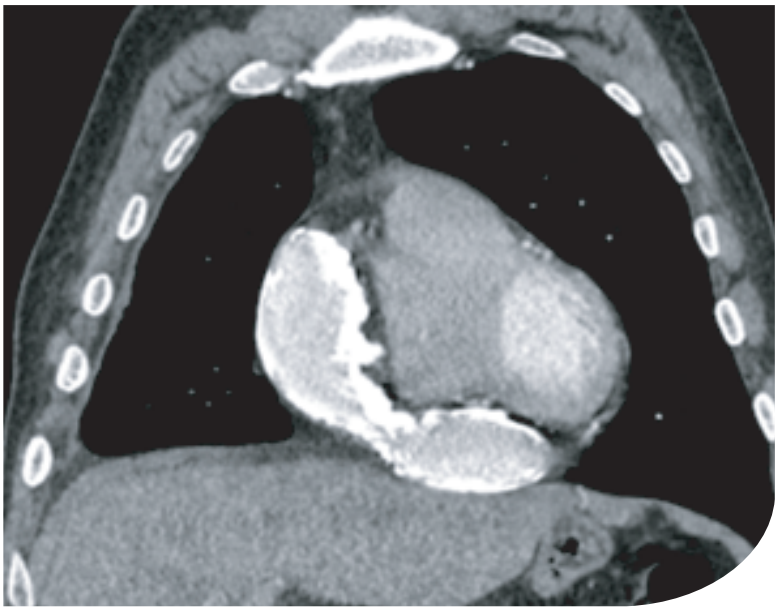
DEHM

Developments and Experiments in Health and Medicine

Volume:40 Issue:1 Year:2026
e-ISSN: 3062-2948



EDITORIAL BOARD

Statistic Editor

Language Editor

Advisory Board

Please note that the order in which the Editors and Advisory Board appear on this page is alphabetical.

Publishing Coordinator
Müjde UZHAN

Managerial Office
Dokuz Eylül University
Dean's Office, Faculty of Medicine
35340 Inciraltı / Balçova - IZMIR / TÜRKİYE

Contact Information
Editorial correspondence should be addressed to
Hale ÖREN
e-mail: hale.oren@deu.edu.tr

Cover & layout design for this issue was kindly contributed by Çınla YÜCEBAŞ

URL
https://dergipark.org.tr/en/pub/dehm

Phone
+90 232 412 22 90

e-mail
dehm@deu.edu.tr

Developments and Experiments in Health and Medicine (DEHM) is a peer reviewed academic journal, electronically published four-times (January, April, July, and October) in a year.

Correspondence Address:
Dokuz Eylül University
Publication Committee of the
Faculty of Medicine, Dean's Office
35340 Inciraltı / Balçova - IZMIR / TÜRKİYE

DEHM is indexed in Index Copernicus Master List, TUBITAK ULAKBIM TR Medical Index, and Turkish Citation Index.

Developments and Experiments in Health and Medicine

Aims and Scope

Developments and Experiments in Health and Medicine (ISSN: 1300-6622; e ISSN: 2602- 3148) is an international, double-blind peer-reviewed, open access publication of Dokuz Eylül University Faculty of Medicine which is published quarterly in January, April, July, and October.

It publishes articles of original research conducted using scientific methods with appropriate hypotheses in all areas of medicine. In addition, it publishes reviews on current issues, rare medical cases, and letters to the editor containing the experiences and comments of specialist physicians in the field. Manuscripts are publishable in English. Developments and Experiments in Health and Medicine does not charge any fees to the author(s) for the evaluation and/or publication of submitted articles.

The aim of this journal is to provide scientists with the opportunity to publish their original scientific studies in the field of medicine and health, to share their discoveries, new original ideas and theories in this field.

The target audience of Developments and Experiments in Health and Medicine is physicians, specialists, researchers, specialists, and doctoral students in all areas of medicine as well as medical faculty students. It aims to contribute to the spread of continuous professional development and research culture.

Developments and Experiments in Health and Medicine is indexed in Index Copernicus Master List, TUBITAK ULAKBIM TR Medical Index, and Turkish Citation Index. The index value for 2020 was calculated as 80.48.

The abbreviation of Developments and Experiments in Health and Medicine is "Dev Exp Health Med". It should be denoted as it when referenced.

Thank you for your contributions to our journal as an author and reviewer.

Subject Areas

This journal welcomes the papers from all clinical and pre-clinical medical disciplines. Basic, translational and clinical research conducted through interdisciplinary collaborations, community-based research, studies on medical devices and artificial intelligence in the medical field are given priority in the journal.

Publication Ethics Statement

Developments and Experiments in Health and Medicine Editorial Board, in accordance with the "DEU Faculty of Medicine Journal Directive", carries out its work by observing the ethical rules of international organizations [International Council of Medical Journal Editors (ICMJE), World Association of Medical Editors (WAME), Council of Science Editors (CSE), Committee on Publication Ethics (COPE), and European Association of Science Editors (EASE)].

Developments and Experiments in Health and Medicine takes the responsibility to enforce a rigorous peer-review together with strict ethical policies and standards to ensure to add high quality scientific works to the field of scholarly publication. Unfortunately, cases of plagiarism, data falsification, inappropriate authorship credit, and the like, do arise. To verify the originality of content submitted to our journals, articles sent to the journal are accepted with an iThenticate or Turnitin report. A maximum of 15% similarity is accepted as a result of the report. The author must perform the similarity report when uploading the article to the system. If the rate exceeds 15%, the article can be sent back to the author with the report.

Copyright / Open Access

Developments and Experiments in Health and Medicine
DEHM
Volume 40/ Issue 1 / January
2026

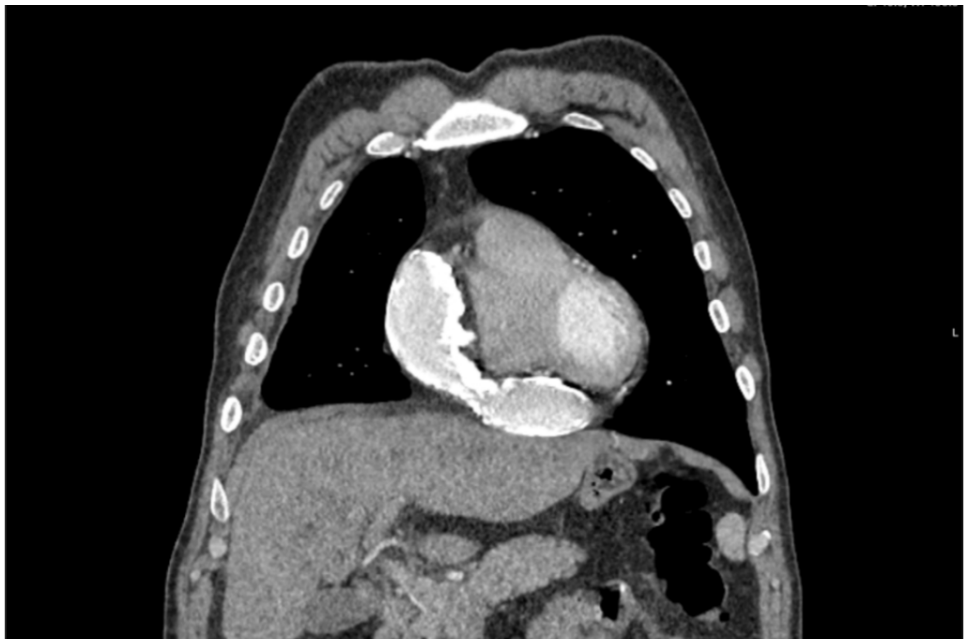
Contents

Review

Research Articles

Case Report

COVER PHOTO:



Non-infectious, caseous necrosis involving constrictive pericarditis treated with pericardiectomy: A case report

Perikardiyektomi ile tedavi edilen non-enfeksiyöz, kazeifikasyon nekrozu içeren konstriktif perikardit hastası: Vaka raporu

Barış AVŞAR, Onur Barış DAYANIR, Osman Nejat SARIOSMANOĞLU

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

Nutritional risk factors related to non-communicable diseases in the world

Dünyada bulaşıcı olmayan hastalıklar konusunda beslenme ile ilgili risk faktörleri

Raife KOTZAOGLAN[1]
Dilek ASLAN[2]

[1]Hacettepe University, Institute of Health Sciences, Department of Public Health, Nutrition and Food Sciences Program Graduate, Ankara, Türkiye.
[2] Hacettepe University, Faculty of Medicine, Department of Public Health, Ankara, Türkiye.

Non-communicable diseases and nutrition
Received: 01.12.2024
Accepted: 18.09.2025
DOI:10.18614/dehm.1873505

Corresponding author
Raife KOTZAOGLAN
ORCID ID: 0009-0001-3840-6714
raifekotzaoglan@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

ABSTRACT

The global burden of non-communicable diseases is increasing, with unhealthy diets being a key contributing factor. The Western diet, which is now widespread due to technology, food industry practices, and globalization, conflicts with the dietary principles of the World Health Organization. Consisting of high-calorie, nutrient-poor foods, it contributes to increased mortality and morbidity related to non-communicable diseases. This review examines the links between nutrition-related risk factors and non-communicable diseases by searchingthe PubMed, Scopus, Web of Science, and Google Scholar, as well as the World Health Organization and United Nations reports. The emphasis was placed on recent, authoritative sources, with data collected from January 2024 to August 2025 and updated based on reviewer feedback.

KEYWORDS
Healthy dietary pattern, non-communicable diseases, nutrition, nutritional risk factors, western diet

ÖZ

Bulaşıcı olmayan hastalıkların küresel yükü giderek artmakta, sağlıksız beslenme ise bu artışın temel etkenlerinden biri olarak öne çıkmaktadır. Teknolojik gelişmeler, gıda endüstrisinin uygulamaları ve küreselleşme ile yaygınlaşan Batı tipi beslenme, Dünya Sağlık Örgütü'nün sağlıklı beslenme ilkeleriyle çelişmektedir. Yüksek enerji içerikli ancak besin değeri düşük gıdalarla karakterize bu beslenme biçimi, bulaşıcı olmayan hastalıklara bağlı mortalite ve morbiditeyi artırmaktadır. Bu derleme, beslenme ile ilişkili risk faktörleri ile bulaşıcı olmayan hastalıklar arasındaki ilişkiyi incelemektedir. Literatür taraması PubMed, Scopus, Web of Science ve Google Scholar kullanılarak yapılmıştır; ayrıca Dünya Sağlık Örgütü ve Birleşmiş Milletler raporları incelenmiştir. Güncel ve güvenilir kaynaklara öncelik verilmiştir, veriler Ocak 2024–Ağustos 2025 arasında toplanmış ve hakem önerileri doğrultusunda düzenlenmiştir.

ANAHTAR KELİMELER
Bulaşıcı olmayan hastalıklar, beslenme, beslenme risk faktörleri, batı tipi beslenme, sağlıklı beslenme modeli

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

Non-communicable diseases (NCDs) pose a significant public health challenge today, with increasing mortality and morbidity rates (1). Various risk factors contribute to the development of NCDs, with nutrition being one of the most critical. The development and progression of many conditions, including cardiovascular diseases, diabetes, and cancer, are closely linked to nutritional behaviors (2). The aim of this article is to define NCDs and their context, explore the connection between NCDs and nutritional behavior, identify nutritional risk factors associated with the development of these diseases, and assess the current global situation with regard to risky behaviors. Additionally, it aims to evaluate the relationship between the food industry and the Western diet, outline healthy dietary patterns, highlight successful global practices from around the world, and provide recommendations for improving nutrition and health.

Materials and Methods

This review is based on scientific documents obtained through a literature search conducted between January 2024 and August 2024, and was updated with additional literature including August 2025 during revisions in response to the journal reviewer's comments. The databases used for the search included PubMed, Scopus, Web of Science, and Google Scholar. In addition to peer-reviewed journal articles, the review and analysis included official reports, and data from international organizations such as the World Health Organization (WHO), the United Nations (UN), and the Institute for Health Metrics and Evaluation (IHME). Keywords in both the Turkish and English languages were used with the primary words being 'non-communicable disease', 'disease burden', 'nutrition and disease', and 'nutrition and non-communicable disease'. All reports, websites, and other reference materials used in this review were carefully selected to reflect the most current and authoritative data available at the time of writing. Priority was given to the most recent versions of official documents, primarily published in 2023 and 2024. All organizational websites consulted (e.g. WHO, UN, and IHME) were accessed during the literature search period and verified to contain up-to-date statistics, policy documents, and global estimates. This approach was taken to ensure that the review's findings are based on the most reliable and timely evidence available.

Noncommunicable diseases: conceptual framework

For centuries, infectious diseases have been the leading cause of death worldwide. Due to uncontrolled epidemics, life expectancy at birth has historically remained low. However, after World War II, significant advancements in vaccination practices, the use of antibiotics, and improvements in living conditions led to a successful battle against infectious diseases. Consequently, the burden of non-communicable diseases (NCDs), which remains a critical public health issue today, has come to the fore (3). NCDs are defined as conditions that are not caused by acute infections, lead to long-term health effects, and requiring prolonged treatment and care (4). Another definition suggests that NCDs are diseases that are typically non-contagious and not transmitted from the affected person to others (5). Although there is no universally accepted definition of NCDs, the term is often preferred to "chronic diseases." The latter primarily describes the long-term nature of a condition, regardless of whether it is contagious. Some sources also use the term "lifestyle-related diseases". Nevertheless, "NCDs" is the terminology favored by the World Health Organization and it is the term most commonly encountered in current literature (6,7). The non-communicable diseases with the highest mortality and morbidity rates include cardiovascular diseases (such as heart attacks and strokes), cancer, chronic respiratory diseases (such as chronic obstructive pulmonary disease and asthma), and diabetes mellitus (1). As communicable diseases have become less prevalent, these four categories have emerged as a significant burden on health systems, particularly in developed countries. Initially, NCDs were associated with wealth and described as "diseases of the rich." However, since the early 2000s, their prevalence has increased globally, particularly in developing countries. This trend can be explained by the epidemiological transition theory (3). For instance, economic development and industrialization lead to greater access to food and subsequent changes in dietary behaviors. These dietary changes, coupled with a more sedentary lifestyle, have resulted in adverse health outcomes (8). Consequently, in the early 2000s, developing countries began facing a dual burden of both communicable and NCDs (9).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

Today, an increasing number of deaths result from NCDs. Approximately 41 million deaths occur each year due to NCDs, accounting for 74% of all global deaths. Around 17 million individuals die from NCDs before the age of 70 each year, and 86% of these premature deaths occur in low- and middle-income countries. These regions account for 77% of all NCD-attributable deaths (1). NCDs not only cause premature deaths but also contribute to increased healthcare expenditures and significant economic losses due to their complexity and the chronic nature of care required. It is estimated that the cost of NCDs in low- and middle-income countries will exceed 7 trillion USD between 2011 and 2025 (10). Examining country classifications based on income reveals that the percentage of deaths due to NCDs increases with income levels. However, it is essential to recognize that the regions with the highest number of NCD-related deaths remain low- and middle-income countries (11). Cardiovascular diseases alone cause 17.9 million deaths annually worldwide, making them the leading cause of NCD deaths, followed by cancers (9.3 million), chronic respiratory diseases (4.1 million), and diabetes (which includes 2.0 million deaths from kidney disease caused by diabetes) (1). NCDs lead not only premature death but also limit the number of healthy life years in populations. The burden of NCDs on disability-adjusted life years (DALYs) has increased over time. Between 2000 and 2019, the number of DALYs from infectious diseases like HIV/AIDS and diarrheal diseases decreased by 50%. In contrast, DALYs from diabetes increased by over 80%, and those from Alzheimer's disease doubled (12,13). In 2019, NCDs accounted for 63% of DALYs worldwide, with the rate in the WHO European region reaching 84% (14). Cardiovascular diseases make the highest global contribution to disability-adjusted life years (DALYs), representing 15.52% of the total. The next highest contributors are cancers, neonatal diseases, musculoskeletal disorders, respiratory tract infections, and mental illnesses.

Table 1 shows the Human Development Index (HDI) for different countries, along with their life expectancy at birth, gross national product (GNP), and the frequency of factors contributing to DALYs in these countries. Analysis of life expectancy and GNP reveals that these values tend to decrease as the level of human development declines. In developed countries, non-communicable diseases (NCDs) are expected to contribute more significantly to DALYs compared to other factors. For example, NCDs account for 86.32% of DALYs in Switzerland, which has a very high level of human development, and 88.69% in Bulgaria, which is classified as having a high level of human development. By contrast, the contribution of NCDs in Venezuela, categorized as having a medium HDI, is 69.44%, while in Nigeria, classified as having low HDI, it reaches only 26.78%. The difference between these countries provides insight into the varying impacts of NCDs in countries with different levels of human development (15,16).

Figure 1 illustrates the data presented in Table 1, showing the average percentage contribution of NCDs to DALYs for each development category. It is evident that the contribution of NCDs to DALYs decreases as the level of human development declines.

Non-communicable diseases; risk factors

Risk factors are defined as any characteristic or exposure that increases an individual's likelihood of contracting a disease or sustaining an injury (17). According to the World Health Organization, the risk factors that increase the frequency of NCDs are categorized into three main groups including behavioural, metabolic, and environmental risk factors. Among these, the most significant risk factors for NCDs are tobacco use, physical inactivity, alcohol consumption, unhealthy diets, and air pollution (1). Approximately 8 million people die each year because of tobacco use, with more than 1 million of those being passive smokers. Unhealthy diets are responsible for 19% of deaths from NCDs annually, and it is estimated that 1.8 million deaths each year are related to excessive salt or sodium intake. Alcohol consumption is linked to several diseases, including liver cirrhosis and various types of cancer. It accounts for around 3 million deaths annually due to its harmful effects. Despite the well known benefits of physical activity in preventing and treating NCDs one in three women, one in four men, and over 80% of adolescents do not engage in enough physical activity to maintain a healthy lifestyle. It is estimated that physical inactivity contributes to approximately 830,000 deaths each year. Air pollution, both outdoors and indoors, poses a significant health risk and is a major environmental driver of NCDs. Every year, 6.7 million people die from NCDs related to air pollution, including chronic obstructive pulmonary disease (COPD) and lung cancer. High blood pressure is the leading global metabolic risk factor, accounting for around 19% of all

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

deaths. Currently, 1.3 billion people aged 30 to 79 suffer from high blood pressure, two-thirds of whom reside in low- and middle-income countries. Being overweight is also a critical metabolic risk factor. In 2022, it was estimated that 2.5 billion people were overweight, 890 million of whom were obese. Obesity significantly increases the risk of cardiovascular diseases, diabetes, musculoskeletal disorders, and certain cancers. While obesity has been a major health issue in high-income countries for decades, it has recently emerged as a public health concern in low- and middle-income countries too. Hyperglycemia, characterized by elevated blood sugar levels, can lead to serious health issues if sustained over time. It is estimated that hyperglycemia contributes to 20% of deaths related to cardiovascular diseases. High blood cholesterol levels, a component of hyperlipidemia, also negatively impact cardiovascular health. Factors such as unhealthy diets, excessive body weight, insufficient physical activity, tobacco use, and excessive alcohol consumption can also elevate cholesterol levels, although high cholesterol can be hereditary. According to estimates, high blood cholesterol levels were responsible for around 3.9 million deaths in 2017 (1,18).

Table 1. Life expectancy at birth, gross domestic product, and disability adjusted life years in four countries, according to their human development index category.

Country	**HDI (2023)**		**Life expectancy at birth** (years)	**Gross domestic product** (USD)	**DALY (%)**		
	***Category**	**Value**			**NCDs**	**CDs+maternal, perinatal, nutritional factors**	**İnjuries**
Switzerland	Very High	0.967	84.3	689.433	86.32	3.75	9.92
Bulgaria	High	0.799	71.5	23.921	88.69	3.49	7.82
Venezuela	Medium	0.699	71.1	6.184	69.44	12.79	17.77
Nigeria	Low	0.548	53.6	4.755	26.78	68.74	4.47

*The Human Development Index classifies countries into 4 categories according to the values they receive; very high, high, medium and low. The country at the top of each category is shown in the table.
HDI, Human Development Index; DALY, Disability Adjusted Life Years; NCDs, Non-communicable diseases; CDs: Communicable diseases

NCDs result from a combination of factors, including genetic, environmental, and physiological influences. These can be classified as either modifiable or non-modifiable risk factors. However, as certain unmodifiable characteristics (like age and gender) impact the risk of developing NCDs, it is insufficient to examine only the modifiable factors. Therefore, an alternative classification model has been proposed (2). This model groups risk factors associated with NCDs into five categories: genetic factors, environmental factors, sociodemographic factors, factors related to self-management, and factors related to medical conditions. All of these factors interact with one another and influence an individual's risk of developing a disease. For example, advancing age may lead to retirement, resulting in social isolation and financial stress. Furthermore, various factors can influence nutritional status, including a person's socioeconomic status, level of education, the technological resources available in their country, and their region's access to food. Thus, there are complex structures underlying modifiable risk factors (Figure 2).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

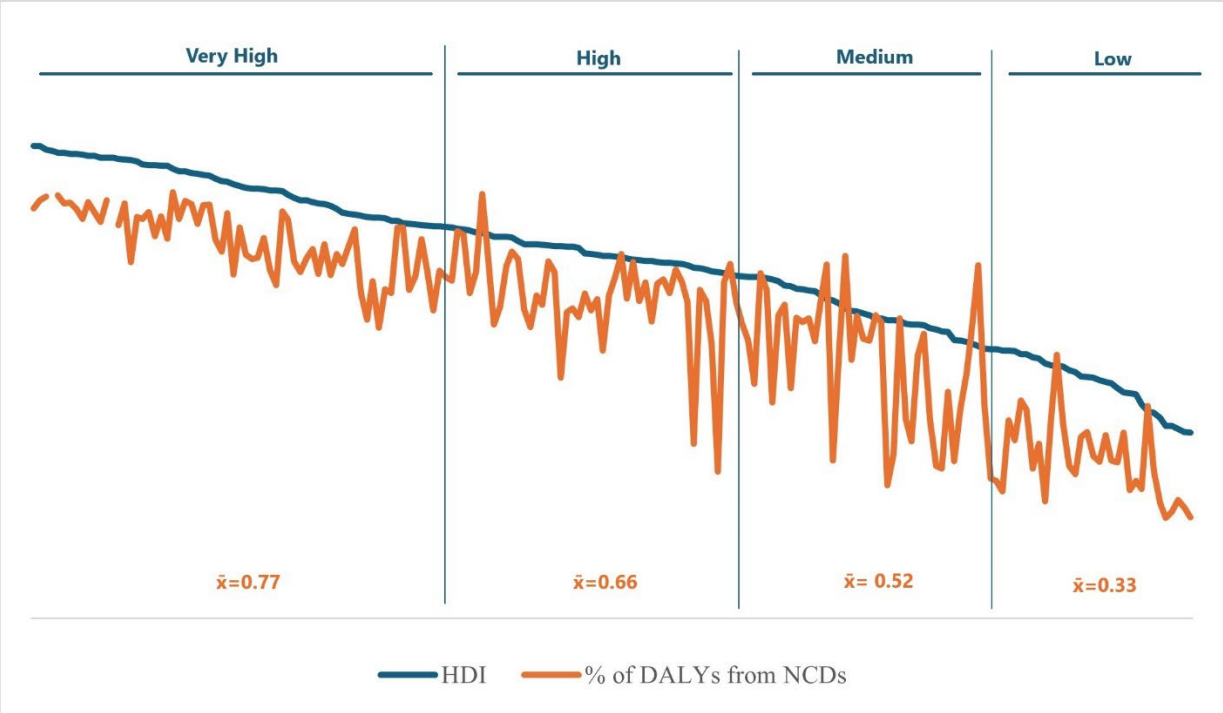


Figure 1. Comparison the contribution of NCDs to DALYs according to the HDI scores countries

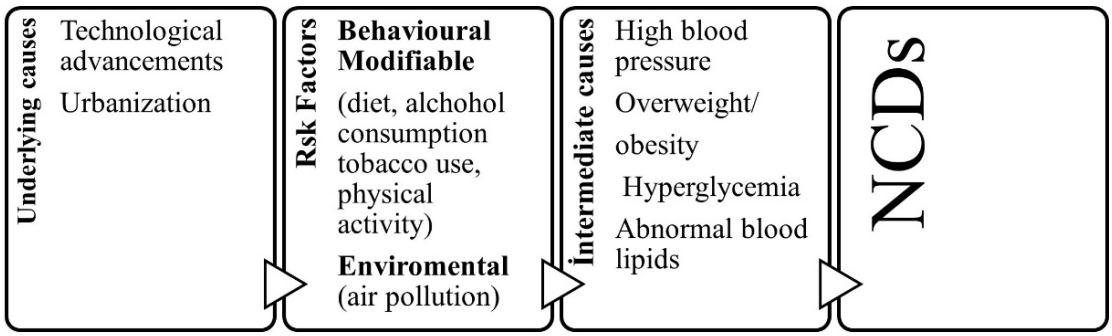


Figure 2. Underlying causes of NCDs

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

Country-specific context: The case of Türkiye

In Türkiye, NCDs are one of the leading causes of illness and death, accounting for approximately 90% of all fatalities (19). In 2019, ischemic heart disease was the primary cause of disease-related deaths, accounting for 95.9% of cases, followed by stroke at 49.1%, various types of cancer at 39.7%, chronic obstructive pulmonary disease at 28.0%, diabetes at 20.1%, and hypertensive heart disease at 16.3% (20). In 2022, NCDs were responsiblefor 389,100 deaths in Türkiye, with a 16% probability of preventable premature death from these diseases (19). In response to this public health challenge, the Ministry of Health launched the "Türkiye Multisectoral Noncommunicable Diseases Action Plan", covering the period from 2017 to 2025 (21). This plan aims to monitor and reduce risk factors following the STEPwise approach recommended by the World Health Organization (WHO) (22). As part of this initiative, the "Türkiye Household Health Survey" was conducted in 2017 and again in 2023. Data from both studies indicates that behavioral and metabolic risk factors, such as an unhealthy diet, physical inactivity, and obesity, significantly contribute to the prevalence of NCDs in Türkiye. The 2023 survey revealed that 87.9% of adults consume fewer than five portions of fruits and vegetables per day, highlighting a widespread nutritional risk. Furthermore, physical inactivity affects 32.1% of the population, with a notable gender disparity: men average 64.3 minutes of daily physical activity, while women average only 34.3 minutes. Encouragingly, the prevalence of obesity declined from 28.8% in 2017 to 25.4% in 2023, primarily due to a reduction among women. These findings emphasize both persistence of behavioral risk factors and areas of progress, underlining the importance of Türkiye's ongoing multi-sectoral strategies to promote healthy diets, increase physical activity, and reduce the burden of NCDs (23).

Noncommunicable diseases associated with nutritional behavior

Healthy nutrition is defined as a diet that promotes health and prevents disease (24). In contrast, an unhealthy nutrition leads to what is known as 'malnutrition.' Malnutrition encompasses deficiencies or excesses in nutritional intake, imbalances of essential nutrients, or impaired nutrient utilization (25). The increasing prevalence of NCDs worldwide, along with increased mortality and disability rates, has highlighted the importance of nutrition-related risk factors (26). Since the early 2000s, nutritional behaviors have changed significantly on an international scale. Globalization and urbanization have led to a growing preference for ready-to-eat food and drink, as well as more frequent dining out. These inexpensive, ready-to-consume food and drink products are often classified as "ultra-processed." They typically contain high levels of energy, fat, salt, and sugar, but lack nutritional value. Ultra-processed foods and beverages tend to have a long shelf life, which makes them more appealing for businesses than fresh products. Intensive marketing efforts, particularly those aimed at children, have also contributed to the increased consumption of these unhealthy products. As a result, ultra-processed foods are rapidly replacing fresh, nutritious, and minimally processed alternatives, thereby altering the nutritional patterns and food systems within society. Vulnerable populations worldwide often struggle to access and maintain a healthy diet; and it is in these environments that ultra-processed food and beverage products are most prevalent (27).

Nutrition related NCDs include overweight and obesity (which are linked to high blood pressure, high cholesterol, diabetes, cardiovascular diseases, stroke, certain cancers, and insulin resistance), cardiovascular diseases, type 2 diabetes, hypertension, and specific types of cancer (such as esophageal, lung, oral cavity, nasopharynx, colon, and rectal cancers). The underlying risk factors for these diseases include high sodium intake, excessive sugar consumption, high trans fatty acid consumption, and low consumption of vegetables, fruits, whole grains, and oilseeds. High salt intake raises blood pressure, thereby increasing the risk of cardiovascular diseases, stroke, chronic kidney disease, and some cancers. Consuming high sugar can lead to weight gain, contributing to obesity and its associated diseases. Trans fatty acids have been linked to an increased risk of cardiovascular disease and stroke (27). As illustrated in Figure 3, a single dietary risk factor can lead to multiple diseases, just as a noncommunicable disease can serve as a risk factor for other diseases. Diet-related factors are the third largest contributor to the global burden of disease, after high blood pressure and tobacco use. Poor nutrition increases the risk of various health issues. In 2019, dietary risk factors were associated with 7.9 million deaths and 187.7

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

million disability-adjusted life years (DALYs) (28). The leading risky dietary behaviors globally in terms of mortality and DALYs include high sodium intake, low whole grain intake, and low fruit consumption (Figure 4) (29). High sodium intake is the dietary risk factor that has the most significant impact on health, primarily due to its association with cardiovascular diseases such as ischemic heart disease and hypertensive heart disease. In 2019, sodium intake was linked to 1.9 million deaths (28). Additionally, a low consumption of healthy foods—like fruits, vegetables, legumes, and whole grains—greatly increases the risk of cardiovascular diseases within a population. In 2017, unhealthy diets accounted for 22% of all adult deaths, with cardiovascular diseases identified as the leading cause of diet-related fatalities (30, 31). A 2022 study indicated that increasing daily vegetable consumption from zero grams to 306 - 372 grams reduced the risk of ischemic stroke by 23.2%, the risk of ischemic heart disease by 22.9%, the risk of haemorrhagic stroke by 15.9%, and the risk of esophageal cancer by 28.5% (32).

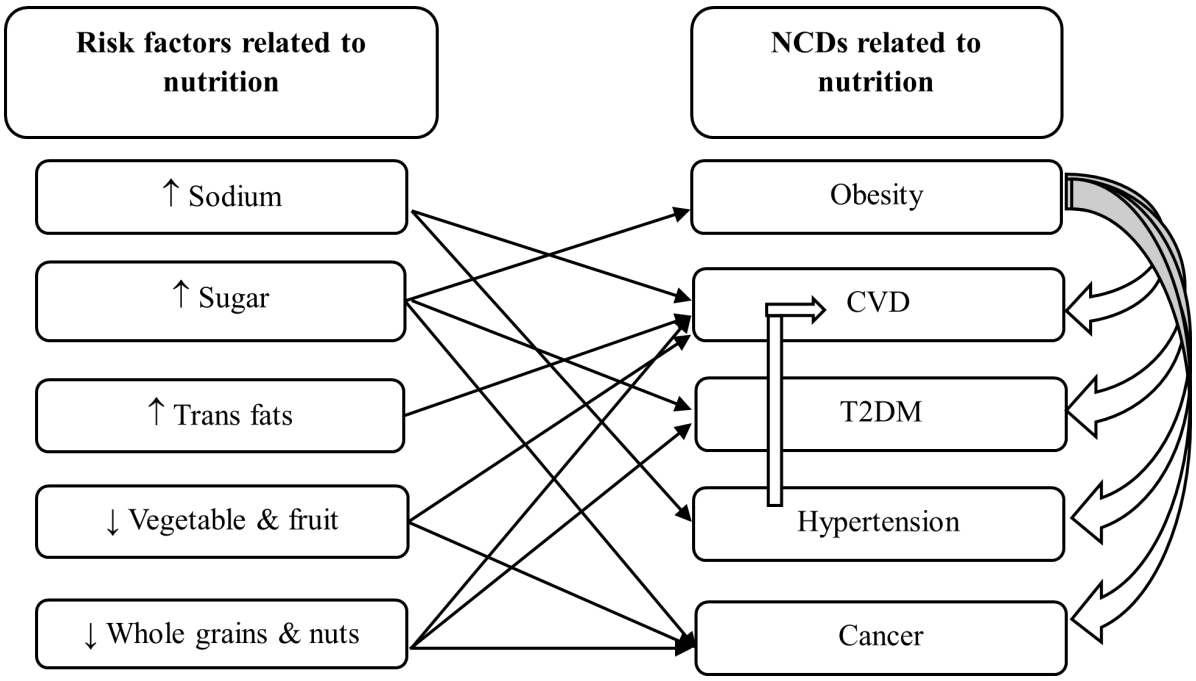


Figure 3. Nutritional risk factors for non-communicable diseases

Healthy dietary patterns

Healthy nutrition is one of the most important elements in a person's growth and development, protection against diseases, and overall quality of life. Poor eating habits are a significant risk factor contributing to the global disease burden (33). Over the past few decades, a focus on individual nutrients has improved our understanding of diseases associated with vitamin deficiencies. However, examining macro or micronutrients alone fails to explain nutrition's role in chronic conditions. Instead, the combination of nutrients and foods in a person's diet provides greater benefits than any individual food or nutrient. The dietary model approach is currently being used to analyze the nutritional behaviors of societies and their relationship with disease burden. The dietary model is defined by the amount, variety, or combination of different foods and beverages consumed, as well as how regularly they are consumed (34). Rather than assessing specific food groups or nutrients separately, dietary model analysis considers nutritional factors as a whole (35).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

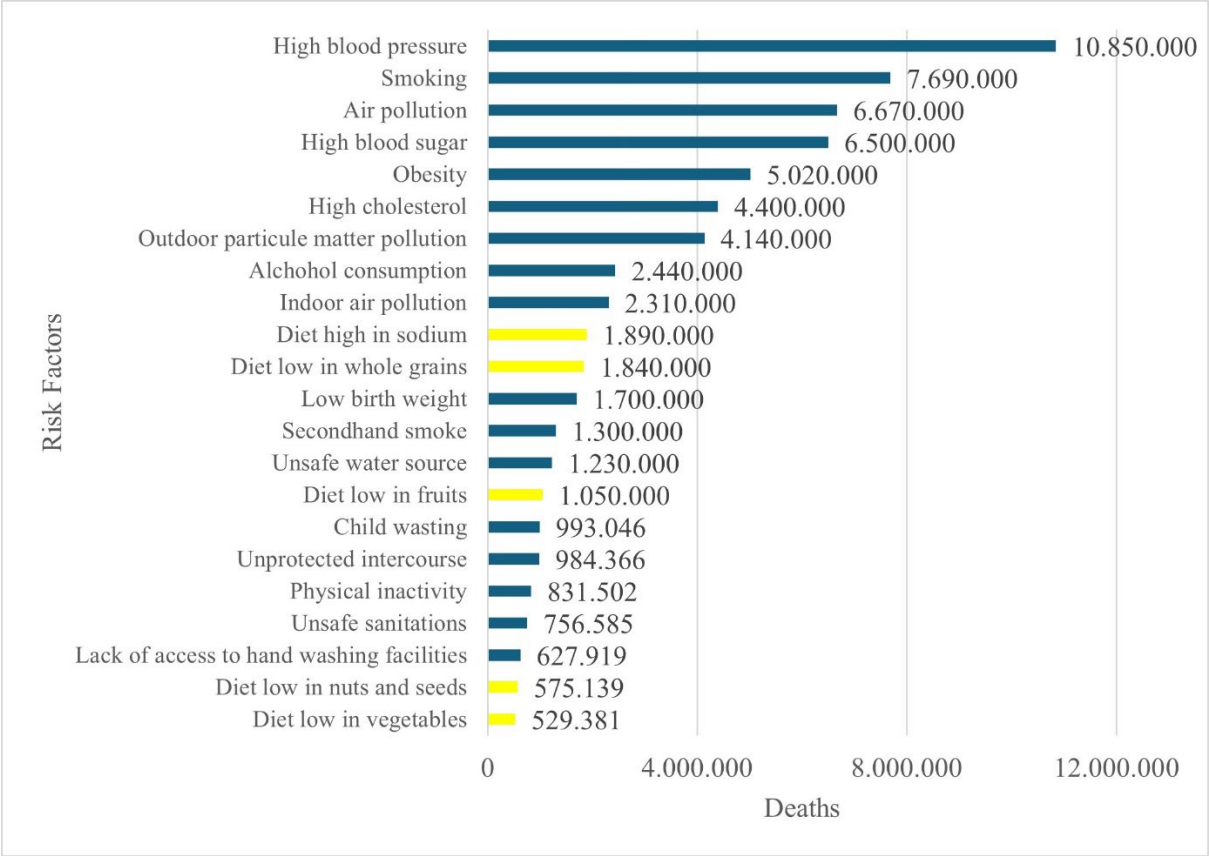


Figure 4. Number of deaths by risk factors (World), 2019

The content of a healthy dietary model may vary from person to person based on factors such as age, gender, disease status, lifestyle, cultural characteristics, local foods, and cuisine. Nevertheless, the fundamental principles of healthy nutrition are the same for everyone (33). According to the World Health Organization, a healthy dietary model should adhere to the following principles: (a) Energy intake and energy expenditure should be balanced, (b) The sources of energy, protein, vitamins, and minerals should primarily come from a diverse, plant-based diet, (c) Energy should mainly be derived from carbohydrates, such as whole grains and legumes, (d) Fat intake should constitute no more than 30% of total energy, favoring unsaturated fatty acids over saturated fatty acids, while eliminating industrial trans fats, (e) Added sugar intake should be less than 10% of total energy (ideally less than 5%), (f) Daily sodium intake should be limited to less than 2 grams (equivalent to 5 grams of salt), (g) Adults are recommended to consume at least 400 grams (5 portions) of fruits and vegetables daily. In order to achieve these health goals, it is important to include fresh vegetables with every meal. Additionally, fresh fruits and raw vegetables should be preferred as snacks between meals, with a focus on seasonal options. Boiling or steaming methods should be preferred over frying to reduce saturated fat intake. The use of vegetable/seed oils over solid fats is advised. When it comes to meat, selecting lean cuts is advisable. Fried or baked pastries, as well as pre-packaged foods that contain high levels of trans fats should be avoided. To limit daily sodium intake, consumption of packaged foods should be minimized, salt should be eliminated from the table, and low-sodium items should be opted for. Finally, to

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

minimize consumption of simple sugars, sugary snacks, sugar-sweetened beverages, energy drinks, and ready-to-drink iced teas and coffees have to be avoided (33, 36).

The western diet and the role of the food industry

The modern nutritional pattern that has become widespread around the world is known as the "Western Diet". Emerging with the Industrial Revolution, this dietary approach has gained prominence in the 21st century. Technological advances in food industry have accelerated the production of foods with a long shelf life and greater sensory appeal. Due to their sensory properties and ease of access, these foods have become increasingly popular. Today, processed and ultra-processed foods make a large part of the Western diet. These foods are often high in sugar, sodium, and fat but low in fiber, vitamins, and minerals. Research indicates that consuming ultra-processed foods is linked to various health issues. The Western diet is characterized by high intakes of processed and refined foods, red and processed meats, added sugars, and saturated and trans fats, while lacking in fruits, vegetables, whole grains, and oilseeds. This shift in dietary habits differs starkly from that of previous generations and is contrary to human physiology, potentially causing numerous health problems. The Western diet has been associated with diseases such as type 2 diabetes, cardiovascular diseases, and certain types of cancer (37, 38).

One reason for the popularity of ultra-processed foods—beyond their long shelf life and improved sensory properties—is the aggressive marketing and sales strategies employed by the food industry. The promotion of these foods is pervasive, reaching consumers through television advertisements, online promotions, and physical posters or banners at points of sale (39). Studies have shown that advertising directed at children significantly increases the likelihood of these foods being consumed shortly after exposure, leading to an overall increase in total energy intake (40). Sales tactics such as "discounted prices," "promotional products," and "bargain items" further encourage the purchase of unhealthy foods (41). According to a systematic review, promotional pricing is more common for unhealthy food groups, especially packaged foods sold in large sizes (42). In 2021, the United Kingdom government introduced the first law addressing food promotions. This regulation aims to ban quantity-based promotions (e.g., "buy one, get one free") for unhealthy food and drink products in stores and online. However, the implementation of this law has been delayed and is expected to take effect in October 2025 (43). Another strategy employed by the food industry to increase sales is to manipulate the claims and labels on food packaging to create theimpression that the products are healthier than they actually are. This practice is often referred to as "healthwashing" or creating a "health halo." These terms describe techniques that mislead consumers into believing that unhealthy products are healthy by associating them with fitness or a healthy lifestyle (44, 45). For example, foods labeled as "low fat" are often perceived as healthy, even though they may contain high levels of sugar. Similarly, protein bars are often mistakenly considered a healthy option simply because they include the word "protein" in their name, regardless of their sugar content and other nutritional aspects (46). Food fortification initiatives aimed at preventing micronutrient deficiencies are intended to protect and improve public health (47). However, food suppliers may take advantage of this by fortifying ultra-processed foods (such as breakfast cereals, ready-made fruit juices, and fruit-flavored milk), which can mask their unhealthy nature. Such foods may be marketed as "rich in vitamins/minerals" or "high in nutrients," which misleads consumers and encourages higher consumption of ultra-processed options. Therefore, it is emphasized that voluntary food fortification should be regulated, and the fortification of ultra-processed foods should be restricted (48).

Examples of good practices worldwide

In the fight against NCDs, the United Nations (UN) and the World Health Organization (WHO) have developed and continue to develop various policies. The Global Nutrition Goals, published in 2014 and running until 2025, provide a comprehensive implementation plan focused on the nutrition of mothers, infants, and young children (49). Another important action plan emphasizing nutritional targets is the Sustainable Development Goals (SDGs), which were established in 2015 and will continue until 2030. This development plan consists of 17 goals, with SDG-2: "Zero Hunger" and SDG-3: "Good Health and Well-being" specifically addressing issues closely related to nutrition and NCDs (50). To accelerate progress towards these action plans

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

and ensure success for partner countries, period from 2016 to 2025 has been designated the United Nations Decade of Action on Nutrition (51). In order to achieve these goals, countries need to implement and sustain evidence-based nutrition policies and interventions that have demonstrated effectiveness. Implementing nutrition programs is a complex process influenced by several factors, including adequate budget allocation, sufficient logistics, and workforce, the qualifications and motivation of project managers, community participation, and continuous monitoring and evaluation (52).

When examining successful practices from around the world, one of the most significant focus areas is reducing salt consumption. Cardiovascular diseases, the leading cause of death among NCDs, are linked to high salt intake, making salt reduction interventions both effective and cost-efficient. Three main areas of action are typically defined: product reformulation, consumer awareness, education (including clear and comprehensive labeling), and monitoring public salt consumption. Finland and the United Kingdom are pioneers in salt reduction initiatives. In Finland, a program initiated in 1970 primarily aimed to raise public awareness. By 1993, it had become mandatory to display the amount of salt content on food labels and to include warning signs on foods high in salt. To help consumers identify healthier options, a label indicating "better choice" was introduced for low-salt foods. As a result of these regulations, Finland's salt consumption decreased from 12 grams per day in the 1970s to 6.5 grams per day by 2002. In the UK, the focus was on reformulating food and collaborating with the food sector. Over 100 food groups responsible for the majority of the salt consumption were targeted, achieving a 25-45% reduction in the salt content in food to date. It has been reported that overall salt consumption in the UK has decreased by 10-15% since the program's inception in 2003-2004. The policies implemented by both Finland and the UK have served as models for other member states.

Another critical area of action addresses trans fatty acids, which are formed during the production of ultra-processed foods such as margarine, and these fatty acids are linked to both cardiovascular diseases and certain types of cancer. Eliminating industrially produced trans fats from the food supply is considered as one of the simplest public health interventions to enhance nutrition and reduce the risk of NCDs. Denmark was the first country to take action in this regard, implementing a ban on the sale of foods containing trans fatty acids in 2003, with a maximum limit of 2 grams of trans fats per 100 grams of product. Following this legislation, the food industry shifted towards healthier fat options, thereby improving the overall food profile. Recent decreases in cardiovascular disease-related deaths in Denmark can be partly attributed to this intervention (53).

As childhood obesity has increased over the years, the importance of school nutrition programs has grown. . In Slovenia, a school food law was introduced in 2013, banning vending machines selling food and drinks in schools. This law, in addition to the previously existing school fruit program and school nutrition education, has had positive effects (54, 55). Another intervention aimed at children is restricting food advertising. South Korea took action against food advertising aimed at children in 2008. Advertisements for certain foods (high energy, low nutrition) have been prohibited during the hours when children watch TV the most (17:00–19:00). Additionally, presenting and advertising any food or promotional products as gifts has been prohibited. The total number of advertisements related to undesirable foods has decreased by 58% since the program came into effect (55, 56).

Finally, the application of an excise tax to unhealthy foods in many countries has led to positive outcomes. For example, the public health product tax that came into effect in Hungary aimed to reduce the consumption of certain foods (those with a high salt, sugar or caffeine content) in 2011. Taxed products include sugar-sweetened beverages, energy drinks, candies, salty snacks, condiments, broth cubes, flavored alcoholic beverages, and fruit jams. As a result, it has been observed that the sales of these products have decreased by 27% and it is estimated that consumption has decreased by approximately 20-35%. It has also been emphasized that the food industry has resorted to reformulation to reduce the use of taxed materials. Additionly, this taxation system increased consumers' awareness of he difference between healthy and unhealthy food (55).

Although individual commitments of countries are important for achieving the goal, cooperation between countries will accelerate the process and lead to more effective results. For this reason, the UN recommends the establishment of 'Action Networks', a mechanism to strengthen cooperation between countries. Action Networks are informal coalitions of

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:1-14

countries focused on a specific action area related to nutrition to promote dialogue and facilitate and develop local action. For example, the global action coalition titled 'Sustainable food from the oceans and seas for food security and nutrition' led by Norway has been established. This coalition aims to raise awareness about the consumption of sustainable and safe seafood, transfer knowledge and experience between countries, share good practices and identify obstacles (57).

Conclusion

NDCs have become the most significant health problem of our time. These diseases are caused by multiple risk factors, one of which is an unhealthy nutrition and the metabolic imbalances that result from it. The primary principle of nutritional interventions worldwide regarding NCDs is to reduce the intake of salt, sugar, and trans fatty acids. Although these programs are ongoing in many countries today, global statistics show a rising burden of NCDs over the years. This trend indicates that current interventions must be strengthened and that countries are likely facing challenges in implementing effective policies. To achieve the desired outcomes, it is essential to focus on multiple aspects. During the policy development phase, the needs of society must be identified, and appropriate communication and motivation techniques should be employed. Public participation is vital, so all available tools and networks should be evaluated to raise awareness. At this stage, collaborating with civil society organizations is crucial for effectively engaging the public. Furthermore, developing solution proposals through a partnership between the government and the food sector will help establish more practical and realistic targets. Once this foundation has been established, it will be easier and more effective to encourage public engagement and the involvement of other stakeholders.

Conflict of interest

The authors declare that there are no conflicts of interest regarding this study.

Sources of funding

This study received no funding of any kind.

Acknowledgements

None.

References

1. World Health Organization (Internet). Noncommunicable diseases. (Access Date: 5 January 2024) Available from: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases.
2. Budreviciute A, Damiati S, Sabir DK, Onder K, Schuller-Goetzburg P, Plakys G, et al. Management and Prevention Strategies for Non-communicable Diseases (NCDs) and Their Risk Factors. Front Public Health. 2020;8:574111.
3. Omran AR. The epidemiologic transition theory revisited thirty years later. World health statistics quarterly. 1998;53(2, 3, 4):99-119.
4. PAHO (Internet). Noncommunicable Diseases. (Access Date: 5 January 2024) Available form: https://www.paho.org/en/topics/noncommunicable-diseases.
5. National Center for Biotechnology Information. MeSH (Internet). Non-communicable diseases (Access Date: 17 January 2024) Available form: https://www.ncbi.nlm.nih.gov/mesh/?term=non-communicable+disease.
6. Adjaye-Gbewonyo K, Vaughan M. Reframing NCDs? An analysis of current debates. Glob Health Action. 2019;12(1):1641043.
7. Ackland M, Choi BC, Puska P. Rethinking the terms non-communicable disease and chronic disease. J Epidemiol Community Health. 2003;57(11):838-9.
8. Habib SH, Saha S. Burden of non-communicable disease: global overview. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2010;4(1):41-7.
9. Boutayeb A, Boutayeb S. The burden of non communicable diseases in developing countries. International journal for equity in health. 2005;4:1-8.
10. World Bank Group (Internet). Responding to the Challenge of Non-Communicable Diseases. (Access Date: 17 January 2024) Available form: http://documents.worldbank.org/curated/en/208501570807014679/Responding-to-the-Challenge-of-Non-Communicable-Diseases.
11. World Health Organization (Internet). Global health estimates: Leading causes of death: (Access Date: 2 February 2024) Available form: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death.

12. Our World In Data 'Internet). Burden of Disease. (Access Date: 2 February 2024) Available form: https://ourworldindata.org/burden-of-disease.
13. World Health Organization (Internet). Global health estimates: Leading causes of DALYs: (Access Date: 5 March 2024) Available form: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/global-health-estimates-leading-causes-of-dalys.
14. Global Health Estimates 2020: Disease burden by Cause, Age, Sex, by Country and by Region, 2000-2019. Geneva: World Health Organization; 2020.
15. Institute for Health Metrics and Evaluation (IHME) (Internet). GBD Compare Data Visualization. (Access Date: 5 March 2024) Available form: https://vizhub.healthdata.org/gbd-compare/
16. UNDP (United Nations Development Programme). 2024. Human Development Report 2023-24: Breaking the gridlock: Reimagining cooperation in a polarized world. New York.
17. OECD Library (Internet). Health Risks. (Access Date: 5 March 2024) Available form: https://www.oecd-ilibrary.org/social-issues-migration-health/health-risks/indicator-group/english_1c4df204-en.
18. Invisible numbers: the true extent of noncommunicable diseases and what to do about them. World Health Organization; 2022.
19. World Health Organization. Noncommunicable diseases progress monitor 2025. World Health Organization; 2025 Jun 5.
20. T.C. Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü (Kronik Hastalıklar ve Yaşlı Sağlığı Daire Başkanlığı). Türkiye Hanehalkı Sağlık Araştırması: Bulaşıcı Olmayan Hastalıkların Risk Faktörleri Prevalansı 2017-2023 Çalışmalarının Karşılaştırılması. Sağlık Bakanlığı Yayın No: 1306. Ankara: Halk Sağlığı Genel Müdürlüğü; 2025.
21. Republic of Turkey, Ministry of Health. Multisectoral Action Plan of Türkiye for Noncommunicable Diseases 2017–2025. Ministry of Health Publication No. 1057. Ankara; 2017.
22. World Health Organization. STEPwise approach to NCD risk factor surveillance (STEPS) (Internet). Geneva: World Health Organization; 2025 (Access date: 2025 Aug 10). Available from: https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps.
23. World Health Organization Regional Office for Europe. Türkiye completes national household survey on noncommunicable disease risk factors (Internet). Geneva: World Health Organization; 2025 May 28 (Access date: 2025 Aug 10). Available from: WHO Regional Office for Europe news release.
24. Neufeld LM, Hendriks S, Hugas M. Healthy Diet: A Definition for the United Nations Food Systems Summit 2021. In: von Braun J, Afsana K, Fresco LO, Hassan MHA, editors. Science and Innovations for Food Systems Transformation. Cham (CH): Springer Copyright 2023, The Author(s). 2023. p. 21-30.
25. World Health Organization (Internet). Malnutrition. (Access Date: 7 March 2024) Available form: https://www.who.int/news-room/fact-sheets/detail/malnutrition.
26. World Health Organization. Sustainable healthy diets: Guiding principles. Food & Agriculture Org.; 2019 Oct 15.
27. Ncd Alliance (Internet). Diet related non communicable diseases. [Access Date: 18 March 2024]. Available form: https://ncdalliance.org/why-ncds/risk-factors-prevention/unhealthy-diets-and-malnutrition.
28. Institute For Health Metrics and Evaluation (Internet). Diet. (Access Date: 18 March 2024). Available form: https://www.healthdata.org/research-analysis/health-risks-issues/diet.
29. Our World in Data (Internet). Deaths by risk factor, World, 2019. [Access Date: 31 May 2024]. Available form: https://ourworldindata.org/grapher/number-of-deaths-by-risk-factor?time=latest.
30. Qiao J, Lin X, Wu Y, Huang X, Pan X, Xu J, et al. Global burden of non-communicable diseases attributable to dietary risks in 1990-2019. J Hum Nutr Diet. 2022;35(1):202-13.
31. Wang F, Mubarik S, Zhang Y, Shi W, Yu C. Risk assessment of dietary factors in global pattern of ischemic heart disease mortality and disability-adjusted life years over 30 years. Front Nutr. 2023;10:1151445.
32. Stanaway JD, Afshin A, Ashbaugh C, Bisignano C, Brauer M, Ferrara G, et al. Health effects associated with vegetable consumption: a Burden of Proof study. Nature medicine. 2022;28(10):2066-74.
33. World Health Organization; (Internet). Healthy Diet.[Access Date: 31 May 2024] Available form: https://www.who.int/health-topics/healthy-diet.
34. Sánchez-Villegas A, Marchínez-Lapiscina EH. A healthy diet for your heart and your brain. 2018.

35. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Current opinion in lipidology. 2002;13(1):3-9.
36. World Health Organization (Internet). Healthy Diet.Access Date: 31 May 2024) Available form: https://www.who.int/news-room/fact-sheets/detail/healthy-diet.
37. Cordain L, Eaton SB, Sebastian A, Mann N, Lindeberg S, Watkins BA, et al. Origins and evolution of the Western diet: health implications for the 21st century. Am J Clin Nutr. 2005;81(2):341-54.
38. Clemente-Suárez VJ, Beltrán-Velasco AI, Redondo-Flórez L, Marchín-Rodríguez A, Tornero-Aguilera JF. Global Impacts of Western Diet and Its Effects on Metabolism and Health: A Narrative Review. Nutrients. 2023;15(12).
39. Alkharfy KM. Food advertisements: to ban or not to ban? Ann Saudi Med. 2011;31(6):567-8.
40. Sadeghirad B, Duhaney T, Motaghipisheh S, Campbell NR, Johnston BC. Influence of unhealthy food and beverage marketing on children's dietary intake and preference: a systematic review and meta-analysis of randomized trials. Obes Rev. 2016;17(10):945-59.
41. Hawkes C. Sales promotions and food consumption. Nutr Rev. 2009;67(6):333-42.
42. Riesenberg D, Backholer K, Zorbas C, Sacks G, Paix A, Marshall J, et al. Price Promotions by Food Category and Product Healthiness in an Australian Supermarket Chain, 2017-2018. Am J Public Health. 2019;109(10):1434-9.
43. Obesity Evidence Hub (Internet). Unhealthy food price promotions. [Access Date: 31 May 2024] Availableform:https://www.obesityevidencehub.org.au/collections/prevention/new-approaches-restrictions-on-price-promotions.
44. Health Desk. (Internet). What is health-washing, and what does the label “real food” mean to consumers? : (Access Date: 31 May 2024) Available form: https://health-desk.org/articles/what-is-health-washing-and-what-does-the-label-real-food-mean-to-consumers.
45. Gundersen Health System (Internet). Health Halos: What they are and why you need to avoid them. (Access Date: 31 May 2024) Available form: https://www.gundersenhealth.org/health-wellness/eat-move/health-halos-what-they-are-and-why-you-need-to-avoid-them
46. Fernan C, Schuldt JP, Niederdeppe J. Health Halo Effects from Product Titles and Nutrient Content Claims in the Context of "Protein" Bars. Health Commun. 2018;33(12):1425-33.
47. Klassen-Wigger P, Barclay DV. Market-driven fortification. Food fortification in a globalized world: Elsevier; 2018. p. 63-7.
48. Kroker-Lobos MF, Mazariegos M, Guamuch M, Ramirez-Zea M. Ultraprocessed Products as Food Fortification Alternatives: A Critical Appraisal from Latin America. Nutrients. 2022;14(7).
49. Global nutrition targets 2025: policy brief series. World Health Organisation; 2014.
50. United Nations (Internet). Sustainable developement goals. (Access Date: 31 May 2024) Available form: https://sdgs.un.org/goals.
51. United Nations (Internet). Decade of Action On Nutrition. (Access Date: 31 May 2024). Available form: https://www.un.org/nutrition/un-decade-action-nutrition-2016-2025.
52. de Romana DL, Greig A, Thompson A, Arabi M. Successful delivery of nutrition programs and the sustainable development goals. Current Opinion in Biotechnology. 2021;70:97-107.
53. A snapshot from across Europe, Successful nutrition policies - country examples. World Health Organization Europe, 2014.
54. School Food Policy Country Factsheets-Slovenia. European Commission, 2011.
55. Food policy highlights from around the world. World Cancer Research Fund International; 2014.
56. Hunter College New York City Food Policy Center (Internet). Food Advertising Restrictions for Youth, South Korea: Urban Food Policy Snapshot. (Access Date: 31 May 2024) Available form: https://www.nycfoodpolicy.org/food-advertising-restrictions-youth-south-korea-urban-food-policy-snapshot/
57. Global Action Network (Internet). Sustainable Food from the Oceans and Inland Waters for Food Security and Nutrition. (Access Date: 31 May 2024) Available form: https://nettsteder.regjeringen.no/foodfromtheocean/

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

Genomic biomarkers for immunotherapy response in pediatric solid tumors

Pediatrik solid tümörlerde immünoterapi yanıtı için genomik biyobelirteçler

Sefayi Merve ÖZDEMİR[1]
Tekincan Çağrı AKTAŞ[1]
Özde Elif GÖKBAYRAK[1]
Safiye AKTAŞ[2]

[1]Dokuz Eylül University Institute of Health Sciences, Izmir, Türkiye
[2] Department of Pathology, Faculty of Medicine, Dokuz Eylül University, Izmir, Türkiye

Biomarkers in Pediatric Solid Tumors
Received: 21.01.2025
Accepted: 12.11.2025
DOI:10.18614/dehm.1873512

Corresponding author
Safiye AKTAŞ
ORCID ID: 0000-0002-7658-5565
safiyeaktas@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

ABSTRACT

Immunotherapy is an increasingly popular treatment strategy offering hope for many cancers. The FDA (Food and Drug Administration) has just approved the use of immune checkpoint inhibitors for treating malignancies in both adults and children. Immune checkpoint inhibitors have been more successful in treating adult cancers than in pediatric cancers. Adult tumors have a higher tumor mutation burden (TMB) than pediatric tumors. The level of microsatellite instability (MSI) in adult tumors is greater than in pediatric solid tumors due to DNA-mismatch deficiency. TMB in tumors correlates with MSI. TMB and MSI analysis are genomic biomarkers for immune checkpoint blockade response in tumors. TMB and MSI analyses have been used in clinical practice to predict which patients are candidates for immunotherapy. This review evaluates the use of TMB and MSI analysis to predict the immunotherapy response of pediatric tumors.

KEYWORDS
Biomarker, immunotheraphy, microsatellite instability, pediatric solid tumors, tumor mutation burden.

ÖZ

İmmünoterapi, birçok kanserin tedavisinde umut vadeden büyüyen bir stratejidir. FDA, (Gıda ve İlaç İdaresi) hem yetişkinlerde hem de çocuklarda maligniteleri tedavi etmek için immün kontrol noktası inhibitörlerinin kullanımını onayladı. İmmün kontrol noktası inhibitörleri, yetişkin kanserlerinde pediatrik kanserlere göre daha başarılı olmuştur. Yetişkin tümörler, pediatrik tümörlere kıyasla daha yüksek tümör mutasyon yüküne (TMB) sahiptir. Yetişkin tümörlerde mikrosatelit instabilitesine (MSI) neden olan DNA uyumsuzluğu eksikliği seviyesi, pediatrik solid tümörlere göre daha yüksektir. Tümörlerdeki TMB, MSI ile ilişkilidir. TMB ve MSI, tümörlerde immün kontrol noktası blokaj yanıtı için genomik biyobelirteçlerdir. TMB ve MSI analizi, klinikte immünoterapi adayı hastaları tahmin etmek için kullanılmıştır. Bu derlemede, pediatrik tümörlerin immünoterapi yanıtı için TMB ve MSI analizi değerlendirilmiştir.

ANAHTAR KELİMELER
Biyobelirteç, immünoterapi, mikrosatelit instabilitesi, pediatrik katı tümörler, tümör mutasyon yükü

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

The primary factor leading to disease-related mortality in children and adolescents is pediatric tumors. Despite having high heterogeneity, pediatric tumors constitute only approximately %1 of tumor types. A broad classification of childhood malignancies is based on their anatomical, molecular, cellular, or genetic characteristics. It is estimated that 300,000 children (0–19 years old) have a cancer diagnosis each year worldwide (1,2). In 2022, 206,362 cases of childhood cancer that were newly reported worldwide. Of these, 80,104 of these cases resulted in death (3). The Surveillance, Epidemiology and End Results (SEER) reports that less than 200 cases of pediatric cancer occur annually, and over 50% of these cases are rare (4). About thirty percent of juvenile cancers are solid tumors, even though hematological cancers account for the majority of these cases. Among youngsters under the age of 15, brain malignancies account for 26% of all cancer cases (5). Neuroblastoma (15%), rhabdomyosarcoma (7%), Wilms tumor (6%), Ewing sarcoma (8%), retinoblastoma (5%), and other malignancies are among the more prevalent types (6,7).

Over the past few decades, there has been significant progress in the treatment of childhood solid tumors due to our growing understanding of their molecular and cellular dynamics. The development of cytotoxic chemotherapy and multimodal strategies has led to a significant survival improvement of more than 50% since the 1970s. In addition, molecular and diagnostic developments have resulted in more accurate stratification procedures, determining the choice of those patients who require intensified therapy and decreasing long-term toxicities. Although most kinds of pediatric cancers have a survival rate greater than 80% after treatment, some cancers have a poor prognosis. In addition, treating childhood malignancies that are recurrent and resistant to treatment remains difficult (8,9). Radiation therapy, cytotoxic chemotherapy, and surgery are typically used to treat children cancers. Cytotoxic chemotherapy can have negative long-term effects (10,11). Immunotherapy is a developing discipline that has demonstrated promise in treating children brain cancers that do not respond well to traditional treatment (9). The use of personalized and targeted treatments based on molecular markers for childhood and adult cancers have been increased. However, insufficient progress has been made in improving outcomes. In pediatric oncology, molecular biomarkers are routinely investigated for diagnosis and risk group stratification.

In precision medicine, the detection of genomic alterations in cancers has become significant. Genetic data from pediatric tumors provides information about their molecular composition. In order to improve recovery rates in pediatric patients, molecular targeting research using tumor molecular profiling in children must continue. In recent years, profiling studies utilising next-generation sequencing (NGS) have made the extensive localisation of childhood malignancies easier. This has resulted in the fragmentation of numerous biomarkers in numerous childhood cancers with both minor changes and copy number variants (12–15). Genomic mutations in cancers, such as single nucleotide variants (SNVs), minor indels, copy number variants (CNVs), and fusion genes, can be observed using NGS. Whole genome, exome, or transcriptome sequencing has been utilized in clinical settings for cancer diagnosis. Custom-designed or targeted NGS panels have been developed for clinical use. These panels are used to identify biomarkers for the diagnosis and prognosis of cancer (14,16).

Sequencing studies have revealed potential biomarkers with clinical and therapeutic value in pediatric tumors. Genetic mutations have been identified for targeted therapy of pediatric tumors. Unfortunately, these have had no impact on the survival of patients with childhood tumors. Despite this, MEK and BRAFV600E inhibitors have shown efficiency in children with low-grade glioma, regardless of molecular changes (17). Current chemotherapy strategies remain ineffective against relapsed/refractory cancers with late toxicities. Immunotherapy strategies have had a significant impact on the treatment of hematological and adult tumors such as lung and colorectal cancers. However, immunotherapy studies with pediatric tumors have not been effective, because of their immune cold characteristics (18). Adult tumors contain a higher mutation load than childhood cancers, so the response to immunotherapy is higher in adult tumors. The mutation frequency has increased in pediatric tumors that are refractory/recurrent compared to adult tumors (19). Nevertheless, there are cases where immunotherapy has been successful in pediatric tumors. TMB and MSI, as revealed by genomic profiling studies, are suggested to be biomarkers that can predict response to immune checkpoint inhibition (20).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

Genetic alterations in pediatric tumors

The frequencies and genetic changes of childhood cancers may differ from those of adult tumors (21). Although childhood cancers involve fewer genetic changes than those in adults, they often contain single and multiple nucleotide variants and insertions/deletions. They are also more likely to occur through gene splicing and copy number mutations. Different pediatric tumors have DNA mutations that are the main factors. Examples include ATRX, p53, BRAF and PTEN mutations in gliomas, ALK mutations in neuroblastomas, PTCH1 in medullablastomas, and MTOR alterations in rhabdomyosarcomas (12).

Genomic profiling of tumors, including whole genome analyses, reveals their molecular pathogenesis, and allows the origins of different malignancy types and subtypes to be distinguished. Recent research has determined the genetic landscapes of solid tumors in adults and children, including particular driver alterations for precision and targeted therapy (12). Researchers have demonstrated that genomic changes, mutation burdens, and mutation signatures are present in the molecular pathology of diverse malignancies. The most striking discovery in genomic investigations is the absence of large mutation loads in the majority of juvenile cancers, with very few exceptions. Osteosarcomas include a higher number of mutations than other childhood tumors. TP53, RB1, ATRX, and PTEN mutations are mostly seen in patients with osteosarcoma (22). BRAFV600E variations have been detected in low-grade glioma with worse outcome (23). Pediatric high-grade gliomasexhibit certain epigenetic alterations involving PTEN and EGFR mutations (24). Medulloblastoma is one of the childhood tumors characterized by TP53, CTNNB1, and TERT mutations (17,25). The types of sporadic and hereditary retinoblastoma have RB1 gene mutations (26).

Tumor mutation burden

Current treatment for pediatric solid tumors includes enhancement and consolidation, with or without radiation therapy. The prognosis remains poor for children with highly likely metastatic and/or recurrent disease. There is clearly an unmet need for less toxic and more effective treatments. Immunotherapy shows promise in treating resistant disease and improving long-term survival. However, the effects of immunotherapy on pediatric solid tumors are still unclear. Tumor mutation burden (TMB) is an emerging genomic biomarker in cancer, showing an improved response to immune checkpoint inhibition (ICIs) in adult cancers (27,28). TMB refers to the total number of somatic mutations per tumor genome coding region. It is generally expressed as mutations per megabase (mut/Mb) (29,30). A high TMB capacity is an emerging biomarker that is related to sensitivity to immune checkpoint blockade. Studies have shown that TMB is more closely related to response to PD-1/PD-L1 blockade immunotherapy than PD-1 or PD-L1 expression as determined by immunohistochemistry (IHC) (31).

Tumor mutational load varies depending on the type and histology of cancer (31). In recent years, many studies have contributed to the c characterisation of TMB variations in diseases, reporting that TMB levels are highest in melanoma, followed by NSCLS and squamous cancers. Pediatric tumors and leukemias demonstrate low levels of TMB. TMB was first described as a biomarker of response to ICIs in melanoma (32). Environmental factors, including UV, smoking and ageing, etc., lead to genomic mutations and are mutational processes in melanoma and NSCLS. APOBEC cytidine deaminase mutations in sub clonal mutations are observed in many cancer types following chemotherapy, such as temozolomide (33,34). As can be seen in Figure 1, environmental factors and errors in the DNA mismatch repair system cause different patterns of alterations, resulting in MHC (major histocompatibility complex) diversity and an increasing number of mutations. MHC diversity determines how different neoantigens are presented and can be identified by the T- cell recognition reportaire (34).

The TMB of cancer patients was first investigated in detail using whole exome sequencing (WES). The WES method covers 40-50 Mb of the genome and provides an accurate estimation of tumor mutational load in the coding regions. Although TMB values obtained from WES are currently considered the gold standard, the method is not routinely used in diagnostics due to its high cost and time-consuming nature. Therefore, it is suggested that targeted NGS gene panels are a cheaper and more feasible method for TMB prediction than WES (29,35). Targeted panels have been designed with a minimum 1 Mb panel size for identifying somatic mutations in cancer associated genes (29). While cost-effective for routine

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

use, small panel size NGS tests (<1 Mb) are clinically suboptimal for predicting response to immunotherapy due to imprecise tumour distribution programming (36,37).

Pediatric tumors have a lower mutation load than those in adults (21,38). There were much fewer SNVs and indels in the malignancies during this period. For example, osteosarcoma exhibits a greater number of compartments than other childhood malignancies. However, the TMB level in childhood malignancies is still much lower than TMB levels that observed in adult tumors (39,40). Parisi et al. showed that high TMB levels in children with brain tumors were related to poor outcomes in their multi-institutional analysis (41). In a study in which the comprehensive genomic profiling of 723 pediatric brain tumor patients (aged ≤21 years) was performed, TMB was categorized as low (between 0 and 6), intermediate (at the 6-20 interval) or high (greater than 20 mut/megabase). Among these patients, 91.8% had low TMB, 6.1% had intermediate TMB, and 2.1% had high TMB. Low-TMB tumors are associated with BRAF alterations, whereas high-TMB tumors are associated with TP53 mutations (42).

TMB refers to the total number of somatic mutations within a tumor sample. It has been reported that the higher mutational burden shows different neoantigen formation that is potentially recognized by T cell, clinically related with better ICI responses. According to FDA approval, a TMB value of 10 mut/Mb or greater is defined as a high mutation burden resulting in neoantigen formation.. In order to define a high TMB status, consideration should be given to the NGS panel assay's panel size, gene content, germline filtering, and the bioinformatics tools used for TMB calculations (43,44). Generally, studies consider non-synonymous mutations, chromosomal translocations, and indels mutations for estimating TMB. Synonymous mutations are not thought to contribute to TMB prediction. This is because nonsynonyms mutations and indels have the potential to contribute to the formation of neoantigens, in contrast to synonymous mutations (30). Different approaches have been used in different studies involving patient samples. For example, a study using the FoundationOne CDx (F1CDx) NGS panel included synonymous mutations in the TMB calculation, but excluded hotspot driver mutations (33,35). Copy number variations are indicative of immune infiltration and immunotherapy efficacy and are positively associated with TMB (45).

TMB analysis in pediatric oncology has faced several challenges. Pediatric tumors exhibit high levels of intra-tumor heterogeneity, meaning that different tumor regions may have various mutational profiles. This heterogeneity can affect the accuracy of TMB analysis and its ability to predict immunotherapy response. Pediatric tumors demonstrate lower mutation rates, so the threshold for determining high TMB can be different from adult cancers. There is a lack of standardization in TMB assessment methods and thresholds for defining high TMB in pediatric tumors. This makes it difficult to compare results from different studies and reduces the usefulness of TMB as a predictive biomarker in this population.

Microsatellite Instability

Microsatellites (MS) are short repeated sequences (1-6 base pair motifs) in regions of 10-60 base pairs in the genome. They account for 3% of the whole genome and are polymorphic among individuals. Microsatellites can be found in many regions of the genome including introns, exons, promoter, and terminal sites (46,47). MSs play a role in chromosomal structure, including the formation of heterochromatin. The location of a microsatellite within chromatin domains may affect the replication and gene expression associated with diseases. Complex molecular mechanisms exist between chromatin structure, chromatin remodelling, and the DNA mismatch repair system (MMR) in relation to microsatellite instability (48,49). The formation of MS is caused by unequal crossing over or DNA slippage during replication. Mismatch base groups between the template strand and slippage strands are repaired by the MMR system which corrects DNA replication errors in normal cells. Disruption to the MMR system results in an inability to regulate the lengths of microsatellites during replication. Following cell division, varying lengths develop in the microsatellite sequences of cells with a defective MMR system (26). Mutations in MMR genes result in a defective mismatch repair system, and the possibility of genome instability increases in tumor cells (46).

The mismatch repair system consists of main genes encoding proteins: MLH1, MSH2 (MutS homologue 2 protein), MSH6 (MutS homologue 6 protein), and PMS2 (PMS1 homologue 2

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

protein). These proteins form heterodimers as MSH2 interacting with MSH6 or MSH3 and then, MLH1 binding with PMS2 or MLH3 (Figure2). The MSH2/MSH6/MH3 protein complex detects mismatch base pairs. This protein complex then recruits the MLH1/PMS2/MSH6 complex. These complexes can induce Exonuclease 1 (EXO1) to excise the DNA strand. The DNA strand break is then filled by DNA polymerase ξ/D and replication protein A (RPA) (Figure 2) (50) . The methylation of MMR genes, especially the hypermethylation of promoter in MLH1 gene (associated with MLH1 protein inactivation) is the driving mechanism for MSI in sporadic tumors. A study of MSI analysis in 36 medullablastoma patients showed mild hypermethylation levels of the MSH6 gene in two patients with MSI (29). Biallelic inactivation of MMR genes due to somatic or germline mutations, or epigenetic silencing increases the rate of mutations (50,51). Epigenetic silencing of MLH1 is frequent in retinoblastoma tumors (52). These repetitive DNA sequences, known as MSI-H+ (high-level MSI), exhibit uneven expansion and/or contraction due to somatic (acquired) or germline (inherited) mutations in the DNA mismatch repair (MMR) proteins (40). MSI is a marker of the dMMR system. Roughly 15% of MSI-high tumors have germline mutations in mismatch repair genes. The inactivation of MMR genes resulting in mismatch repair deficiency causes to missing insertions/deletions in microsatellites by repeating multiple times(53,54). MSI tumors include MMR gene deficiencies, but the genes that lead to high MSI are unclear. MSI tumors have single nucleotide mutations in the coding regions of many genes, including BRAFV600E, TGFβRII, BAX, and IGFIIR (55).

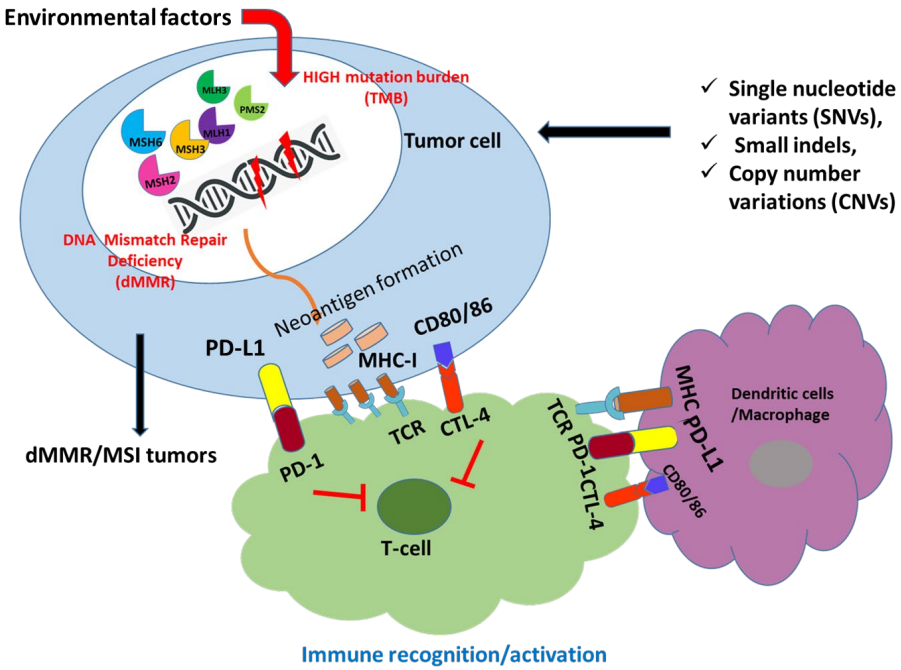


Figure 1. The schematic representation of tumor cells recognized by T-lymphocytes in TME. TMB and MSI are genomic biomarker for immune checkpoint response. High mutation burden is resulted from SNVs, CNVs, and indels in tumor genome. The hypermutation of MMR genes containing MLH1, MSH2, MSH3, MSH6, MLH3, and PMS2 also cause high mutation load and microsatellite instability. Tumors with high TMB and MSI include MHC diversity and produce neoantigen that is detected by TCR. The interactions between PD-L1 and PD-1 or CTL4 and CD80/CD86 play role in immune escape of tumors cells. MHC, Major histocompatibility complex; TCR, T cell receptor; CTLA-4, Cytotoxic T lymphocyte antigen-4; PD-1, Programmed cell death-1; PD-L1, Programmed cell death receptor-1/-2 ligand.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

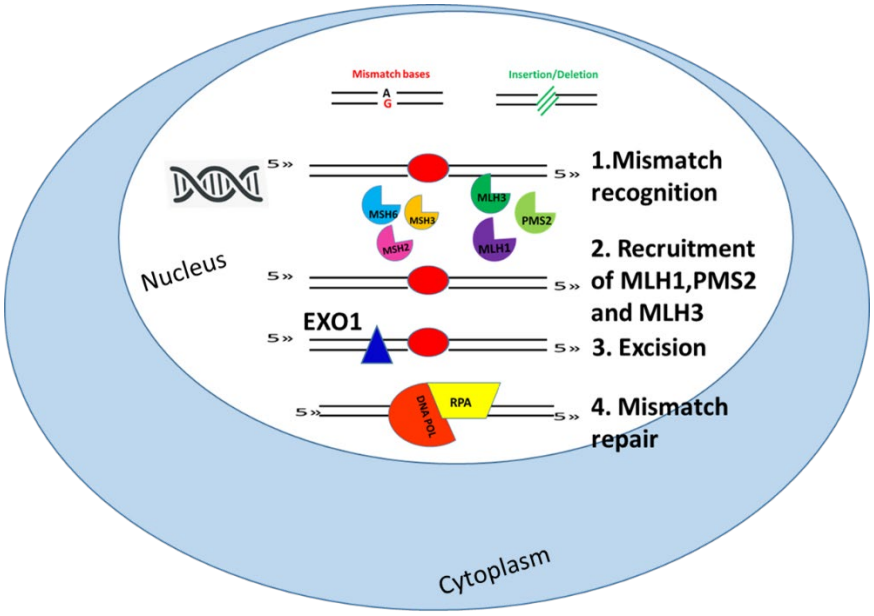


Figure 2. The illustration of DNA mismatch repair mechanisms. 1. MSH2/MSH6/MH3 proteins detects mismatch base. 2. This protein complex recruits MLH1/PMS2/MSH6. 3. EXO1, is activated to excise strand.4. DNA strand break is filled by DNA polymerase ξ/D and RPA.EXO1, exonuclease 1; RPA, replication protein A.

MSI is mostly seen in cancer patients with Lynch syndrome, colorectal, prostate, endometrial, and ovarian cancers, and glioblastoma (46,56). MSI is found about 15% of patients with colorectal cancers and impact the colorectal cancer management (57). The frequency of MSI in pediatric CNS tumors is more than in adult CNS tumors. According to a study, MSI is more common in pediatric high grade gliomas with 19.7% than adults with 6.8% (58). MSI is a strong mutational signature created by defective DNA mismatch repair. The inactivation of DNA mismatch repair (MMR) genes both genetically and epigenetically increases the frequency of frameshift mutations in many cancer-related genes linked to tumor growth. When comparing malignancies with high-frequency MSI (MSI-L) to low-frequency MSI (MSI-L) or microsatellite stable (MSS) tumors, distinct molecular, pathological, and clinical features are seen that are independent of the tumor tissue origin (59).

The MSI/dMMR profile of a cancer can be identified using IHC to detect the loss of MMR proteins and doing molecular tests such as PCR based and NGS-based tests to show microsatellite alterations. NGS analysis can target cancer-related genes by sequencing the genome to reveal MSI in tumor samples. To compare the microsatellite loci found in tumor tissues with conventional DNA, multiplex fluorescence PCR is utilized. According to the recommendation of the National Cancer Institute, the two single nucleotide repeat loci BAT-25 and BAT-26, as well as the three multi-nucleotide repeat loci D2S123, D5S346, and D17S250 can be used as microsatellite markers to determine MSI status. IHC is a simple and practical method to evaluate MSI status by detecting the expressions of MMR proteins (46). MSI analysis by IHC is routinely used to detect Lynch syndrome (60).

A high MSI is an important genomic indicator of a high tumor mutation load. The high MSI phenotype is correlated with MMR deficient cancers. Indeed, TMB-H with ≥20 mutations/Mb is present in around 83% of MSI-H malignancies (31,34). Tumor mutation load and deficient mismatch repair are caused by environmental and endogenous mutagens. Impaired mismatch repair results in high TMB and the formation of neoantigens that can be recognized by the host immunity (61). Specific genomic mutations, MHC and T cell diversity provide important clues for determining the response to immune checkpoint inhibitors.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
REVIEW
Pages:15-26

The high-expression of PD-L1, a ligand of PD-1, helps cancer cells evade recognition and destruction by the body's adaptive immune system.. Blocking the PD-1/PD-L1 interaction primes the patient's immune system to combat cancer cells that were previously considered "invisible" (28). Numerous studies have demonstrated favorable associations between MSI-H+ status and total TMB, as well as increased PD-1/PD-L1 expression. Pembrolizumab was approved by FDA in 2017, and it is a PD-1 inhibitor used to treat metastatic and unresectable tumors in adults and children with MSI-high (MSI-H) or MMR deficient (dMMR) tumors. The FDA then approved nivolumab (a PD-1 inhibitor) plus ipilimumab (a CTLA-4 inhibitor) for treating MSI-H or dMMR metastatic colorectal cancer in adults and children (43,62). Another PD-1 inhibitor, Dostarlimab, is used in combination with carboplatin and paclitaxel to ameliorate progression-free survival in recurrent and primary endometrial cancer with dMMR-MSI-H profile (63). Das et al. found that patients with childhood solid tumors treated with temozolomide showed higher TMB (defined as ≥5 mutations per megabase) and dMMR, as reported by They found that patients with higher TMB and dMMR levels did not response to nivolumab. Patients with high-grade glioma showed an overall response rate of 50% and a prolonged survival period when treated with nivolumab. This demonstrated the role of immune checkpoint inhibition in pediatric tumor treatment for the first time (64).

Advances in immunotherapy of pediatric solid tumors

Immunotherapy has become a cutting-edge method of treating cancer, offering new hope to patients with various forms of cancers. Numerous immunotherapeutic approaches, such as immune checkpoint inhibitors, vaccine therapy, and adoptive immunotherapy, which includes viral therapy and chimeric antigen receptor T cell (CART) therapy, have been used to treat adult malignancies. These approaches have also been examined in pediatric cancers. One of the most commonly studied forms of immunotherapy for pediatric tumors is immune checkpoint inhibitors (ICIs). These drugs target antigens on immune cells or cancer cells, impairing the signals that enable cancer cells to evade the immune system. For example, PD-1 inhibitors can interfere with the PD-1/PD-L pathway, thereby preventing cancer cells from evading immune surveillance (Figure 1). CD8 + tumor infiltrating lymphocytes (TILs) are correlated with PD-1 expression (65). The expression of PD-L1 in pediatric tumors have been found to be low compared to subtypes with a poor prognosis (66). ICIs have shown promising results in neuroblastoma, osteosarcoma, and certain brain tumors. Drugs such as nivolumab and pembrolizumab, which block the PD-1 (programmed cell death 1)/PD-L1 (programmed cell death 1 ligand) pathway, have demonstrated efficacy in some pediatric cancers, leading to long-lasting responses and improved survival rates (67). It was thought that upregulating PD-1 expression in pediatric tumor cell lines such as neuroblastoma could enhance the efficacy of ICIs. A phase I/II trial combined nivolumab and ipilimumab to treat children and adolescents with relapsed/refractory solid tumors. This trial demonstrated some clinical activity for this combination, but an increased dose of nivolumab and ipilimumab led to toxicity without any clinical benefit (68).

PD-1 antibodies alone are insufficient for the treatment of pediatric tumors. Strategies combining PD-1 antibodies with other treatments have improved outcomes for pediatric cancers. In addition to this, PD-1 is a biomarker that can be used to identify pediatric cancer patients who might be candidates for immunotherapy. Therefore, more molecular markers must be introduced to the ICI regime (69).

CAR T-cell therapy is another groundbreaking approach to immunotherapy, particularly for hematological malignancies. To combat cancer cells that express specific surface antigens, this method involves genetically modifying a patient's T cells to produce chimeric antigen receptors. Initially evaluated for leukemia and lymphoma, CAR T-cell therapy is now being studied for solid cancers, such as pediatric neuroblastoma, sarcomas, and brain tumors (70). Early clinical trials have shown promising results, with some patients achieving complete remissions and prolonged survival. However, immunotherapy in pediatric tumors presents unique challenges and considerations compared to adult cancers (71,72).

Pediatric tumors often have lower mutational burdens and different immune microenvironments such as low PD-1 expression and TILs which influence their response to immunotherapy (73). Additionally, the developing immune system in children may respond differently to

immunomodulatory agents than the immune systemin adults. Despite using various processes, immunotherapy techniques all stimulate the immune system and have the potential to inflame the site of the disease. This can have a significant impact on the area of interest, potentially resulting in serious neurological adverse effects, particularly in children with cancers of the central nervous system. Furthermore, the long-term effects of immunotherapy on pediatric patients' growth, development, and immune function require careful evaluation (74).

Conclusions

The development of pediatric immunotherapies has accelerated in recent decades. Alongside this, identifying biomarkers to predict which childhood tumour patients are likely to respond to immunotherapy has become significant. TMB and MSI are biomarkers of immune checkpoint response in adult malignancies. There is a correlation between mutational load and MSI. This provides new insight into utilising them as immunotherapy biomarkers. Studies on TMB and MSI analysis in pediatric solid tumors have demonstrated that these tumors have a low mutational load and MSI. This is associated with a poor response to immunotherapy in children. However, specific genetic alterations and their contribution to mutation load provide new insights into the immunotherapy of children with respect to personalized medicine. Mismatch repair deficiency resulting from the methylation of MMR genes contributes to mutation burden and MSI. Genomic profiling to identify individuals with high TMB and dMMR/MSI tumours has a significant impact on the detection of immunotherapy candidates.

Author contributions

Safiye AKTAŞ determined the subject and design of this manuscript. Sefayi Merve ÖZDEMİR conducted the literature search. Sefayi Merve wrote this manuscript and scratched all figures. Özde Elif GÖKBAYRAK and Tekincan Çağrı AKTAŞ prepared manuscript design draft reviewed the manuscript, and made critical revisions. Safiye AKTAŞ approved this manuscript.

Acknowledgements

Figures are created by Microsoft Office PowerPoint program.

Funding

There is no funding for this study.

Conflict of interest statements

The authors declare no conflicts of interest

References

1. Childhood cancer [Internet]. [cited 2023 Oct 4]. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer-in-children
2. Lupo PJ, Spector LG. Cancer Progress and Priorities: Childhood Cancer. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2020 Jun;29(6):1081–94.
3. Huang J, Chan SC, Ngai CH, Lok V, Zhang L, Lucero-Prisno III DE, et al. Global incidence, mortality and temporal trends of cancer in children: A joinpoint regression analysis. Cancer Med. 2023;12(2):1903–11.
4. Surveillance, Epidemiology, and End Results Program [Internet]. [cited 2024 Apr 24]. Available from: https://seer.cancer.gov/
5. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. CA Cancer J Clin. 2022 Jan;72(1):7–33.
6. Childhood Cancer Epidemiology: Overview, Tools of Study, Cancer Incidence. 2023 Sep 21 [cited 2023 Oct 14]; Available from: https://emedicine.medscape.com/article/989841-overview?form=fpf
7. LaQuaglia MP, Gerstle JT. ADVANCES IN THE TREATMENT OF PEDIATRIC SOLID TUMORS: A 50 YEAR PERSPECTIVE. J Surg Oncol. 2022 Oct;126(5):933–42.
8. Zahnreich S, Schmidberger H. Childhood Cancer: Occurrence, Treatment and Risk of Second Primary Malignancies. Cancers. 2021 May 26;13(11):2607.
9. Shalita C, Hanzlik E, Kaplan S, Thompson EM. Immunotherapy for the treatment of pediatric brain tumors: a narrative review. Transl Pediatr. 2022 Dec;11(12):2040–56.
10. Schilter KF, Smith BA, Nie Q, Stoll K, Felix JC, Jarzembowski JA, et al. Analytical validation and implementation of a pan cancer next-generation sequencing panel, CANSeqTMKids for molecular profiling of childhood malignancies. Front Genet [Internet]. 2023 [cited 2023 Oct 14];14. Available from:

https://www.frontiersin.org/articles/10.3389/fgene.2023.1067457
11. Kulubya ES, Kercher MJ, Phillips HW, Antony R, Edwards MSB. Advances in the Treatment of Pediatric Brain Tumors. Children. 2022 Dec 27;10(1):62.
12. Hiemenz MC, Ostrow DG, Busse TM, Buckley J, Maglinte DT, Bootwalla M, et al. OncoKids: A Comprehensive Next-Generation Sequencing Panel for Pediatric Malignancies. J Mol Diagn JMD. 2018 Nov;20(6):765–76.
13. Cipri S, Abenavoli L, Boccuto L, Del Baldo G, Mastronuzzi A. How Genetics and Genomics Advances Are Rewriting Pediatric Cancer Research and Clinical Care. Medicina (Mex). 2022 Oct 2;58(10):1386.
14. Surrey LF, MacFarland SP, Chang F, Cao K, Rathi KS, Akgumus GT, et al. Clinical utility of custom-designed NGS panel testing in pediatric tumors. Genome Med. 2019 May 28;11:32.
15. Gröbner SN, Worst BC, Weischenfeldt J, Buchhalter I, Kleinheinz K, Rudneva VA, et al. The landscape of genomic alterations across childhood cancers. Nature. 2018 Mar 15;555(7696):321–7.
16. Budczies J, Allgäuer M, Litchfield K, Rempel E, Christopoulos P, Kazdal D, et al. Optimizing panel-based tumor mutational burden (TMB) measurement. Ann Oncol. 2019 Sep 1;30(9):1496–506.
17. Bornhorst M, Hwang EI. Molecularly Targeted Agents in the Therapy of Pediatric Brain Tumors. Pediatr Drugs. 2020 Feb 1;22(1):45–54.
18. Bosse KR, Giudice AM, Lane MV, McIntyre B, Schürch PM, Pascual-Pasto G, et al. Serial Profiling of Circulating Tumor DNA Identifies Dynamic Evolution of Clinically Actionable Genomic Alterations in High-Risk Neuroblastoma. Cancer Discov. 2022 Dec 2;12(12):2800–19.
19. Schramm A, Köster J, Assenov Y, Althoff K, Peifer M, Mahlow E, et al. Mutational dynamics between primary and relapse neuroblastomas. Nat Genet. 2015 Aug;47(8):872–7.
20. Palmeri M, Mehnert J, Silk AW, Jabbour SK, Ganesan S, Popli P, et al. Real-world application of tumor mutational burden-high (TMB-high) and microsatellite instability (MSI) confirms their utility as immunotherapy biomarkers. ESMO Open. 2022 Feb 1;7(1):100336.
21. Vogelstein B, Papadopoulos N, Velculescu VE, Zhou S, Diaz LA, Kinzler KW. Cancer Genome Landscapes. Science. 2013 Mar 29;339(6127):1546–58.
22. Chen X, Bahrami A, Pappo A, Easton J, Dalton J, Hedlund E, et al. Recurrent Somatic Structural Variations Contribute to Tumorigenesis in Pediatric Osteosarcoma. Cell Rep. 2014 Apr 10;7(1):104–12.
23. Dougherty MJ, Santi M, Brose MS, Ma C, Resnick AC, Sievert AJ, et al. Activating mutations in BRAF characterize a spectrum of pediatric low-grade gliomas. Neuro-Oncol. 2010 Jul;12(7):621–30.
24. Korshunov A, Ryzhova M, Hovestadt V, Bender S, Sturm D, Capper D, et al. Integrated analysis of pediatric glioblastoma reveals a subset of biologically favorable tumors with associated molecular prognostic markers. Acta Neuropathol (Berl). 2015 May;129(5):669–78.
25. Sursal T, Ronecker JS, Dicpinigaitis AJ, Mohan AL, Tobias ME, Gandhi CD, et al. Molecular Stratification of Medulloblastoma: Clinical Outcomes and Therapeutic Interventions. Anticancer Res. 2022 May 1;42(5):2225–39.
26. Odemis DA, Kebudi R, Bayramova J, Erciyas SK, Turkcan GK, Tuncer SB, et al. RB1 gene mutations and genetic spectrum in retinoblastoma cases. Medicine (Baltimore) [Internet]. 2023 Sep 9 [cited 2024 May 21];102(36). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10489529/
27. Aggarwal C, Ben-Shachar R, Gao Y, Hyun SW, Rivers Z, Epstein C, et al. Assessment of Tumor Mutational Burden and Outcomes in Patients With Diverse Advanced Cancers Treated With Immunotherapy. JAMA Netw Open. 2023 May 2;6(5):e2311181.
28. Fumet JD, Truntzer C, Yarchoan M, Ghiringhelli F. Tumour mutational burden as a biomarker for immunotherapy: Current data and emerging concepts. Eur J Cancer. 2020 May 1;131:40–50.
29. Meri-Abad M, Moreno-Manuel A, García SG, Calabuig-Fariñas S, Pérez RS, Herrero CC, et al. Clinical and technical insights of tumour mutational burden in non-small cell lung cancer. Crit Rev Oncol Hematol. 2023 Feb 1;182:103891.
30. Gubin MM, Artyomov MN, Mardis ER, Schreiber RD. Tumor neoantigens: building a framework for personalized cancer immunotherapy. J Clin Invest. 2015 Sep 1;125(9):3413–21.
31. Chalmers ZR, Connelly CF, Fabrizio D, Gay L, Ali SM, Ennis R, et al. Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden. Genome Med. 2017 Apr 19;9(1):34.
32. Snyder A, Makarov V, Merghoub T, Yuan J, Zaretsky JM, Desrichard A, et al. Genetic basis for clinical

response to CTLA-4 blockade in melanoma. N Engl J Med. 2014 Dec 4;371(23):2189–99.

33. Chan TA, Yarchoan M, Jaffee E, Swanton C, Quezada SA, Stenzinger A, et al. Development of tumor mutation burden as an immunotherapy biomarker: utility for the oncology clinic. Ann Oncol. 2019 Jan 1;30(1):44–56.
34. Jardim DL, Goodman A, de Melo Gagliato D, Kurzrock R. The Challenges of Tumor Mutational Burden as an Immunotherapy Biomarker. Cancer Cell. 2021 Feb 8;39(2):154–73.
35. Noskova H, Kyr M, Pal K, Merta T, Mudry P, Polaskova K, et al. Assessment of Tumor Mutational Burden in Pediatric Tumors by Real-Life Whole-Exome Sequencing and In Silico Simulation of Targeted Gene Panels: How the Choice of Method Could Affect the Clinical Decision? Cancers. 2020 Jan 17;12(1):230.
36. Buchhalter I, Rempel E, Endris V, Allgäuer M, Neumann O, Volckmar AL, et al. Size matters: Dissecting key parameters for panel-based tumor mutational burden analysis. Int J Cancer. 2019 Feb 15;144(4):848–58.
37. Makrooni MA, O'Sullivan B, Seoighe C. Bias and inconsistency in the estimation of tumour mutation burden. BMC Cancer. 2022 Aug 2;22(1):840.
38. Rahal Z, Abdulhai F, Kadara H, Saab R. Genomics of adult and pediatric solid tumors. Am J Cancer Res. 2018 Aug 1;8(8):1356–86.
39. Perry JA, Kiezun A, Tonzi P, Van Allen EM, Carter SL, Baca SC, et al. Complementary genomic approaches highlight the PI3K/mTOR pathway as a common vulnerability in osteosarcoma. Proc Natl Acad Sci U S A. 2014 Dec 23;111(51):E5564–73.
40. Yoshida T, Muramatsu H, Wakamatsu M, Taniguchi R, Ichikawa D, Nakaguro M, et al. Microsatellite instability-high is rare events in refractory pediatric solid tumors. Pediatr Hematol Oncol. 2022 Aug;39(5):468–74.
41. Parisi R, Patel RR, Rood G, Bowden A, Turco G, Korones DN, et al. Multi-institution analysis of tumor mutational burden and outcomes in pediatric central nervous system tumor patients. Pediatr Blood Cancer. 2023;70(3):e30139.
42. Patel RR, Ramkissoon SH, Ross J, Weintraub L. Tumor mutational burden and driver mutations: Characterizing the genomic landscape of pediatric brain tumors. Pediatr Blood Cancer. 2020 Jul;67(7):e28338.
43. Marcus L, Fashoyin-Aje LA, Donoghue M, Yuan M, Rodriguez L, Gallagher PS, et al. FDA Approval Summary: Pembrolizumab for the treatment of tumor mutational burden-high solid tumors. Clin Cancer Res Off J Am Assoc Cancer Res. 2021 Sep 1;27(17):4685–9.
44. Sung MT, Wang YH, Li CF. Open the Technical Black Box of Tumor Mutational Burden (TMB): Factors Affecting Harmonization and Standardization of Panel-Based TMB. Int J Mol Sci. 2022 May 3;23(9):5097.
45. Lei Y, Zhang G, Zhang C, Xue L, Yang Z, Lu Z, et al. The average copy number variation (CNVA) of chromosome fragments is a potential surrogate for tumor mutational burden in predicting responses to immunotherapy in non-small-cell lung cancer. Clin Transl Immunol. 2021 Jan 4;10(1):e1231.
46. Li K, Luo H, Huang L, Luo H, Zhu X. Microsatellite instability: a review of what the oncologist should know. Cancer Cell Int. 2020 Jan 13;20(1):16.
47. Pećina-Šlaus N, Kafka A, Salamon I, Bukovac A. Mismatch Repair Pathway, Genome Stability and Cancer. Front Mol Biosci [Internet]. 2020 Jun 26 [cited 2024 May 6];7. Available from: https://www.frontiersin.org/articles/10.3389/fmolb.2020.00122
48. Goellner EM. Chromatin remodeling and mismatch repair: Access and excision. DNA Repair. 2020 Jan;85:102733.
49. Baretti M, Le DT. DNA mismatch repair in cancer. Pharmacol Ther. 2018 Sep;189:45–62.
50. Li GM. Mechanisms and functions of DNA mismatch repair. Cell Res. 2008 Jan;18(1):85–98.
51. Schöniger S, Rüschoff J. Mismatch Repair Deficiency and Microsatellite Instability. Encyclopedia. 2022 Sep;2(3):1559–76.
52. Choy KW, Pang CP, Fan DSP, Lee TC, Wang JH, Abramson DH, et al. Microsatellite Instability and MLH1 Promoter Methylation in Human Retinoblastoma. Invest Ophthalmol Vis Sci. 2004 Oct 1;45(10):3404–9.
53. Sinicrope FA, Sargent DJ. Molecular Pathways: Microsatellite Instability in Colorectal Cancer: Prognostic, Predictive and Therapeutic Implications. Clin Cancer Res. 2012 Mar 15;18(6):1506–12.
54. Lu Y, Soong TD, Elemento O. A Novel Approach for Characterizing Microsatellite Instability in Cancer Cells. PLoS ONE. 2013 May 6;8(5):e63056.
55. GRADY WM, CARETHERS JM. Genomic and Epigenetic Instability in Colorectal Cancer

Pathogenesis. Gastroenterology. 2008 Oct;135(4):1079–99.
56. Hause RJ, Pritchard CC, Shendure J, Salipante SJ. Classification and characterization of microsatellite instability across 18 cancer types. Nat Med. 2016 Nov;22(11):1342–50.
57. Guyot D'Asnières De Salins A, Tachon G, Cohen R, Karayan-Tapon L, Junca A, Frouin E, et al. Discordance between immunochemistry of mismatch repair proteins and molecular testing of microsatellite instability in colorectal cancer. ESMO Open. 2021 Apr 28;6(3):100120.
58. Viana-Pereira M, Lee A, Popov S, Bax DA, Al-Sarraj S, Bridges LR, et al. Microsatellite Instability in Pediatric High Grade Glioma Is Associated with Genomic Profile and Differential Target Gene Inactivation. PLoS ONE. 2011 May 26;6(5):e20588.
59. Yamamoto H, Watanabe Y, Maehata T, Imai K, Itoh F. Microsatellite instability in cancer: a novel landscape for diagnostic and therapeutic approach. Arch Toxicol. 2020 Oct 1;94(10):3349–57.
60. Hampel H, Frankel WL, Martin E, Arnold M, Khanduja K, Kuebler P, et al. Feasibility of Screening for Lynch Syndrome Among Patients With Colorectal Cancer. J Clin Oncol. 2008 Dec 10;26(35):5783–8.
61. Dudley JC, Lin MT, Le DT, Eshleman JR. Microsatellite Instability as a Biomarker for PD-1 Blockade. Clin Cancer Res Off J Am Assoc Cancer Res. 2016 Feb 15;22(4):813–20.
62. Zhong Y, Xu F, Wu J, Schubert J, Li MM. Application of Next Generation Sequencing in Laboratory Medicine. Ann Lab Med. 2021 Jan;41(1):25–43.
63. Mirza MR, Chase DM, Slomovitz BM, dePont Christensen R, Novák Z, Black D, et al. Dostarlimab for Primary Advanced or Recurrent Endometrial Cancer. N Engl J Med. 2023 Jun 8;388(23):2145–58.
64. Das A, Tabori U, Sambira Nahum LC, Collins NB, Deyell R, Dvir R, et al. Efficacy of Nivolumab in Pediatric Cancers with High Mutation Burden and Mismatch Repair Deficiency. Clin Cancer Res. 2023 Dec 1;29(23):4770–83.
65. Caraban BM, Matei E, Cozaru GC, Aşchie M, Deacu M, Enciu M, et al. PD-L1, CD4+, and CD8+ Tumor-Infiltrating Lymphocytes (TILs) Expression Profiles in Melanoma Tumor Microenvironment Cells. J Pers Med. 2023 Jan 27;13(2):221.
66. Aoki T, Hino M, Koh K, Kyushiki M, Kishimoto H, Arakawa Y, et al. Low Frequency of Programmed Death Ligand 1 Expression in Pediatric Cancers. Pediatr Blood Cancer. 2016 Aug;63(8):1461–4.
67. Mokhtari RB, Sambi M, Qorri B, Baluch N, Ashayeri N, Kumar S, et al. The Next-Generation of Combination Cancer Immunotherapy: Epigenetic Immunomodulators Transmogrify Immune Training to Enhance Immunotherapy. Cancers. 2021 Jul 18;13(14):3596.
68. Davis KL, Fox E, Isikwei E, Reid JM, Liu X, Minard CG, et al. A Phase I/II Trial of Nivolumab plus Ipilimumab in Children and Young Adults with Relapsed/Refractory Solid Tumors: A Children's Oncology Group Study ADVL1412. Clin Cancer Res Off J Am Assoc Cancer Res. 2022 Dec 1;28(23):5088–97.
69. Long AH, Morgenstern DA, Leruste A, Bourdeaut F, Davis KL. Checkpoint Immunotherapy in Pediatrics: Here, Gone, and Back Again. Am Soc Clin Oncol Educ Book Am Soc Clin Oncol Annu Meet. 2022 Apr;42:1–14.
70. Wang C, Wang J, Che S, Zhao H. CAR-T cell therapy for hematological malignancies: History, status and promise. Heliyon. 2023 Nov 7;9(11):e21776.
71. Peterson C, Denlinger N, Yang Y. Recent Advances and Challenges in Cancer Immunotherapy. Cancers. 2022 Aug 17;14(16):3972.
72. Rohit Reddy S, Llukmani A, Hashim A, Haddad DR, Patel DS, Ahmad F, et al. The Role of Chimeric Antigen Receptor-T Cell Therapy in the Treatment of Hematological Malignancies: Advantages, Trials, and Tribulations, and the Road Ahead. Cureus. 13(2):e13552.
73. Hutzen B, Ghonime M, Lee J, Mardis ER, Wang R, Lee DA, et al. Immunotherapeutic Challenges for Pediatric Cancers. Mol Ther Oncolytics. 2019 Aug 28;15:38–48.
74. Tanda ET, Croce E, Spagnolo F, Zullo L, Spinaci S, Genova C, et al. Immunotherapy in Adolescents and Young Adults: What Remains in Cancer Survivors? Front Oncol. 2021 Sep 23;11:736123.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

Sedoanalgesia-based anesthesia approach in pediatric extracorporeal shock wave lithotripsy cases

Pediatrik ekstrakorporeal şok dalga litotripsi olgularında ayaktan anestezi uygulamaları

Sibel BÜYÜKÇOBAN[1]
Erkan ÖZDURAN[2]
Leyla İYİLİKÇİ[1]
Özlem ÖNER[3]
Aykut KEFİ[4]
Muzaffer DOĞU TAŞDEMİR[5]

[1] Dokuz Eylül University Faculty Of Medicine Department of Anesthesiology And Reanimation, Izmir, Türkiye
[2] Sivas Numune Hospital, Department of Physical Medicine and Rehabilitation/Algology, Sivas, Türkiye
[3] Izmir Democracy University Buca Seyfi Demirsoy Education and Research Hospital, Department of Anesthesiology and Reanimation, Subdivision of Critical Care Medicine, Izmir, Turkiye
[4] Dokuz Eylül University Faculty Of Medicine Department of Urology, Izmir, Türkiye
[5] Private Can Hospital, Department of Urology, Izmir, Turkiye

Pediatric ESWL with Sedoanalgesia
Received: 09.07.2024
Accepted: 18.09.2025
DOI:10.18614/dehm.1873523

Corresponding author
Erkan ÖZDURAN
ORCID ID: 0000-0003-3425-313X
erkanozduran@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

ABSTRACT

BACKGROUND
The aim of the study is to evaluate the safety, feasibility, and effectiveness of sedoanalgesia in pediatric patients undergoing extracorporeal shock wave lithotripsy (ESWL).

METHODS
This retrospective study included pediatric patients who underwent ESWL under a standardized sedoanalgesia protocol consisting of intravenous midazolam (0.0] mg/kg), fentanyl (1 mcg/kg), propofol (0.5–1 mg/kg), and ketamine (0.5–1 mg/kg) as needed. Any complications or adverse events related to sedoanalgesia were documented.

RESULTS
A total of 190 pediatric patients underwent 453 ESWL sessions. All procedures were completed successfully without conversion to general anesthesia. Spontaneous ventilation was preserved in all patients, and airway instrumentation was not required. Minor complications included transient desaturation (3.3]%) and nausea/vomiting (19.2%). No major anesthesia-related adverse events were observed. The mean stone size was 9 ± 2.86 mm for the kidney and 8 ± 2[14 mm for the ureter. The average number of sessions per patient was 2.4.

CONCLUSION
The fundamental principle of pediatric anesthesia is to use the lowest effective and shortest-acting anesthetic agents through careful titration. Our findings demonstrate that ESWL can be safely and effectively performed in children using a balanced sedoanalgesia protocol.

KEYWORDS
ESWL, fentanyl, ketamine, midazolam,non-operating room anesthesia,pediatric anesthesia,procedural sedation,propofol,sedoanalgesia

ÖZ

AMAÇ
Bu çalışmada, ekstrakorporal şok dalga litotripsi (ESWL) uygulanan pediatrik hastalarda sedoanaljezi kullanımının güvenliği, uygulanabilirliği ve etkinliğinin değerlendirilmesi amaçlanmıştır.

GEREÇ YÖNTEM
Bu retrospektif çalışmada, standart sedoanaljezi protokolü altında ESWL uygulanan pediatrik hastalar incelenmiştir. Kullanılan protokol intravenöz midazolam ([0].[05] mg/kg), fentanil ([1] mcg/kg), propofol ([0].[5]–[1] mg/kg) ve gerektiğinde ketamin ([0].[5]–[1] mg/kg) içermektedir. Komplikasyonlar ve advers olaylar kaydedilmiştir.

BULGULAR
Toplam 190 pediatrik hastaya 453 ESWL seansı uygulanmıştır. Tüm işlemler genel anesteziye geçilmeden başarıyla tamamlanmıştır. Hastaların tamamında spontan ventilasyon korunmuş ve hava yolu enstrümantasyonu gerekmemiştir. Minör komplikasyonlar arasında geçici desatürasyon (%[3],[3]) ve bulantı/kusma (%[19],[2]) yer almaktadır. Majör anesteziye bağlı advers olay gözlenmemiştir. Ortalama taş boyutu böbrek için [9] ± [2],[86] mm, üreter için [8] ± [2],[14] mm olup, ortalama seans sayısı [2],[4] olarak saptanmıştır.

SONUÇ
Pediatrik anestezide temel yaklaşım, en düşük etkili dozda ve kısa etkili ajanların titrasyonla uygulanmasıdır. Bulgularımız, ESWL işlemlerinin dengeli bir sedoanaljezi protokolü ile güvenli ve etkili bir şekilde gerçekleştirilebileceğini göstermektedir.

ANAHTAR KELİMELER
Ameliyathane dışı anestezi, ESWL, fentanil, girişimsel sedasyon, ketamin, midazolam, pediatric anestezi, propofol, sedoanaljezi

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

Though urolithiasis is less common in children than in adults, it has shown an increasing incidence in recent years, particularly among children under 15 years of age (1,2). Standard treatment approaches for pediatric urolithiasis have evolved with the development of minimally invasive and non-invasive techniques. Among these, extracorporeal shock wave lithotripsy (ESWL) has become the primary modality for treating upper urinary tract stones in children due to its efficacy and non-invasive natüre (3,4).

The success of ESWL is influenced by several factors, including stone size, location, composition, and number. Despite their relatively small ureters, the stone fragment passage rates in children are higher than in adults, likely due to the flexibility and elasticity of the pediatric ureter, as well as the body's higher fluid content and smaller volume, which improves shock wave conduction (3,5). Numerous studies have confirmed the safety and effectiveness of ESWL in children, including infants (5,6).

However, the success of ESWL also depends heavily on adequate pain control and patient immobility during the procedure. Although ESLW is non-invasive, it is associated with deep and sharp pain that requires appropriate anesthesia or sedation. Unlike adult patients, children often require sedation or general anesthesia to tolerate the procedure and remain immobile (7).

Various anesthetic approaches have been reported to date, ranging from general anesthesia to combinations of intravenous sedatives and analgesics. Each technique has its own advantages and risks. General anesthesia provides deep sedation and complete immobility but it can require a longer preparation and recovery time. When performed properly, , sedoanalgesia offers a more time- and resource-efficient option, especially in outpatient settings. The most commonly used agents for pediatric sedation in ESWL procedures are propofol, ketamine, midazolam, and fentanyl, either alone or in combination (8,9,10).

In this study, we aimed to evaluate the 10-year clinical experience of a standardized sedoanalgesia-based anesthesia protocol in pediatric ESWL procedures. We investigated the feasibility, safety, and effectiveness of this approach, documenting any adverse events or complications that occurred.

Materials and Methods

This retrospective study included pediatric patients under the age of 18 who underwent ESWL at the Dokuz Eylül University ESWL Unit between November 9th, 2009, and November 18th, 2019. Ethical approval was obtained from the Dokuz Eylül University Non-Invasive Research Ethics Committee (Date: 01.06.2020; Decision No: 2020/11-60). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient selection and data collection

A total of 190 pediatric patients were included. Demographic data, stone characteristics (size, location), number of ESWL sessions, anesthetic drugs used, and perioperative parameters were collected retrospectively from electronic medical records, ESWL unit charts, and non-operating room anesthesia documentation.

ESWL procedure

All ESWL procedures were performed using a PCK Stone Lith v3 Lithotriptor, under the supervision of two urologists experienced in the treatment of pediatric stone disease. Shock waves were initiated at low energy and gradually increased to a maximum of 18 kV. The number of shock waves applied per session generally exceeded 1500 pulses. The number of sessions per patient ranged from 1 to 4, scheduled at 7-day intervals. If stone fragments remained after three sessions, ESWL was considered unsuccessful and alternative treatment options were considered. However, a fourth ESWL session was performed for patients whose parents had declined surgical treatment.

Patient positioning was guided by stone localisation, with ESWL performed in the supine, lateral, or prone position as appropriate. Pre-procedural imaging included kidney-ureter-bladder (KUB) radiography and/or urinary ultrasonography.

Anesthesia and sedation protocol

All patients underwent a pre-anesthesia evaluation in the outpatient clinic. In accordance with the United Nations Convention on the Rights of the Child, informed consent was

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

obtained from the parents and age-appropriate assent from the children.

On the day of the procedure, patients were accompanied by their parents to the premedication area.

No oral sedative premedication was administered. An intravenous (IV) line was inserted in the presence of the parents to minimize anxiety. After being separated from their parents, sedation was initiated in the ESWL room.

The standardized sedoanalgesia protocol consisted of

IV midazolam (0.05 mg/kg)

IV fentanyl (1 µg/kg)

IV propofol 10% (0.5–1 mg/kg), administered just before the procedure

IV ketamine (0.5–1 mg/kg), used in selected cases when additional sedation was required

IV fluid: 4 mL/kg of 1/3 isotonic solution (Izomix)

Sedation depth was monitored and titrated to maintain a Modified Ramsay Sedation Score of 3–4/6. All patients received oxygen via face mask at 2 L/min during the procedure. The average duration of the ESWL procedure was approximately 15 minutes; however, the total procedural time including IV access, positioning, sedation, awakening, and recovery averaged around 45 minutes.

To prevent postoperative nausea and vomiting, 2–4 mg of IV dexamethasone was administered either before or immediately after the procedure, depending on clinical judgement. Despite prophylaxis, the incidence of nausea and vomiting was relatively high. Potential contributing factors such as opioid use, positioning, and procedure-related stimulation are discussed in the Results section.

Monitoring and discharge

All patients were monitored continuously using pulse oximetry and intermittent non-invasive blood pressure monitoring during and after the procedure. Following the procedure, patients were observed in the recovery area of the ESWL unit for at least 4 hours. They were discharged in the company of their parents once they were clinically stable.

Statistical analysis

Statistical analyses were performed using SPSS version 24.0. Descriptive data are presented as mean ± standard deviation (min–max). Associations between stone size or number of sessions and variables such as gender, age group, and stone location were assessed using the Student's t-test, with $p < 0.05$ considered statistically significant.

Results

Table 1. Demographic and procedural characteristics of pediatric patients undergoing ESWL

Characteristic	Value
Total patients (n)	190
Male (%)	95 (50%)
Female (%)	95 (50%)
Median age (years)	5
Age range (years)	1–17
Mean kidney stone size (mm)	9 ± 2.86
Mean ureter stone size (mm)	8 ± 2.14
Total ESWL sessions	453
Average sessions per patient	2.4
Single-session patients (n)	87
Multiple-session patients (n)	103

A total of 190 pediatric patients 95 males, 95 females who underwent 453 ESWL sessions were included in the analysis. The median age of the patients was 5 years (range: 1–17). The mean kidney stone size was 9 ± 2.86 mm, and the mean ureteral stone size was 8 ± 2.14 mm.

All patients received sedoanalgesia using a combination of intravenous midazolam (0[05 mg/kg), fentanyl (1 mcg/kg), propofol (0.5–1 mg/kg), and ketamine (0.5–1 mg/kg) when needed. The protocol ensured borh spontaneous ventilation and minimal airway intervention. All procedures were completed successfully.

The number of shock waves per session ranged from 1000 to 2000, with most sessions exceeding 1500 shocks. The average number of sessions per patient was 2.4. A single session was sufficient for 87 patients, while the remaining patients required multiple sessions.

In terms of safety, transient desaturation occurred in 15 patients (7.9%) and was managed with supplemental oxygen and airway repositioning. Nausea and vomiting occurred in 87 patients (45.8%) despite the prophylactic administration of dexamethasone (Figure 1).

Ecchymosis at the shock site was observed in 35 patients (18.4%). There were no major complications or need for endotracheal intubation. The method's feasibility was demonstrated by the absence of unplanned hospital admissions and the rapid discharge of all cases. The sedation

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

protocol was well-tolerated, with no patients requiring conversion to general anesthesia.

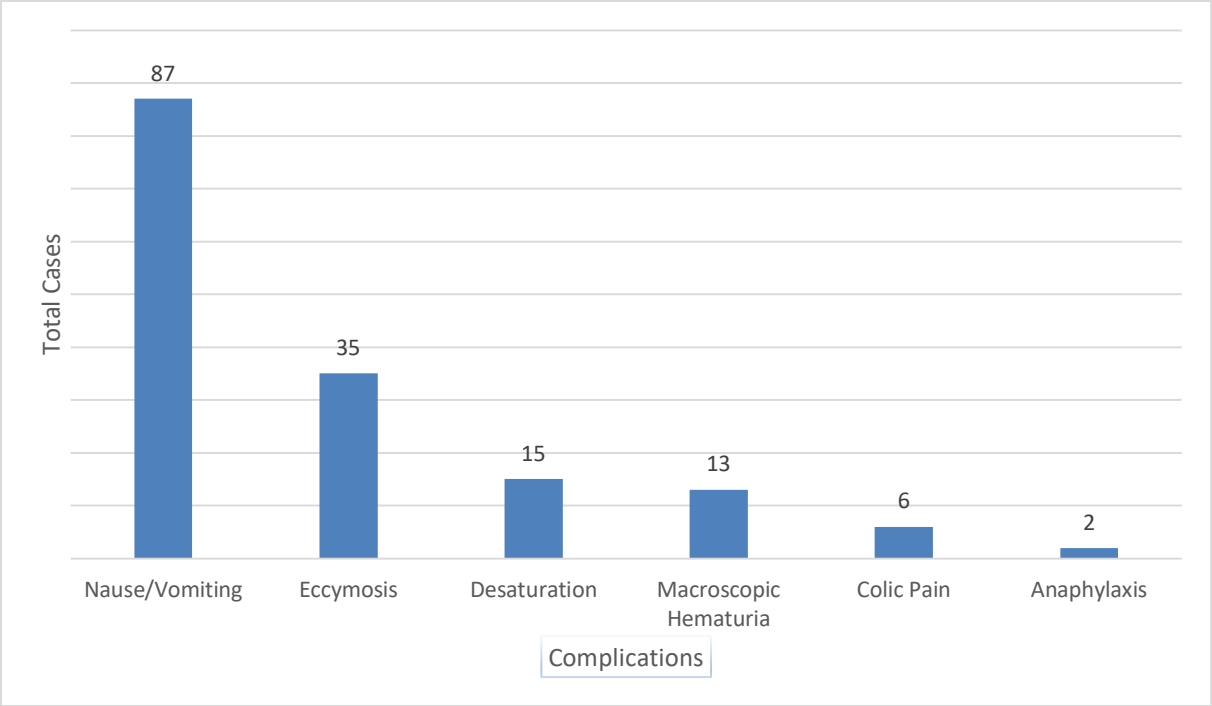


Figure 1. Complications in ESWL cases during Sedoanalgesia.

Discussion

This retrospective study presents a 10-year experience using a sedoanalgesia-based anesthesia protocol during ESWL procedures in pediatric patients. The protocol, which comprises midazolam, fentanyl, propofol, and ketamine, enabled procedures to be completed without conversion to general anesthesia and demonstrated an acceptable safety profile (1).

ESWL is widely employed as a first-line treatment for urinary tract stones in pediatric patients. However, there is no consensus on the optimal anesthesia method, especially in outpatient settings (2). Effective analgesia and immobilization are essential for the successful completion of procedures on children. While general anesthesia can achieve these outcomes, it may be more costly and time-consuming. When administered by experienced teams under appropriate monitoring and standardized protocols, sedoanalgesia offers a practical alternative (3).

In our study, transient desaturation occurred in 15 patients (7.8%), all of whom responded to standard airway maneuvers and supplemental oxygen. No advanced airway intervention was required. This finding highlights the importance of continuous monitoring and preparedness for airway management during the procedure (3,5).

Postoperative nausea and vomiting (PONV) was observed in 35 patients (18.4 %) despite the prophylactic use of dexamethasone. This rate suggests that the current antiemetic prophylaxis may be insufficient, given the emetogenic potential of opioid and ketamine combinations (5). Future applications of multimodal antiemetic strategies may therefore be beneficial. Reducing PONV would enhance discharge efficiency and improve the quality of outpatient care (6).

Local ecchymosis was noted in 35 patients (18.4%) and resolved spontaneously. No major complications, such as perirenal hematoma, severe allergic reactions, or long-term neurological events, were encountered (7). Additional interventions, such asureteral stent placement in 14 patients and hospitalization for renal colic in 6 patients, were attributed

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

to underlying urological conditions rather than the anesthesia technique. A notable strength of our protocol is its flexibility. Midazolam provided anxiolysis and amnesia, fentanyl ensured potent analgesia, propofol enabled a rapid onset and easy titration, and ketamine was reserved for cases requiring deeper dissociative anesthesia (8). This combination enabledreduced the dosages of individual agents, thereby lowering the risk of adverse effects. However, ketamine may cause hallucinations or agitation, particularly if not co-administered with benzodiazepines (9).

Compared to general anaesthesia, sedoanalgesia during pediatric ESWL offers advantages such as faster recovery, reduced cost, and compatibility with outpatient or rural healthcare settings (11). However, this approach requires skilled personnel, continuous monitoring, and preparedness for airway intervention. In centers without dedicated anesthesiologists, adherence to established sedation guidelines published by major anesthesia societies is essential (12).

Recent literature suggests the usefulness of novel sedation protocols and risk stratification models for pediatric ambulatory urological procedures (18,19).

When administered under proper monitoring by experienced personnel, sedoanalgesia is a viable alternative to general anesthesia for pediatric ESWL procedures, as supported by recent literature advocating for individualized sedation strategies (13,14). It is safe, practical, and well-suited to outpatient conditions. Recent publications support the development of new sedation protocols and the implementation of risk stratification models in ambulatory urological interventions (15,16,17).

Limitations

This study has several limitations, primarily due to its retrospective design. Important radiological parameters, such as stone density on computed tomography scans, skin-to-stone distance, and infundibulopelvic angle measurements, were unavailable and could therefore not be included in the analysis.

Additionally, the timing of drug administration, premedication duration (including separation time from parents), and the overall procedure duration were not consistently recorded, partly due to technical delays during patient positioning. These factors were influenced by external variables, such as the intellectual and emotional characteristics of the family, as well as the patient's age and gender. Consequently, procedure time was excluded from the analysis.

Moreover, patients were referred from various geographic regions of Turkeyoften only for the ESWL sessions. For this reason, we were unable to conduct follow-ups with all patients after the procedure, meaning that the stone-free rate (SFR) could not be calculated.

Most notably, no objective measurements were taken to evaluate the effectiveness of the analgesia. Parameters such as intra-procedural pain scales, the need for patient repositioning due to movement, sedation-related costs, and total procedural time were not evaluated. These omissions are the main methodological limitations when assessing the effectiveness and feasibility of the sedoanalgesia protocol.

Conclusion

Pediatric anesthesia procedures, particularly those performed outside the operating theatre, such as ESWL,, require careful planning to achieve a balance between efficacy and safety. Our experience demonstrates that for selected paediatric ESWL cases, sedoanalgesia can be a feasible and safe alternative to general anesthesia. This approach, using short-acting agents at minimal effective doses, allowed the completion of procedures without the need for conversion to general or neuraxial anesthesia, thereby reducing anesthesia-related risks and recovery time.

Despite its retrospective limitations, this study suggests that anesthesia practices for pediatric outpatient procedures—particularly remote anesthesia procedures—should continue to evolve towards less invasive yet effective methods. Further prospective studies with standardized analgesia assessment metrics are necessary to validate these findings and optimize sedoanalgesia protocols for broader clinical use.

Disclosure

The authors of this work have nothing to disclose.

Funding

The authors received no financial support for the research or authorship of this article.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:27-33

References

1. Cevik B, Tuncer M, Erkal KH, Eryildirim B, Sarica K. Procedural sedation and analgesia for pediatric shock wave lithotripsy: a 10 year experience of single institution. *Urolithiasis*. 2018;46(4):363-367. DOI:10.1007/s00240-017-0992-z
2. Akelma H, Kiliç ET, Salik F, Kaydu A. Comparison of Ketamine with Midazolam versus Ketamine with Fentanyl for Pediatric Extracorporeal Shock Wave Lithotripsy Procedure: A Randomized Controlled Study. *Anesth Essays Res*. 2018;12(2):464-469.
3. Simonini A, Brogi E, Cascella M, Vittori A. Advantages of ketamine in pediatric anesthesia. *Open Med (Wars)*. 2022;17(1):1134-1147. Published 2022 Jul 6. DOI:10.1515/med-2022-0509
4. Chang Y, Xie X, Liu Y, Liu M, Zhang H. Exploring clinical applications and long-term effectiveness of benzodiazepines: An integrated perspective on mechanisms, imaging, and personalized medicine. *Biomed Pharmacother*. 2024;173:116329. DOI:10.1016/j.biopha.2024.116329
5. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. *Anesthesiology*. 2002;96(4):1004-1017. DOI:10.1097/00000542-200204000-00031
6. Brookes CD, Berry J, Rich J, Golden BA, Turvey TA, Blakey G 3rd, et al. Multimodal protocol reduces postoperative nausea and vomiting in patients undergoing Le Fort I osteotomy. *J Oral Maxillofac Surg*. 2015;73(2):324-33DOI:10.1016/j.joms.2014.08.007
7. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med. 2004;350(24):2441-2451. DOI:10.1056/NEJMoa032196
8. D'Addessi A, Vittori M, Racioppi M, Pinto F, Sacco E, Bassi P. Complications of extracorporeal shock wave lithotripsy for urinary stones: to know and to manage them-a review. *ScientificWorldJournal*. 2012;2012:619820. DOI:10.1100/2012/619820
9. Strayer RJ, Nelson LS. Adverse events associated with ketamine for procedural sedation in adults. *Am J Emerg Med*. 2008;26(9):985-1028. DOI:10.1016/j.ajem.2007.12.005
10. Green SM, Roback MG, Kennedy RM, Krauss B. Clinical practice guideline for emergency department ketamine dissociative sedation: 2011 update. *Ann Emerg Med*. 2011;57(5):449-461. DOI:10.1016/j.annemergmed.2010.11.030
11. Mason KP. Sedation trends in the 21st century: the transition to dexmedetomidine for radiological imaging studies. *Paediatr Anaesth*. 2010;20(3):265-272. DOI:10.1111/j.1460-9592.2009.03224.x
12. Krauss B, Green SM. Sedation and analgesia for procedures in children. *N Engl J Med*. 2000;342(13):938-945. DOI:10.1056/NEJM200003303421306
13. Zaccagnini ME, Baughman G, Lee AR. Innovations in pediatric urologic sedation: a [2022] update. J Pediatr Urol. 2022;18([1):45-52.
14. Ahmed S, Tran K. Sedation risk stratification in ambulatory pediatric procedures: a practical review. Curr Opin Anaesthesiol. 2023;36(2):115–122.
15. Türkçapar N, Sarica K, Resorlu B Pediatric stone disease: an overview and current treatment strategies. Urolithiasis. 2019;47(2):109-118.
16. Ugur B, Oguzturk H, Gezer E Sedation and analgesia for pediatric extracorporeal shock wave lithotripsy: comparison of propofol, ketamine, and midazolam combinations. J Pediatr Urol. 2020;16(3):310.e1–310.e7.
17. Rewari V, Trivedi S, Kumar R. Pediatric anesthesia for urological procedures: Advances and updates. Indian J Urol. 2021;37(4):314–321.
18. Havidich JE. Sedation/anesthesia in pediatric patients for procedures outside the operating room. Curr Opin Anaesthesiol. 2020;33(4):465–471.
19. Liu Z, Chen L, Wang R. Emerging advancements in pediatric sedation protocols: toward precision anesthesia. Pediatr Anesth. 2025;35(3):145–152.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Investigation of the relationship between prolonged PCR positivity and mortality rate in COVID-19 patients with hematological malignancy admitted to the intensive care unit

Yoğun bakım ünitesine yatırılan hematolojik maligniteli COVID-19 hastalarında uzun süreli PCR pozitifliği ile mortalite oranı arasındaki ilişkinin araştırılması

Özlem ÖNER[1]
Hakan AKTUNA[2]
Hüseyin DÖNGELLİ [1]
Merve BALCIOĞLU[3]
Ejder Kamil ÖZTÜRK[4]
Mehmet Çağatay GÜRKOK[5]
Mehmet Nuri YAKAR[6]
Begüm ERGAN[7]
Volkan HANCI[8]
Erdem YAKA[9]
Ali Necati GÖKMEN[8]

[1] İzmir Democracy University Buca Seyfi Demirsoy Education and Research Hospital, Department of Anesthesiology and Reanimation, Subdivision of Critical Care Medicine, İzmir, Türkiye
[2] Menderes State Hospital, Department of Internal Medicine, İzmir, Türkiye
[3] Dokuz Eylul University Faculty of Medicine, Department of Internal Medicine, İzmir, Türkiye
[4] Kırklareli Education and Research Hospital, Department of Internal Medicine, Subdivision of Critical Care Medicine, Türkiye
[5] Şanlıurfa Education and Research Hospital, Department of General Surgery, Subdivision of Critical Care, Türkiye
[6] Şişli Hamidiye Etfal Education and Research Hospital, Subdivision of Critical Care Medicine, İstanbul, Türkiye
[7] Dokuz Eylül University Faculty of Medicine, Department of Pulmonary, Subdivision of Critical Care Medicine, İzmir, Türkiye
[8] Dokuz Eylül University Faculty of Medicine, Department of Anesthesiology and Reanimation, Subdivision of Critical Care Medicine, İzmir, Türkiye
[9] Dokuz Eylül University Faculty of Medicine, Department of Neurology, Subdivision of Critical Care Medicine, İzmir, Türkiye

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Investigation of prolonged PCR positivity and mortality in patients with hematological malignancies

Received: 06.01.2025
Accepted: 19.10.2025
DOI:10.18614/dehm.1873586

Corresponding author
Özlem ÖNER
ORCID ID: 0000-0001-6171-2114
namdaroner@gmail.com

ABSTRACT

BACKGROUND

In patients with hematological malignancies followed in the intensive care unit, the relationship between the number of days of prolonged polymerase chain reaction (PCR) positivity and mortality has not been clarified.

METHODS

All patients with hematological malignancies followed in the intensive care unit and who had a positive PCR test were included in the study. Patients were divided into two groups according to whether they survived or not. The relationship between the number of days of PCR positivity and mortality rate was investigated in these patients.

RESULTS

Among 31 COVID-19 patients with hematological malignancies admitted to the intensive care unit, 7 (22.6%) survived and 24 (77.4%) patients succumbed to the disease. The median duration of PCR positivity was 14 days (6-24) for the entire patient cohort, 11 (4-21) days for survivors, and 24 (21-52) days for non-survivors. Significantly longer PCR positivity times were observed in patients who died compared to survivors (p = 0.019). Acute respiratory distress syndrome (ARDS) was diagnosed in 22 (71%) patients and there was a statistically significant 22 (91.7%) mortality rate in hematologic malignancy patients with ARDS (p = 0.001). Furthermore, the mortality rate in patients receiving invasive mechanical ventilation was 23 (95.8%) (p = 0.001).

CONCLUSION

A relationship between long-term PCR positivity and mortality rates has been demonstrated in patients with hematologic malignancies. This patient group is at unique risk for long-term viral persistence and progressive and fatal respiratory symptoms. We believe that evidence-based strategies that promote viral clearance should be developed to prevent or manage persistent infection.

KEYWORDS

Hematological malignancy, intensive care unit, mortality, prolonged PCR positivity

ÖZ

AMAÇ

Yoğun bakım ünitesinde (YBÜ) takip edilen hematolojik maligniteli hastalarda uzamış PCR pozitifliğinin gün sayısı ile mortalite arasındaki ilişki açıklığa kavuşturulmamıştır.

GEREÇ YÖNTEM

YBÜ'de takip edilen ve PCR testi pozitif olan hematolojik maligniteli tüm hastalar çalışmaya dahil edildi. Hastalar sağ kalıp kalmamalarına göre iki gruba ayrıldı. Bu hastalarda PCR pozitifliğinin gün sayısı ile mortalite oranı arasındaki ilişki araştırıldı.

BULGULAR

YBÜ'ne yatırılan hematolojik maligniteli 31 COVID-19 hastası arasında 7 (%22,6) hasta sağ kalırken 24 (%77,4) hasta hastalığa yenik düştü. Tüm hasta kohortu için PCR pozitifliğinin ortanca süresi 14 gün (6-24), sağ kalanlar için 11 (4-21) gün ve sağ kalamayanlar için 24 (21-52) gündü. Ölen hastalarda sağ kalanlara kıyasla anlamlı derecede daha uzun PCR pozitiflik süreleri gözlendi (p = 0,019). Akut solunum sıkıntısı sendromu 22 (%71) hastada teşhis edildi ve ARDS'li hematolojik malignite hastalarında istatistiksel olarak anlamlı 22 (%91,7) ölüm oranı vardı (p = 0,001). Ayrıca, invaziv mekanik ventilasyon uygulanan hastalarda mortalite oranı 23 (%95,8) idi (p = 0,001).

SONUÇ

Hematolojik maligniteli hastalarda uzun vadeli PCR pozitifliği ve mortalite oranları arasında bir ilişki gösterilmiştir. Bu hasta grubu, uzun vadeli viral persistans ve ilerleyici ve ölümcül solunum semptomları açısından benzersiz bir risk altındadır. Kalıcı enfeksiyonu önlemek veya yönetmek için viral temizliği destekleyen kanıta dayalı stratejilerin geliştirilmesi gerektiğine inanıyoruz.

ANAHTAR KELİMELER

Hematolojik malignite, mortalite, uzun süreli PCR pozitifliği, yoğun bakım ünitesi.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Since December 2019, the coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has evolved into a global pandemic, posing a significant threat to public health worldwide (1). Diagnosis of the disease relies on a real-time reverse transcription polymerase chain reaction (RT-PCR) assay to detect SARS-CoV-2 RNA in respiratory specimens, predominantly obtained from nasopharyngeal swabs (2). Severe and fatal outcomes of the disease are particularly prevalent in populations with various comorbidities and hematological malignancies (3). Patients with hematological malignancies represent a distinct group characterized by substantially high rates of hospitalization (77%) and admission to intensive care units (ICUs) (81%) (4). Despite efforts to manage this specific patient group in the same way as those without hematological malignancies, there remains a lack of studies comparing the disease progression in these populations (4).

A literature review reveals that prolonged PCR positivity may occur in COVID-19 patients, with viral RNA shedding persisting or fluctuating over time (5). However, the correlation between prolonged PCR positivity and symptom severity, infectiousness, or the strength of the patient's antibody response remains unclear (4). Notably, in immunosuppressed individuals with hematologic malignancies, prolonged PCR positivity may indicate chronic viral syndromes, accompanied by radiographic findings and respiratory and systemic symptoms, suggestive of intrahost viral evolution (6).

In addition to direct viral toxicity, prolonged PCR positivity presents challenges in managing hematological malignancies, potentially resulting in delays to cancer-related treatments and poorer outcomes (7). Moreover, persistent COVID-19 infections and prolonged PCR positivity may pose a significant public health threat due to the emergence of concerning mutations emerging from intrahost viral evolution (8). Patients with hematological malignancies, who are likely to harbour higher viral loads, may contribute to increased nosocomial transmission, particularly in hematology and oncology services, where the likelihood of nosocomial clusters is heightened (9). Patients with lymphoid malignancies may serve as a reservoir host, especially for the formation of viral mutants that escape suppressed immune systems (10). Given these considerations, PCR testing, which is widely used in disease diagnosis and management, is critical for planning infection control strategies (9).

In this study; we hypothesized that prolonged PCR positivity may be associated with increased morbidity and mortality rates among patients with hematological malignancies who are followed-up in intensive care unit (ICU) with a diagnosis of SARS-CoV-2 infection. Against this backdrop, the study aimed to investigate this association.

Materials and Methods

This study was designed as a retrospective observational investigation. Following approval by the Ethics Committee on 30.11.2022 (approval no: 2022/38-13), data were collected from the designated ICU for the management and monitoring of COVID-19 patients. The inclusion criteria were admission to the ICU, a diagnosis of hematological malignancy according to the World Health Organization (WHO) classification, confirmation of COVID-19 infection via polymerase chain reaction (PCR) testing of nasopharyngeal swabs, an age of 18 years or over, and a minimum ICU stay of 24 hours. Exclusion criteria included being under 18 years of age, an ICU stay of less than 24 hours, inadequate medical information or history, and pregnancy or lactation. Written consent was not obtained from patients due to the nature of the study. Data on the number of days between patients' initial positive and first negative PCR tests were recorded from the hospital's medical database. Throughout the pandemic, patients were consistently managed by the same medical team and transferred to the same ICU as required. Demographic information, medical histories, laboratory parameters, ventilation statuses, and other relevant clinical data were extracted from the hospital database. The following parameters were also recorded: Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores, Sequential Organ Failure Assessment (SOFA) scores, Charlson Comorbidity Index (CCI) scores upon ICU admission, admitting service, COVID-19 vaccination status (including type of vaccine), type of malignancy, duration of ICU stay, and morbidity and mortality rates. Patient identities and personal information were anonymized to ensure confidentiality.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Statistical analysis

Statistical analysis involved presenting continuous variables as mean ± standard deviation (SD) or median (interquartile range [IQR]) and categorical variables as numbers and percentages (%). Normality of continuous variables was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. Student's t-test or Mann-Whitney U test was employed for continuous variables based on normality test results, while categorical variables were analyzed using the chi-square test or Fisher's exact test. Statistical significance was set at $p < 0.05$.

Results

Of the 31 COVID-19 patients with hematological malignancies admitted to the ICU, 7 (22.6%) survived while 24 (77.4%) died from the disease. Of these patients, 16 (51.6%) were female, with a median age of 63 years (range 57-70 years) (Table 1).

The median duration of PCR positivity was 14 days (range 6-24) for the entire patient cohort, 11 days (range 4-21) for survivors, and 24 days (range 21-52) for non-survivors. Significantly longer PCR positivity durations were observed in patients who died compared to survivors ($p = 0.019$; Mann-Whitney U test) (Table 1).

Table 1. Characteristic features of COVID-19 patients with hematological malignancies followed in the intensive care unit

Characteristics:	**All Patients (n =31)**	**Survivors (n = 7)**	**Non-survivors (n = 24)**	**p**
Age	63 (57-70)	59 (56-66)	65 (57-73)	0.253
Sex:				0.539
-Female	16 (51.6 %)	4 (57.1%)	12 (50%)	
-Male	15 (48.4 %)	3 (42.9%)	12 (48.4%)	
Number of PCR positive days	14 (6-24)	11 (4-21)	24 (21-52)	**0.019**
COVID serology positivity				
IgG	19 (61.3)	7 (100)	12 (50.0)	**0.026**
IgM	18 (58.1)	0 (0)	18 (75.0)	**0.001**
Omicron Variant	8 (25.8)	0 (0)	8 (33.3)	0.146
APACHE II Score	28 (25-30)	28 (25-30)	27 (26-30)	0.729
SOFA Score	8 (7-10)	8 (7-10)	8 (8-10)	0.835
CCI	6 (5-7)	6 (5-7)	6 (6-7)	0.764
Hematologic malignancy:				
- AML	5 (16.1%)	1 (14.3%)	4 (16.7%)	0.831
- ALL	2 (6.5%)	0 (0%)	2 (6.5%)	
- KLL	10 (32.3%)	2 (28.6%)	8 (33.3%)	
- Hodgkin lymphoma	1 (3.2%)	0 (0%)	1 (4.2%)	

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

- MM	10 (32.3%)	4 (57.1%)	6 (25.0%)	
- MDS-RAEB 2	1 (3.2%)	0 (0%)	1 (4.2%)	
- Non Hodgkin lymphoma	1 (3.2%)	0 (0%)	1 (4.2%)	
- New presentation hematological malignancy, subtype determination could not be made due to current clinic.	1 (3.2%)	0 (0%)	1 (4.2%)	
Chemotherapy number:				0.702
0	6 (19.4%)	1 (14.3%)	5 (20.8%)	
1	9 (29%)	1 (14.3%)	8 (33.3%)	
2	8 (25.8%)	3 (42.9%)	5 (20.8%)	
3	5 (16.1%)	1 (14.3 %)	4 (16.7%)	
4	1 (3.2%)	0 (0%)	1 (4.2%)	
5	2 (6.5%)	1 (14.3%)	1 (4.2%)	
Time elapsed between last chemotherapy session to admission *(months) median (IQR)*	2 (2)	1 (1)	2 (2)	**0.005**
Bone marrow transplantation:				0.625
-No	21 (67.7%)	4 (57.1%)	17 (70.8%)	
-Allogeneic bone marrow transplantation	1 (3.2%)	0 (0%)	1 (4.2%)	
-OHSCT	8 (25.8%)	3 (42.9%)	5 (20.8%)	
-AbMT and OHSCT	1 (3.2%)	0 (0%)	1 (4.2%)	
Bone marrow transplantation:				0.401
-No:	21 (67.7%)	4 (57.1%)	17 (70.8%)	
-Yes:	10 (32.3%)	3 (42.9%)	7 (29.2%)	
Pre-ICU service:				0.662
-Hematology service	27 (87.1%)	6 (85.7%)	21 (87.5%)	
-Emergency service	4 (12.9%)	1 (14.3%)	3 (12.5%)	

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Status of malignancy:				0.098
-New diagnosis:	4 (12.9%)	2 (28.6%)	2 (8.3%)	
-Refractory malignancy:	23 (74.2%)	3 (42.9%)	20 (83.3%)	
- Remission:	4 (12.9%)	2 (28.6%)	2 (12.9%)	
Malignancy-related clinical condition:				0.451
-Hyperviscosity syndrome	2 (6.5%)	1 (14.3%)	1 (4.2%)	
-graft-versus host reaction:	2 (6.5%)	1 (14.3%)	1 (4.2%)	
- Tumor lysis syndrome:	3 (9.7%)	0 (0%)	3 (12.5%)	
- No:	24 (77.4%)	5 (71.4%)	19 (79.2%)	
Precense of confusion:				0.415
- central nervous system invasion	3 (14.3%)	1 (33.3%)	2 (11.1%)	
-Seizure:	2 (9.5%)	1 (5.6%)	1 (33.3%)	
-Intracranial hemorrhage:	2 (9.5%)	0 (0%)	2 (11.1%)	
-post cardiopulmonary arrest:	1 (4.8%)	0 (0%)	1 (5.6%)	
No:	13 (61.9%)	1(33.3%)	12 (66.7%)	
Number of vaccinations:				0.378
0:	14 (46.7%)	2 (28.6%)	12 (52.2%)	
1:	1 (3.3%)	0 (0%)	1 (4.3%)	
2:	6 (20%)	1 (14.3%)	5 (21.7%)	
3:	3 (10%)	2 (28.6%)	1 (33.3%)	
4:	5 (16.7%)	2 (28.6%)	3 (13%)	
5:	1 (3.3%)	0 (0%)	1 (4.3%)	
Number of with Biontech vaccinations:	24 (77.4%)	5 (71.4%)	19 (79.2%)	0.751
0:	2 (6.5%)	1 (14.3%)	1 (4.2%)	
1:	4 (12.9%)	1 (14.3%)	3 (12.5%)	
2:	1 (3.2%)	0 (0%)	1 (3.2%)	
3:				
Number of with Synovac vaccinations:				
0:	15 (48.4%)	2 (28.6%)	13 (54.2%)	0.253
1:	1 (3.2%)	0 (0%)	1 (4.2%)	
2:	12 (38.7%)	3 (42.9%)	9 (37.5%)	
3:	1 (3.2%)	1 (14.3%)	0 (0%)	
4:	2 (6.5%)	1 (14.3%)	1 (4.2%)	
ICU length of stay (days)	8 (2-17)	4.5 (1.25-12.50)	15 (8-25)	0.094

All values are expressed as numbers (percentages) or median (interquartile range).
APACHE, Acute physiology and chronic health evaluation; CCI, Charlson comorbidity index; SOFA, Sequential organ failure assessment score; AML, Acute myeloid leukemia; ALL, Acute lymphoblastic leukemia; MM, Multiple myeloma; MDS rEAB 2, Myelodysplastic syndrome rEAB 2

Among the cohort, 5 patients with AML (16.1%) predominantly received 7+3 or FLAG-based induction, 2 patients with ALL (6.5%) were treated with Hyper-CVAD or CALGB protocols, 10 patients with CLL (32.3%) received FCR or BR therapy, 1 patient with Hodgkin lymphoma (3.2%) was treated with ABVD, 10 patients with multiple myeloma (32.3%) received VCD or VRD regimens, 1 patient with MDS-RAEB-2 (3.2%) was treated with hypomethylating agents, and 1 patient

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

with non-Hodgkin lymphoma (3.2%) received R-CHOP or BR therapy. The median (IQR) time from the last chemotherapy session to hospitalization (months) was 1 (1) in the survivor group and 2 (2) in the non-survivor group, which was found to be statistically significant (p = 0.005) (Table 1).

When all patients were evaluated, it was determined that the mean time since the last chemotherapy session was 2 months for non-survivors and 1 month for survivors, which was statistically significant (p = 0.005).

In the entire patient group, IgG positivity was detected in 19 patients (61.3%), while IgM positivity ws observed in 18 patients (58.1%). In the group of patients who did not survive, IgG positivity was observed in 12 patients (50%), while IgM positivity was detected in 18 patients (75%).This difference was statistically significant (p = 0.026 and p = 0.001, respectively) (Table 1).

Regarding hematologic malignancy types, there were 5 (16.1%) cases of acute myeloid leukemia, 2 (6.5%) cases of acute lymphoid leukemia, 1 (3.2%) case of Hodgkin lymphoma, 10 (32.3%) cases of chronic lymphoid leukemia, 10 (32.3%) cases of multiple myeloma, 1 (3.2%) case of non-Hodgkin lymphoma, and 1 (3.2%) case of an unspecified newly diagnosed hematologic malignancy (p = 0.831). Among ICU-admitted patients, 2 (6.5%) developed hyperviscosity syndrome, 2 (6.5%) developed graft-versus-host disease, and 3 (9.7%) developed tumor lysis syndrome. The median ICU stay duration for all COVID-19 patients with hematological malignancies was 8 days (range 2-17), 4.5 days (range 1.25-12.5) for survivors, and 15 days (range 8-25) for deceased patients. There was no significant difference between the two groups (p = 0.094; Mann-Whitney U test) (Table 1). However, no significant association was found between these malignancy-related clinical conditions and mortality rates (p = 0.451; chi-square test) (Table 2).

Table 2. Comorbidities, symptoms, and treatment modalities of COVID-19 patients with hematological malignancy admitted to the ICU

Comorbidities:	**All patients (n=31)**	**Survivors (n=7)**	**Non-survivors (n=24)**	**p**
Diabetes mellitus:				0.132
No:	19 (61.3%)	6(85.7%)	13(54.2%)	
Yes:	12 (38.7%)	1(14.3%)	11(45.8%)	
Hypertension				0.435
No:	19 (61.3%)	5 (71.4%)	14 (58.3%)	
Yes:	12 (38.7%)	2 (28.6%)	10 (41.7%)	
Coronary artery disease:				0.594
No:	29 (93.5%)	7 (100%)	22 (91.7%)	
Yes:	2 (6.5%)	0 (0%)	2 (8.3%)	
Congestive heart failure:				0.406
No:	29 (93.5%)	6 (85.7%)	23 (95.8%)	
Yes:	2 (6.5%)	1 (14.3%)	1 (4.2%)	
COPD:				0.594
No:	29 (93.5%)	7 (100%)	22 (91.7%)	
Yes:	2(6.5%)	0(0%)	2(8.3%)	
Chronic liver disease:				**0**.774
No:	30 (96.8%)	7 (100%)	23 (95.8%)	
Yes:	1 (3.2%)	0(0%)	1(4.2%)	
Chronic renal failure:				0.639
No:	28 (90.3%)	6 (%85.7)	22 (91.7%)	

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Yes:	3 (9.7%)	1 (14.3%)	2 (8.3%)	
ARDS:				**0.001**
No:	9 (29%)	7 (100%)	2 (8.3%)	
Yes:	22 (71%)	0 (0%)	22 (91.7%)	
	Respiratory support:			
Nasal cannula and oxygen mask				0.247
No:	4 (12.9%)	0 (0%)	4 (16.7%)	
Yes:	27 (87.1%)	7 (100%)	20 (83.3%)	
High flow nasal cannula:				0.017
No:	12 (38.7%)	0 (0%)	12 (50%)	
Yes:	19 (61.3%)	7 (100%)	12 (50%)	
Noninvazive mechanical ventilation:				0.798
No:	19 (61.3%)	4 (57.1%)	15 (62.5%)	
Yes:	12 (38.7%)	3 (42.9%)	9 (37.5%)	
Invazive mechanical ventilation:				**0.001**
No:	8 (25.8%)	7 (100%)	1 (4.2%)	
Yes:	23 (74.2%)	0 (0%)	23 (95.8%)	
	Symptoms:			
Myalgia:				0.104
No:	7 (22.6%)	0 (0%)	7 (29.2%)	
Yes:	24 (77.4%)	7 (100%)	17 (70.8%)	
Fever:				0.813
No:	10 (32.3%)	2 (28.6%)	8 (33.3%)	
Yes:	21 (67.7%)	5 (71.4 %)	16 (66.7%)	
Weakness:				
No:	(13.2%)	0 (0%)	1 (4.2%)	0.583
Yes:	30(96.8%)	7 (100%)	23 (95.8%)	
Chest pain:				0.849
No:	23 (74.2%)	5 (71.4%)	18 (75%)	
Yes:	8(25.8%)	2 (28.6%)	6 (25%)	
Dyspnea:				0.594
No:	2(6.5%)	0 (0%)	2 (8.3%)	
Yes:	29(93.5%)	100 (7%)	22 (91.7%)	
Cough :				0.183
No:	11(35.5%)	1 (14.3%)	10 (41.7%)	
Yes:	20(64.5%)	6 (85.7%)	14 (58.3%)	
Palpitaiton:				0.329
No:	22(71%)	6 (85.7%)	16 (66.7%)	
Yes:	9(29%)	1 (14.3%)	8 (33.3%)	
	Treatment Modalities:			
LMWH:				0.187
No:	5 (16.1%)	0 (0%)	5 (20.8%)	
Yes:	26 (83.9%)	7 (100%)	19 (79.2%)	

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

ASA:				0.062
No:	14 (45.2%)	1 (14.3%)	13 (54.2%)	
Yes:	17 (54.8%)	6 (85.7%)	11 (45.8%)	
Dpyridamol:				0.880
No:	26 (83.9%)	6 (85.7%)	20 (83.3%)	
Yes.	5 (16.1%)	1 (14.3%)	4 (16.7%)	
Aditionally anticoagulant therapy:				0.060
No:	30 (96.8%)	6 (85.7%)	24 (100%)	
Yes:	1 (3.2%)	1 (14.3%)	0 (0%)	
Pulse steroid therapy:				0.429
No:	8 (25.8%)	1(14.3%)	7 (29.2%)	
Yes:	23 (74.2%)	6 (85.7%)	17 (70.8%)	
Methyl prednisolone :				0.054
No:	9 (29%)	0 (0%)	9 (37.5%)	
Yes:	22 (71%)	7 (100%)	15 (62.5%)	
Dexametazone :				0.329
No :	22 (71%)	6 (85.7%)	16 (66.6%)	
Yes:	9 (29%)	1 (14.3%)	8 (33.3%)	
Hydroxychloroquine:				
No:	28 (90.3%)	7 (100%)	21 (87.5%)	0.450
Yes:	3 (9.7%)	0 (0%)	3 (12.5%)	
Favipiravir :				0.889
No:	17 (54.8%)	4 (57.1%)	13 (54.2%)	
Yes:	14 (45.2%)	3 (42.9%)	11 (45.8%)	
Osetalmivir – Enfluvir :				0.774
No :	30(96.8%)	7(100%)	30 (96.8%)	
Yes:	1(3.2%)	0(0%)	1 (3.2%)	
Molnupiravir :				0.160
No:	27 (87.1%)	5 (71.4%)	22 (91.7%)	
Yes:	4 (12.9%)	2 (26.6%)	2 (8.3%)	
Tocizilizumab :				0.774
No:	30 (96.8%)	7 (100%)	23 (95.8%)	
Yes:	1 (3.2%)	0 (0%)	1 (4.2%)	

All values are expressed as numbers (percentages) or median (interquartile range)

ARDS, Acute respiratory distress syndrome; COPD, Chronic obstructive pulmonary disease; LMWH, Low molecular weight heparine; ASA, Acetyl salicylic acid

Regarding treatment modalities, pulse steroids were administered to 23 (74.2%) patients, methylprednisolone to 22 (71%) patients, and dexamethasone to 9 (29%) patients. No significant difference in mortality rates was observed among the three drugs (p = 0.429, p = 0.554, and p = 0.329, respectively; Fisher's Exact Test). The number of vaccinated patients was 3 (range 0-4) among survivors and 0 (range 0-2) among deceased patients (p = 0.226; Mann-Whitney U test). Additionally, there was no significant difference in mortality rates based on the type of vaccine administered (BioNTech SE and Sinovac) (p = 0.835 and p = 0.153, respectively; chi-square test) (Table 1, Table 2).

ARDS was diagnosed in 22 (71%) patients, with a statistically significant mortality rate of 22 (91.7%) among hematological malignancy patients with ARDS (p = 0.001; Fisher's Exact Test) (Table 2). Furthermore, the mortality rate

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

was 23 (95.8%) among patients receiving invasive mechanical ventilation (p = 0.001; Fisher's Exact Test) (Table 2). No statistically significant difference was detected between the two groups in terms of laboratory data (Table 3). Additionally, all patients and the two groups of culture results were added to Table 4.

Table 3. Laboratory findings of patients.

	All Patients (n =31)	Survivors (n = 7)	Non survivors (n = 24)	p
White blood cell count, 10^3 /mL	6500 (3900-22300)	7150 (3350 -25450)	4400 (3900-22200)	0.627
Neutrophill 10^3 /mL	3800 (2500-11100)	4400 (1450-10875)	4400 (3900-222000)	0.444
Lymphocyte 10^3 /mL	600 (200-4600)	1250 (225-4675)	3800 (3300-2140)	0.317
AST, IU/L	82.85±102.29	86.05±114.44	78.56±84.48	0.932
ALT, IU/L	54.35±70.15	58.13±85.91	49.29±40.95	0.747
Blood urea nitrogen, mg/dL	42.19±30.91	41.4±30.16	43.24±32.23	0.994
Creatinine, mg/dL	2.09±0.98	1.06±0.65	3.37±1.12	0.356
Glucose, mg/dL	146.42±60.57	143.89±67.3	149.8±50.76	0.257
Albumin, g/dL	1.64±0.78	1.48±0.61	1.84±0.94	0.350
C-reactive protein	114 (61-228)	114(20-185)	124(63-232)	0.695
Procalsitonin	0.67(0.13-1.87)	0.7(0.22-2.05)	0.94(0.23-1.83)	0.253
D-dymer	2100(1360-6410)	1480(1360-6410)	2395(1350-7800)	0.502
pH	7.35±0.13	7.37±0.14	7.38±0.12	0.703
pO_2	70±27.63	71.38±32.75	68.66±18.99	0.813
pCO_2	38.01±13.14	36.93±11.48	39.46±15.13	0.830
Lactat	2.86±1.41	2.39±1.59	2.13±1.11	0.472
P/F ratio	56.59±11.14	55.91±9.38	57.51±13.22	0.657

ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; PaO_2, Arterial partial oxygen pressure; $PaCO_2$, Arterial partial carbon dioxide pressure; CRP, C-Reactive protein; FiO_2, Fraction of inspired oxygen; HCO_3, Bicarbonate; LDH, Lactate dehydrogenase; sCr, Serum creatinine

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

Table 4. Culture results of patients

	Patients (n =31)	Survivors (n = 7)	Non survivors (n = 24)	p
Blood cultures				
Acinetobacter spp	12 (38.7%)	2 (28.57%)	10 (41.66%)	0.04
Klebsiella spp	9 (29%)	3 (42.85%)	6 (25%)	0.05
Enterbacter spp	6 (19.35%)	2 (28.57%)	4 (16.66%)	0.065
Pseudomonas spp	5 (55.55%)	2 (28.57%)	3 (12.5%)	0.71
Respiratory sample culture				
Acinetobacter spp.	19 (61.29%)	5 (71.42%)	14 (58.33%)	0.03
Klebsiella spp.	15 (48.38%)	6 (85.71%)	9 (37.5%)	0.04
Pseudomonas spp.	9 (29%)	4 (57.14%)	5 (20.83%)	0.07
Enterobacter spp.	8 (25.8%)	3 (42.85%)	5 (20.83%)	0.06
Urine culture spp.				
Acinetobacter spp.	4 (12.9%)	1 (14.28%)	3 (12.5%)	0.8
Klebsiella spp.	3 (9.67%)	1 (14.28%)	2 (8.33%)	0.07
Pseudomonas spp.	3 (9.67%)	1 (14.28%)	2 (8.33%)	0.09
Enterobacter spp.	1 (3.22%)	0 (0%)	1 (4.16%)	0.06
E.Coli spp	16 (51.6%)	5 (71.4%)	9 (37.5%)	0.04
Candida spp.	10 (32.2%)	4 (57.1%)	6 (25%)	0.03

Discussion

In our study, we observed a significant association between prolonged PCR positivity and high mortality rates among ICU patients with haematological malignancies. Additionally, a higher rate of IgM positivity was detected in the non-survivor group, which was interpreted as evidence of active infection. However, we foundno significant associations between mortality rates and the source of admission to the ICU, type of hematologic malignancy, receipt of chemotherapy, performance of allogeneic or autologous hematopoietic stem cell transplantation, presence of comorbidities, treatment modalities, vaccination status, or type of vaccine administered. Nevertheless, we found a significant association between the development of acute respiratory distress syndrome and the need for invasive mechanical ventilation support with mortality rates among patients with hematological malignancies admitted to the ICU.

Patients with hematological cancers are at an increased risk of complications associated with COVID-19 (11). A meta-analysis of 38 studies involving patients with hematological cancers who contracted COVID-19 reported a pooled mortality risk of 39%, rising to 50% among patients aged 60 years and over (12). Although the presence of

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

hematological cancer is associated with an increased risk of mortality, its impact on the risk of long term effects of the COVID-19 remains unclear (13). In our study, we found that deceased patients exhibited significantly prolonged PCR positivity, with a median duration of 24 days (range 21-52). Similarly, Yasuda et al. reported persistent COVID-19 pneumonia and ongoing PCR positivity for 2 months in a patient with follicular lymphoma, with PCR positivity persisting until day 46 (14). The authors noted the resolution of lung lesions at the 12- month follow-up stage, and the patient never developed COVID-19 antibodies. Hueso et al. reported persistent COVID-19 infection in 15 patients with hematological cancer (15). Of these patients who received anti-CD20 monoclonal antibody therapy within the past 2 years, the interval between the last rituximab infusion and symptom onset was 4 months, with patients experiencing COVID-19 symptoms for a median of 56 days (range 7-83 days). Subsequently, Betrains et al. reported one of the first studies to demonstrate reduced neutralizing antibody titers and prolonged PCR positivity, indicative of diminished viral clearance, in 5 lymphoma patients (16). In this study, the authors demonstrated a clear association between the presence of COVID-19 symptoms and the absence of PCR positivity and neutralizing antibodies in this study (16). In their study of 111 lymphoma patients hospitalized for COVID-19, Duléry et al. reported a median hospital stay of 14 days (range 1-235) and a 6-month survival rate of 69% (17). The authors highlighted viral persistence, with PCR positivity observed in nasopharyngeal swabs and bronchoalveolar lavage samples up to 143 days after the onset of illness in these patients (17).

Studies investigating factors influencing the duration of PCR positivity in critically ill patients with hematological malignancies are limited (13). While the reasons for this remain unclear, patients with hematological malignancies and COVID-19 may require longer follow-up due to the prolonged viral phase (stages 1 and 2A), delayed hyperinflammatory phase (stage 3), and a later onset of clinical deterioration (12-20 days), suggesting a need for extended monitoring (18). This phenomenon may be related to the role of T-cell responses in determining severity of a patient's clinical presentation of the disease, and to the importance of B-cell functions in achieving viral clearance (19, 20). Prolonged viral persistence in the nasopharynx and high viral loads in patients can complicate disease management (4). Prolonged carriage of the COVID-19 can complicate the treatment of inflammatory events of viral origin (21). The use of immunomodulatory agents without effective antiviral therapy may inadvertently exacerbate viral disease (22). Uncontrolled prolonged viral disease may delay chemotherapy treatments and contribute to disease progression. Additionally, patients with hematological cancers with high viral loads may pose an increased risk of nosocomial epidemic outbreaks due to increased infectivity (9). Understanding the duration of viral shedding in immunocompromised patients is crucial for guiding the treatment of these patients and understanding disease spread (4).

There are growing concerns about epidemiological issues arising from high mutation rates in the immunosuppressed patient population (7). Supporting this concern, the sudden emergence of the Omicron variant in South Africa and Botswana in November 2021, and its connection to a fatal strain isolated in 2020, suggest that Omicron may have emerged as a result of intrahost evolution in immunosuppressed individuals (23, 24). This phenomenon has been demonstrated in several case reports, including patients with hematological malignancies and poorly controlled Human Immunodeficiency Virus (HIV) infection (25). Unfortunately, it remains unclear whether current treatment strategies used to prevent or treat chronic infection reduce the risk of intrahost evolution (26).

Another significant threat observed in patients with hematological malignancies who are infected with COVID-19 is cytokine storm syndrome (CSS) (27). CSS may contribute to the pathogenesis of COVID-19 and lead to multiorgan failure, ARDS, and ultimately death (28). In our study, we found a significant association between the development of ARDS and the need for invasive mechanical ventilation with higher mortality rates among patients with hematological malignancies admitted to the ICU. A reviewof the literature by Lee et al. evaluated persistent COVID-19 in 382 patients with hematological cancer (7). They reported that 72% of the included patients required supplemental oxygen therapy, 31% were admitted to the ICU, and 22% required mechanical ventilation. The mortality rate was 31%. Similarly, another study reported a 20% mortality rate in cancer patients with COVID-19, with those admitted to the ICU requiring invasive

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:35-49

ventilation experiencing a 3.5-fold increase in mortality (29). Consistent with these findings, our study identified an increased mortality rate associated with both the development of ARDS and the application of invasive mechanical ventilation in this patient group. This is consistent with the majority of studies that suggest lung damage associated with COVID-19 is a result of an excessive immune response rather than the virus itself (30, 31).

Vaccination remains a crucial option for preventing COVID-19 infection, which has a broad clinical spectrum and serious consequences (32). Despite the widespread administration of COVID-19 vaccines, the likelihood of achieving targeted immune responses, particularly in patients with hematologic cancers, is lower (33). Studies support the idea that patients with hematological cancers exhibit low humoral responses to vaccination and fail to generate high levels of anti-COVID-19 antibodies (34). In our patient cohort, we found no significant relationship between the number of vaccinations or the type of vaccine and survival. A meta-analysis on this matter found a significantly lower seroconversion rate and heterogeneous, decreased serological response in patients with hematologic malignancies (35). However, it is still believed that vaccination significantly reduces the risk of complications related to SARS-CoV-2 infection in these patients, as T-cell memory responses can be generated in 50-75% of non-responders after vaccination (10). This T-cell immunity has been demonstrated in patients undergoing treatment for hematological malignancies as well as those receiving B-cell-depleting therapy for rheumatologic disorders (20). Therefore, vaccination is recommended in guidelines for preventing COVID-19 infection and/or reducing disease severity even in patients who do not develop adequate humoral responses.

Limitations

The most significant limitation of our study is the small sample size due to the specific patient population. A second limitation is that PCR positivity was used as both a diagnostic test and evidence of prolonged viral persistence in patients with COVID-19, since viral cell culture was not performed. Finally, as a retrospective study, our research is subject to inherent limitations.

Conclusion

Our results clearly demonstrate a relationship between prolonged PCR positivity and mortality rates among patients with hematological malignancies and COVID-19. Additionally, our study reveals that this patient group is particularly vulnerable to progressive and fatal respiratory symptoms alongside prolonged viral persistence. Moreover, the long-term consequences of chronic viral infections in immunosuppressed patients can have broad epidemiological consequences that extend beyond individual outcomes. Although vaccines have generally reduced the mortality risk associated with COVID-19, their efficacy against prolonged COVID-19 in patients with hematological malignancies remains uncertain, as observed in our study where no association was found.

In conclusion, given that prolonged COVID-19 infection primarily occurs in immunosuppressed patients and is associated with high mortality rates, we believe that evidence-based strategies to promote viral clearance should be developed to prevent or manage persistent infection in these patients.

Funding

No institutional departmental funds were received in the conduct of the study.

Conflict of interest

Authors have not disclosed any potential conflicts of interest.

References

1. Fu Y, Li Y, Guo E, He L, Liu J, Yang B, et al. Dynamics and Correlation Among Viral Positivity, Seroconversion, and Disease Severity in COVID-19 : A Retrospective Study. Ann Intern Med. 2021;174(4):453–61.
2. Rabaan AA, Tirupathi R, Sule AA, Aldali J, Mutair AA, Alhumaid S, et al. Viral Dynamics and Real-Time RT-PCR Ct Values Correlation with Disease Severity in COVID-19. Diagnostics (Basel). 2021;11(6).
3. Passamonti F, Cattaneo C, Arcaini L, Bruna R, Cavo M, Merli F, et al. Clinical characteristics and risk factors associated with COVID-19 severity in patients with haematological malignancies in Italy: a retrospective, multicentre, cohort study. Lancet Haematol. 2020;7(10):e737–e45.
4. Arcani R, Colle J, Cauchois R, Koubi M, Jarrot PA, Jean R, et al. Clinical characteristics and outcomes of

patients with haematologic malignancies and COVID-19 suggest that prolonged SARS-CoV-2 carriage is an important issue. Ann Hematol. 2021;100(11):2799–803.

5. 5. Cento V, Colagrossi L, Nava A, Lamberti A, Senatore S, Travi G, et al. Persistent positivity and fluctuations of SARS-CoV-2 RNA in clinically-recovered COVID-19 patients. J Infect. 2020;81(3):e90–e2.

6. Kemp SA, Collier DA, Datir RP, Ferreira I, Gayed S, Jahun A, et al. SARS-CoV-2 evolution during treatment of chronic infection. Nature. 2021;592(7853):277–82.

7. Lee CY, Shah MK, Hoyos D, Solovyov A, Douglas M, Taur Y, et al. Prolonged SARS-CoV-2 Infection in Patients with Lymphoid Malignancies. Cancer Discov. 2022;12(1):62–73.

8. Aydillo T, Gonzalez-Reiche AS, Aslam S, van de Guchte A, Khan Z, Obla A, et al. Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer. N Engl J Med. 2020;383(26):2586–8.

9. Eser F, Kayaaslan B, Güner R, Hasanoğlu I, Kaya Kalem A, Aypak A, et al. The Effect of prolonged PCR Positivity on patient Outcomes and Determination of Isolation period in COVID-19 patients. Int J Clin Pract. 2021;75(5):e14025.

10. Laracy JC, Kamboj M, Vardhana SA. Long and persistent COVID-19 in patients with hematologic malignancies: from bench to bedside. Curr Opin Infect Dis. 2022;35(4):271–9.

11. Ocheni S, Nwagha TU, Amu N, Obodo OI, Okereke K, Chikezie K, et al. COVID-19 in hematological malignancies: Case series and literature review. Ann Afr Med. 2023;22(3):381–4.

12. Vijenthira A, Gong IY, Fox TA, Booth S, Cook G, Fattizzo B, et al. Outcomes of patients with hematologic malignancies and COVID-19: a systematic review and meta-analysis of 3377 patients. Blood. 2020;136(25):2881–92.

13. Ichikawa T, Tamura T, Takahata M, Ishio T, Ibata M, Kasahara I, et al. Prolonged shedding of viable SARS-CoV-2 in immunocompromised patients with haematological malignancies: A prospective study. Br J Haematol. 2024;204(3):815–20.

14. Yasuda H, Tsukune Y, Watanabe N, Sugimoto K, Uchimura A, Tateyama M, et al. Persistent COVID-19 Pneumonia and Failure to Develop Anti-SARS-CoV-2 Antibodies During Rituximab Maintenance Therapy for Follicular Lymphoma. Clin Lymphoma Myeloma Leuk. 2020;20(11):774–6.

15. Hueso T, Pouderoux C, Péré H, Beaumont AL, Raillon LA, Ader F, et al. Convalescent plasma therapy for B-cell-depleted patients with protracted COVID-19. Blood. 2020;136(20):2290–5.

16. Betrains A, Godinas L, Woei AJF, Rosseels W, Van Herck Y, Lorent N, et al. Convalescent plasma treatment of persistent severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection in patients with lymphoma with impaired humoral immunity and lack of neutralising antibodies. Br J Haematol. 2021;192(6):1100–5.

17. Duléry R, Lamure S, Delord M, Di Blasi R, Chauchet A, Hueso T, et al. Prolonged in-hospital stay and higher mortality after Covid-19 among patients with non-Hodgkin lymphoma treated with B-cell depleting immunotherapy. Am J Hematol. 2021;96(8):934–44.

18. Siddiqi HK, Mehra MR. COVID-19 illness in native and immunosuppressed states: A clinical-therapeutic staging proposal. J Heart Lung Transplant. 2020;39(5):405–7.

19. Marasco V, Carniti C, Guidetti A, Farina L, Magni M, Miceli R, et al. T-cell immune response after mRNA SARS-CoV-2 vaccines is frequently detected also in the absence of seroconversion in patients with lymphoid malignancies. Br J Haematol. 2022;196(3):548–58.

20. Ghione P, Gu JJ, Attwood K, Torka P, Goel S, Sundaram S, et al. Impaired humoral responses to COVID-19 vaccination in patients with lymphoma receiving B-cell-directed therapies. Blood. 2021;138(9):811–4.

21. Cattaneo C, Daffini R, Pagani C, Salvetti M, Mancini V, Borlenghi E, et al. Clinical characteristics and risk factors for mortality in hematologic patients affected by COVID-19. Cancer. 2020;126(23):5069–76.

22. Martinot M, Jary A, Fafi-Kremer S, Leducq V, Delagreverie H, Garnier M, et al. Emerging RNA-Dependent RNA Polymerase Mutation in a Remdesivir-Treated B-cell Immunodeficient Patient With Protracted Coronavirus Disease 2019. Clin Infect Dis. 2021;73(7):e1762–e5.

23. Viana R, Moyo S, Amoako DG, Tegally H, Scheepers C, Althaus CL, et al. Rapid epidemic expansion of the SARS-CoV-2 Omicron variant in southern Africa. Nature. 2022;603(7902):679–86.

24. Tian D, Sun Y, Xu H, Ye Q. The emergence and epidemic characteristics of the highly mutated SARS-CoV-2 Omicron variant. J Med Virol. 2022;94(6):2376–83.

25. Voloch CM, da Silva Francisco R, Jr., de Almeida LGP, Brustolini OJ, Cardoso CC, Gerber AL, et al. Intra-host evolution during SARS-CoV-2 prolonged infection. Virus Evol. 2021;7(2):veab078.
26. Maneikis K, Šablauskas K, Ringelevičiūtė U, Vaitekėnaitė V, Čekauskienė R, Kryžauskaitė L, et al. Immunogenicity of the BNT162b2 COVID-19 mRNA vaccine and early clinical outcomes in patients with haematological malignancies in Lithuania: a national prospective cohort study. Lancet Haematol. 2021;8(8):e583–e92.
27. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the `Cytokine Storm' in COVID-19. J Infect. 2020;80(6):607–13.
28. Rumende CM, Susanto EC, Sitorus TP. The Management of Cytokine Storm in COVID-19. Acta Med Indones. 2020;52(3):306–13.
29. Suárez-García I, Perales-Fraile I, González-García A, Muñoz-Blanco A, Manzano L, Fabregate M, et al. In-hospital mortality among immunosuppressed patients with COVID-19: Analysis from a national cohort in Spain. PLoS One. 2021;16(8):e0255524.
30. Moore JB, June CH. Cytokine release syndrome in severe COVID-19. Science. 2020;368(6490):473–4.
31. Fajgenbaum DC, June CH. Cytokine Storm. N Engl J Med. 2020;383(23):2255–73.
32. Hadj Hassine I. Covid-19 vaccines and variants of concern: A review. Rev Med Virol. 2022;32(4):e2313.
33. Bitoun S, Henry J, Vauloup-Fellous C, Dib N, Belkhir R, Mouna L, et al. Response to COVID-19 mRNA vaccination in multiple myeloma is conserved but impaired compared to controls. J Hematol Oncol. 2021;14(1):166.
34. Perry C, Luttwak E, Balaban R, Shefer G, Morales MM, Aharon A, et al. Efficacy of the BNT162b2 mRNA COVID-19 vaccine in patients with B-cell non-Hodgkin lymphoma. Blood Adv. 2021;5(16):3053–61.
35. Becerril-Gaitan A, Vaca-Cartagena BF, Ferrigno AS, Mesa-Chavez F, Barrientos-Gutiérrez T, Tagliamento M, et al. Immunogenicity and risk of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection after Coronavirus Disease 2019 (COVID-19) vaccination in patients with cancer: a systematic review and meta-analysis. Eur J Cancer. 2022;160:243–60.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

The effect of peripheral blood eosinophil/lymphocyte ratios on chemotherapy response and prognosis before and after neoadjuvant chemotherapy in patients with locally advanced breast cancer

Lokal ileri evre meme kanserli hastalarda neoadjuvan kemoterapi öncesi ve sonrası periferik kan eozinofil/lenfosit oranlarının kemoterapi yanıtına ve prognoza etkisi

Öykü ÜNSAL[1]
Tuğba YAVUZŞEN[2]
Işıl SOMALI[2]

[1] Department of Internal Medicine, Dokuz Eylül University, Faculty of Medicine, Izmir, Türkiye
[2] Department of Medical Oncology, Dokuz Eylül University, Faculty of Medicine, Izmir, Türkiye

Peripheral Blood Eosinophil/Lymphocyte Ratios in Patients with Locally Advanced Breast Cancer

Received: 07.01.2025
Accepted: 18.09.2025
DOI:10.18614/dehm.1873599

Corresponding author
Öykü ÜNSAL
ORCID ID: 0000-0001-7366-1158
droykuunsal@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

ABSTRACT

BACKGROUND

This study aims to examine the peripheral blood eosinophil/lymphocyte ratio (ELR) as a simple, affordable and easily accessible marker to predict neoadjuvant chemotherapy (NACT) response and prognosis in patients with locally advanced breast cancer (LABC).

METHODS

The study included 102 female patients over the age of 18 who were diagnosed with LABC in 2010-2019 and were treated with NACT at Dokuz Eylül University Faculty of Medicine, Department of Internal Medicine, Medical Oncology. The patients were retrospectively examined for demographic, clinical, pathological and laboratory data. Laboratory data (leukocyte count, eosinophil count and percentage, lymphocyte count and percentage, ELR and eosinophil x lymphocytes) were evaluated before chemotherapy, before surgery and before relapse. Single and multi-variable regression analyses were performed to determine risk factors important for pathological complete response (pCR) and relapse development. The Kaplan-Meier survival analysis method was used to determine the effects of these factors on PFS (progression-free survival).

RESULTS

The mean diagnostic age was 50.8±13.0 years, the follow-up time was 41.0±27.0 months, and the average time from NACT to operation was 7.9±2.5 months. Mortality rate was 10.8%, relapse rate was 14.7%, and PCR incidence rate was 27.5%. No statistically significant differences were found in the ELR and eosinophil x lymphocyte parameters before and after NACT in terms of their value in pCR and relapse prediction. The most important predictive clinical and pathological features for pCR were found to be low count of positive lymph nodes (LN) (OR = 0.342, p = 0.04) and ER negativity (OR = 2.6, p = 0.035). The risk of recurrence in patients with a positive LN count of three and above was 3.8 times greater (OR = 3.8, p = 0.008) and the duration of PFS was shorter. The risk of recurrence in patients with a pre-NACT lymphocyte percentage of 26.75 and below was 4.2 times greater (OR = 4.2, p = 0,016), and the duration of PFS was shorter.

CONCLUSION

The study suggests that if more patients are evaluated and over a long follow-up period, markers such as peripheral blood ELR or eosinophil x lymphocyte could be used as affordable, easily accessible predictive and prognostic markers for predicting NACT response.

KEYWORDS

Locally advanced breast cancer, neoadjuvant chemotherapy, pathological complete response, prognostic marker, recurrence

ÖZ

AMAÇ

Lokal ileri evre meme kanserli (LİMK) hastalarda neoadjuvan kemoterapi (NAKT) yanıtı ve prognozu öngörmek için; basit, uygun fiyatlı ve kolay ulaşılabilir bir belirteç olarak periferik kan eozinofil/lenfosit oranının (ELR) incelenmesidir.

GEREÇ YÖNTEM

Çalışmaya 18 yaş üzeri, Dokuz Eylül Üniversitesi Tıp Fakültesi İç Hastalıkları Anabilim Dalı Tıbbi Onkoloji Bilim Dalı'nda 2010-2019 yılları arasında LİMK kanseri tanısı alan ve NAKT verilen 102 kadın hasta dahil edildi. Hastaların retrospektif olarak demografik, klinik, patolojik ve laboratuvar verileri incelendi. Laboratuvar verileri (lökosit sayısı, eozinofil sayı ve yüzdesi, lenfosit sayı ve yüzdesi, ELR ve eozinofilxlenfosit) kemoterapi öncesi, operasyon öncesi ve nüks öncesinde değerlendirildi. Patolojik tam yanıt (pCR) ve nüks gelişimi açısından önemli olan risk faktörlerini belirlemek amacıyla tek ve çok değişkenli regresyon analizleri uygulandı. Bu faktörlerin PFS (progresyonsuz sağkalım) üzerine etkilerini belirlemek için Kaplan-Meier sağkalım analiz yöntemi kullanıldı.

BULGULAR

Ortalama tanı yaşı 50,8±13,0 yıl, takip süresi 41,0±27,0 ay; NAKT'den operasyona kadar geçen süre ortalama 7,9±2,5 ay olarak hesaplandı. Mortalite oranı %10,8, nüks oranı %14,7, pCR görülme oranı ise %27,5 bulundu. NAKT öncesi ve sonrası ELR ve eozinofil x lenfosit parametrelerinde; pCR ve nüksü öngörmedeki değeri açısından istatistiksel anlamlı farklılık bulunmadı. pCR için en önemli öngörü değerine sahip klinik ve patolojik özellikler; pozitif lenf nodu(LN) sayısının az olması (OR = 0,342, p = 0,04) ve ER negatifliği (OR = 2,6, p = 0,035) olarak bulundu. Pozitif LN sayısı üç ve üzeri olan hastalarda nüks gelişme riski; 3,8 kat daha fazla (OR = 3,8, p = 0,008), PFS süresi daha kısa bulundu. NAKT öncesi lenfosit yüzdesi 26,75 ve altı olan hastalarda nüks gelişme riski; 4,2 kat daha fazla (OR = 4,2, p = 0,016), PFS süresi daha kısa bulundu.

SONUÇ

Daha fazla hasta sayısı ve uzun takip süresinde değerlendirme yapıldığında; periferik kan ELR veya eozinofil x lenfosit gibi belirteçlerin, NAKT yanıtını öngörmede uygun fiyatlı, kolay erişilebilir prediktif ve prognostik belirteçler olarak kullanılabileceği düşünülmektedir.

ANAHTAR KELİMELER

Lokal ileri evre meme kanseri, neoadjuvan kemoterapi, nüks, patolojik tam yanıt, prognostik belirteç

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

Breast cancer is the most common cancer in women both globally and in Türkiye. In a healthy population, a woman has a 12.9% risk of developing breast cancer during her lifetime, with one in eight women being diagnosed with the disease. In the United States, breast cancer is the second leading cause of cancer-related death in women, after lung cancer. Among women aged 20-59, it is the leading cause of cancer-related deaths (1). In Türkiye, the age-standardized incidence of breast cancer in women is 47.7 per 100,000. Regarding the percentage distribution of the most common cancers in women of all age groups, breast cancer accounts for 25.5% of cases (2).

The definition of locally advanced stage breast cancer is heterogeneous; it includes stage IIB (T3N0) and stage IIIA, IIB, IIIC breast cancers. This group includes both slow-growing and aggressive tumors. The standard treatment approach in LABC (locally advanced breast cancer) is NACT (neoadjuvant chemotherapy) treatment (3–6). The most important factor determining treatment success and survival is pCR (pathological complete response) (3). The most widely accepted definition of pCR includes no residual invasive disease in the breast and no measurable disease in the axillary lymph nodes sampled (ypT0/ypN0) (3,7,8).

Patients who achieved a pathologic pCR after neoadjuvant chemotherapy had a higher survival rate than those who did not. Therefore, numerous studies are investigating clinical and pathological characteristics that can be used to predict whether pCR can be achieved in patients receiving NACT, as well as laboratory data that can surve as markers. However, due to their cost and limited accessibility, genetic and molecular tests are not widely used in clinical practice. Simpler, cost-effective, and easily accessible markers are needed to predict the NACT response (9,10).

The main functions of eosinophils in the immune system include the elimination of foreign substances (their role in parasitic infections) and the regulation of inflammation (they respond to cytokines secreted from lymphocytes, secrete factors that have anti-tumor effects or stimulate tumor progression, act as antigen-presenting cells and can stimulate and influence lymphocyte functioning) (11,12). Eosinophils stimulate the anti-tumor response by attracting CD8+T cells to the tumor site with various chemokines that they secrete. However, some studies suggest that they promote tumour growth by inducing angiogenesis with growth factors such as VEGF (vascular endothelial growth factor), TGF-α (transforming growth factor-alpha), TGF-β (transforming growth factor-beta), and GM-CSF (granulocyte macrophage colony stimulating factor (12–14). Although tumoral eosinophilia is considered to be associated with a poor prognosis in Hodgkin lymphoma, it has been shown to be associated with a good prognosis in colorectal, breast, and prostate cancers (12).

The purpose of our study is to analyze the use of peripheral blood eosinophil/lymphocyte ratio (ELR) before and after NACT in LABC as a marker of treatment response and prognosis. Based on studies showing that tumoral eosinophilia is associated with a good prognosis in breast cancer (12), it is thought that peripheral blood eosinophilia may also have prognostic significance.

Materials and Methods

The study began after receiving approval from the Dokuz Eylül University Ethics Board for Non-Invasive Research. Women aged 18 years and older who were diagnosed with LABC and received NACT between 2010 and 2019 at the Department of Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Dokuz Eylül University were included. Participants were excluded from the study if they were under 18 years of age, if the necessary demographic and clinical information was absent from the hospital records, or if they were male. The data were obtained by scanning electronic file system records (Probel Hbys) of Dokuz Eylül University Medical Faculty Hospital and archival materials in the Department of Archives and Medical Statistics. The laboratory data were obtained retrospectively from the central laboratory of the Dokuz Eylül University Medical Faculty Hospital, which is ISO 15189 accredited. Hemogram parameters within the scope of accreditation were studied usingthe impedance method on a Beckman Coulter LH 780 analyzer (MLTR.505.105) in blood with EDTA.

The independent variables were pathological complete response, relapse, mortality, whilethe dependent variables were determined as age, histological type, tumor diameter, positive lymph node count, estrogen receptor, progesterone receptor, human epidermal growth factor

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

receptor, and peripheral blood parameters. Demographic and clinical data are shown in Table 1. Tumor histology, receptor status, and pathological response are shown in Table 2 including histological type (ductal, lobular, mixed, other), ER status and PR status, HER2 status, Ki-67 proliferation index (<20%, ≥20%, unknown), lymphocytes infiltrating the tumor, lymphovascular invasion, perineural invasion, and pathological response.

Table 1. Demographic, clinical and histopathological data

Total number of patients (n)		102
Age of diagnosis (years) (mean ± sd) (min-max)		50.8±13.0 (26.7-82.4)
Relapse rate (n, %)		15 (14.7 %)
Mortality rate (n, %)		11 (10.8%)
Follow-up time (months) (mean±sd) (min-max)		41.0±27.0 (0.3-129.8)
Tumor diameter (mm) (mean±sd) (min-max)		27.2±16.1 (3.0-80.0)
Number of lymph nodes (mean±sd) (min-max)		9.7±6.5 (1.0-32.0)
Number of positive lymph nodes (mean±sd) (min-max)		2.3±3.8 (0.0-28.0)
Chemotherapy (n, %) EC→T		76 (74.5%)
FEC→T		18 (17.6%)
Carbo→T		3 (2.9%)
Unknown		2 (2.0%)
Other		3 (2.9%)
KT type (n, %) Taxane-based		94 (92.2%)
Other		8 (7.8%)
Trastuzumab (n, %) Yes		40 (39.2%)
No		62 (60.8%)
Radiotherapy (n, %) Yes		86 (84.3%)
No		16 (15.7%)
Histological type (n, %)		69 (67.6%)
	Lobular	18 (17.6%)
	Mixed	12 (11.8%)
	Other	3 (2.9%)
Estrogen receptor (ER) (n, %)	+	4 (3.9%)
	++	12 (11.8%)
	+++	54 (52.9%)
	-	32 (31.4%)
Progesterone receptor (PR) (n, %)	+	7 (6.9%)
	++	18 (17.6%)
	+++	29 (28.4%)
	-	48 (47.1%)
HER2 (n, %)	Positive	25 (24.5%)
	Negative	77 (75.5%)
Triple negative (n, %)	Yes	17 (16.7%)
	No	85 (83.3%)
Ki-67 proliferation index (n, %)	< 20%	21 (20.6%)
	≥20%	69 (67.6%)
	Unknown	12 (11.8%)
Tumor infiltrating lymphocytes (TIL) (n, %)	Low	29 (28.4%)
	Moderate	14 (13.7%)
	High	8 (7.8%)
	Unknown	49 (48.0%)
	None	2 (2.0%)
Lymphovascular invasion (LVI) (n, %)	Yes	55 (53.9%)

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

	None	46 (45.1%)
	Unknown	1 (1.0%)
Perineural invasion (n, %) (PNI)	Yes	16 (15.7%)
	None	85 (83.3%)
	Unknown	1 (1.0%)
Pathological complete response (pCR) (n, %)	pCR	28 (27.5%)
	DCIS, LN-negative	10 (9.8%)
	DCIS, LN-positive	13 (12.7%)
	Residual invasive carcinoma, LN-negative	10 (9.8%)
	Residual invasive carcinoma, LN-positive	40 (39.2%)
	Unknown	1 (1.0%)

CT, Chemotherapy; EC→T, Epirubicin, Cyclophosfamide then docetaxel or Paclitaxel; FEC → T, Fluorouracil, Epirubicin, Cyclofosfamide then Docetaxel or Paclitaxel, Carbo→T, Carboplatin then paclitaxel

Table 2. Demographic, clinical and histopathological characteristics of patients according to pathological response

		pCR positive n=28	**No pCR n=74**	**P**
Age of diagnosis (years) (mean ± sd)		50.3±13.1	50.9±13.0	0.838
Relapse rate		1 (3.6%)	14 (18.9%)	0.051
Tumor diameter (mm) (mean ± sd)		30.4±14.4	26.1±16.6	0.229
Number of LN (median) (min-max)		6.0 (1.0-21.0)	9.5 (1.0-32.0)	**0.035**
Number of positive LN (median) (min-max)		0.0 (0.0-2.0)	2.0 (0.0-28.0)	**<0.001**
Chemotherapy (n, %)	EC→T	22 (78.6%)	54 (73.0%)	0.654
	FEC→T	5 (17.9%)	13 (17.6%)	
	Carbo→T	0 (0.0%)	3 (4.1%)	
	Unknown	1 (3.6%)	1 (1.4%)	
	Other	0 (0.0%)	3 (4.1%)	
CT type (n, %)	Taxane-based	27 (96.4%)	67 (90.5%)	0.440
	Other	1 (3.6%)	7 (9.5%)	
Transtuzumab (n, %)	Yes	14 (50.0%)	26 (35.1%)	0.170
	No	14 (50.0%)	48 (64.9%)	
Radiotherapy (n, %)	Yes	21 (75.0%)	65 (87.8%)	0.132
	No	7 (25.0%)	9 (12.2%)	
Histological type (n, %)	Ductal	24 (85.7%)	45 (60.8%)	0.083
	Lobular	2 (7.1%)	16 (21.6%)	
	Mixed	1 (3.6%)	11 (14.9%)	
	Other	1 (3.6%)	2 (2.7%)	
ER (n, %)	Positive	13 (46.4%)	57 (77.0%)	**0.003**
	Negative	15 (53.6%)	17 (23.0%)	
PR (n, %)	Positive	10 (35.7%)	44 (59.5%)	**0.032**
	Negative	18 (64.3%)	30 (40.5%)	
HER2 (n, %)	Positive	11 (39.3%)	14 (18.9%)	**0.033**
	Negative	17 (60.7%)	60 (81.1%)	
Triple negative (n, %)	Yes	9 (32.1%)	8 (10.8%)	**0.016**
	No	19 (67.9%)	66 (89.2%)	
Ki-67 (n, %)	< 20%	2 (7.1%)	19 (25.7%)	0.050
	≥20%	24 (85.7%)	45 (60.8%)	
	Unknown	2 (7.1%)	10 (13.5%)	

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

TIL (n, %)	Low	7 (25.0%)	22 (29.7%)	0.993
	Moderate	4 (14.3%)	10 (13.5%)	
	High	2 (7.1%)	6 (8.1%)	
	Unknown	14 (50.0%)	35 (47.3%)	
	None	1 (3.6%)	1 (1.4%)	
LVI (n, %)	Yes	11 (39.3%)	44 (59.5%)	0.127
	None	17 (60.7%)	29 (39.2%)	
	Unknown	0 (0.0%)	1 (1.4%)	
PNI (n, %)	Yes	3 (10.7%)	13 (17.6%)	0.671
	None	25 (89.3%)	60 (81.1%)	
	Unknown	0 (0.0%)	1 (1.4%)	

pCR, Pathological complete response; LN, Lymph node; CT, Chemotherapy; EC→T, Epirubicin, Cyclophosfamide then docetaxel or Paclitaxel; FEC → T, Fluorouracil, Epirubicin, Cyclofosfamide then Docetaxel or Paclitaxel, Carbo→T, Carboplatin then paclitaxel; ER, Estrogen receptor; PR, Progesterone receptor; HER2, Human epidermal growth factor receptor 2; TIL, Tumor infiltrating lymphocytes; LVI, Lymphovascular invasion; PNI, Perineural invasion

The presence of HER2 was evaluated using the immunohistochemical method (IHC) and fluorescent in-situ hybridization (FISH) methods. Patients with HER2 (3+) were considered positive, while patients with HER2 (0) and (1+) were considered negative. Patients with HER2 (2+) were categorized as either positive or negative following further evaluation using the FISH method. Laboratory data were classified as follows: Leukocyte count (103/ul), eosinophil percentage (%), eosinophil count (103/ul), absolute eosinophil count (103/ul), lymphocyte percentage (%), lymphocyte count (103/ul), absolute lymphocyte count (103/ul), eosinophil/lymphocyte ratio (the number of eosinophils divided by lymphocytes), and eosinophil x lymphocyte (the number of eosinophils multiplied by lymphocytes). The laboratory data were examined before NACT, before the operation (post-NACT), and before relapse.

Statistical analyses were performed with SPSS software version 22.0 (IBM, New York, USA). After making descriptive statistics, Shapiro-Wilk and Kolmogorov-Smirnov normality tests were used to determine whether the continuous data was distributed normally. The Mann-Whitney U test was used to compare variables that did not show normal distribution between groups, and the Student-T test was used to compare normal distribution variables. The results of these analyses were presented as mean ± standard deviation, median and minimum-maximum values. Categorical data between the groups was compared using Chi-Square and Fisher's exact test. The results were given in numbers and percent (%).

Single-variable regression analysis was applied to determine variables with predictive value in predicting pathological full response. In single-variable regression analysis, variables with an alpha value less than 0.2 were included in the multi-variable regression analysis. The results were presented with 95% confidence intervals. P<0.05 was taken to indicate statistical significance.

A single-variable regression analysis was performed to determine the most important risk factors for recurrence development. In single-variable regression analysis, parameters with an alpha value less than 0.2 were included in the multi-variable regression analysis (Cox regression analysis). The results were presented with 95% confidence intervals. P<0.05 was taken to indicate statistical significance. As a result of regression analyses, ROC analyses were applied for the parameters determined as risk factors. Cut-off values were determined using AUC and Youden index ratios. Sensitivity and specificity rates were determined for such cut-off values. Using cut-off values, patients were divided into high-risk and low-risk groups.

The Kaplan-Meier survival analysis method was used based on the survival analyzes to determine the effects of effective risk factors on relapse on PFS. The estimated PFS times were given with confidence intervals of 95% as an average ± standard deviation. In all statistical analyses, $p < 0.05$ was taken to indicate statistical significance.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

Results

A total of 102 women diagnosed with LABC and treated with NACT were included in the study. The mean age at diagnosis of the patients was 50.8±13.0 years, and the mean follow-up period was 41.0±27.0 months. The mortality rate was calculated as 10.8%, while the relapse rate was 14.7%. Other demographic, clinical and histopathological characteristics are summarized in Table 1.

The NACT regimens used are listed in Table 1. Taxane based NACT regimens include EC→T (Epirubicin, Cyclophosfamide then docetaxel or Paclitaxel), FEC → T (Fluorouracil, Epirubicin, Cyclofosfamide then Docetaxel or Paclitaxel) and Carbo→T (Carboplatin then paclitaxel). Missing values in categorical variables were coded as an 'unknown' category and included in the analyses. The duration of the patients from NACT to operation was calculated as 7.9 ± 2.5 months on average. When the patients' demographics and clinical characteristics were compared with their pathological response, a higher positive LN count was observed in patients without pCR ($p < 0.001$). A comparison of the tumor histology and receptor status in patients with PCR showed that the proportion of ER- and PR-positive patients was significantly lower ($p = 0.003$ and 0.032, respectively). The percentage of HER2-positive patients was higher in the pCR group ($p = 0.033$). A higher percentage of patients were triple-negative in the pCR group ($p = 0.016$). No statistically significant differences were found when other pathological features were compared (Table 2). Additonally, no significant differences were observedbetween all peripheral blood parameters before NACT in patients with and without pCR.

The parameters that may predict whether pCR will be observed in LABC patients receiving NACT were compared using single and multi-variable analyses. According to the multivariate regression analysis, the clinical and pathological characteristics that were found to have the most important predictive value for pCR in patients receiving NACT were found to have a low number of positive LN ($p = 0.04$) and ER negativity ($p = 0.035$) (Table 3).

Table 3. Single and multi-variable regression analysis for pathological complete response

	Univariate analysis (single variable)				Multivariate analysis (multiple variable)			
Parameters	**β**	**OR**	**95% GA**	**p**	**β**	**OR**	**95% GA**	**P**
Number of LN	-0.073	0.930	0.863-1.002	0.057	0.025	1.026	0.926-1.137	0.627
Number of positive LN	-1.129	0.323	0.166-0.629	0.001	-1.073	0.342	0.165-0.708	**0.004**
ER positive vs negative	1.353	3.869	1.543-9.700	0.004	1.254	2.603	1.470-14.448	**0.035**
PR positive vs negative	0.971	2.640	1.072-6.504	0.035	-0.966	0.381	0.081-1.796	0.222
HER2 negative vs positive	1.020	2.773	1.066-7.217	0.036	1.178	3.249	0.625-16.888	0.161
Triple-negative vs non-triple-negative	1.363	3.908	1.326-11.513	0.013	1.544	4.683	0.420-52.211	0.210

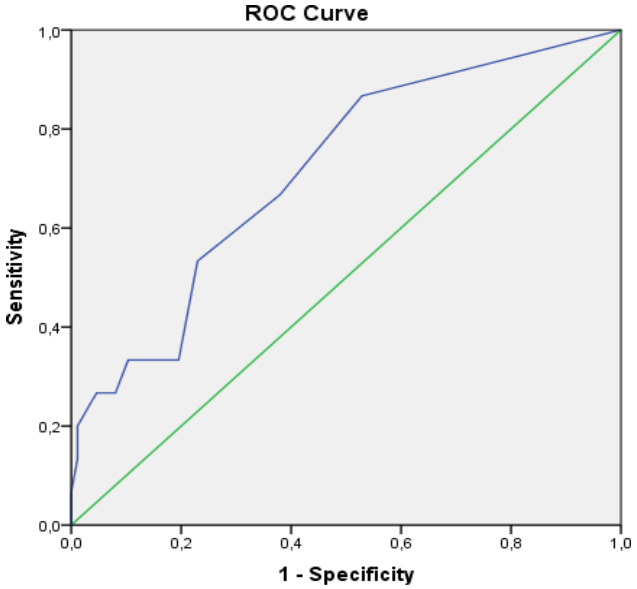
LN, Lymph node; ER, Estrogen receptor; PR, Progesterone receptor; HER2, Human epidermal growth factor receptor 2

When patients who relapsed after NACT were compared to patients who did not relapse, the number of positive LNs was found to be significantly higher in patients who relapsed ($p = 0.006$). No statistically significant difference was found in terms of tumor histology and receptor status between relapsing and non-relapsing patients.

However, relapsed patients were found to have lower percentages of lymphocytes alone in the peripheral circulation before chemotherapy than patients who did not relapse ($p = 0.016$). According to the ROC analysis conducted to evaluate the prediction of relapse development of positive LN number, cut-off value was 2.5 and the risk of relapse in patients with 3

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

or more positive lymph nodes was 3.8 times greater than in patients with less than 3 positive LNs Figure 1



	AUC	95% CI	P	Sensitivity	Specificity	Cut-off value	PPV	NPV	OR (95% CI)
Positive LN number	0.715	0.576-0.854	0.008	53.3%	77.0%	2.5	28.6%	90.5%	3.83 (1.24-11.86)

Figure 1. Relationship of positive LN to relapse in the ROC analysis curve

ROC analysis was performed to evaluate the ability of peripheral blood lymphocyte percentage to predict relapse development. The cut-off value was determined to be 26.75, and it was found that the risk of relapse was 4.2 times higher in patients with a pre-NACT lymphocyte percentage of 26.75 or below than in patients with a percentage above this value Figure 2.

The PFS of patients was found to be 92.7±4.5 months (83.7-101.6) with 95% CI Figure 3.

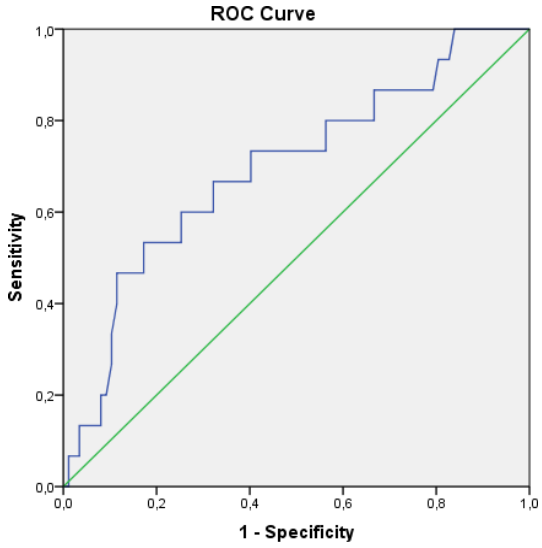
PFS was found to be shorter (p=0.013) in patients with a positive LN count of 3 and above than in patients with a count below 3 Figure 4.

PFS was found to be shorter (p=0.027) in patients with peripheral blood lymphocyte percentages of 26.75 or less than in patients with percentages above 26.75 Figure 5.

No statistically significant ELR value before or after NACT was determined to predict relapse, no cut-off value was calculated Figure 6.

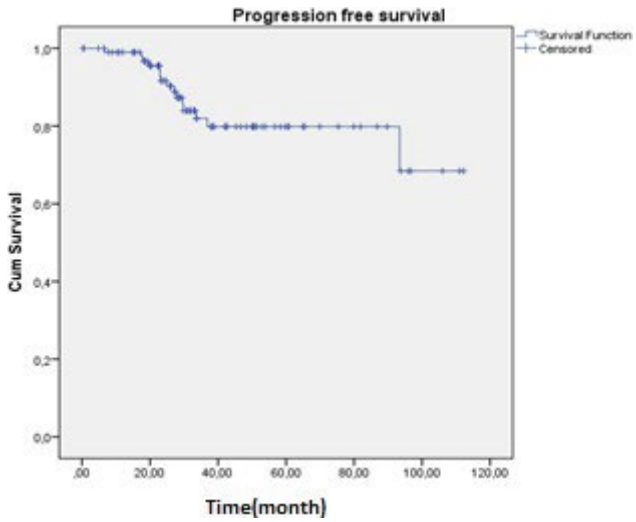
In single-variable analysis, parameters involved in relapse development in patients include age at diagnosis, positive LN count, and low lymphocyte percentage before chemotherapy. However, single-variable regression analysis of peripheral blood ELR before and after NACT found no significant results to include in the multivariate model ($p > 0.20$). In the multivariate analysis of the model created from parameters $P < 0.20$ (Cox regression), the prominent risk parameters for relapse development in this group of patients during follow-up were observed as positive LN count and low percentage of lymphocytes before chemotherapy, although no statistical significance was found ($p = 0.076$ and $p = 0.097$) (Table 4).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64



	AUC	95% CI	P	Sensitivity	Specificity	Cut-off value	PPV	NPV	OR (95% CI)
Pre-NACT lymphocyte %	0,696	0.547-0.845	0,016	66.7%	67.8%	26.75	26.3%	92.2%	4.21 (1.32-13.50)

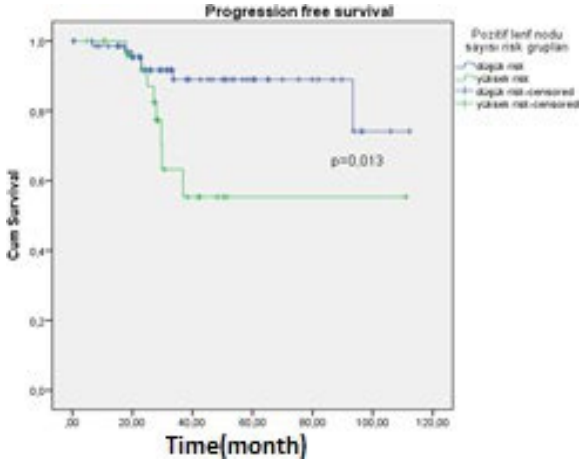
Figure 2. Relation of peripheral blood lymphocyte percentage to relapse in the ROC analysis curve



Time (months)	0	20	40	60	80	100	120
No at risk	102	79	34	17	10	3	0
No of events	4	10	0	0	1	0	0

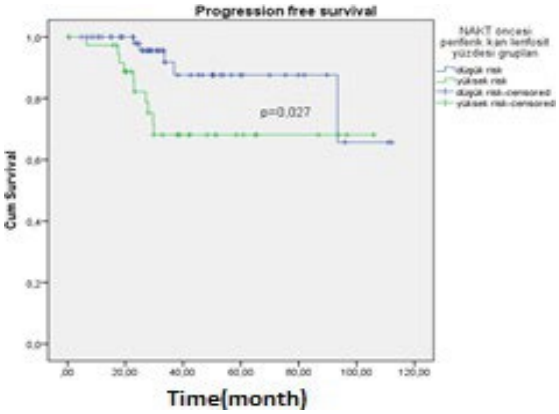
Figure 3. PFS analysis (Kaplan-Meier survival analysis)

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64



Number of positive LN	PFS (month)	95% CI	P
<3 low risk	99.5±4.5	90.6-108.4	**0.013**
≥3 high risk	74.1±10.2	54.0-94.2	

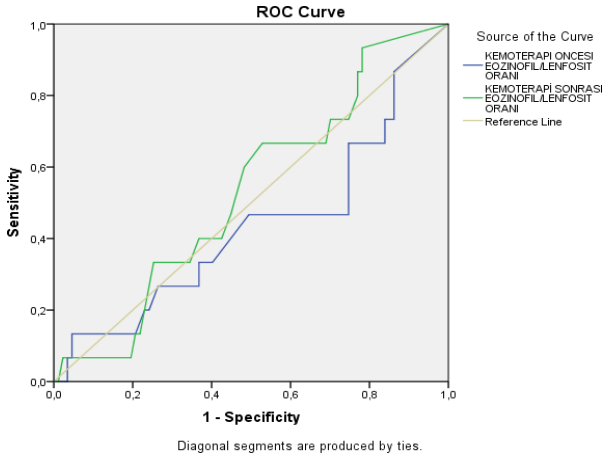
Figure 4. The effect of positive LN count on PFS (Kaplan-Meier analysis)



Pre-NACT lymphocyte percentage	PFS (month)	95% CI	P
> 26.75 low risk	**98.1±5.8**	**86.7-109.4**	**0.027**
≤ 26.75 high risk	**79.5±7.0**	**65.8-93.2**	

Figure 5. Effect of the percentage of lymphocytes in peripheral blood before NACT on PFS (Kaplan-Meier analysis)

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64



	AUC	95% CI	P	Sensitivity	Specificity	Cutoff value	PPV	NPV	OR (95% CI)
Pre-NACT ELR	0,434	0,266-0,603	0,419	-	-	-	-	-	-
Post-NACT ELR	0.530	0.384-0.676	0.713	-	-	-	-	-	-

Figure 6. Relationship of peripheral blood ELR before and after NACT in the ROC analysis curve

Table 4. Single and multi-variable regression analysis of the predictive values of the parameters for relapse

	Univariate analysis (single variable)				Multivariate analysis (multiple variable)			
Parameters	**β**	**OR**	**95% GA**	**p**	**β**	**OR**	**95% GA**	**p**
Age at diagnosis	-0.042	0.959	0.918-1.002	**0.062**	-0.036	0.964	0.924-1.007	0.099
Tumor size	0.014	1.014	0.988-1.040	0.296				
Number of positive LN Low vs High risk	1.226	3.407	1.223-9.491	**0.019**	0.975	2.652	0.903-7.792	0.076
Pre-NACT lymphocyte % Low vs High risk	1.148	3.151	1.076-9.227	**0.036**	0.935	2.547	0.844-7.691	0.097
Pre-NACT ELR	-3.738	0.024	0.000-481.015	0.460				
Post-NACT ELR	-0.824	0.439	0.000-2868.911	0.854				

LN, Lymph node; NACT, neoadjuvant chemotherapy; ELR, eosinophil/lymphocyte ratio

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

Discussion

In our study, the proportion of HER2-positive and triple-negative patients achieving pCR after NACT was significantly higher, whereas the proportion of patients with ER and/or PR receptor positive patients were statistically lower. Many other studies in the literature have reported similar findings, namely that the likelihood of pCR after NACT is highest in hormone-negative and HER2-positive tumors, followed by triple-negative tumors (15,16).

In both univariate and multivariate analyses, the two statistically significant factors with the greatest predictive value for pCR were identified as the low number of positive LN and negative ER status. A similar study conducted by Iwamoto et al., found factors predicting a high pCR rate after NACT were high-grade tumor, negative ER, and post-NACT cN0 (17). In a study by Omranipur et al., factors that predicted high pCR rates after NACT were found to be under 50 years of age, PR negativity, and high Ki-67 (15).

In our study, a positive LN count of 3 or more (3.8-fold) and a pre-NACT lymphocyte percentage of 26.75 or less (4.2-fold) were determined to be values that increase the risk of relapse. Similarly, many studies have found thata high number of axillary LNs involved in breast cancer has been found as a parameter that increases the risk of relapse (18). In the literature, it has been determined that pre-treatment lymphopenia is a parameter that predicts tumor relapse in breast cancer and is associated with poorer overall survival (19). Notably, previous studies have focused on absolute lymphocyte counts but the relationship between changes in lymphocyte percentage and relapse has not been checked.

In our study, we observed that LN positivity was elevated in patients with shorter PFS, and pre-NACT peripheral blood lymphocyte percentages were low. Similarly, Ownby et al. reported that a low pre-NACT peripheral blood lymphocyte count (<1500 cells/mm3) was associated with reduced PFS (20).

When we examined whether the ELR and eosinophil x lymphocyte parameters before and after NACT contributed to predicting CT response and prognosis, results revealed no significant associations with pCR, recurrence, or mortality. In a study conducted by Onesti et al. on 112 breast cancer patients treated with standard NACT, improvement in breast cancer-specific survival was observed in patients with high eosinophil and lymphocyte counts before treatment. Additionally, patients with high eosinophil counts before treatment had an increased rate of achieving pCR, particularly the pCR rate was higher in patients with eosinophil x lymphocytes ≥ 35.8 (21).

Peripheral blood cell-derived ratios, including lymphocyte/monocyte ratio (LMR), neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR), have been associated with prognosis and survival in breast cancer. Specifically, high LMR and low NLR correlated with reduced relapse risk and longer survival, whereas elevated PLR predicted shorter survival (22,23). All these studies have shown that markers containing peripheral blood cells may be associated with prognosis and survival in cancers, but studies incorporating eosinophil-based markers are limited. Endometrial cancer study have shown that higher ELR predicts poorer OS (24). In another study on endometrial cancer, higher pre-treatment ELR (≥ 0.1) and ENLR (eosinophil x neutrophil/lymphocyte ratio) (≥ 0.5) were found to be independently associated with worse overall survival (25). Low preoperative eosinophil counts and low ELR are independently associated with poorer overall survival in patients with stage II resectable pancreatic cancer (26). Additionally prostate cancer study found that higher pre-treatment ELR was associated with increased Gleason score (23). The number of studies investigating the ELR in breast cancer is limited.

The main limitations of our study are the small number of patients who have relapsed, the uneven distribution of patients across breast cancer subtypes, the short follow-up period, and the inability to exclude deaths that are not related to breast cancer or to conduct prospective monitoring.

This study's strength lies in its novel evaluation of the potential of ELR, lymphocyte count and percentage as predictive and prognostic markers for relapse and mortality in patients with LABC undergoing NACT. Our findings contribute valuable insight to the literature by addressing this gap. Other strengths include a meaningful dataset comprising 102 LABC patients, a separate assessment of parameters associated with both pCR and recurrence, and the use of ROC analyses to determine cut-off values, providing clinically applicable information. The lack of statistical significance in the ELR is also an important negative result that is worth reporting.

Although our study did not demonstrate a statistically significant association between ELR and clinical outcomes, this biomarker may still have clinical relevance. Biologically, ELR reflects the balance between eosinophils, which have been implicated in anti-tumor immunity, and lymphocytes, which are essential for adaptive immune responses. Previous studies have reported that systemic inflammatory ratios, including ELR and NLR, may serve as prognostic or predictive indicators in several malignancies, including breast cancer (7,27). Moreover, our relatively limited sample size and the heterogeneity of subgroups may have

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:51-64

restricted statistical power, raising the possibility that a true association might be observed in larger, more homogeneous cohorts. Therefore, the prognostic and predictive significance of ELR requires further clarification in prospective studies with larger patient populations.

Conclusion

In conclusion, when larger patients and extended follow-up periods are evaluated, peripheral eosinophil and lymphocyte count, as well as combined markers such as the ELR or eosinophil x lymphocyte containing both of these cells together can be used as cost-effective, easily accessible predictive and prognostic markers for NACT response. Further comprehensive studies are needed to validate these observations. Our findings provide a foundation for such future investigations.

It was presented as a specialization thesis at Dokuz Eylül University, Department of Medical Oncology on November 18, 2021 (registered in Yöktez as thesis number 702996). Izmir Uğur Yılmaz Oncology Days, IX. Rare Tumors Symposium, Izmir, Türkiye, 25 - 27 February 2022, presented as an oral presentation.

Supporting institution and/or person
None.

Conflict of interest statement
The authors have no conflict of interest.

References

1. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin. 2021;71(1):7–33.
2. Türkyılmaz M, Öztürk M, Dündar S. Türkiye Kanser İstatistikleri. T.C. Halk Sağlığı Kurumu Ankara. 2017. 75–77 p.
3. Güler N, Karabulut B, Koçdor MA. Lokal İleri Meme Kanseri 2010 İstanbul Konsensus Toplantısı. J Breast Heal. 2011;7(2):68–89.
4. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin. 2017;67(2):93–9.
5. Waks AG, Winer EP. Breast Cancer Treatment: A Review. JAMA. 2019 Jan 22;321(3):288–300.
6. Barni S, Mandalà M, Williams L, Barni S. Locally advanced breast cancer. Curr Opin Obstet Gynecol. 2006;18:47–52.
7. Ethier JL, Desautels D, Templeton A, Shah PS, Amir E. Prognostic role of neutrophil-to-lymphocyte ratio in breast cancer: a systematic review and meta-analysis. Breast Cancer Res. 2017 Jan 5;19(1):1–13.
8. Simon RM, Paik S HD. Use of archived specimens in evaluation of prognostic and predictive biomarkers. J Natl Cancer Inst. 2009;101(21):1446–1452.
9. Eren T, Karacin C, Ucar G, Ergun Y, Yazici O, İmamoglu İ, et al. Correlation between peripheral blood inflammatory indicators and pathologic complete response to neoadjuvant chemotherapy in locally advanced breast cancer patients. Medicine (Baltimore). 2020 May 29;99(22):e20346.
10. Cortazar P, Zhang L, Untch M, Mehta K, Costantino JP, Wolmark N, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. Lancet. 2014;384(9938):164–72.
11. Weller PF, Lim K. Human Eosinophil-Lymphocyte Interactions. Mem Inst Oswaldo Cruz, Rio Janeiro. 1997;92:173–82.
12. Sakkal S, Miller S, Apostolopoulos V, Nurgali K. Eosinophils in Cancer: Favourable or Unfavourable? Curr Med Chem. 2016 Jan 20;23(7):650–66.
13. Balkwill FR, Mantovani A. Cancer-related inflammation: Common themes and therapeutic opportunities. Semin Cancer Biol. 2011;22:33–40.
14. Carretero R, Sektioglu IM, Garbi N, Salgado OC, Beckhove P, Hämmerling GJ et all. Eosinophils orchestrate cancer rejection by normalizing tumor vessels and enhancing infiltration of CD8(+) T cells. Nat Immunol. 2015 May 19;16(6):609–17.
15. Omranipour R, Jalili R, Yazdankhahkenary A, Assarian A, Mirzania M, Eslami B et all. Evaluation of Pathologic Complete Response (pCR) to Neoadjuvant Chemotherapy in Iranian Breast Cancer Patients with Estrogen Receptor Positive and HER2 Negative and impact of predicting variables on pCR. Eur J breast Heal. 2020 Jun 24;16(3):213–8.
16. Simos D, Clemons M, Ginsburg OM, Jacobs C. Definition and consequences of locally advanced breast cancer. Curr Opin Support Palliat Care. 2014;8(1):33–8.
17. Iwamoto N, Aruga T, Horiguchi S, Saita C, Onishi M, Goto R, et al. Predictive factors of an axillary pathological complete response of node-positive breast cancer to neoadjuvant chemotherapy. Surg Today. 2020 Feb 1;50(2):178–84.

18. Chang JM, Leung JWT, Moy L, Ha SM, Moon WK. Axillary Nodal Evaluation in Breast Cancer: State of the Art. Radiology. 2020 Jun 1;295(3):500–15.
19. Bai YG, Gao GX, Zhang H, Zhang S, Liu Y-H, Duan X-N, et al. Prognostic value of tumor-infiltrating lymphocyte subtypes in residual tumors of patients with triple-negative breast cancer after neoadjuvant chemotherapy. Chin Med J (Engl). 2020 Mar 5;133(5):552–60.
20. Ownby HE, Roi LD, Isenberg RR, Brennan MJ. Peripheral Lymphocyte and Eosinophil Counts as Indicators of Prognosis in Primary Breast Cancer. Cancer. 1983;52:126–30.
21. Onesti CE, Josse C, Poncin A, Frères P, Poulet C, Bours V. Predictive and prognostic role of peripheral blood eosinophil count in triple-negative and hormone receptor-negative/HER2-positive breast cancer patients undergoing neoadjuvant treatment. Oncotarget. 2018 Sep 1;9(72):33719–33.
22. Losada B, Guerra JA, Malón D, Jara C, Rodriguez L, Barco S Del, et all. Pretreatment neutrophil/lymphocyte, platelet/lymphocyte, lymphocyte/monocyte, and neutrophil/monocyte ratios and outcome in elderly breast cancer patients. Clin Transl Oncol. 2019 Jul 10;21(7):855–63.
23. Ferro M, Musi G, Serino A, Cozzi G, Mistretta FA, Costa B, et al. Neutrophil, Platelets, and Eosinophil to Lymphocyte Ratios Predict Gleason Score Upgrading in Low-Risk Prostate Cancer Patients. Urol Int. 2019 Jan 1;102(1):96–101.
24. Holub K, Conill C. The Impact of Inflammatory Biomarkers on Overall Survival of Patients with Pancreatic Cancer Treated with Chemoradiation. Elsevier. 2018;29(5):135.
25. Holub K, Biete A. New pre-treatment eosinophil-related ratios as prognostic biomarkers for survival outcomes in endometrial cancer. BMC Cancer. 2018;18:1280. DOI:10.1186/s12885-018-5131-x
26. Ohkuma R, Kubota Y, Horiike A, Ishiguro T, Hirasawa Y, Ariizumi H, et al. The prognostic impact of eosinophils and the eosinophil-to-lymphocyte ratio on survival outcomes in stage II resectable pancreatic cancer. Pancreas. 2021 Feb 1;50(2):167–75. DOI:10.1097/MPA.0000000000001731
27. Poncin A, Onesti CE, Josse C, Boulet D, Thiry J, Bours V, et al. Immunity and breast cancer: Focus on eosinophils. Biomedicines. 2021;9(9):1087. DOI:10.3390/biomedicines9091087.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

Compliance of comprehensive care in children with Duchenne muscular dystrophy: Real-world experience of a pediatric neuromuscular diseases center

Duchenne musküler distrofili çocuklarda kapsamlı bakıma uyum: Bir pediatrik nöromüsküler hastalıklar merkezinin gerçek dünya deneyimi

İsmail Burak YEYEN[1]
Çağatay GÜNAY[2]
Semra HIZ KURUL[2]
Uluç YİŞ[2]

[1] Dokuz Eylul University Faculty of Medicine, Department of Pediatrics, Izmir, Türkiye
[2] Dokuz Eylul University Faculty of Medicine, Department of Pediatric Neurology, Izmir, Türkiye

Care in Children with Duchenne Muscular Dystrophy
Received: 11.02.2025
Accepted: 18.09.2025
DOI:10.18614/dehm.1873614

Corresponding author
Çağatay GÜNAY
ORCID ID: 0000-0001-7860-6297
cagataygunaymd@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

ABSTRACT

BACKGROUND

Although international care considerations for Duchenne muscular dystrophy (DMD) were revised in 2018, compliance in clinical practice remains unknown. The objective of this study was to investigate the parental compliance with care considerations in a tertiary hospital in Türkiye.

METHODS

A questionnaire was administered to parents of patients with DMD to assess compliance with recommended frequencies of visits to healthcare providers and clinical tests. The data collected from the questionnaires were analyzed using cross-tables to explore if there were differences between ambulant and non-ambulant patients.

RESULTS

Sixty-one participants completed the questionnaire, most of whom were parents of ambulant patients (n= 44, 72.1%). The majority of parents complied with the recommended frequency of cardiac assessments. However, suboptimal compliance was observed in the rest of the assessments, including the PPSV23 and influenza vaccination rates, which were notably low across all patient groups. Compliance with anthropometric assessments and the use of corticosteroids with proper posology was significantly higher in ambulant patients. Compliance with respiratory and orthopedic evaluations was significantly higher among non-ambulant patients.

CONCLUSION

This study showed several areas in which compliance is insufficient. To improve compliance, future work should focus on home-based assessments, educational programs for patients, parents, and physicians, as well as raising awareness about the importance and timing of recommended vaccinations

KEYWORDS

Compliance, Duchenne muscular dystrophy, delivery of health care, guideline

ÖZ

AMAÇ

Duchenne Musküler Distrofisi (DMD) için uluslararası bakım önerileri 2018 yılında güncellenmiştir, ancak klinik uygulamalardaki uyum bilinmemektedir. Bu çalışmanın amacı, Türkiye'deki bir üçüncü basamak hastanede ebeveynlerin bakım önerilerine uyumunu araştırmaktır.

GEREÇ YÖNTEM

DMD'li çocukların ebeveynlerine, bakım önerilerinden elde edilen önerilen sıklıklara göre sağlık hizmeti sağlayıcı ziyaretleri ve klinik testlere uyumlarını değerlendiren bir anket uygulanmıştır. Anketlerden elde edilen veriler, ambulatuvar ve non-ambulatuvar hastalar arasında fark olup olmadığını incelemek amacıyla çapraz tablolar kullanılarak analiz edilmiştir.

BULGULAR

Ankete 61 ebeveyn katılmış olup, katılımcıların çoğunluğu ambulatuvar hastaların ebeveynlerinden oluşmaktaydı (n = 44, %72,1). Çoğu ebeveyn, kardiyak değerlendirmeler için önerilen sıklıklara uyum göstermiştir. Ancak PPSV23 ve influenza aşı oranları dahil diğer değerlendirmelerde optimal düzeyde uyum sağlanamamıştır. Antropometrik değerlendirmeye uyum ve kortikosteroidlerin uygun dozda kullanımı ambulatuvar hastalarda anlamlı olarak daha yüksek bulunmuştur. Solunum ve ortopedik değerlendirmelere uyum ise non-ambulatuvar hastalarda anlamlı olarak daha yüksektir.

SONUÇ

Bu çalışma, bakım önerilerine uyumun yetersiz olduğu çeşitli alanları ortaya koymuştur. Uyumun artırılması için evde yapılabilecek değerlendirmeler, hastalar, ebeveynler ve hekimler için eğitim programları ve önerilen aşıların önemi ve zamanlaması konusunda farkındalığın artırılması üzerinde durulmalıdır.

ANAHTAR KELİMELER

Duchenne musküler distrofisi, kılavuz, sağlık hizmetleri aktarımı, uyum

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

Pathogenic changes in the dystrophin-encoding DMD gene gives rise to life-threatening Duchenne muscular dystrophy (DMD), which is the most common muscular dystrophy with an incidence of approximately 1:5000 to 1:20000 in male live births (1). The variable but usually severe clinical course makes the multidisciplinary approach and strict follow-up indispensable. Experience and disease-specific clinical approach are essential for best-practice management of rare diseases including DMD. However, a lack of knowledge regarding the recognition of multisystem involvement and complications may cause delayed guidance and suboptimal management for the patients, leading to a worse health status and subsequently lower levels of participation and quality of life (2). Recently, a considerable literature has grown up around the theme of addressing the needs of patients whose survival time is quite prolonged by the efforts of multidisciplinary teams led by neuromuscular specialists. However, disruptions in the comprehensive care for individuals with DMD continue to ocur (3–5). This study seeks to assess the compliance of the parents of individuals with DMD regarding follow-up recommendations and to what extent the care complies with the international care considerations.

Materials and Methods

The present study was conducted on patients who were aged between 0 and 20 years old with DMD, who attended pediatric neurology department of Dokuz Eylül University Faculty Of Medicine during a period of 10 years between 2008 and 2017. Telephone interviews were conducted to assess parental compliance with internationally recommended care considerations. During the calls, parents were informed about the purpose of the study, and verbal consent was obtained. Demographic data were also recorded. The interviews included structured, closed-ended questions that focused on whether families adhered to the recommended follow-up schedule in various domains, including neuromuscular, respiratory, cardiac, and bone health assessments, physical rehabilitation, endocrine and orthopedic evaluations, swallowing-gastrointestinal management, steroid treatment, immunization, psychosocial functions, and genetic counseling. For each domain, parents were specifically asked whether the recommended evaluations or interventions had been performed at the suggested frequency based on international care guidelines. Compliance was categorized as either 'performed at recommended frequency' or 'not performed at recommended frequency'. The recommended frequency for assessingeach item was determined based on care considerations (3–5).

Evaluation of muscle strength, range of motion, and motor function tests at least twice per year, as well as twice per year visits to a neuromuscular specialist were considered optimal care for neuromuscular management (3). The outcome measures for cardiac management included a baseline evaluation at the time of diagnosis and an annual visit with a pediatric cardiologist. Baseline cardiac evaluation consisted of past and present cardiac medical history, family history, physical examination, electrocardiogram and non-invasive imaging techniques (echocardiogram for <6-7 years old children, cardiac magnetic resonance imaging for ≥6-7 years old children). Annual cardiological assessment included cardiac medical history, physical examination, electrocardiogram and non-invasive imaging techniques. The optimal assessment frequency for patients with cardiac symptoms was determined based on a recommendation of a pediatric cardiologist. Respiratory management consisted of annual and bi-annual spirometric evaluations for ambulant and non-ambulant patients, respectively (4). Orthopedic management consisted of a visit to an orthopedic surgeon and visual inspection of spine annually and bi-annually for ambulant and non-ambulant patients, respectively (4). Optimal gastrointestinal evaluations included twice-yearly assessments of dysphagia, constipation, gastroesophageal reflux, and gastroparesis. Since the recommended care considerations of nutritional and anthropometric profile assessments are covered by both gastroenterological and endocrinological evaluations, these particular items were analyzed among subgroups of endocrinological evaluations to avoid confusion. Outcome measures for endocrinological management consisted of screening for overweight, growth retardation, delayed puberty, and bone demineralization. Optimal anthropometric evaluations consisted of weight, height, and body mass index measurements were taken twice a year. The optimal frequency of puberty assessment using Tanner staging was performed every six months by the age of nine.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

Monitoring of bone health included annual assessments of dietary calcium intake and serum 25-hydroxy-vitamin D concentration (3). For the item of psychosocial assessment, due to the lack of a certain recommended frequency in 2018 guideline (5) except for at the time around diagnosis, before school entry and after a psychological function change, optimal compliance was evaluated according to whether or not they were screened during the aforementioned periods and whether or not they followed the recommendation to refer the patients to psychiatrists, psychologists, and therapeutic educators for psychological and neuropsychological assessments and interventions when necessary. Besides the National Immunization Program (NIP) of Türkiye (Table 1), (6) the pneumococcal polysaccharide vaccine 23 (PPSV23) and the annual inactivated influenza vaccines were questioned. For the item of genetic counseling, families were specifically asked whether they had received formal counseling from certified genetic specialists. While neurologists may provide basic genetic information, our study focused on evaluating compliance with formal genetic counseling recommendations.

Table 1. Turkish ministry of health national immunization program

Vaccines	Birth	End of 1 month	End of 2 months	End of 4 months	End of 6 months	End of 12 months	End of 18 months	End of 24 months	Elementary 1 degree	Elementary 8 degree
HepB	I	II			III					
BCG			I							
PCV			I	II		B				
DaPT-IPV-Hib			I	II	III		B			
OPV					I		II			
VAR						I				
MMR						I			II	
HepA							I	II		
DaPT-IPV									B	
Td										B

HepB, Hepatitis B Vaccine; BCG, Bacille Calmette-Guérin (Tuberculosis) Vaccine; PCV, Pneumococcal Conjugate Vaccination; OPV, Oral Polio Vaccine; VAR, Varicella vaccine; MMR, Measles, Mumps & Rubella Vaccine; HepA,Hepatitis A Vaccine; DaPT-IPV, Diphtheria and tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine;
Td,Tetanus and diphtheria toxoids adsorbed; B, Booster.

The data from the questionnaires were validated with hospital electronic system and archival records. Patients with data incongruity between interview results and archive records were not included. The data collected from the questionnaire were evaluated in terms of significant difference between patients with/without corticosteroid therapy, and ambulant/non-ambulant patients. These subgroup variables were selected because ambulation status reflects a major milestone in the disease course, directly influencing both accessibility to hospital visits, and parental psychological responses, whereas steroid therapy is the cornerstone of treatment in DMD, usually discontinued after loss of ambulation. In addition, parental concerns about steroid-related side effects may particularly affect their compliance with vaccination and preventive care, making it a relevant variable for analysis.

Ethical approval

The present study was conducted in accordance with the 1964 Declaration of Helsinki and approved by the Ethics Committee of Dokuz Eylül University Hospital (number of approval: 2017/21-56).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

Statistical analysis

All statistical analyses were conducted using Statistical Package for Social Sciences (SPSS) version 24.0 software for Windows (IBM Corp, Armonk, New York). The variables were investigated using visual (histograms and probability plots) and analytical methods (Kolmogorov–Smirnov test) to determine whether they were normally distributed. While continuous variables were expressed as mean ± standard deviation (SD) and median with minimum-maximum, categorical variables were expressed as a number and percentage. The chi-square and Fisher's exact tests were used to evaluate differences in categorical variables. A p value <0.05 was established as the threshold for determining statistical significance.

Results

Demographic features

A total of 78 patients were evaluated for a diagnosis of DMD, of whom 6 were excluded due to lack of telephone accessibility and 10 were excluded due to failure to obtain consent. One patient was further excluded because of the data inconsistency between the interview results and the electronic archive records. A total of 61 patients were enrolled, all of whose parents agreed to participate in the study. The cohort consisted entirely of male patients, with a median age of 106 (8-240) months. The majority of the cohort was ambulant (n= 44, 72.1%).

Compliance of the parents of the ambulant and non-ambulant patients

Fifty-seven percent (n= 34) of the interviewees reported regularly neuromuscular clinical visits, muscle strength assessment, and validated range of motion and motor function tests. Although compliance with neuromuscular follow-ups was more common in ambulant patients (n = 26, 29.1%), no significant difference was obtained (p = 0.396). Home-based and inpatient physical rehabilitations were received by 42 (68.8%) and 39 (64%) patients, respectively. There were no significant differences between ambulant and non-ambulant patients in either physical rehabilitation setting. While an orthopedic evaluation was not regularly performed for even half of the ambulant group, the majority of non-ambulant patients (n = 14, 82.3%) were regularly assessed in this particular respect, resulting in a significant difference between the two subgroups (p = 0.014). Overall, 57.4% (n = 35) of the cohort complied with orthopedic care considerations.

The majority of those who responded to the item about cardiological evaluations, regular electrocardiographic and echocardiographic examination rates were relatively high, with 52 patients each (85.2%). Neither of ambulant and non-ambulant patients demonstrated significant difference in electrocardiography (p = 0.692) and echocardiography (p = 0.682) rates. Cardiac magnetic resonance imaging was not performed in any of the patients. The relatively high rate of cardiac evaluations was not valid for the recommended visit frequency for a respiratory clinical assessment with spirometric examination, which was complied by only 15 (24.6%) patients. Subgroup analysis revealed that just over half of the non-ambulant patients (n = 9, 53%) were followed up with regular respiratory clinical assessments that included spirometric examinations, while only 13.6% (n = 6) of the patients complied with respiratory care considerations, resulting a significant difference between these subgroups (p = 0.001).

Detailed gastroenterological evaluations including assessments of dysphagia, constipation, gastroesophageal reflux, and gastroparesis were performed regularly in 30 (49.2%) patients without any significant difference between ambulant and non-ambulant patients (p = 0.132). Moreover, in 47.5% (n = 29) of the cohort, a complete endocrinological evaluation encompassing preventive strategies against impaired bone health, growth, and puberty was conducted. In the first part of the endocrinological evaluation, participants were asked whether they acted on the recommendation of monitoring anthropometric profiles. Of whom, 77% (n = 47) were followed up on a regular basis and the difference between the ambulant (n = 37, 84.1%) and non-ambulant (n = 10, 58.8%) groups was significant (p = 0.035). However, assessments of puberty and bone health were much lower in both ambulant and non-ambulant patients without any significant difference (p = 0.078). In 28 (46%) patients, psychosocial assessment was found to be optimal in align to care considerations.

The entire cohort was vaccinated according to the NIP of Türkiye which includes the pneumococcal conjugate vaccine (PCV13), but not the PPSV23. All patients were given a primary series of PCV13, at ages 2 and 4 months with a booster at age 12 months. However, the influenza and PPSV23 vaccines were

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

equally low in the cohort (n = 17, 27.9%) and its subgroups (ambulant; n = 15, 34.1% and non-ambulant; n = 2, 11.7%), revealing no significant difference (p = 0.081). Table 2 presents the results obtained from the statistical analysis of ambulant and non-ambulant patients.

Table 2. Compliance rates of the parents of ambulant and non-ambulant patients with Duchenne muscular dystrophy

	Ambulant (n= 44) *n, %*	Non-ambulant (n= 17) *n, %*	*P*
Neuromuscular evaluation			
Neuromuscular specialist visit	26 (59.1%)	8 (47%)	0.396
Muscle strength assessment	26 (59.1%)	8 (47%)	0.396
Range of motion assessment	26 (59.1%)	8 (47%)	0.396
Motor function tests	26 (59.1%)	8 (47%)	0.396
Physical rehabilitation (home-based)	32 (72.2%)	10 (58.8%)	0.293
Physical rehabilitation (inpatient)	30 (68.2%)	9 (53%)	0.266
Cardiac evaluation			
Baseline evaluation at diagnosis	44 (100%)	17 (100%)	ND
Electrocardiography	38 (86.4%)	14 (82.3%)	0.692
Echocardiography	37 (84.1%)	15 (88%)	0.682
Cardiac MRI	0	0	ND
Respiratory evaluation – spirometry	6 (13.6%)	9 (53%)	**0.001**
Orthopedic evaluation	21 (47.7%)	14 (82.3%)	**0.014**
Swallowing and gastrointestinal evaluation	19 (43.2%)	11 (64.7%)	0.132
Endocrinological evaluation			
Growth (height)	37 (84.1%)	10 (58.8%)	**0.035**
Weight	37 (84.1%)	10 (58.8%)	**0.035**
Bone health	24 (54.5%)	5 (29%)	0.078
Puberty	24 (54.5%)	5 (29%)	0.078
Psychosocial evaluation	19 (43.2%)	9 (53%)	0.493
Routine immunization schedule	44 (100%)	17 (100%)	ND
Influenza vaccine	15 (34.1%)	2 (11.7%)	0.081
Pneumococcal vaccine (PPSV23)	15 (34.1%)	2 (11.7%)	0.081
Genetic counselling	40 (91%)	15 (88%)	0.753
Corticosteroid therapy	24 (54.5%)	5 (29.4%)	0.078
Prednisolone	14 (32%)	1 (5.8%)	**0.035**
Deflazacort	10 (22.8%)	4 (23.5%)	0.947
Proper posology	23 (52.3%)	4 (23.5%)	**0.043**

*: Patients were evaluated with one or more of the motor function tests including six-minute walk test, North Star Ambulatory Evaluation, Brooke Upper Extremity Scale, and Vignos Lower Extremity Scale.
PPSV23, pneumococcal polysaccharide vaccine 23;ND, no difference sufficient for statistical analysis; MRI, magnetic resonance imaging; A p-value < 0.05 was considered as significant.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

Compliance of the parents of the patients with and without corticosteroid therapy

Twenty-nine (47.5%) patients were receiving corticosteroid therapy, in whom most of them were ambulant (n = 24, 54.5%). There was no significant difference in steroid use between ambulant and non-ambulant patients (p = 0.078). The median age of corticosteroid therapy initiation was 4.2 (4–5 years) years. Prednisolone use was significantly higher among ambulant patients (n = 14, 32%, p = 0.035). Deflazacort, however, was not significantly associated with the motor function classification of the patients (p = 0.947). Among patients receiving corticosteroid therapy, the use of guideline-recommended dosages (0.75 mg/kg/day for prednisolone and 0.9 mg/kg/day for deflazacort) were significantly more common in ambulant patients compared to non-ambulant patients (52.3% vs. 23.5%, p = 0.043). (Table 1).

Influenza vaccination rates were low in both the corticosteroid group (n= 8, 27.6%) and the no corticosteroid (n= 9, 29%) group withno significant difference between the two groups (p= 0.901). A similar result was observed for the pneumococcal vaccination rates between the two groups (p= 0.225); 7 (24.1%) and 12 (38.7%) patients received pneumococcal vaccine in the corticosteroid and no corticosteroid groups, respectively. Figure 1 provides the results obtained from chi-square analysis of vaccination status of the patients depending on wheter they received or not reeived corticosteroid therapy.

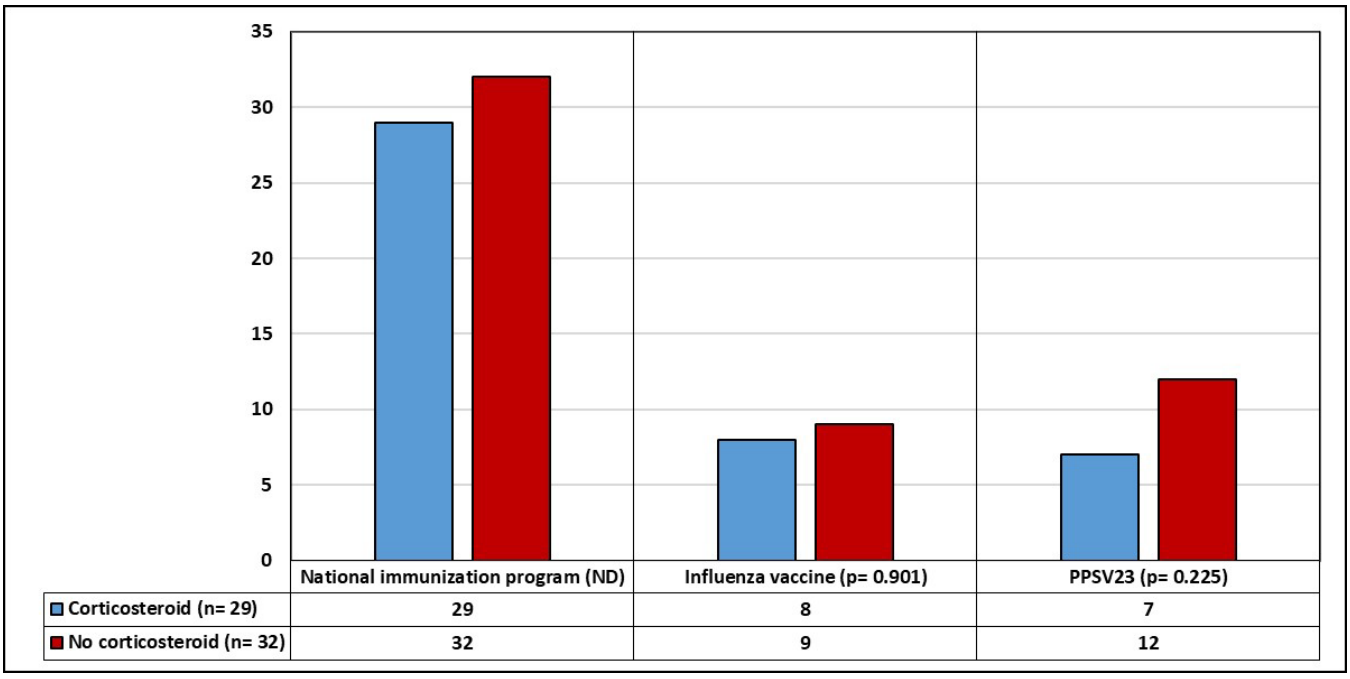


Figure 1. Bar graph showing vaccination status of individuals with Duchenne muscular dystrophy with and without corticosteroid therapy. ND, No difference sufficient for statistical analysis; PPSV23: Pneumococcal polysaccharide vaccine 23

Discussion

The present study revealed that the real-world experience of parental compliance among individuals with DMD in Türkiye falls short of the standards specified in international care considerations in many aspects. In which, the crucial role of regular visits to a neuromuscular specialist and the indispensability of various neuromuscular assessments, such as muscle strength, range of motion, and motor functional tests were highlighted (3). In our cohort, just over half of the participants met the recommendation to visit a neuromuscular specialist twice a year. Despite the results in a wide spectrum of 27-86.9% reported from different countries, (7–10). it is clear that more comprehensive education is needed

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

to ensure the parental compliance to these visits at the recommended frequency. Of note, in the present cohort, the frequency of neuromuscular assessments was the same with that of visit a neuromuscular specialist who performed these evaluations. In fact, rates of neuromuscular assessments were consistent with that of motor function tests ranging between 23 and 53.8% and range of motion assessments ranging from 31.9 and 64% in the literatüre (7,9). Despite no significant difference between ambulant and non-ambulant patients, lower compliance with neuromuscular evaluation in non-ambulant patients corresponds to suboptimal results in other studies (7,9,10) This result may be explained by the challenges in transportation of non-ambulant patients to the hospital as well as difficult transfer from a wheelchair to a treatment table, where these assessments are performed. The assessment methods should be revised so that these particular tests can also be performed while sitting on a wheelchair, especially in late-stage non-ambulant patients. More effort is therefore needed to increase parental compliance, since regular monitoring of function decline and prominence of contractures is essential for early interventions that have a major impact on mortality and morbidity.

In a larger-cohort study of patients from Germany, Italy, UK, and USA, insufficient compliance with cardiological evaluation recommendations was demonstrated, ranging between 34 and 66% (10). Nevertheless, there are a few areas in our study where practice was aligned with international care considerations about cardiac assessments, including baseline cardiological evaluation. Moreover, despite no significant difference between ambulant and non-ambulant patients, the rate of performing electrocardiographic and echocardiographic examinations at the recommended frequency was high, consistent with the recent literatüre (7,9) The observed increase in compliance rates in recent studies could be attributed to higher awareness of parents and patients, as well as easier accessibility to cardiac specialists over time.

In contrast to earlier findings with relatively high compliance rates of respiratory care considerations, (7,9,10) no evidence of sufficient follow-up for this particular item was detected in the present study. Moreover, in our study, poor compliance was significantly higher in ambulant patients, which is not in agreement with those obtained by Heutinck et al., (7) who reported a higher compliance in ambulant group.

The authors speculated that all recommended tests were no longer clinically relevant and might only cause burden on the non-ambulant individuals requiring non-invasive ventilation (7). On the other hand, several reports have shown similar proportions of compliance for both ambulant and non-ambulant patients (10–12). Our results displayed the expected pattern of increased compliance with care considerations in advanced disease stages, where there is growing concern about prognosis for patients and parents. Similarly, significantly higher rate in non-ambulant patients was valid for orthopedic evaluation with higher compliance rates in both groups. In fact, the rate observed in this study (57.4%) is far above the reported range of 18.5 and 40% in several studies (7,9,10). Although the rates of respiratory and orthopedic evaluations are higher than those reported in the literature, regular monitoring of both functions is imperative for early intervention. Therefore, these rates should be increased even more.

Swallowing dysfunction (dysphagia), which usually begins in the teenage years, is universal and progressive in patients with DMD, leading to weight loss, dehydration, episodes of suffocations, and aspirations (3,13) Although underlined in care considerations, very little attention has been paid to obtain data about constipation, gastroesophageal reflux, and gastroparesis in DMD patients, which are all assumed to be highly prevalent, underrecognized, and undertreated (3,14,15).Optimal swallowing and gastroenterological assessment at recommended frequency was achieved in only half of the cohort. This result highlights the fact that both physicians and parents should pay more attention to this particular issue in order to prevent further complications and increase the quality of life.

Due to multifactorial etiology, particularly corticosteroids, disruptions in growth, bone health and puberty are common in DMD patients (3,16,17) However, limited data on compliance with these care considerations have been published (7,9). Compliance with the recommended frequency of weight and height measurements was reported between 50.7and 63% and 29.2 and 57%, respectively (7,9). Our study with a compliance rate of 77% suggests that attention of the parents to this item has increased over time, although the frequency at which more intense focus is needed is still

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

insufficient. Nonetheless, compliance with evaluation of anthropometric profile was not specified separately in ambulant and non-ambulant patients, which was found at a significantly higher rate in ambulant patients in the present study, which could be partly attributed to difficulty of these measurements secondary due to the immobility. Another significant poor compliance was detected in assessments of bone health with a rate of 47.5% in our study, consistent with reported rates ranging from 29.5% to 68% (7,9).

Although the psychologically distressing effect of delayed puberty is stated in care considerations, (3) there remains a paucity of studies evaluating compliance of patients and/or parents with this particular issue. Although evaluations of bone health and puberty at the recommended frequency were higher in ambulant patients, these differences were not statistically significant in the present study, necessitating further works with larger cohorts and education for both parents and physicians, as corticosteroids remain the core therapy.

Along with longer survival in DMD patients who now live in their thirties and beyond, a whole new set of concern topics about mental health and psychosocial care requires to be brought on the agenda (18,19. However, the rate of compliance with psychosocial assessments remained low, with reported compliance rates varying between 15-64%. In our cohort, less than 50% of patients complied with an optimal psychosocial assessment, indicating that increased effort must be devoted to further integrate psychosocial management throughout entire disease course.

In our study, we assessed whether families had accessed specialty services, but we did not systematically evaluate how effectively these follow-ups were maintained. It is important to note that obtaining timely appointments with relevant specialties and subspecialties can be challenging due to health system limitations. These difficulties may contribute to reduced adherence to international care recommendations, as families may encounter barriers in securing regular follow-up visits. Although our findings suggest that such systemic challenges could negatively affect compliance, this remains a possible explanation rather than a directly measured outcome in our cohort.

Corticosteroids are the core standard therapy for patients with DMD based on evidence that they improve muscle strength and motor function, delay loss of ambulation, improve pulmonary function, reduce the need for scoliosis surgery, delay onset of cardiomyopathy, and overall leading to longer survival (20). However, corticosteroid use differed substantially in several recent studies, ranging between 46.4and 73%. (7–9,21). Despite vigorous efforts and education, the rate of past or current corticosteroid status was less than 50% in our cohort.

The low rates are thought to be largely due to concerns about possible side effects (8,21). Even though care considerations clearly and unequivocally emphasize the indispensable role of corticosteroids, concerns regarding the side effects of daily regimens have led to several alternative dosing schedules with lower/higher doses or intermittent pattern (21). Over time, initial posology and titration protocols have been established for deflazacort and prednisolone/prednisone (3). However, in the present study, inappropriate posology was common probably due to limited compliance with medical treatment, fear of side effects, or poor compliance with weight management. The fact that the proper posology was more common in ambulant patients can be explained by better compliance of these patients with neuromuscular management and anthropometric measurements.

Under the NIP of Türkiye, vaccines provide protection against 13 different infectious agents with 10 sessions in a total of 21 individual vaccinations (6] Although the PCV13, one of the vaccines included in the NIP, was given to each patient according to the schedule recommended by CDC and care consideration (5,22), the PPSV23 vaccine failed to be administered in the recommended schedule. At least eight weeks following completion of PCV13 vaccination, these patients were recommended to get the first of two doses of PPSV23, spaced five years apart (5,22). According to this schedule, the PPSV23 vaccination rate was only 27.9%, which was also valid for the inactivated influenza vaccine. A possible explanation for the very low vaccination rates compared to 75and 91.6% in current studies (7,9). is that the PPSV23 and influenza vaccines are expensive, unlike free of charge vaccines included in the NIP. This possible explanation is also supported by the fact of no significant difference between the influenza and PPSV23 vaccines in patients with and without corticosteroid therapy; the rates of these vaccines were almost

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:65-75

equally low in both groups, whereas vaccines in NIP were consummate.

These results suggested that the low vaccination rates may be due to economic reasons rather than corticosteroid-vaccine interaction concerns. Although economic concerns were frequently mentioned informally by caregivers during clinical encounters, the survey did not include a structured item addressing this issue. Therefore, this interpretation should be considered preliminary. Additionally, it is highly likely that insufficient awareness among caregivers and even some healthcare providers about the importance and timing of vaccines such as PPSV23 and the influenza vaccine for patients with DMD also contributes significantly to the low vaccination rates observed in our study. Further work-up should be undertaken to improve vaccination rates by increasing the availability of these vaccinations and efforts to reduce possible prejudices against vaccines.

Overall, poor compliance with many assessments can be explained by the large number of assessments recommended based on care considerations, and it may not be feasible for parents to implement all of these assessments. However, aside from giving up these frequencies, even more frequent evaluations may be required in personalized programs. Besides, as the disease progresses, the increase in compliance with cardiac, respiratory and gastroenterological evaluations may have led to the neglect of evaluations in other areas. Developing home-based care strategies for patients who fail frequent hospital visits may be the solution for optimal care.

Conclusion

We demonstrated that iseveral areas of care considerations need improvement. However, there are a few areas in which practice aligns well with recommendations. We recommend increasing efforts even further to educate patients and parents in detail about the incontrovertible benefits of full compliance with care considerations.

Funding
None.

Conflict of Interest
None.

Acknowledgments
We thank all the patients and families who participated in the study.

References

1. Waldrop MA, Flanigan KM. Update in Duchenne and Becker muscular dystrophy. Curr Opin Neurol 2019;32:722–7. https://doi.org/10.1097/WCO.0000000000000739
2. Bendixen RM, Senesac C, Lott DJ, Vandenborne K. Participation and quality of life in children with Duchenne muscular dystrophy using the International Classification of Functioning, Disability, and Health. Health Qual Life Outcomes 2012;10:43. https://doi.org/10.1186/1477-7525-10-43
3. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and neuromuscular, rehabilitation, endocrine, and gastrointestinal and nutritional management. Lancet Neurol 2018;17:251–67. https://doi.org/10.1016/S1474-4422(18)30024-3
4. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 2: respiratory, cardiac, bone health, and orthopaedic management. Lancet Neurol 2018;17:347–61. https://doi.org/10.1016/S1474-4422(18)30025-5
5. Birnkrant DJ, Bushby K, Bann CM, et al. Diagnosis and management of Duchenne muscular dystrophy, part 3: primary care, emergency management, psychosocial care, and transitions of care across the lifespan. Lancet Neurol 2018;17:445–55. https://doi.org/10.1016/S1474-4422(18)30026-7
6. Republic of Türkiye Ministry of Health, National Immunization Program in Türkiye, Available from https://asi.saglik.gov.tr/bagisiklama-programi-ve-asi-takvimi/asi-takvimi.html (Accessed October 24, 2025)
7. Heutinck L, Houwen-van Opstal SLS, Krom YD, et al. Compliance to DMD Care Considerations in the Netherlands. J Neuromuscul Dis 2021;8:927–38. https://doi.org/10.3233/JND-210670
8. Vry J, Gramsch K, Rodger S, et al. European Cross-Sectional Survey of Current Care Practices for Duchenne Muscular Dystrophy Reveals Regional and Age-Dependent Differences. J Neuromuscul Dis 2016;3:517–27. https://doi.org/10.3233/JND-160185
9. Andrews JG, Conway K, Westfield C, et al. Implementation of Duchenne Muscular Dystrophy

Care Considerations. Pediatrics 2018;142. https://doi.org/10.1542/peds.2017-4006
10. Landfeldt E, Lindgren P, Bell CF, et al. Compliance to Care Guidelines for Duchenne Muscular Dystrophy. J Neuromuscul Dis 2015;2:63–72. https://doi.org/10.3233/JND-140053
11. Rodger S, Woods KL, Bladen CL, et al. Adult care for Duchenne muscular dystrophy in the UK. J Neurol 2015;262:629–41. https://doi.org/10.1007/s00415-014-7585-3
12. Finder JD, Birnkrant D, Carl J, et al. Respiratory care of the patient with Duchenne muscular dystrophy: ATS consensus statement. Am J Respir Crit Care Med 2004;170:456–65. https://doi.org/10.1164/rccm.200307-885ST
13. Toussaint M, Davidson Z, Bouvoie V, Evenepoel N, Haan J, Soudon P. Dysphagia in Duchenne muscular dystrophy: practical recommendations to guide management. Disabil Rehabil 2016;38:2052–62. https://doi.org/10.3109/09638288.2015.1111434
14. Kraus D, Wong BL, Horn PS, Kaul A. Constipation in Duchenne Muscular Dystrophy: Prevalence, Diagnosis, and Treatment. J Pediatr 2016;171:183–8. https://doi.org/10.1016/j.jpeds.2015.12.046
15. Borrelli O, Salvia G, Mancini V, et al. Evolution of gastric electrical features and gastric emptying in children with Duchenne and Becker muscular dystrophy. Am J Gastroenterol 2005;100:695–702. https://doi.org/10.1111/j.1572-0241.2005.41303.x
16. Lamb MM, West NA, Ouyang L, et al. Corticosteroid Treatment and Growth Patterns in Ambulatory Males with Duchenne Muscular Dystrophy. J Pediatr 2016;173:207-213.e3. https://doi.org/10.1016/j.jpeds.2016.02.067
17. West NA, Yang ML, Weitzenkamp DA, et al. Patterns of growth in ambulatory males with Duchenne muscular dystrophy. J Pediatr 2013;163:1759-1763.e1. https://doi.org/10.1016/j.jpeds.2013.08.004
18. Colvin MK, Poysky J, Kinnett K, et al. Psychosocial Management of the Patient With Duchenne Muscular Dystrophy. Pediatrics 2018;142:S99–109. https://doi.org/10.1542/peds.2018-0333L
19. Saito T, Kawai M, Kimura E, et al. Study of Duchenne muscular dystrophy long-term survivors aged 40 years and older living in specialized institutions in Japan. Neuromuscul Disord 2017;27:107–14. https://doi.org/10.1016/j.nmd.2016.11.012
20. Biggar WD, Skalsky A, McDonald CM. Comparing Deflazacort and Prednisone in Duchenne Muscular Dystrophy. J Neuromuscul Dis 2022;9:463–76. https://doi.org/10.3233/JND-210776
21. Griggs RC, Herr BE, Reha A, et al. Corticosteroids in Duchenne muscular dystrophy: major variations in practice. Muscle Nerve 2013;48:27–31. https://doi.org/10.1002/mus.23831
22. Centers for Disease Control and Prevention. Pneumococcal Vaccine Recommendations. Updated October 26, 2024. Available from: https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/index.html (Accessed October 24, 2025)

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Attitudes of health professionals towards healthy nutrition and prevention of hypertension; cross-sectional correlational study

Sağlık çalışanlarının sağlıklı beslenme ve hipertansiyondan korunmaya yönelik tutumları: Kesitsel-ilişki arayıcı çalışma

Hakime ASLAN[1]
Feride KAPLAN[2]
Hanife ÇELİK[3]

[1] Department of Fundamental of Nursing, Faculty of Nursing, Inonu University, Malatya, Türkiye
[2] Department of Medical Services and Techniques, Goksun Vocational School, Kahramanmaras Sutcu Imam University, Kahramanmaras, Türkiye
[3] Disabled Care and Rehabilitation Program, Vocational School of Health Services, Bingol University, Bingol, Türkiye

Healthy Nutrition and Hypertension
Received: 05.03.2025
Accepted: 23.09.2025
DOI:10.18614/dehm.1873836

Corresponding author
Hakime ASLAN
ORCID ID: 0000-0003-1495-3614
hakime.aslan@inonu.edu.tr

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

ABSTRACK

BACKGROUND

This study was conducted to evaluate the attitudes of healthcare professionals toward healthy nutrition and the prevention of hypertension.

METHODS

The study was a cross-sectional-correlational study. The study was conducted in a public hospital in eastern Türkiye between September and December of 2022. The study population consisted of all healthcare professionals working in the hospital (N:957). A sample of 356 professionals was selected based on a power analysis. 37.1% of the population was surveyed. 'The Attitude Scale for Healthy Nutrition' and 'Attitudes Scale towards Prevention of Hypertension' were used to collect data. The data were analysed using the SPSS 22 package program. Numbers, percentages, means, one-way ANOVA, independent sample t-test, Pearson correlation and linear regresion tests were used to evaluate the data.

RESULTS

Health workers received a total score of 73.19±11.30 on the attitude scale for healthy nutrition and demonstrated positive attitudes. They received 107.21±23.65 points on the attitudes scale towards prevention of hypertension and also had positive attitudes. A weak positive correlation was found between attitudes toward healthy nutrition and attitudes toward preventing hypertension (r : 0.386). Weekly working hours, alcohol consumption, dieting, and healthy nutrition were determined to be variables affecting attitudes toward healthy nutrition. Educational level, years of employment, weekly working hours, and healthy nutrition were found to affect attitudes toward the prevention of hypertension.

CONCLUSION

As a result, health professionals had positive attitudes toward healthy nutrition and preventing hypertension. As positive attitudes toward healthy nutrition increased, so did attitudes toward preventing hypertension.

KEYWORDS

Hypertension, healthy nutrition, health professional

ÖZ

AMAÇ

Bu araştırma, sağlık çalışanlarının sağlıklı beslenme ve hipertansiyondan korunmaya yönelik tutumlarını değerlendirmek amacıyla yürütülmüştür.

GEREÇ YÖNTEM

Çalışma kesitsel-ilişki arayıcı türde bir çalışmadır. Çalışma Eylül-Aralık 2022 tarihleri arasında Türkiye'nin doğusundaki bir kamu hastanesinde yürütülmüştür. Çalışma evrenini hastanede çalışan tüm sağlık çalışanları oluşturmuştur (N:957). Örneklemini, power analizi ile belirlenen 356 profesyonel oluşturmuştur. Evrenin %37,1'ine ulaşılmıştır. Veri toplamak için, 'Sağlıklı Beslenmeye İlişkin Tutum Ölçeği' ve 'Hipertansiyondan Korunma Tutumları Ölçeği' kullanılmıştır. Veriler SPSS 22 paket programı kullanılarak analiz edildi. Verilerin değerlendirilmesinde sayı, yüzde, ortalama, tek yönlü varsans analizi (ANOVA), t-testi, Pearson korelasyon ve Linear regresyon testleri kullanıldı.

BULGULAR

Sağlık çalışanlarının sağlıklı beslenmeye ilişkin tutum ölçeğinden toplam 73,19±11,30 puan aldıkları ve olumlu tutuma sahip oldukları bulunmuştur. Hipertansiyondan korunma tutumları ölçeğinden ise toplam 107,21±23,65 puan aldıkları ve tutumlarının olumlu olduğu bulunmuştur. Sağlıklı beslenmeye yönelik tutum ile hipertansiyondan korunma tutumları arasında pozitif yönde zayıf düzeyde anlamlı ilişki olduğu belirlenmiştir (r: 0,386, p < 0,001). Haftalık çalışma saati, alkol tüketimi, diyet ve sağlıklı beslenmeye önem verme durumu sağlıklı beslenme konusundaki tutumları etkileyen değişkenler olduğu belirlenmiştir. Eğitim düzeyi, çalışma süresi, haftalık çalışma saati ve sağlıklı beslenmeye önem verme durumu, hipertansiyonun önlenmesi konusundaki tutumları etkileyen değişkenler olduğu belirlenmiştir.

SONUÇ

Sonuç olarak, sağlık çalışanlarının sağlıklı beslenme ve hipertansiyondan korunmaya yönelik tutumlarının olumlu olduğu ve sağlıklı beslenmeye yönelik olumlu tutum arttıkça hipertansiyondan korunmaya yönelik tutumların da olumlu yönde arttığı belirlendi.

ANAHTAR KELİMELER

Hipertansiyon, sağlıklı beslenme, sağlık çalışanı

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Nutrition is essential for sustaining life, ensuring growth and development, promoting productivity, and protecting health. Adequate nutrition is defined as ingesting the energy required to perform the bodily functions, while a balanced diet is defined as ingesting the required amount of energy from all nutrients (1). An adequate and balanced diet make up healthy nutrition and is defined as an intake of foods that is appropriate for the age, sex and physiological status of the individual (1, 2). Healthy nutrition is important for health at all stages of development. While a healthy diet reduces the risk of developing chronic diseases, it is also important for improving quality of life alongside other lifestyle changes (1, 3). Failure to maintain a healthy nutrition can increase susceptibility to many diseasessuch as diabetes, obesity, cancer, osteoporosis, and high blood pressure (3, 4).

Healthy nutrition is also one of the factors influencing the productivity of working people (5). It enables the working individuals to gain resistance to disease by strengthening the immune system, to be more efficient in the working environment, to increase the level of attendance at work and to reduce the rate of occupational accidents (5, 6). Differences in the working conditions affect employees' nutrition (7). This situation affects health workers who work on a shift schedule more. In these individuals, healthy eating is affected by situations such as the absence of daily and social life due to shift work, changes in eating times and frequency due to irregular sleep and working conditions, the acquisition of negative eating habits by resorting to food in the form of snacks, excessive fat and carbohydrate content of meals, generally cold intake and consumption, and less daily exercise programmes (7, 8). Nutritional and metabolic disorders and elevated triglyceride and cholesterol levels have been reported in healthcare workers who are unable to maintain a healthy nutrition. There is also an increased risk of gastrointestinal diseases such as gastritis and ulcers, metabolic diseases such as diabetes mellitus, and cardiovascular diseases such as deep vein thrombosis and hypertension (7-9).

Hypertension is the most common chronic disease among healthcare workers. It is a cardiovascular disease affecting 1.13 billion people worldwide, remaining a global public health problem, and causing high mortality and morbidity rates (10-12). Hypertension, defined as systolic and diastolic blood pressure >140/90 mm/Hg, is one of the leading causes of premature death by significantly increasing the risk of heart, brain, kidney, and other diseases (10, 13). It is possible to reduce the prevalence of hypertension by improving the quality of the diet of healthcare workers, whose susceptibility to hypertension is increased by the irregularity of shift work, and by promoting a healthy diet (12). At this point, it is very important to educate health care workers to eat a diet rich in vegetables, fruits and seafood; to use olive oil in meals; to reduce alcohol consumption and sodium intake; to consume high-fibre, low-fat foods in a varied and balanced way, as much as the body needs; to create an environment that allows them to be physically active; to ensure that their body weight remains at an ideal level; to take remedial steps towards a healthy diet; and to ensure that health care workers comply with these steps (15-18). One study reported that in order to achieve the expected quality of life, working people should make healthy eating a way of life, develop healthy eating behaviour change programmes, introduce physical activity policies, and encourage working people by building gyms in working areas (6). Health services are provided by health workers and it is very important to improve the quality of life of health workers, to ensure their physical, mental and social well-being and to protect their health in order to prevent any disruption of these services, material and moral loss and negative situations such as occupational accidents (12, 14). Considering the prevalence of HT worldwide and in Türkiye, and despite the constant emphasis on the importance of healthy nutrition in prevention, it has been observed that the relationship between the two concepts has been addressed to a very limited extent in national and international literature. In particular, there is a severe lack of research evaluating the attitudes of healthcare professionals, who form the basis of patient care, on this subject. It is believed that evaluating the attitudes of healthcare workers towards healthy nutrition and prevention of hypertension will both raise awareness on the subject and contribute to the improvement of patient care.

In light of this information, the purpose of this study is to contribute to the existing research on this topic by examining the attitudes of healthcare professionals regarding healthy nutrition and the prevention of hypertension.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Materials and Methods

Type of research

This is a cross-sectional correlational study. It assessed the attitudes of health professionals working in a hospital in eastern Türkiye toward healthy nutrition and their approaches to preventing hypertension, examining the possible relationships between these variables. This study is both cross-sectional, as it aims to describe the current situation through data collectedover a specific time period, and descriptive-corelational, as it aims to analyse the relationships between variables.

Population and sample of the study

The study population consisted of 957 healthcare professionals (nurses, midwives, doctors, pharmacists, physiotherapists, dieticians, paramedics, radiographers, laboratory technicians, anaesthetists) working in a Kahramanmaraş province in eastern Türkiye. As a result of the power analysis performed to determine the sample size, it was determined that a minimum of 327 participants should be included in the study based on the criteria of 5% bias, 95% confidence interval, 0.5% effect size, and 97% population representativeness. The data collection process continued in this direction until a sufficient sample size of 356 participants was reached, at which point the research was completed. Participants were selected from the population using simple random sampling.

Inclusion criteria

- At least 1 year of professional experience,
- Healthcare workers who volunteered to participate in the study were included.

Exclusion criteria

- Incorrect/incomplete filling out of data collection forms,

Data collection and instruments

Data were collected between September and December of 2022. Ethics committee and institutional approvals were obtained before the study began, and informed consent was obtained from participants by adding an explanatory text to the beginning of the form that explained the purpose of the study. After obtaining institutional approval from the hospital where the study would be conducted, the online form was shared with the managers and the form was given to the healthcare professionals. To reach members of all professions, data collection forms were shared via WhatsApp groups after consulting with the departments responsible for healthcare personnel, including the chief physician's office, the nursing services directorate, and personnel managers. An explanation of the study was included at the beginning of the data collection form, and participants who agreed to take part were asked to indicate their consent by checking a box before answering the questions. Do to the voluntary nature of participation and the use of an online survey, we were enable to reach an equal number of participants from each profession or at the desired level. The subjectivity and potential for response bias inherent in self-report data collection methods could not be completely eliminated. “Information Form”, “Attitude Scale for Healthy Nutrition (ASHN)” and “Attitudes Scale towards Prevention of HT (ASPH)” were used to collect data.

Information form

The researchers designed the form in accordance with the literature (5, 6, 19). It consists of 14 questions that assess the age, sex, marital status, level of education, smoking and alcohol consumption habits, exercise habits, presence of chronic diseases, and nutritional status of healthcare workers.

Attitude scale for healthy nutrition (ASHN)

Tekkurşun Demir and Cicioğlu developed the ASHN, and validity and reliability studies were conducted (2). The ASHN consists of 21 items and four sub-dimensions. The lowest score that can be obtained from the scale is 21 and the highest score is 105. Participants’ scores are evaluated as 21 points very low, 23-42 points low, 43-63 points medium, 64-84 points high, and 85-110 points ideally high attitudes towards healthy nutrition.

The internal consistency coefficients of the scale were found to be 0.83 for the ASHN factor (2). In this study, the Cronbach alpha coefficient of the scale was found to be 0.75.

Attitudes scale towards prevention of HT (ASPH)

The ASPH is the first attitude scale developed by Albayrak and Şengezer to prevent hypertension (19). The scale consists of 26 items and five sub-dimensions. The ASPH is a 5-point Likert scale, with items ranging from 'strongly disagree' to 'strongly agree'. The range of scores that can be obtained from the scale varies between 26 and 130, and high scores indicate that individuals have a positive attitude towards hypertension prevention. The Cronbach alpha internal consistency coefficient of the scale was found to be 0.91 in the

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

original study (19). In this study, the Cronbach alpha coefficient of the scale was calculated to be 0.98.

Analysis

Data were analysed using the SPSS 22 package. Numbers, percentages, means, one-way ANOVA (Bonferroni for further analysis), Mann-Whitney U-test, t-test in independent groups, Kruskal-Wallis H-test, and correlation tests were used to evaluate data related to descriptive characteristics. As a result of the normality test (Shapiro-Wilk), parametric tests were used in the data set that was accepted as normal, and non-parametric tests were used in the data set that did not show a normal distribution. Linear regression Enter model was used to evaluate the effect of healthy eating attitudes on attitudes toward preventing hypertension. The results were evaluated with 95% confidence interval and significance at $p<0.05$ level.

Ethical considerations

Permission was obtained from the Ethics Committee for Scientific Research and Publication at Inönü University of Health Sciences (approval number: E-33117789-044-74764). The necessary permissions were obtained from the scale owners via e-mail. When participants clicked on the participation link, the purpose of the study was explained and they were informed that participation was voluntary.

Results

The mean age of the health workers who participated in the study was 30.7±7.82 years. 62.4% were female and 53.9% were Bachelor's degree. 45.5% of the participants were nurses, and 45.8% had 0-5 years of work experience. 46.6% worked 40 hours per week, and 56.7% worked in shifts. In terms of body mass index, 67.1% were of normal weight. 70.5% did not smoke, 88.2% did not drink alcohol, 52.5% took occasional exercise, 46.1% had a family history of hypertension, and 90.2% considered a healthy nutrition important (Table 1).

Table 1. Sociodemographic characteristics of participants

Variable		Group	Number	Percent
Age	30.7±7.82			
Gender		Woman	222	62.4
		Male	134	37.6
Education level		High school (SML)	23	6.5
		Associate degree	92	25.8
		Bachelor's degree	192	53.9
		Master's degree	49	13.8
		Doctor	36	10.1
Profession		Nurse	162	45.5
		Midwife	48	13.5
		Dietitian	5	1.4
		Health technicians	67	18.8
		Other	38	10.7
Marital status		Married	189	53.1
		Single	161	45.2
		Divorced	6	1.7
Occupation		Doctor	36	10,1
		Nurse	162	45,5
		Midwife	48	13,5
		Dietitian	5	1,4
		Health technicians	67	18,8
		Other	38	10,7
Year of employment		0-5 years	163	45.8
		6-10 years	96	27.0
		11-14 years	41	11.5
		15 years and over	56	15.7
Weekly working hours		32 hours	20	5.6

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

	40 hours	166	46.6
	48 hours	102	28.7
	56 hours and over	68	19.1
How it working	Daytime only	127	35.7
	Night only	27	7.6
	Day/night shifts	202	56.7
Body mass index (BMI)	<18.5 (Weak)	13	3.7
	18.5-24.9 (Normal)	239	67.1
	25.0-29.9 (Fat)	88	24.7
	>30.0 (Overweight)	16	4.5
Smoking status	Uses	90	11.8
	Does not use	251	70.5
	Dropped out	15	4.2
Alcohol use status	Uses	42	11.8
	Does not use	314	88.2
Sporting habits	I do sports regularly	33	9.3
	I do sports occasionally	187	52.5
	I don't do sport	136	38.2
Dieting status	Yes	105	29.5
	No	251	70.5
Family history of hypertension	Yes	164	46.1
	No	192	53.9
Attaching importance to healthy nutrition	Yes	321	90.2
	No	35	9.8

SML, Health Vocational High School; %,Percentage

Healthcare workers received a total score of 73.19±11.30 on the ASHN. These results demonstrate that healthcare workers have positive attitudes towards healthy nutrition. Additionally, it was also found that healthcare professionals' attitudes were positive and high on the sub-dimensions of this scale, including knowledge of nutrition, feelings about nutrition, and perceptions of healthy and unhealthy nutrition.

Healthcare professionals received a total score of 107.21±23.65 on the ASPH. This result shows that the attitudes of healthcare professionals towards hypertension prevention are positive and high. It was found that their attitudes to the sub-dimensions of the scale, namely prevention and control, habit and lifestyle, dietary attitudes, mental status and physical activity, and knowledge of diseases and risks were also high (Table 2). The comparison of the socio-demographic characteristics of the participants and the mean scores of the ASHN and the ASPH are shown in Table 3.

A comparison of the socio-demographic characteristics of the participants and the mean scores of the ASHN revealed a statistically significant difference between the mean scores of the ASHN and the variables of weekly working hours (the group that created a significant difference: those who worked 32 hours per week), alcohol consumption status, dieting status and the importance of healthy eating ($p < 0.05$). No significant difference were found between other demographic variables and ASHN mean scores.

A statistically significant difference ($p < 0.05$) was found between the participants' levels of education (the group that made a significant difference: those with an associate degree), years of employment (the group that made a significant difference: those who had worked more than 15 years), weekly working hours (the group that made a significant difference: those who worked 32 hours a week), and the variables of importance attached to healthy nutrition and the mean scores of the ASPH. Individuals who prioritize healthy nutrition may have contributed to this result by participating in the study at a higher rate. No significant difference was found between the other variables and the mean scores of the ASPH (Table 3).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Table 2. Mean scores of the ASHN and ASPH and its sub-dimensions

Scale Dimensions	Min	Max	X ± SD	Cronbach α
Information about nutrition	5.00	25.00	19.15±6.51	
Feeling towards nutrition	6.00	30.00	18.92±5.79	
Positive nutrition	5.00	25.00	16.07±5.69	0.75
Malnutrition	5.00	25.00	19.03±4.60	
Attitude Scale for Healthy Nutrition (ASHN)	27.00	100.00	73.19±11.30	
Prevention and control	8.00	40.00	32.89±7.89	
Habits and lifestyle	6.00	30.00	24.64±6.07	
Nutrition attitude	4.00	20.00	16.09±3.36	
Mental state and physical activity	3.00	15.00	12.68±2.57	
Disease and risk information	5.00	25.00	20.89±5.03	0.98
Attitudes Scale towards Prevention of HT (ASPH)	29.00	130.00	107.21±23.65	

X, Mean; SD, Standard deviation

Table 3. Comparison of participants' socio-demographic characteristics and mean scores on the ASHN and ASPH

Variable	Group	Number	ASHN Test and significance	ASPH Test and significance
Gender	Woman	222	73.9±11.3	108.4±23.3
	Male	134	71.9±11.2	105.1±24.1
			t:1.644	t:1.271
			p = 0.101	p = 0.205
Education level	High school (SML)	23	71.0±9.8	109.6±21.8
	Associate degree[F]	92	72.5±11.0	100.2±29.3
	Bachelor's degree	192	73.9±11.7	108.7±21.5
	Master's degree	49	73.2±10.4	113.0±16.9
			KW:4.792	KW:7.302
			p = 0.188	**p = 0.007***
Marital status	Married	189	73.9±11.8	108.2±21.0
	Single	161	72.1±10.5	106.3±25.7
	Divorced	6	78.7±13.8	106.2±32.9
			KW:4.827	KW:0.508
			p = 0.185	p = 0.917
Occupation	Doctor	36	73.0±9,8	109.6±20,8
	Nurse	162	72.5±10,8	110.2±19,2
	Midwife	48	73,9±10,7	108.7±19,2
	Dietitian	5	74.2±10,2	113,0±20,7
	Health technicians	67	71.0±9,8	107.6±21,8
	Other	38	72.1±10,4	108.2±20,3
			KW:0.407	KW:1.779

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

			p = 0.418	p = 0.103
Year of employment	0-5 years	163	71.9±10.1	106.4±25.5
	6-10 years	96	74.7±12.4	113.5±14.6
	11-14 years	41	74.1±12.6	104.0±25.0
	15 years and over[F]	56	73.3±11.4	100.8±27.1
			F:1.420	F:4.004
			p = 0.454	**p = 0.008***
Weekly working hours	32 hours[F]	20	67.8±8.5	92.5±13.5
	40 hours	166	74.2±11.6	109.9±21.2
	48 hours	102	74.1±11.2	105.7±22.9
	56 hours and over	68	70.7±10.7	108.0±23.4
			KW:3.407	KW:4.779
			p = 0.018*	**p = 0.003***
How it working	Daytime only	127	73.6±12.0	105.2±26.4
	Night only	27	73.6±11.0	106.6±22.4
	Day/night shifts	202	72.8±10.8	108.4±21.9
			KW:0.221	KW:0.291
			p = 0.895	p = 0.865
Body mass index (BMI)	<18.5 (Weak)	13	73.3±11.7	111.7±10.0
	18.5-24.9 (Normal)	239	73.1±11.6	104.1±23.5
	25.0-29.9 (Fat)	88	74.1±10.7	103.7±25.7
	>30.0 (Overweight)	16	73.7±8.7	108.0±20.4
			KW:0.047	KW:2.751
			p = 0.988	p = 0.432
Smoking status	Uses	90	71.4±11.3	104.2±26.5
	Does not use	251	73.9±11.2	108.3±22.5
	Dropped out	15	70.3±11.6	105.9±23.0
			KW:4.545	KW:1.378
			p = 0.103	p = 0.502
Alcohol use status	Uses	42	69.5±11.2	105.5±26.7
	Does not use	314	73.6±11.2	107.4±23.2
			t:,-2.235	t:-0.472
			p = 0.026*	p = 0.638
Sporting habits	I do sports regularly	33	77.4±11.7	106.3±26.1
	I do sports occasionally	187	73.0±11.8	105.5±24.7
	I don't do sport	136	72.3±10.2	105.7±21.2
			F:2.777	F:1.249
			p=0.064	p=0.288
Dieting status	Yes	105	75.1±12.4	108.5±24.6
	No	251	72.3±10.7	106.6±23.2
			t:2.127	t:0.685
			p = 0.034*	p = 0.494
Family history of HT	Yes	164	74.2±11.6	106.5±24.0
	No	192	72.3±11.0	107.7±23.3
			t:1.589	t:-0.485
			p = 0.113	p = 0.628
Attaching importance to healthy nutrition	Yes	321	73.8±11.3	110.7±23.2
	No	35	67.1±9.14	101.9±23.2
			t:3.380	t:2.383
			p = 0.001*	**p = 0.016***

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Age	r: 0.102 p = 0.054	r : -0.079 p = 0.139

*p < 0.05; 𝒯: Tukey test; F, One way ANOVA (Tukey); t, independent sample t-test; KW, Kruskal Wallis H-testi

There was a moderately significant positive relationship between attitudes towards healthy eating and attitudes towards hypertension prevention (r : 0.386, p < 0.001). Once again, a positive and moderately significant relationship was found between knowledge of diet (r : 0.655, p < 0.001) and positive dietary habits (r : 0.503, p < 0.001) and attitudes toward preventing hypertension. However, a weakly significant negative correlation was found between feelings about food (r :-0.373, p < 0.001) and poor dietary habits (r : -0.131, p < 0.05) and attitudes toward hypertension prevention. There was a negative correlation between negative feelings about food, poor dietary attitudes and attitudes toward hypertension prevention (Table 4).

Table 4. The relationship between nurses' ASHN and ASPH

		1	2	3	4	5	6	7	8	9	10	11
Information about nutrition (1)	r	1										
	p											
Emotion towards nutrition (2)	r	-0.536**	1									
	p	0.000										
Positive nutrition (3)	r	0.726**	-0.426**	1								
	p	0.000	0.000									
Malnutrition (4)	r	-0.206**	0.530**	-0.056	1							
	p	0.000	0.000	0.295								
Attitude Scale for Healthy Nutrition (ASHN) total (5)	r	0.583**	0.205**	0.681**	0.532**	1						
	p	0.000	0.000	0.000	0.000							
Prevention and control (6)	r	0.652**	-0.387**	0.507**	-0.163**	0.366**	1					
	p	0.000	0.000	0.000	0.002	0.000						
Habits and lifestyle (7)	r	0.629**	-0.384**	0.479**	-0.181**	0.333**	0.949**	1				
	p	0.000	0.000	0.000	0.001	0.000	0.000					
Attitude to nutrition (8)	r	0.562**	-0.252**	0.430**	-0.003	0.410**	0.799**	0.790**	1			
	p	0.000	0.000	0.000	0.961	0.000	0.000	0.000				
Mental state and physical activity (9)	r	0.554**	-0.239**	0.428**	0.026	0.422**	0.794**	0.761**	0.791**	1		
	p	0.000	0.000	0.000	0.630	0.000	0.000	0.000	0.000			
Knowledge of disease and risk (10)	r	0.636**	-0.390**	0.484**	-0.153**	0.348**	0.960**	0.949**	0.786**	0.802**	1	
	p	0.000	0.000	0.000	0.004	0.000	0.000	0.000	0.000	0.000		
Attitudes Scale towards Prevention of HT (ASPH) total (11)	r	0.655**	-0.373**	0.503**	-0.131*	0.386**	0.981**	0.970**	0.865**	0.852**	0.976**	1
	p	0.000	0.000	0.000	0.014	0.000	0.000	0.000	0.000	0.000	0.000	

**. Correlation value is significant at <0.01 level

*. Correlation value is significant at <0.05 level

The effect of attitudes towards healthy nutrition on attitudes towards hypertension prevention was analysed using regression analysis. The relationship between dependent and independent variables was examined graphically, and the predicted and observed values showed a linear distribution. The normality of regression residuals was tested using the

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Shapiro-Wilk test, and the significance level was found to be p = 0.194. In addition, histogram and P-P plot graphs also supported normality. Homoscedasticity Assumption: When the distribution of the residuals with the predicted values was examined, it was seen that the assumption of constant variance was met. The residuals were randomly distributed and no distinct pattern was observed. Autocorrelation Assumption: The Durbin-Watson test result was found to be 1.92, and this value indicates that there is no autocorrelation (1.5 < DW < 2.5). As a result, the validity of the findings is supported because the regression model meets the basic assumptions. The study found that health workers' attitudes toward healthy nutrition positively affected their attitudes toward hypertension prevention (β=0.386). Furthermore, 14.9% of the total variance in the dependent variable of ASHN was explained by the total ASPH score and this result was statistically significant (R = 0.386, R2=0.149, p < 0.001) (Table 5).

Table 5. The effect of attitudes towards healthy nutrition on hypertension prevention attitudes

	Unstandardised Coefficients		**Standardised Coefficients**						
Model	B	SE	Beta	t	Sig.	F	Sig	R	R^2
Constant	48.135	7.594		6.338	0.000				
ASHN total	0.807	0.103	0.386	7.872	0.000	61.963	0.000[b]	0.386[a]	**0.149**

Dependent variable, ASHN total ; Predictors, (Constant), ASPH total

Discussion

This study showed that the attitudes of healthcare professionals towards healthy nutrition and hypertension prevention were generally positive. The high scores obtained on the Attitude Scale for Healthy Nutrition and the Attitude Scale for Prevention of Hypertension indicate that healthcare professionals are highly awarene of these issues. Their awareness of nutrition and lifestyle issues is important for protecting their own health and providing the right advice to their patients.

This study showed that healthcare professionals had very positive attitudes toward healthy nutrition. High scores were obtained in the sub-dimensions of knowledge of nutrition, feelings about nutrition, positive nutrition, and poor nutrition. Consistent with the findings of this study, Bıçakcı's study of healthcare workers revealed that their attitudes toward healthy nutrition were generally positive (20). Overall, the literature shows that healthcare workers generally have positive attitudes toward healthy nutrition and chronic disease prevention. Torquati et al., assessed the dietary and physical activity habits of healthcare workers and found that healthcare professionals had a positive tendency to adopt a healthy lifestyle (21). When the sub-dimensions of the Attitude Scale for Healthy Nutrition Attitude Scale for Healthy Nutrition were analysed, it was found that healthcare professionals had a high level of nutritional knowledge and positive attitudes toward nutrition. This shows that healthcare workers use the information in their daily lives and value healthy nutrition highly. Spronk et al., reported in their study that people who focus on nutrition are more likely to adopt healthy nutrition habits, positively affecting their overall health (22).

When analysing the relationship between attitudes towards healthy nutrition and demographics, this study found that there was a significant difference between weekly working hours, alcohol consumption, diet and the importance of healthy nutrition. In particular, those who worked 40 hours per week were found to have more positive attitudes than those working more hours. These findings are consistent with the literature on the impact of working hours on health, suggesting a direct correlation between working hours and employees' quality of life and health behaviors. Dembe et al., reported that working hours and personal habits directly affecthealth behaviour (23). In Bıçakçı's study, when gender differences were examined, it was found that the total scores and nutritional knowledge levels of female participants on the ASHN scale were significantly higher than those of male participants, which was interpreted as women developing more positive attitudes towards healthy nutrition and having

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

more awareness of nutritional knowledge (20). However, this study did not find a significant relationship between ASHN scores and gender. This difference may be due to various factors such as the sampling characteristics of the study, the level of professional knowledge, and the nutritional awareness of the participants. Because healthcare professionals are more aware of healthy living due to their profession, there may not have been a significant difference between male and female participants. It should also be considered that sample size and distribution may also affect this result. Future studies examining the effect of gender variables on attitudes toward healthy nutrition with larger, more heterogeneous samples will contribute to a more comprehensive evaluation of the findings in the literature.

The results of this study showed that healthcare professionals had positive attitudes towards hypertension prevention. Similarly, this study found that attitudes regarding prevention and control, habits and lifestyle, dietary habits, mental state and physical activity, and knowledge of the disease and risks were also highly positive. Furthermore, the study found that health professionals were aware of the importance of these sub-dimensions. The high score obtained from the ASPH developed by Albayrak and Şengezer indicates that healthcare workers are willing to take necessary precautions to reduce the risk of hypertension (19). According to a study conducted by Sengwan and Puoane the level of knowledge of hypertension among healthcare professionals plays an important role in people's attitudes towards the disease and the quality of interventions offered (24). This clearly demonstrates the impact that healthcare professionals have on promoting healthy lifestyles and reducing the prevalence of hypertension in the community. Although participants in structured interviews identified heredity, physical inactivity, and excessive consumption of salty and fatty foods as risk factors for hypertension, the study concluded that their knowledge of these risk factors was limited (24).

This study examined the relationship between the ASPH and demographics and found that variables such as education level, years of employment, weekly working hours, and the importance of healthy nutritionsignificantly affected attitudes toward hypertension prevention. The observation of more positive attitudes, especially among participants with more than 15 years of work experience and had a bachelor's degree, suggests that experience and education effectively develop awareness and attitudes. This finding supports that experience and education play an important role in strengthening the attitudes of healthcare workers toward hypertension prevention. A study conducted in India by Gupta et al., analysed the relationship between hypertension awareness, treatment and control, as well as educational level and found that educational level significantly affected attitudes toward hypertension prevention (25). It was found that individuals with higher levels of education were more aware of hypertension and had more positive attitudes toward hypertension, whereas individuals with lower levels of education had lower levels of awareness of hypertension, diabetes and hypercholesterolaemia, adherence to treatment, and smoking cessation. Similarly, Bıçakcı found that health perceptions increased with higher levels of education (20).

Additionally,health perceptions were higher among participants with an underweight or normal body mass index than among overweight or obese individuals. These findings show that an ideal weight positively affects health perception. On the other hand, Owolabi et al., found that a significant proportion of healthcare professionals were affected by work-related stress and that perceived work stress was significantly associated with a higher prevalence of hypertension (26). Johnson and Lipscomb reported that long working hours are associated with acute effects such as stress and fatigue, as well as negative health behaviours such as smoking. They are also associated with chronic effects such as cardiovascular and musculoskeletal diseases (27). According to the Attitude Scale for Prevention of Hypertension developed by Albayrak and Şengezer, the high awareness and positive attitudes of healthcare professionals are an important factor in hypertension prevention (19). These findings are consistent with the World Health Organization report which states that healthcare professionals play a critical role in the prevention and management of hypertension and that increased awareness of hypertension will have a positive impact on public health (28). In this study, it was also found that there is a significant difference between the importance given to healthy nutrition and attitudes toward hypertension prevention. It is believed that the positive relationship between thoughts and attitudes played a role in this outcome.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:77-90

Additionally, the higher participation rate of individuals who are more concerned about healthy nutrition may have influenced the results, since the data for this study were collected online. Future research studies should take potential volunteer bias into account. This study found a significant positive relationship between a healthy nutrition and attitudes toward hypertension prevention. In a study conducted by Hajjar and Kotchen, it was found that the southern region of the United States of America had the highest systolic and diastolic blood pressure, the highest consumption of monounsaturated fatty acids, polyunsaturated fatty acids, cholesterol, and the lowest amount of fibre (29). Cena and Calder reported that fresh fruits and vegetables, whole grains, legumes, beans, seeds and nuts were more common among healthy foods, while fatty and processed meats, and animal products were less common (30). The study also found that dietary patterns reduce the risk of cardiovascular disease, cancer and other non-communicable diseases. In this direction, they reported that more efforts should be made to integrate healthy nutrition and lifestyles into the daily lives of communities around the world and to make healthy diets accessible, affordable and sustainable. They also reported that high salt intake may increase susceptibility to the later development of hypertension in children, and that the basis for healthy blood pressure is a healthy diet, adequate physical activity, stress reduction, and adequate potassium intake (31). This study found that there was a positive and moderately significant relationship between attitudes toward healthy eating and attitudes toward hypertension prevention. In addition, negative emotions toward nutrition and poor nutritional attitudes were found to negatively affect hypertension prevention attitudes, while healthcare professionals' positive attitudes toward healthy nutrition were found to positively affect hypertension prevention attitudes.

Limitations and bias of the study

In this study, data were collected via an online form and distributed to participants on a voluntary basis. Limitations related to various types of bias were considered. Selection Bias: This study is limited to healthcare professionals working in the same institutional structure in a specific geographical region. This limits the generalisability of the results to the entire population of healthcare professionals.

However, since the aim of the study is to reveal the current situation in a specific institutional context, this sample is considered appropriate for the intended research purpose. Volunteer Bias: The questionnaire was distributed on a voluntary basis. Therefore, it is possible that individuals who are more interested or sensitive to the subject participated. This situation was noted when interpreting the results, and it was stated that this tendency could affect the representativeness of the data.

Observation bias

The questions in the survey form were prepared to be as clear and understandable as possible; to prevent misunderstanding by participants, the necessary sections were revised by five nurses after a pre-application. However, the subjectivity and response bias inherent in data collection processes based on self-reporting cannot be completely eliminated. This situation has been noted in the data collection process.

Survivorship bias

It was determined that 72.8% of the participants had less than 10 years of experience in the profession. This indicates that the sample consisted predominantly of younger healthcare workers who had recently started their careers. This limited the generalisability of the results, and differences based on experience level were considered when making interpretations.

Conclusion

This study shows that healthcare professionals generally have positive attitudes toward healthy nutrition and the prevention of hypertension. Weekly working hours, alcohol consumption, dieting, and healthy nutrition were found to affect attitudes toward healthy nutrition. Educational level, years of employment, weekly working hours, and healthy nutrition were found to affect attitudes toward the prevention of hypertension.

Based on the results of this study, healthcare professionals' positive attitudes toward healthy nutrition and prevention of hypertension should be supported, and strategies should be developed to further strengthen these attitudes. Regular in-service training programmes should be organised on healthy nutrition and prevention of

hypertension. Training should be structured specifically for those with low levels of education, those who are new to the profession, those with long professional experience, and those working in health technician fields. It is recommended that healthcare personnel working in shift systems be provided with special support programmes on healthy nutrition and stress management, and that their weekly working hours be regulated. Considering that alcohol consumption and dieting affect attitudes, individual health responsibility awareness should be developed. Healthcare workers should be encouraged to be role models. In addition, seminars/workshops focused on hypertension and nutrition should be organised to update the knowledge of all healthcare workers.

Although the limitations of the sample group included in this study reduce the generalisability of the research results, this does not completely invalidate the study. Future studies should include larger and more heterogeneous sample groups.

Informed consent

The researchers informed the participants about the study and obtained their consent.

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

Acknowledgements

We thank all of the health professionals who participated in the study.

References

1. T.C. Ministry of Health. Healthy eating and physical activity teacher handbook [Internet]. Ankara: Ministry of Health; 2019.
2. Tekkurşun Demir G, Cicioğlu Hİ. Attitude Scale for Healthy Nutrition (ASHN): validity and reliability study. Gaziantep Univ J Sport Sci. 2019;4(2):256-274. doi:10.31680/gaunjss.559462
3. Şengün N, Pala R, Çınar V, Akbulut T, Larion A, Padulo J, et al. Alterations in biomarkers associated with cardiovascular health and obesity with short-term lifestyle changes in overweight women: the role of exercise and diet. Medicina (Kaunas). 2024;60(12):2019. doi:10.3390/medicina60122019
4. Gürbüz P, Yetiş K. Determination of nutritional habits of health services vocational school students. J Inonu Univ Voc Sch Health Serv. 2018;6(2):54-63.
5. Demir HP, Elkin N, Barut AY, Bayram HM, Averi S. Evaluation of sleep duration and nutritional status of health personnel working in shifts. IGUSABDER. 2017;2:89-107.
6. Yurtseven E, Eren F, Vehid S, Köksal S, Erginöz E, Erdoğan M. Evaluation of the dietary habits of white-collar workers. KTD. 2014;15(1):20-26. doi:10.18229/ktd.74513
7. Learthart S. Health effects of internal rotation of shifts. Nurs Stand. 2000;14(47):34-36. doi:10.7748/ns2000.08.14.47.34.c2895
8. Özdemir GP, Ökmen CA, Yılmaz O. Shift work disorder and psychological and physical effects of shift work. Curr Approaches Psychiatry. 2018;10(1):71-83.
9. Dominguez LJ, Gea A, Ruiz-Estigarribia L, Sayón-Orea C, Fresán U, Barbagallo M, et al. Low dietary magnesium and overweight/obesity in a Mediterranean population: a detrimental synergy for the development of hypertension. The SUN Project. Nutrients. 2021;13(1):125. doi:10.3390/nu13010125
10. World Health Organization. Hypertension [Internet]. Geneva: WHO; 2022.
11. Geaney F, Fitzgerald S, Harrington JM, Kelly C, Greiner BA, Perry IJ. Nutrition knowledge, diet quality and hypertension in a working population. Prev Med Rep. 2015;2:105-113. doi:10.1016/j.pmedr.2014.11.008
12. Kılıç M, Çetinkaya F. Prevalence of health problems in health workers in Yozgat city centre and factors affecting them. J Health Sci. 2011;20(3):184-194.
13. Jiang SZ, Lu W, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. Exp Ther Med. 2016;12(4):2395-2399. doi:10.3892/etm.2016.3667
14. Çalışkan Z, Saykılı S. Healthy lifestyle behaviors and anthropometric measurements of provincial health directorate employees. Ankara J Health Sci. 2020;9(2):1-12. doi:10.46971/ausbid.769912

15. Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek EPIC study. Am J Clin Nutr. 2004;80(4):1012-1018. doi:10.1093/ajcn/80.4.1012
16. Unal RN. Nutrition in the prevention and treatment of hypertension: current approaches. Bes Diy Derg. 2015;43(1):78-86.
17. Ekim M. The importance of nutrition and lifestyle changes in the treatment of hypertension. Bozok Med J. 2018;8(2):80-85. doi:10.16919/bozoktip.335813
18. Demir H. Investigation of healthy lifestyle behaviours of health workers [master's thesis]. Konya: Necmettin Erbakan University; 2024.
19. Albayrak Z, Şengezer T. Attitude Scale for Prevention of HT development in individuals who have a family member with hypertension. Turk J Fam Pract. 2022;26(2):53-65. doi:10.54308/tahd.2022.52296
20. Bıçakçı HS. Evaluation of health perception and nutritional habits of university hospital health personnel during the COVID-19 pandemic [expertise thesis]. Konya: Necmettin Erbakan University; 2022.
21. Torquati L, Pavey T, Kolbe-Alexander T, Leveritt M. Promoting diet and physical activity in nurses. Am J Health Promot. 2017;31(1):19-27. doi:10.4278/ajhp.141107-LIT-562
22. Spronk I, Kullen C, Burdon C, O'Connor H. Relationship between nutrition knowledge and dietary intake. Br J Nutr. 2014;111(10):1713-1726. doi:10.1017/S0007114514000087
23. Dembe AE, Erickson JB, Delbos RG, Banks SM. The impact of overtime and long work hours on occupational injuries and illnesses. Occup Environ Med. 2005;62(9):588-597. doi:10.1136/oem.2004.016667
24. Sengwana MJ, Puoane T. Knowledge, beliefs and attitudes of community health workers about hypertension. Curationis. 2004;27(1):65-71. doi:10.4102/curationis.v27i1.958
25. Gupta R, Sharma KK, Gupta BK, Gupta A, Gupta RR, Deedwania PC. Educational status-related disparities in cardiovascular risk factors in India. Heart Asia. 2015;7(1):1-6. doi:10.1136/heartasia-2014-010551
26. Owolabi AO, Owolabi MO, OlaOlorun AD, Olofin A. Work-related stress perception and hypertension among health workers. Afr J Prim Health Care Fam Med. 2012;4(1):307. doi:10.4102/phcfm.v4i1.307
27. Johnson JV, Lipscomb J. Long working hours, occupational health and work organization. Am J Ind Med. 2006;49(11):921-929. doi:10.1002/ajim.20383
28. Global Health Council. A global brief on hypertension: silent killer, global public health crisis [Internet]. Washington DC; 2013.
29. Cena H, Calder PC. Defining a healthy diet: evidence for contemporary dietary patterns. Nutrients. 2020;12(2):334. doi:10.3390/nu12020334
30. Samadian F, Dalili N, Jamalian A. Lifestyle modifications to prevent and control hypertension. Iran J Kidney Dis. 2016;10(5):237-263.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

Impact of previous abdominal surgery on shunt revision in pediatric ventriculoperitoneal shunt cases at a single center

Önceden geçirilmiş abdominal cerrahinin pediatrik ventrikülöperitoneal şant revizyonu üzerindeki etkisi: Tek merkezli bir çalışma

Koray UR[1]
Ege COŞKUN[1]
Fazlı Oğuzhan DURAK[1]
Hatun Mine ŞAHİN[1]
Oktay ULUSOY[2]
Ceren KIZMAZOĞLU[1]
Orhan KALEMCİ[1]
Ercan ÖZER[1]
Serhat ERBAYRAKTAR[1]

[1] Dokuz Eylul University Faculty of Medicine, Department of Neurosurgery, Izmir, Türkiye
[2] Dokuz Eylul University Faculty of Medicine, Department of Pediatric Surgery, Izmir, Türkiye

Impact of Abdominal Surgery on Pediatric Shunt Revision
Received: 17.07.2025
Accepted: 23.12.2025
DOI:10.18614/dehm.1873851

Corresponding author
Hatun Mine ŞAHİN
ORCID ID: 0000-0003-4537-2599
sahinhatunmine@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

ABSTRACT

BACKGROUND

The main problems encountered during postoperative follow-up after ventriculoperitoneal shunt surgeries are ventriculoperitoneal shunt malfunction and related complications. One of the reasons for malfunction is problems with the distal catheter. This study aimed to analyze pediatric cases and establish whether there is a link between a history of abdominal surgery and the need for shunt revision.

METHODS

We conducted a retrospective analysis of 138 pediatric patients who underwent surgery at our institution between 2010 and 2018.

RESULTS

In the first year postoperatively, 33.2% of the patients required shunt revision. Furthermore, we found a significant relationship between a history of abdominal surgery and the requirement for shunt revision ($p < 0.0001$). Additionally, the length of the proximal catheter inside the ventricles appeared to affect the need for shunt revision ($p < 0.001$).

CONCLUSION

Similar to other studies, we believe that our findings show that a history of abdominal surgery impacts the need for shunt revision. This contributes to existing literature on the topic.

KEYWORDS

Abdominal surgery, pediatric, shunt revision, ventriculoperitoneal shunt surgery

ÖZ

AMAÇ

Ventriküloperitoneal (VP) şant disfonksiyonu ve ilişkili komplikasyonlar, VP şant cerrahileri sonrası postoperatif takipte karşılaşılan başlıca sorunlardır. Şant disfonksiyonunun nedenlerinden biri distal katetere ilişkin sorunlardır. Bu çalışmada, çocuk hastalar retrospektif olarak analiz edilerek, önceden geçirilmiş abdominal cerrahinin şant revizyon ihtiyacıyla olası ilişkisi araştırılmıştır.

GEREÇ YÖNTEM

2010 ile 2018 yılları arasında kurumumuzda cerrahi müdahale geçirmiş 138 pediatrik hasta retrospektif olarak analiz edilmiştir.

BULGULAR

Ameliyat sonrası ilk yıl içinde hastaların %33,2'sinde şant revizyonu gerekmiştir. Önceden geçirilmiş abdominal cerrahi öyküsü ile şant revizyon gereksinimi arasında anlamlı bir ilişki bulunmuştur ($p < 0.0001$). Ayrıca, ventrikül içindeki proksimal kateter uzunluğunun da şant revizyonu üzerinde etkili olduğu saptanmıştır ($p < 0.001$).

SONUÇ

Bulgularımız, önceki çalışmalarla paralel olarak, abdominal cerrahi öyküsünün şant revizyon gereksinimi üzerinde etkisi olduğunu göstermektedir. Bu sonuç mevcut literatüre katkı sağlamaktadır.

ANAHTAR KELİMELER

Abdominal cerrahi, ventrikülperitoneal şant cerrahisi, pediatrik, şant revizyonu

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

Despite its relatively high complication rate, ventriculoperitoneal (VP) shunt surgery is the gold standard for treating pediatric hydrocephalus (1-4). Mechanical and infectious complications persist despite advances in shunt material technology. The shunt malfunction rate in the pediatric population is 20–85% (5); this rate is lower in adults at 17–33% (6,7). The malfunction rate in the first year postoperatively is 30–50% (2, 8-11). The main causes of shunt malfunction are infection, overdrainage, and mechanical obstruction (disconnection, breakdown, or passage obstruction) (8,12).

Patients who have undergone VP shunt surgery may also experience gastrointestinal complications, including (i) abdominal pseudocyst formation, (ii) ascites, (iii) bladder perforation, and (iv) bowel-related complications (appendicitis, intestinal perforation, intestinal adhesions, anal extrusion of the peritoneal catheter, abdominal herniation, and migration of the distal end to the scrotal sac) (13,14).

However, no study has examined the impact of previous abdominal surgery on VP shunt revision rates. Intestinal adhesion after abdominal surgery is a natural process. However, its impact on the risk of shunt revision has not yet been clearly demonstrated. This retrospective study reviewed cases involving pediatric patients with VP shunts. Revisions made during follow-up and complications were analyzed in detail.

Materials and Methods

This study was approved by the ethics committee at our university. We examined all patients who underwent VP shunt placement between 2010 and 2018 and found 328 adult and pediatric patients. Patients >18 years old were excluded, and 138 pediatric cases were eventually included in this study. The demographics, type of hydrocephalus, history of abdominal surgery, duration of hospitalization and follow-up, location of the proximal catheter, complications, reasons for revision, number of shunt surgeries, and number of external ventricular drainage (EVD) surgeries were noted.

The senior neurosurgeon performed all pediatric procedures, and shunt placement was performed free hand, based on the bony landmarks and related measurements; no neuronavigation was used. Preferably, the parietal bone on the right side (if there was no previous surgical scar present) was used, and a burr hole was placed at a point 2–4 cm more cranially located than the Frazier point. The dura was opened cross-shaped, and epidural hemostasis was achieved. Then the proximal shunt catheter was sent as the length measured preoperatively by computed tomography (CT). A mini-laparotomy technique was used for the abdominal portion of the operation. All the patients received perioperative cefazolin as a prophylactic antibiotic.

The preoperative Evans ratio (ER) was calculated for all the patients (2). Postoperatively, we noted the placement of the proximal catheter and its length inside the ventricles. Intraoperative and postoperative complications were assessed, and the time to and reasons for revisions were noted. We then compared the revision rates between patients with and without previous abdominal surgery.

Statistical Package for Social Sciences version 22.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. The mean and standard deviation (SD) were calculated, the t-test was used for group comparisons, and the Kaplan–Meier estimator was used to analyze the cumulative revision-free rates. The log-rank test was used to determine survival rates, and statistical significance was set at $p < 0.05$.

Results

All findings are summarized in Table 1. Of the 138 pediatric patients, 73 (52.9%) were female, and 65 (47.1%) were male. The mean age at diagnosis was 3.66±5.45 years. Additionly, the mean follow-up duration was 2.69±3.05 years. The mean time to revision surgery was 10.84±12.40 months, with 64 (46.4%) patients requiring this surgery.

During the first year postoperatively, 56 (33.2%) patients required shunt revision surgery. A statistically significant relationship was found between a history of abdominal surgery and the need for shunt revision ($p < 0.0001$) (Figure 1). Additionally, a proximal catheter length inside the ventricular system of <2 cm significantly impacted the requirement for shunt revision ($p < 0.001$). The calculated odds ratio values for a history of abdominal surgery and catheter length inside the ventricles were 3.36 (95% confidence interval (CI): 1.85–6.11) and 3.61 (95% CI: 1.75–7.44), respectively.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

Table 1. Patient demographics, postoperative CT findings and complications

	All patients	Patients with previous abdominal operation	Patients without previous abdominal operation
Gender			
Female	73(52.9%)	24(17.4%)	49(35.5%)
Male	65(47.1%)	19(13.8%)	46(33.3%)
Age of diagnosis (years)	3.66±5.45	3.74±5.44	3.63±5.49
Chiari Malformation	10(7.2%)	3(2.2%)	7(5.1%)
Previous operation for meningomyelocele	19(13.8%)	8(5.8%)	11(8%)
Previous operation for intracranial tumour	15(10.9%)	4(2.9%)	11(8%)
Hydrocephalus types			
Communicating	72(52.2%)	20(14.5%)	52(37.7%)
Idiopathic Normal Pressure	3(2.2%)	1(0.7%)	2(1.4%)
Posthemorrhagic	17(12.3%)	8(5.8%)	9(6.5%)
Obstructive	42(30.4%)	14(10.1%)	28(20.3%)
Benign Intracranial Hypertension	4(2.9%)	0	4(2.9%)
# of EVD surgeries (with revisions)	24(17.4%)	11	13
1	13(9.4%)	6(4.4%)	7(5.1%)
2	7(5.1%)	3(2.2%)	4(2.9%)
3	1(0.7%)	1(0.7%)	0(0.0%)
4	2(1.4%)	0(0.0%)	2(1.4%)
7	1(0.7%)	1(0.7%)	0(0.0%)
EVD duration (days)	16.04±19.17	19.81±25.81	12.84±11.76
# of VP shunt surgeries (with revisions)		43(31.2%)	95(68.8%)
1	71(51.4%)	2(1.4%)	69(50%)

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

2	28(20.3%)	16(11.6)	12(8.7%)
3	20(14.5%)	14(10.1)	6(4.3%)
4	7(5.1%)	4(2.9%)	3(2.2%)
5	5(3.6%)	1(0.7%)	4(2.9%)
6	1(0.7%)	1(0.7%)	0(0.0%)
7	4(2.9%)	3(2.2%)	1(0.7%)
9	2(1.4%)	2(1.4%)	0(0.0%)
Duration of follow-up (years)	2.69±3.05	2.63±2.90	2.72±3.10
Exitus	10 (7.2%)	3(2.2%)	7(5.1%)
Preoperative Evans Ratio	0.46±0.13	0.44±0.11	0.46±0.14
Postoperative CT			
Optimal position (correct ventricle at foramen of Monroe level)	49(35.5%)	19(13.8%)	30(21.7%)
Tip crossed the midline towards the contralateral ventricle	50(36.2%)	14(10.1%)	36(26.1%)
Correct ventricle, tip not at foramen of Monroe level	34(24.6%)	8(5.2%)	26(18.8%)
Tip twisted	5(3.6%)	2(1.4%)	3(2.2%)
Proximal catheter, length inside the ventricle (cm)			
<1	10(7.2%)	2(1.4%)	8(5.8%)
1-<1.5	10(7.2%)	5(3.6%)	5(3.6%)
1.5-<2	13(9.4%)	4(2.9%)	9(6.5%)
>2	105(76.9%)	32(23.2%)	73(52.9%)
Complications			
Meningitis	7(5.1%)	5(3.6%)	2(1.4%)
Intraventricular hemorrhage	3(2.2%)	2(1.4%)	1(0.7%)
Subdural hematoma	2(1.4%)	1(0.7%)	1(0.7%)
Subdural hygroma	3(2.2%)	1(0.7%)	2(1.4%)

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

Protrusion of the distal catheter from anus	2(1.4%)	2(1.4%)	0(0%)
Superior sagittal sinus injury	1(0.7%)	1(0.7%)	0(0%)
Peritonitis	3(2.2%)	1(0.7%)	2(1.4%)
Intraabdominal abscess	4(2.9%)	4(2.9%)	0(0%)
Mechanical complicaitons			
Proximal obstruction	15(10.9%)	5 (11.6%)	10(10.5%)
Distal obstruction	7(5.1%)	5(11.6%)	2(2.1%)
Proximal fracture	2(1.4%)	1(2.3%)	1(1.1%)
Distal fracture	2(1.4%)	2(4.7%)	0
Disconnection	19(13.8)	5(11.6%)	14(14.7%)
Intraperitoneal cyst	3(2.2)	2(4.7%)	1(1.1%)
Catheter migration	4(2.9%)	2(4.7%)	2(2.1%)
Lengtening required	2(1.4%)	2(4.7%)	0
No malfunction	5(3.6%)	4(9.3%)	1(1.1%)
Revision			
Yes	64(46.4%)	32(23.2%)	32(23.2%)
No	74(53.6%)	11(8%)	63(45.7%)
Time to revision (months)	10.84±12.40	11.41±13.08	10.29±11.88
< 1 month	10(7.2%)	6(9.2%)	4(6.2%)
1-6 months	26(18.8%)	12(18.5%)	14(21.5%)
6-12 months	10(7.2%)	3(4.6%)	7(10.8%)
12-24 months	6(4.3%)	5(7.7%)	1(1.5%)
> 24 months	13(9.4%)	6(9.2%)	7(10.8%)

Twenty-five patients experienced perioperative or postoperative complications. In one patient with Crouzon syndrome, the burr hole was unintentionally placed on the superior sagittal sinus. The resulting bleeding was controlled, and the surgery was completed using an alternative burr hole. However, the patient required 8 weeks of follow-up in the paediatric intensive care unit (pICU) after surgery. After this challenging and instructive complication, the use of intraoperative Doppler ultrasound in patients with cranial vault anomalies became standardpractice in our clinic. In two patients with a history of abdominal surgery, the distal catheter protruded through the anus. Mechanical complications were observed in 59 (42.8%) patients; the most common cause was disconnection (13.8%).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

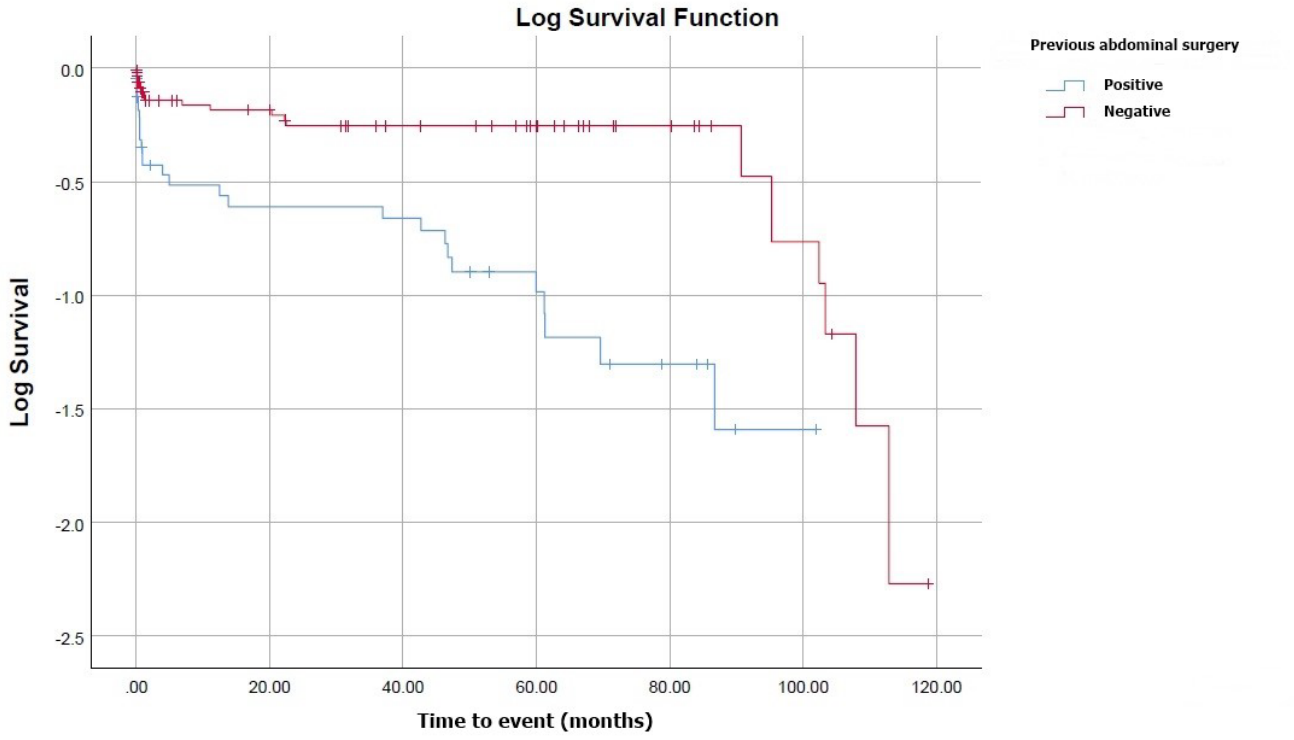


Figure 1. Kaplan-Meier estimator demonstrates time to event (shunt revision). Patients with a history of previous abdominal surgery are shown in blue, while those without are shown in red.

Discussion

Catheters placed during VP shunt surgery are intended to remain in place for the patient's lifetime. Thus, one of the main aims of the surgery is to prevent the need for any revision surgeries (2, 5, 12, 15). The factors affecting the need for revision surgeries have been widely studied. However, the impact of a history of previous abdominal surgery on revision rates has not been extensively investigated; this study retrospectively examined this topic. We also detail the reasons for the surgical revisions and complications.

The three main surgical options for distal catheter placement in VP shunt surgery are mini-laparotomy, laparoscopy, and percutaneous trocar-assisted techniques (16, 17). Possible technical complications include visceral perforation (within three months of surgery), extraperitoneal catheter positioning, distal obstruction, and pseudocyst formation (3). Risk factors for visceral perforation include younger age and the presence of meningomyelocele (18, 19).

Sefarinova et al. demonstrated that the percutaneous trocar-assisted technique carries a risk of abdominal visceral and vascular injury; however, they stated that there was no statistically significant difference between this technique and laparoscopy (3). Schucht et al. compared shunt malfunction rates in the laparoscopic and mini-laparotomy techniques. They found that the only difference was a higher rate of distal catheter malfunction in the mini-laparotomy group. The distal catheter malfunction rate in the mini-laparotomy group was 8%, whereas there were no cases of distal catheter malfunction in the laparoscopy group (1). No statistically significant difference was found when patients with a history of abdominal surgery were compared between the two groups

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

(1). In our study, there was a statistically significant association between a history of abdominal surgery and the need for shunt revision ($p < 0.0001$). However, when focusing specifically on distal catheter malfunction as the cause of revision, this difference was not statistically significant. All patients who underwent revision surgery had laparotomy performed again; however, the placement was performed using a different muscular and fascial route within the same incision.

Correct placement of the ventricular catheter is the most important factor in achieving revision-free survival (20, 21). Wan et al. proposed a five-point grading system based on the length of the catheter inside the ventricle (2). A catheter with a length of >2 cm inside the ventricle was considered a perfectly placed. Ventricle size was the most important factor in ensuring the proximal catheter was perfectly placed in the ventricle (2). In our study, 76.9% of the proximal catheters were >2 cm inside the ventricles. Additionally, the calculated odds ratio for revision was 3.61 (95% CI: 1.75–7.44) if the catheter length inside the ventricle was <2 cm.

Stone et al. demonstrated no relationship between the etiology of hydrocephalus and shunt malfunction in their study of 64 pediatric patients and 234 procedures (22). Anderson et al. showed that 30-day shunt malfunction is related to the etiology of hydrocephalus in adult patients in a study of 321 pediatric and 362 adult patients. However, no significant relationship was found in the pediatric population, despite performing a multivariate analysis. A significant relationship was found between shunt malfunction and whether the surgery was primary or secondary, and whether it was performed by one or multiple surgeons (with secondary surgery and single surgeon being more likely to cause shunt malfunction) (23). Similarly, Rocque et al. found a relationship between the etiology of hydrocephalus and shunt malfunction in univariate analyses. However, they were unable to demonstrate this in multivariate analyses (24).

This study had some limitations. Due to the limited number of patients, the different types of surgeries that patients with a history of abdominal surgery had undergone could not be evaluated in detail. Additionally, it was unclear whether patients had experienced any postoperative surgical site infections.

Very few studies in the current literature have investigated the direct relationship between the length of the peritoneal (abdominal) end of the shunt and the risk of shunt dysfunction (25). Instead, most available reports focus on other factors associated with distal malfunction, such as catheter configuration, the position or patency of distal slit openings, peritoneal adaptation, the relative shortening of the distal catheter due to patient growth, and the formation of abdominal pseudocysts (26, 27, 28, 29).

However, based on the insights gained from the present study and the gaps identified in the existing literature, we plan to systematically record the length of the distal (abdominal) catheter in our future cases. We will also assess its potential influence on shunt function through a prospective study reflecting our own clinical experience. This approach could provide valuable data to clarify whether peritoneal catheter length has a measurable impact on distal complications and contribute to optimization of ventriculoperitoneal shunt placement techniques in the future.

Overall, VP shunt surgery is the first-line treatment for hydrocephalus. Although highly effective, it is associated with a variety of complications. Despite technological and patient care developments, the incidence rates of these complications are far from decreasing. Previous studies have described several of these complications (5, 8, 12). One of the predisposing factors for such complications is a history of abdominal surgery, which was studied in detail in this study. We found that a history of abdominal surgery and a catheter length of less than 2 cm inside the ventricle had the greatest impact on shunt revision rates. We conclude that a previous history of abdominal surgery in the pediatric population increases the risk of shunt failure and thus the need for shunt revisions.

Conclusion

Ventriculoperitoneal shunt malfunction is a common and challenging complication during the postoperative period. Among the various causes, problems related to the distal catheter play a significant role. Prompt recognition and resolution of these issues is essential for enhancing long-term outcomes and reducing the need for shunt revisions in pediatric patients.

Conflicts of interest and source of funding
None declared

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:91-100

Acknowledgements

The authors received no technical, financial, or material support for this study. No individuals or institutions contributed to the work in a manner that requires acknowledgment.

Ethical approval

This study was approved by the Ethics Committee of Dokuz Eylul University with the decision number 2018/21-04, dated August 9, 2018.

References

1. Schucht P, Banz V, Trochsler M, Iff S, Krähenbühl AK, Reinert M, et al. Laparoscopically assisted ventriculoperitoneal shunt placement: a prospective randomized controlled trial. J Neurosurg. 2015 May;122(5):1058–67.
2. Wan KR, Toy JA, Wolfe R, Danks A. Factors affecting the accuracy of ventricular catheter placement. J Clin Neurosci Off J Neurosurg Soc Australas. 2011 Apr;18(4):485–8.
3. Serafimova M, Soleman J, Stoessel T, Guzman R, Constantini S, Roth J. Peritoneal insertion of shunts in children: comparison between trocar and laparoscopically guided insertion. Child's Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. 2021 Jan;37(1):115–23.
4. Hochstetler A, Raskin J, & Blazer-Yost, BL Hydrocephalus: historical analysis and considerations for treatment. Eur J Med Res 27, 168 (2022).
5. Mansoor N, Solheim O, Fredriksli OA, Gulati S. Shunt complications and revisions in children: A retrospective single institution study. Brain Behav. 2021 Nov;11(11): e2390.
6. Merkler AE, Ch'ang J, Parker WE, Murthy SB, Kamel H. The Rate of Complications after Ventriculoperitoneal Shunt Surgery. World Neurosurg. 2017 Feb; 98:654–8.
7. Coll G, Abed Rabbo F, de Schlichting E, Coste A, Chazal J, Garcier J-M, et al. Mechanical complications of cerebrospinal fluid shunt. Differences between adult and pediatric populations: myths or reality? Child's Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. 2021 Jul;37(7):2215–21.
8. Drake JM, Kestle JR, Milner R, Cinalli G, Boop F, Piatt JJ, et al. Randomized trial of cerebrospinal fluid shunt valve design in pediatric hydrocephalus. Neurosurgery. 1998 Aug;43(2):294–5.
9. Bergsneider M, Egnor MR, Johnston M, Kranz D, Madsen JR, McAllister JP 2nd, et al. What we don't (but should) know about hydrocephalus. J Neurosurg. 2006 Mar;104(3 Suppl):157–9.
10. Caldarelli M, Di Rocco C, La Marca F. Shunt complications in the first postoperative year in children with meningomyelocele. Child's Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. 1996 Dec;12(12):748–54.
11. Tuli S, Drake J, Lawless J, Wigg M, Lamberti-Pasculli M. Risk factors for repeated cerebrospinal shunt failures in pediatric patients with hydrocephalus. J Neurosurg. 2000 Jan;92(1):31–8.
12. Erol FS, Ozturk S, Akgun B, Kaplan M. Ventriculoperitoneal shunt malfunction caused by fractures and disconnections over 10 years of follow-up. Child's Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. 2017 Mar;33(3):475–81.
13. Hamid R, Baba AA, Bhat NA, Mufti G, Mir YA, Sajad W. Post ventriculoperitoneal shunt abdominal pseudocyst: Challenges posed in management. Asian J Neurosurg. 2017;12(1):13–6.
14. Crowley RW, Dumont AS, Asthagiri AR, Torner JC, Medel R, Jane JAJ, et al. Intraoperative ultrasound guidance for the placement of permanent ventricular cerebrospinal fluid shunt catheters: a single-center historical cohort study. World Neurosurg. 2014 Feb;81(2):397–403.
15. Basilotta Márquez YNI, Mengide JP, Liñares JM, Saenz A, Argañaraz R, Mantese B. Abdominal complications in patients with a ventriculoperitoneal shunt: proposal for management recommendations from a single pediatric tertiary center. Child's Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. 2021 Jul;37(7):2223–32.
16. Handler MH, Callahan B. Laparoscopic placement of distal ventriculoperitoneal shunt catheters. J Neurosurg Pediatr. 2008 Oct;2(4):282–5.
17. Recinos PF, Pindrik JA, Bedri MI, Ahn ES, Jallo GI, Recinos VR. The periumbilical approach in ventriculoperitoneal shunt placement: technique and long-term results. J Neurosurg Pediatr. 2013 May;11(5):558–63.
18. Park YS, Park IS, Park KB, Lee CH, Hwang SH, Han JW. Laparotomy versus Laparoscopic Placement of Distal Catheter in Ventriculoperitoneal Shunt Procedure. J Korean Neurosurg Soc. 2010 Oct;48(4):325–9.
19. Argo JL, Yellumahanthi DK, Ballem N, Harrigan MR, Fisher WS 3rd, Wesley MM, et al. Laparoscopic versus

open approach for implantation of the peritoneal catheter during ventriculoperitoneal shunt placement. Surg Endosc. 2009 Jul;23(7):1449–55.

20. Kim YB, Lee JW, Lee KS, Lee KC. Image-guided placement of ventricular shunt catheter. J Clin Neurosci Off J Neurosurg Soc Australas. 2006 Jan;13(1):50–4.
21. Dickerman RD, McConathy WJ, Morgan J, Stevens QE, Jolley JT, Schneider S, et al. Failure rate of frontal versus parietal approaches for proximal catheter placement in ventriculoperitoneal shunts: revisited. J Clin Neurosci Off J Neurosurg Soc Australas. 2005 Sep;12(7):781–3.
22. Stone j, Walker CT, Jacobson M, Philips V, Silberstein HJ. Revision rate of pediatric ventriculoperitoneal shunts after 15 years. J Neurosurg Pediatrics 2013; 11:15–19.
23. Anderson IA, Saukila LF, Robins JMW, Akhunbay-Fudge CY, Gooden JR, Tyagi AK, Philips N, Chumas PD. Factors associated with 30-day ventriculoperitoneal shunt failure in pediatric and adult patients. J Neurosurg 2019; 130:145–153.
24. Rocque BG, Waldrop RP, Shamblin I, Arynchyna AA, Hopson B, Kerr T, Johnston JM, Rozelle CJ, Blount JP. Shunt failure clusters: an analysis of multiple, frequent shunt failures. J Neurosurg Pediatr 2021; 27:287–293.
25. Gupta, Mahesh & Digra, N. & Sharma, Narendra & Goyal, Subhash & Agrawal, Amit. (2012). Length of peritoneal end of shunt catheters in hydrocephalus in children and rate of complications. J Cranio Max Dis. 1. 12-16. 10.4103/2278-9588.102468.
26. Pillai, Shibu V. Techniques and Nuances in Ventriculoperitoneal Shunt Surgery. Neurology India 69(Suppl 2):p S471-S475, Nov–Dec 2021.
27. Couldwell WT, LeMay DR, McComb JG. Experience with use of extended length peritoneal shunt catheters. J Neurosurg. 1996 Sep;85(3):425-7.
28. M. Paff, D. Alexandru-Abrams, M. Muhonen, W. Loudon. Ventriculoperitoneal shunt complications: a review. Interdiscipl. Neurosurg., 13 (2018), pp. 66-70.
29. Cozzens, J. W., & Chandler, J. P. (1997). Increased risk of distal ventriculoperitoneal shunt obstruction associated with slit valves or distal slits in the peritoneal catheter. Journal of Neurosurgery, 87(5), 682-686.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

The relationship between smoking and stress hormones in health technician students

Sağlık teknikerliği öğrencilerinde sigara içme ile stres hormonları arasındaki ilişki

Oya SAYIN[1]
Ayla AÇIKGÖZ[2]
Rabia ILGIN[3]
Mehmet ATEŞ[1]

[1] Vocational School Health Services, Department of Medical Laboratuary Techniques, Dokuz Eylul University, Izmir, Türkiye
[2] Vocational School Health Services, Department of Medical Secretarial , Dokuz Eylul University, Izmir, Türkiye
[3] Dokuz Eylul University, School of Medicine, Department of Physiology, Izmir, Turkiye

Smoking and Stress Hormones
Received: 02.11.2025
Accepted: 16.12.2025
DOI:10.18614/dehm.1873863

Corresponding author
Oya SAYIN
ORCID ID: 0000-0003-0879-9091
oya.sayin@deu.edu.tr

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

ABSTRACT

BACKGROUND
Smoking is a common coping mechanism for university students dealing with increasing exam stress. The aim of this study was to examine the effects of smoking on exam stress in health technician students by measuring salivary cortisol and adrenaline levels, recognized as stress biomarkers, and to evaluate the relationship between smoking and exam scores.

METHODS
The study included 64 students (mean age: 21.09 ± 2.05 years) from Dokuz Eylül University's Vocational School of Health Services during the 2023–2024 academic year. Thirty-three smokers (19 female, 14 male) and 31 non-smokers (24 female, 7 male) were included in the study. Data were collected with a form for sociodemographic information, a smoking status questionnaire, the State–Trait Anxiety Inventory Scale (STAI), and saliva samples. Cortisol and adrenaline levels in saliva samples were evaluated by enzyme-linked immunosorbent assay.

RESULTS
The salivary cortisol levels of non-smokers were lower compared to those of smokers (74.43 ± 35.98 vs. 94.35 ± 33.09 ng/mL, respectively; $p = 0.024$). The salivary adrenaline levels of non-smokers were higher compared to those of smokers (928.75 ± 172.57 vs. 727.39 ± 233.96 pg/mL, respectively; $p < 0.001$). The mean exam score was higher for non-smokers (73.97 ± 2.60) compared to smokers (63.84 ± 3.39) ($p = 0.022$). However, there was no significant difference between the groups in terms of the cognitive, psychosocial, or physiological subdimensions of the STAI or mean test achievement score ($p > 0.05$ for all).

CONCLUSION
Non-smoker students had lower cortisol and higher adrenaline levels, positively affecting their exam scores. These findings suggest that smoking status may affect physiological stress markers and exam scores, but not necessarily perceived state anxiety levels.

KEYWORDS
Exam score, salivary adrenaline, salivary cortisol, smoking

ÖZ

AMAÇ
Sigara bağımlılığı artan sınav stresiyle uğraşan üniversite öğrencileri için başa çıkma mekanizması haline gelmiştir. Araştırmanın amacı, sağlık teknisyenliği öğrencilerinde sigara içmenin sınav stresi üzerindeki etkilerini, stres biyobelirteçleri olarak kabul edilen tükürük kortizol ve adrenalin düzeylerini ölçerek araştırmak ve sigara içimi ile sınav başarısı arasındaki ilişkiyi araştırmaktır..

GEREÇ YÖNTEM
Çalışmaya 2023-2024 eğitim-öğretim yılında Dokuz Eylül Üniversitesi Sağlık Hizmetleri Meslek Yüksekokulu'nda öğrenim gören 64 öğrenci (ortalama yaş 21,09 ± 2,05 yıl) dahil edildi. Çalışmaya 33 sigara içen (19 kadın, 14 erkek) ve 31 sigara içmeyen (24 kadın, 7 erkek) dahil edildi. Veriler sosyodemografik bilgiler, sigara içme durumu anketi, Durumluk- Sürekli Kaygı Envanteri Ölçeği (STAI) ve tükürük örnekleri aracılığıyla toplandı. Tükürük örneklerinde kortizol ve adrenalin düzeyleri ELISA kullanılarak değerlendirildi.

BULGULAR
Sigara içmeyen öğrencilerin tükürük kortizol düzeyi sigara içen öğrencilere göre daha düşüktü (sırasıyla 74.43±35.98 ve 94.35±33.09 ng/mL, $p = 0.024$). Sigara içmeyen öğrencilerin tükürüklerindeki adrenalin düzeyi sigara içen öğrencilere göre daha yüksekti (sırasıyla 928.75±172.57 ve 727.39±233.96 pg/mL) $p < 0.001$) Sigara içmeyen öğrencilerin ortalama sınav başarı puanı (73.97 ± 2.60), sigara içen öğrencilere (63.84 ± 3.39) göre daha yüksekti ($p = 0.022$). Ancak STAI'nin bilişsel, psikososyal ve fizyolojik alt boyutları ile test başarı puan ortalamaları açısından gruplar arasında anlamlı bir fark yoktu. ($p > 0.05$).

SONUÇ
Sigara içmeyen öğrencilerin kortizol ve adrenalin düzeylerinin daha düşük olması sınav başarılarını olumlu yönde etkiliyordu. Bu bulgular, sigara içme durumunun fizyolojik stres belirteçlerini ve sınav başarısını etkileyebileceğini, ancak algılanan durumluk kaygı düzeylerini etkilemediğini göstermektedir.

ANAHTAR KELİMELER
Sigara içme, sınav başarısı, tükürük kortizol, tükürük adrenalin

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

Smoking, one of the most important social problems today, has increased dramatically among young adults in recent years, especially university students. The university environment has been identified as an important environment for starting to smoke. The transition to university life often coincides with the removal of significant familial and institutional controls, thereby affording students a greater degree of autonomy in their financial decisions and lifestyle choices. This increase in autonomy may, in some cases, be associated with an increased propensity to initiate smoking (1). Some studies have reported a rise in smoking among Turkish students (2,3). Research conducted within Turkish medical faculties revealed a significant increase in the prevalence of smoking as students advanced through their educational programs (4). Cortisol is a hormone secreted from the hypothalamic-pituitary-adrenal (HPA) axis in response to stress. It is also one of the most widely used markers in psychobiological research (5). Cortisol levels are sensitive to social and psychological stress (6). They respond to acute stress, such as acute loneliness or negative social evaluations, and to chronic stress, such as poverty or family conflict (7,8). Furthermore, the development and adult functioning of the HPA axis is profoundly affected by prior developmental experience. The pervasive effects of cortisol are extensive, exerting influence on cognitive and behavioral functions on a daily basis (9). Consequently, researchers have hypothesized that stress-induced changes in cortisol regulation may mediate the relationship between stress exposure and subsequent developmental and health outcomes (5,9,10), including the emergence and progression of both mental and physical health disorders (11). Optimal cortisol levels are essential for learning and memory, as positive stress can enhance academic performance, while high stress levels and elevated cortisol can impair cognitive functions and reduce academic scores (12-15).

The aim of this study was to investigate the effects of smoking on exam stress in health technician students by measuring salivary cortisol and adrenaline levels, which are utilized as stress biomarkers, and to examine the relationship between smoking and exam scores.

Materials and Methods

Participants and procedures

Data were collected from second-year students enrolled in the Vocational School of Health Services of a state university. The research was approved by the Non-Interventional Research Ethics Committee of Dokuz Eylül University (Decision No: 2023/39-01, 06.12.2023). The study included 33 students who currently smoked and 31 students who had never smoked. Prior to the commencement of data collection, the objective of the study was explained to the participating students by the researchers, who informed them that they could freely decide for themselves whether to participate and that the data would be kept confidential within the scope of the study. The researchers obtained voluntary consent from all participating students. Participants were students aged ≥18 years who were reached in their classrooms on days and hours determined by the school's administration. Data were collected in June 2024, with the survey and saliva sampling procedures being administered prior to the final examination of the course with the highest number of credits. The researchers were present to supervise the distribution and completion of the surveys, which did not contain any information indicating the names or identities of the students.

The inclusion criteria were as follows: being 18 years of age or older and being an actively enrolled student in the Dokuz Eylül University Vocational School of Health Services. Exclusion criteria were as follows: being younger than 18 years of age, being enrolled in the Vocational School of Health Services but having missed classes or suspended the registration, the presence of any chronic illness, and the use of hormone medications that could affect cortisol levels.

Data collection

Data were obtained using the Sociodemographic Information and Smoking Status Questionnaire, the State–Trait Anxiety Inventory (STAI), and saliva samples. Students whose saliva samples were collected were asked to fill out the questionnaire and the STAI under supervision.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

Sociodemographic information and smoking status questionnaire

This questionnaire consisted of 16 questions to determine the sociodemographic and individual characteristics, family characteristics, and smoking habits of the students. The form was created by the researchers based on the literature.

State–Trait anxiety inventory (STAI)

A version of the STAI was used to determine pre-exam anxiety levels among university students. This version was developed by Şahin (16) in 2019 and its validity and reliability were confirmed. It consists of a total of 22 items. The lowest total score that can be obtained from the scale is 22 and the highest total score is 88. There are no items that need to be reverse-coded in this scale. The scale consists of three subdimensions: physiological, psychosocial, and cognitive. The cognitive subdimension includes 9 items (Nos. 3, 4, 7, 9, 14, 16, 18, 20, and 22). The lowest possible score for this subdimension is 9 and the highest is 36. The psychosocial subdimension consists of 5 items (Nos. 6, 10, 12, 13, and 21). The lowest possible score for this subdimension is 5 and the highest is 20. The physiological subdimension includes 8 items (Nos. 1, 2, 5, 8, 11, 15, 17, and 19). The lowest possible score for this subdimension is 8 and the highest is 32. The total Cronbach alpha reliability coefficient of the whole scale was found to be 0.94, while that of the physiological subdimension was 0.85, that of the psychosocial subdimension was 0.84, and that of the cognitive subdimension was 0.93 (16).

Collection of Saliva Samples

Saliva samples were collected in a tube at least 30 min before the exam (09:00 AM), before the participants ate or drank anything. Samples were centrifuged at 3000 rpm for 5 min, transferred to small tubes, and stored at -80 °C under appropriate conditions until the day of analysis.

Biochemical measurements

The measurement of cortisol in saliva samples was performed using the cortisol competitive inhibition enzyme-linked immunosorbent assay (ELISA) method with a commercial kit (ELK 8526 Human Cortisol, ELK Biotechnology, USA) according to the manufacturer's protocol. The cortisol detection limit of this kit is 3.13–200 ng/mL.

The measurement of adrenaline in saliva samples was performed using the human adrenaline competitive inhibition ELISA method with a commercial kit (ELK 9242 Human Adrenaline, ELK Biotechnology, USA) according to the manufacturer's protocol. The adrenaline detection limit of this kit is 31.25–2000 pg/mL.

Statistical analysis

Data analysis was performed using IBM SPSS Statistics 24 (IBM Corp., USA). For descriptive findings, categorical variables were presented as numbers and percentages, and continuous variables were presented as mean, standard deviation, minimum, and maximum values. The conformity of the data to normal distribution was analyzed with the Kolmogorov–Smirnov test and the data were found to be normally distributed. In statistical analyses, Pearson chi-square tests and t-tests in independent groups were used to determine the relationships between independent variables and the dependent variable. Significance was accepted at $p < 0.05$ for all statistics.

Results

Sociodemographic characteristics of students according to smoking status

This study included 64 participants, with 33 smokers and 31 non-smokers. Of the women participating in the study, 19 (44.2%) were smokers and 24 (55.8%) were non-smokers. Of the men, 14 (66.7%) were smokers and 7 (33.3%) were non-smokers. There were no significant differences between smokers and non-smokers in terms of sex, age, mother's educational background, father's educational background, mother's employment status, father's employment status, monthly household income, or the presence of another smoker in the family. Thus, overall, no difference was found in the sociodemographic characteristics of the students according to their smoking behaviors ($p > 0.05$). However, smoking was more common among students who had lived in a city center during their childhood ($p < 0.05$; Table 1).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

Table 1. Sociodemographic characteristics according to smoking status

Variables		Smokers, n (%)	Non-smokers, n (%)	p-value*
Sex	Female	19 (44.2)	24 (55.8)	0.091
	Male	14 (66.7)	7 (33.3)	
Age groups	≤20 years	16 (50.0)	16 (50.0)	0.802
	≥21 years	17 (53.1)	15 (46.9)	
Mother's educational background	<High school	22 (52.4)	20 (47.6)	0.856
	≥High school	11 (50.0)	11 (50.0))	
Father's educational background	<High school	15 (44.1)	19 (55.9)	0.205
	≥High school	18 (60.0)	12 (40.0)	
Mother's employment status	Employed	6 (35.3)	11 (64.7)	0.117
	Unemployed	27 (57.4)	20 (42.6)	
Father's employment status	Employed	22 (56.4)	17 (43.6)	0.332
	Unemployed	11 (40.0)	14 (56.0)	
Monthly household income	<Minimum wage	2 (20.0)	8 (80.0)	0.094
	Minimum wage	8 (57.1)	6 (42.9)	
	>Minimum wage	23 (57.5)	17 (42.5)	
Where did you live when you were a child?	City center	21 (67.7)	10 (32.3)	**0.033**
	District	7 (31.8)	15 (68.2)	
	Village	5 (45.5)	6 (54.5)	
Are there any other smokers in the family?	No	7 (38.9)	11 (61.1)	0.368
	Mother	4 (40.0)	6 (60.0)	
	Father	16 (59.3)	11 (40.7)	
	Sibling	6 (66.7)	3 (33.3)	

*, Pearson chi-square p-value

Table 2. Descriptive characteristics of students

Characteristics	Mean ± SD	Min–max
Age, years	21.09 ± 2.05	18–28
Age at starting smoking, years	15.91 ± 2.43	9–19
Number of cigarettes smoked per day	14.88 ± 6.26	1–25
Duration of smoking, years	5.0 ± 3.48	1–15
Exam score	67.42 ± 20.54	8–100

Results of the smoking habits questionnaire

The questionnaire results indicated that the mean age at which smokers had first started smoking was 15.91 ± 2.43 years. On average, they smoked 14.88 ± 6.26 cigarettes per day. The mean duration of smoking among the participants was 5.0 ± 3.48 years (Table 2).

STAI Scores According to Smoking Status

This study examined the subdimensions of the STAI among smokers and non-smokers. The total cognitive score for smokers was 20.12 ± 5.94, while non-smokers had a total cognitive score of 22.06 ± 6.16 ($p > 0.05$). The total psychosocial score for smokers was 7.58 ± 2.37, while it was 7.35 ± 251 for non-smokers ($p > 0.05$). The total physiological score for smokers was 13.73 ± 3.58, while non-smokers had a total physiological score of 13.74 ± 4.43 ($p > 0.05$). These results indicate no significant differences between smokers and non-smokers in the cognitive, psychosocial, and physiological subdimensions of the STAI (Table 3).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

Table 3. Relationships between biochemical measurements and exam anxiety levels of students according to their smoking habits

Variables		Smokers, mean ± SD	Non-smokers, mean ± SD	p*
Results of biochemical measurements	Adrenaline level in saliva (pg/mL)	727.39 ± 233.96	928.75 ± 172.57	**<0.001**
	Cortisol level in saliva (ng/mL)	94.35 ± 33.09	74.43 ± 35.98	**0.024**
Subdimensions of the STAI #	Total cognitive score	20.12 ± 5.94	22.06 ± 6.16	0.203
	Total psychosocial score	7.58 ± 2.37	7.35 ± 2.51	0.719
	Total physiological score	13.72 ± 3.58	13.74 ± 4.43	0.988
Exam score		63.84 ± 3.39	73.97 ± 2.60	**0.022**

* Independent-samples t test p value # STAI, State–Trait anxiety inventory

Salivary cortisol and adrenalin levels and exam scores

The salivary cortisol levels of non-smokers were lower compared to those of smokers (74.43 ± 35.98 vs. 94.35 ± 33.09 ng/mL, respectively; p = 0.024). The salivary adrenaline levels of non-smokers were higher compared to those of smokers (928.75 ± 172.57 vs. 727.39±233.96 pg/mL, respectively; p < 0.001). The mean exam score was higher for non-smokers (73.97 ± 2.60) compared to smokers (63.84 ± 3.39) (p < 0.05; Table 3).

Discussion

According to the World Health Organization, more than 8 million people die each year due to smoking-related causes (17). In Türkiye, according to the Turkish Statistical Institute, the rate of individuals aged 15 and over who smoke was 28.0% in 2019 and 28.3% in 2022 (18). Factors such as the significant reduction of school and family control over students with the start of university education and the increase in the freedom of students to spend money can facilitate the initiation of smoking among university students. The university period is considered a process during which depression and anxiety are intensely experienced due to many stressful life events, such as the end of adolescence, separation from the home environment and family members, adaption to a new environment, the choosing of new friends and peer groups, preparations for exams, stress related to finding a job after graduation, and economic problems (19). During this period, students may start smoking as a way to cope with the problems they encounter. Initially, smoking begins as a temporary habit, but unfortunately it often evolves into an addiction (2).

In this study, we used saliva samples to measure stress among students. In the literature, saliva samples are commonly used to measure both catecholamines and cortisol. The literature reports that saliva is used in psychobiological research to measure acute stress responses and sympathetic nervous system activity. Although the measurement of catecholamines in saliva has not yet been standardized in routine clinical diagnosis, it is a very useful approach in sports physiology and stress research because of its non-invasiveness. In studies conducted with healthy volunteer groups, it has been reported that norepinephrine levels in saliva are 100–350 pg/mL during rest (sitting) and up to 1000 pg/mL during intense exercise (20,21). Salivary cortisol levels are emerging as a popular and useful biomarker (22-24). Studies have shown correlations between salivary and serum cortisol levels (25-28). Compared to venipuncture, saliva testing has been reported to have several advantages. It is non-invasive, minimizes the possibility of confounding factors, and allows for the collection of a large number of samples without causing ethical issues (25,26) with easy processing of salivary cortisol (27). The simple sampling, processing, and storage of saliva make it an excellent medium for cortisol determination with less analytical variability. Cortisol levels are reported to be between 100 and 750 ng/dL (22,23). In our study, since saliva samples were taken before an exam, we anticipated that the values in both groups might be above the normal range. Therefore, we focused on evaluating the difference between the two groups.

In this study, we tested the hypothesis that exam stress could lead to an increase in the stress hormones cortisol and

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

adrenaline in smokers compared to non-smokers and that it could reduce exam performance. Lundberg and Frankenhaeuser (29) and Frankenhaeuser (30) explained the differentiation between pituitary-adrenal and sympathetic-adrenal system activities with the terms "effort" and "distress." In their studies, they showed that a monotonous wakefulness task evoking both effort and distress caused an increase in adrenaline and cortisol levels. Conversely, they showed that a situation evoking effort but not distress caused an increase in adrenaline levels and a decrease in cortisol levels. The body has two main systems that respond to stress and daily activities, and these can function independently in healthy, non-smoking individuals. The HPA axis, characterized by cortisol, is slow and rhythmic, while the sympathomedullary (SAM) system, characterized by adrenaline and noradrenaline, is fast and reactive and its primary function is to maintain movement and alertness. In our study, adrenaline (i.e., the SAM system) increased while cortisol (i.e., the HPA axis) decreased in non-smokers. Adrenaline is necessary not only for fear but also for focus, attention, and effort. When a non-smoker focuses on a mental or physical task, adrenaline increases to enhance performance. Cortisol is primarily released in situations of loss of control, helplessness, or distress. When a person feels confident and in control of a task, the HPA axis is suppressed and cortisol levels decrease. When a non-smoker faces a stressful task and feels in control, the following messages are produced: "I am here, I am alert [high adrenaline], but I am not in danger and everything is under control [low cortisol]." Therefore, in this study, we found lower cortisol and higher adrenaline levels in non-smokers.

In situations of acute stress such as exam stress, the SAM system is activated. The adrenal medulla is stimulated by the sympathetic nerves, leading to an increase in adrenaline. Blood pressure, blood glucose, and heart rate increase, followed by the activation of the HPA axis and an increase in cortisol. This system acts in the opposite direction of the sympathoadrenal axis, protecting the body and mobilizing energy for necessary responses to cope with stress while suppressing adrenaline. Under normal conditions, this system operates with a negative feedback mechanism to prevent the excessive elevation of cortisol (31,32).

In situations of chronic stress, such as smoking, the different functions of cortisol and adrenaline hormones have been described by various researchers. In Parrott's study (33), for example, nicotine dependence was defined as a withdrawal-induced stress cycle and it was stated that smokers experience recurring stress fluctuations throughout the day. Among the subsequent studies examining the biological basis of this psychological model, high cortisol levels originating from the HPA axis were identified by Steptoe and Ussher (34). In the study by Benowitz (35), it was shown that this effect was due to blunted adrenaline responses due to the receptor desensitization mechanism. Benowitz (36) also showed that nicotine increases the heart rate by stimulating epinephrine or adrenaline release during acute intake, but chronic smokers develop a significant tolerance or desensitization to these effects.

Studies evaluating the effects of smoking on exam scores have shown that smoking can lead to a decrease in academic performance (37-39). Based on our results, we suggest that the high cortisol levels in smokers may affect exam scores due to the suppression of adrenaline. The adrenaline secreted during an exam has a stimulating effect that increases focus and concentration. In non-smoking students, high adrenaline and low cortisol levels may prepare them for exam situations, providing optimal focus and motivation.

We found no statistically significant differences between the smoking and non-smoking groups in terms of the subdimensions of the STAI. This suggests that changes in cortisol and adrenaline levels in smokers and non-smokers are independent of exam stress.

Limitations

The most important limitation of this study is that post-exam cortisol and adrenaline levels could not be evaluated. Another limitation is that the number of students in both groups was relatively small. Despite these limitations, this study contributes to the literature because it reveals the relationship between exam scores and cortisol and adrenaline levels in a group of students who smoke and students who do not. Similar studies should be conducted with larger samples and project support. We further recommend that multidisciplinary studies including smoking cessation counseling and peer education be carried out to protect the health of university students and increase their exam scores.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:101-109

Conclusion

We have demonstrated that low cortisol and high adrenaline levels in non-smoking students positively increased their exam scores, while high cortisol and low adrenaline levels in smokers decreased their achievement levels. No previous studies have evaluated the effects of smoking on exam stress through cortisol and adrenaline in relation to exam scores. Our study has contributed to the literature in this regard.

Authorship contributions

O.S., M.A.: Study idea/Hypothesis; O.S., A.A., M.A.: Design; O.S., A.A., R.I.: Data collection; A.A., R.I.: Analysis; O.S., R.I.: Writing; O.S., R.I.: Literature review; O.S., M.A.: Critical review.

Acknowledgment

We would like to thank Prof. Dr. Osman Açıkgöz for the critical evaluation of our article.

Conflict of interest

There are no conflicts of interest among the authors.

Compliance with ethics

This research was approved by the Non-Interventional Research Ethics Committee of Dokuz Eylül University (Decision No: 2023/39-01, 06.12.2023).

References

1. Şahbaz Y, Yeldan İ. Sigara İçen ve İçmeyen Üniversite Öğrencilerinde Anksiyete, Depresyon, Algılanan Yorgunluk, Dikkat Eksikliği ve Hiperaktivite Bozukluğu Düzeylerinin Karşılaştırılması. Gümüşhane Üniversitesi Sağlık Bilimleri Dergisi 2022;11(3):1086-1094.
2. Celikel FC, Celikel S, Erkorkmaz U. Smoking determinants in Turkish university students. Int J Environ Res Public Health 2009;6(8):2248-2257.
3. Senol Y, Donmez L, Turkay M, Aktekin M. The incidence of smoking and risk factors for smoking initiation in medical faculty students: cohort study. BMC Public Health 2006;6:128.
4. Sönmez Cİ, Başer DA, Aydoğan S, Uludağ, G, Dinçer D, Topaluğurlu B. Düzce Üniversitesi Tıp Fakültesi öğrencilerinin sigara içme sıklığı ve sigara ile ilgili bilgi tutum ve davranışları. Konuralp Medical Journal 2017;9(2):160-166.
5. Adam EK, Quinn ME, Tavernier R, McQuillan MT, Dahlke KA, Gilbert KE. Diurnal cortisol slopes and mental and physical health outcomes: A systematic review and meta-analysis. Psychoneuroendocrinology 2017;83:25-41.
6. Gunnar MR, Talge NM, Herrera A. Stressor paradigms in developmental studies: what does and does not work to produce mean increases in salivary cortisol. Psychoneuroendocrinology 2009;34(7):953-967.
7. Adam EK. Emotion-cortisol transactions occur over multiple time scales in development: implications for research on emotion and the development of emotional disorders. Monographs of the Society for Research in Child Development. 2012;77(2):17–27.
8. Adam EK, Heissel JA, Zeiders KH, Richeson JA, Ross EC, Ehrlich KB, et al. Developmental histories of perceived racial discrimination and diurnal cortisol profiles in adulthood: A 20-year prospective study. Psychoneuroendocrinology 2015;62:279- 291.
9. Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat Rev Neurosci 2009;10(6):434-445.
10. Davis EP, Sandman CA. The timing of prenatal exposure to maternal cortisol and psychosocial stress is associated with human infant cognitive development. Child Dev. 2010;81(1):131-148.
11. Heim C, Newport DJ, Mletzko T, Miller AH, Nemeroff CB. The link between childhood trauma and depression: insights from HPA axis studies in humans. Psychoneuroendocrinology 2008; 33(6):693-710.
12. De Quervain D, Schwabe L, Roozendaal B. Stress, glucocorticoids and memory: implications for treating fear-related disorders. Nat Rev Neurosci 2017;18(1):7-19.
13. Hatungil R. Stres ve Demansta Hipotalamus-Hipofiz-Adrenal ekseninin rolü. MersinÜniversitesi Sağlık Bilimleri Dergisi 2008;1(3):1-7.
14. .Langer K, Wolf OT, Jentsch VL. Delayed effects of acute stress on cognitive emotion regulation. Psychoneuroendocrinology 2021;125:105101.
15. Ouda S, Alaki S, Safi M, Nadhreen A, Johani K. Salivary stress biomarkers–Are they predictors of academic assessment exams stress. J Clin Exp Pathol 2016;15:276-279.
16. Şahin A. Durumluk sınav kaygısı ölçeği (DuSKÖ): Geçerlik ve güvenirlik çalışması. Trakya Eğitim Dergisi, 2019;9(1), 78-90.

17. World Health Organization. Tobacco 2023 https://www.who.int/news-room/fact-sheets/detail/tobacco.
18. TUIK 2022. Türkiye Sağlık Araştırması,2022. https://data.tuik.gov.tr/Bulten/Index?p=Turkiye-Saglik-Arastirmasi-2022-49747.
19. Villatte A, Marcotte D, Potvin A.. Correlates of depression in first-year college students. Canadian Journal of Higher Education 2017;47(1):114-136.
20. Kennedy B, Dillon E, Mills PJ, Ziegler MB. Catecholamines in human saliva Life Sci 2001 May 25;69(1):87-99.
21. Chiappin S, Antonelli G, Gatti R, Palo E. Saliva specimen: a new laboratory tool for diagnostic and basic investigation. Clin Chim Acta 2007 Aug;383(1-2):30-40.
22. Norsham Juliana , Sofwatul Mokhtarah Maluin, Nadia Mohd Effendy, Izuddin Fahmy Abu , Sahar Azmani. Cortisol Detection Methods and the Hormone's Role in Evaluating Circadian Rhythm Disruption. Int J Mol Sci 2025;19:26(18):9141.
23. Gozansky WS, Lynn JS, Laudenslager ML, Kohrt WM. Salivary cortisol determined by enzyme immunoassay is preferable to serum total cortisol for assessment of dynamic hypothalamic--pituitary--adrenal axis activity. Clin Endocrinol 2005;63(3):336-41.
24. Sekar M, Sriramprabha R, Sekhar PK, Bhansali S, Ponpandian N, Pandiaraj M, Viswanathan C. Wearable Sensor Platforms for the Electrochemical Detection of Cortisol. J Electrochem Soc 2020;167:067508.
25. Mio˘cevi´c O, Cole CR, Laughlin MJ, Buck RL, Slowey PD, Shirtcliff EA. Quantitative Lateral Flow Assays for Salivary. Biomarker Assessment: A Review. Front Public Health 2017; 14:5:133.
26. Choi MH. Clinical and Technical Aspects in Free Cortisol Measurement. Endocrinol Metab 2022;37(4):599-607.
27. Bozovic D, Racic M, Ivkoviç N . Salivary cortisol levels as a biological marker of stress reaction. Med Arch 2013;67(5):374-7.
28. Kim YJ, Kim JH, Hong AR, Park KS, Kim SW, Shin CS, Kim SY. Stimulated Salivary Cortisol as a Noninvasive Diagnostic Tool for Adrenal Insufficiency. Endocrinol Metab. 2020;35:628–635.
29. Ludberg U, Frankenhaeuser M. Pituitary-adrenal and sympathetic-adrenal correlates of distress and effort. J Psychosom Res 1980;24(3-4):125-30.
30. Frankenhaeuser M. A biopsychosocial approach to work life issues Int J Health Serv 1989;19(4):747-58.
31. Cool J, Zappetti D. The physiology of stress. Medical student well-being: An essential guide 2019;1-15.
32. Tennison LR, Rodgers LS, Beker D, Vorobjeva KI, Creed ET, Simonenko A. Cortisol and symptoms of psychopathology in Russian and American college students. Int J Psychol 2010;1;45(3):165-73.
33. Parrott AC. Does cigarette smoking cause stress? Am Psychol 1999;54(10):817-820.
34. Steptoe A, Ussher M. Smoking, cortisol and nicotine withdrawal. Psychopharmacology (Berl) 2006;185(2):195-203.
35. Benowitz NL. Nicotine addiction. N Engl J Med 2010;362(24):2295-2303.
36. Benowitz NL. Neurobiology of nicotine addiction: implications for smoking cessation treatment. Am J Med 2008;121(4):S3-S10.
37. Aleidi S, Elayah E, Zraiqat D, Abdallah R, Montaha AI. Factors affecting the academic performance of medical, dental, and pharmacy students in Jordan. Jordan Journal of Pharmaceutical Sciences 2020;13(2):169-183.
38. Attalla SM, Ruhi S, Mud CN. Effect of cigarette smoking on the academic achievement among management and science university students. Mal J Med Health Sci 2020;16(7):18-22.
39. Alqahtani JS, Aldhahir AM, Alanazi Z, Alsulami EZ, Alsulaimani MA. Impact of smoking status and nicotine dependence on academic performance of health sciences students. Subst Abuse Rehabil 2023;14:13-24.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

Determinants of state anxiety in parents of children with lymphadenopathy: A cross-sectional analysis

Lenfadenopatili çocukların ebeveynlerinde görülen kaygı düzeyini belirleyen faktörler: Kesitsel bir analiz

Sultan OKUR ACAR[1]
Mehmet Akif CANSIZ[2]

[1] Manisa City Hospital, Department of Pediatric Hematology and Oncology, Manisa, Türkiye
[2] Manisa City Hospital, Department of Child and Adolescent Psychiatry, Manisa, Türkiye

Parental Anxiety and Lymphadenopathy
Received: 03.11.2025
Accepted: 15.12.2025
DOI:10.18614/dehm.1873876

Corresponding author
Sultan OKUR ACAR
ORCID ID: 0000-0002-5768-0890
sultanokur@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

ABSTRACT

BACKGROUND
Pediatric lymphadenopathy is common and usually benign, but it can cause significant anxiety in parents. We quantified parental state anxiety in cases of pediatric lymphadenopathy and examined clinical and psychosocial correlates, including the use of online information sources.

METHODS
In a single-center cross-sectional study, the parents of 99 consecutive children referred for lymphadenopathy completed the State–Trait Anxiety Inventory (STAI). State anxiety (STAI-1) was the primary outcome and trait anxiety (STAI-2) was treated as a covariate. Child variables included age, sex, duration of lymphadenopathy, and lymph node dimensions (short- and long-axis diameter). Internet searching was recorded as yes/no and perceived helpfulness was also documented. We used parametric and nonparametric tests, correlation analyses, and multivariable linear regression to examine associations between STAI-1 and age, sex, duration, short-axis diameter, internet searching, and STAI-2.

RESULTS
The mean age of the children was 6.87 ± 4.33 years and 60.6% were male. The median duration of lymphadenopathy was 8.0 weeks. The mean short-axis diameter was 9.47 ± 3.67 mm and the mean long-axis diameter was 22.17 ± 7.37 mm. Epstein–Barr virus serology was negative in 98% of cases. The mean parental STAI-1 and STAI-2 scores were 39.59 ± 9.99 and 41.24 ± 8.52, respectively. Internet searching, reported by 43.4% of parents, was not associated with higher STAI-1 or STAI-2 scores, and scores did not differ according to whether the short-axis diameter was ≥10 mm. STAI-1 correlated negatively with duration of lymphadenopathy ($r = –0.204$, $p = 0.045$). In adjusted models, older age of the child ($B = 0.660$, $p = 0.002$) and larger short-axis diameter ($B = 0.562$, $p = 0.019$) independently predicted higher STAI-1 scores, whereas longer duration predicted lower STAI-1 scores ($B = –0.150$, $p = 0.002$). Multicollinearity was negligible (variance inflation factor ≤ 1).

CONCLUSION
Among parents of children evaluated for lymphadenopathy, acute anxiety was more strongly related to objective node size and child age than to internet searching. In contrast, shorter symptom duration, likely reflecting greater uncertainty, was associated with higher anxiety. Structured counseling and clear follow-up plans may help to mitigate parental distress in this setting.

KEYWORDS
Anxiety, Internet use, lymphadenopathy, parents, pediatric hematology, STAI

ÖZ

AMAÇ
Çocuklarda lenfadenopati yaygındır ve genellikle iyi huyludur, ancak ebeveynlerde önemli kaygıya neden olabilir. Ebeveynlerin durumsal kaygısını ölçtük ve çevrimiçi bilgi arama da dahil olmak üzere klinik ve psikososyal ilişkileri inceledik.

GEREÇ YÖNTEM
Tek merkezli kesitsel bir çalışmada, lenfadenopati nedeniyle sevk edilen ardışık 99 çocuğun ebeveynleri Durum-Özellik Kaygı Envanterini (STAI) doldurdu. Birincil sonuç durumsal kaygı (STAI-1) idi; özellik kaygısı (STAI-2) bir kovaryat olarak ele alındı. Çocuk değişkenleri arasında yaş, cinsiyet, lenfadenopati süresi ve lenf düğümü boyutları (kısa ve uzun eksen) yer aldı. İnternet araması (evet/hayır) algılanan yararlılıkla birlikte kaydedildi. Uygun parametrik/parametrik olmayan testler, korelasyonlar ve STAI-1'i yaş, cinsiyet, süre, kısa eksen, internet araması ve STAI-2 ile çok değişkenli doğrusal regresyon modellemesi kullandık.

BULGULAR
Çocukların %60,6'sı erkekti; ortalama yaş 6,87±4,33 yıldı. Lenfadenopati süresinin medyan değeri 8,0 hafta; ortalama kısa eksen 9,47±3,67 mm ve uzun eksen 22,17±7,37 mm idi. Epstein-Barr virüsü serolojisi %98 oranında negatifti. Ebeveynlerin ortalama STAI-1 ve STAI-2 değerleri sırasıyla 39,59±9,99 ve 41,24±8,52 idi. İnternet araması (ebeveynlerin %43,4'ü) daha yüksek STAI-1/2 ile ilişkili değildi ve STAI skorları kısa eksen ≥10 mm'ye göre farklılık göstermedi. STAI-1, süre ile negatif korelasyon gösterdi ($r = −0,204$, $p = 0,045$). Ayarlanmış modellerde, daha büyük çocuk yaşı ($B = 0,660$, $p = 0,002$) ve daha büyük kısa eksen ($B = 0,562$, $p = 0,019$) bağımsız olarak daha yüksek STAI-1'i öngörürken, daha uzun süre daha düşük STAI-1'i öngördü ($B = −0,150$, $p = 0,002$); çoklu doğrusallık ihmal edilebilir düzeydeydi (VIF≈1).

SONUÇ
Lenfadenopati açısından değerlendirilen çocukların ebeveynleri arasında, akut kaygı, internet aramalarından ziyade objektif lenf düğümü boyutu ve çocuk yaşıyla daha fazla ilişkiliydi, daha kısa semptom süresi ise (daha fazla belirsizliği yansıtarak) daha yüksek kaygı ile bağlantılıydı. Yapılandırılmış danışmanlık ve net takip planları, lenfadenopati kliniklerinde sıkıntıyı etkili bir şekilde azaltmaya yardımcı olabilir.

ANAHTAR KELİMELER
Ebeveynler, internet kullanımı, kaygı, lenfadenopati, pediatrik hematoloji, STAI

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

Childhood lymphadenopathy is a common clinical finding most often caused by benign, self-limiting conditions. Infections, particularly viral upper respiratory tract infections, are the most frequent cause of lymphadenopathy in children. However, malignancies (e.g., leukemia and lymphoma), immunological disorders, and granulomatous infections should also be considered in the differential diagnosis. Diagnostic evaluation should take into account lymph node size, location, and duration, as well as the presence of systemic signs and symptoms. From the family's perspective, lymphadenopathy can cause substantial cancer-related fear, which in turn is a major driver of healthcare-seeking behavior (1,2).

Visits to pediatric hematology-oncology clinics often generate considerable stress and uncertainty for families. Receiving or even merely suspecting a diagnosis of a serious hematological or oncological condition can cause substantial emotional distress, particularly among parents. Such stressful encounters may adversely affect caregivers' well-being, their communication with health professionals, and their adherence to medical recommendations.

Parental anxiety is known to influence how medical information is interpreted and how decisions are made in pediatric settings. The State–Trait Anxiety Inventory (STAI), developed by Spielberger et al. (3), is one of the most widely used instruments for assessing transient (state) and dispositional (trait) anxiety in adults. It is frequently administered to caregivers whose children are undergoing evaluation or treatment (3,4).

Numerous studies have shown that parents of children with chronic illnesses, particularly cancer or hematological disorders, have higher anxiety scores than the general population (5,6). These psychological responses are shaped by multiple factors, including the child's clinical status, parental educational level, previous health-related experiences, and exposure to medical information online (7).

Understanding the factors that contribute to parental anxiety during hematology-oncology consultations is crucial for developing effective communication strategies and supportive interventions. This study aimed to evaluate state and trait anxiety levels in parents of children referred to a pediatric hematology-oncology clinic for lymphadenopathy and to examine how those levels correlated with selected sociodemographic and clinical characteristics.

Materials and Methods

This single-center cross-sectional observational study included parents of children who were referred to the Pediatric Hematology-Oncology Outpatient Clinic of Manisa City Hospital for peripheral lymphadenopathy. Consecutive patients were enrolled at the time of their initial evaluations.

The primary objective was to quantify parental anxiety and identify clinical and psychosocial factors associated with it. Children under 18 years of age who were referred for an initial hematology-oncology evaluation because of peripheral lymphadenopathy and were accompanied by their primary caregiver (mother, father, or legal guardian) were included in the study. While the presence of palpable or measurable lymphadenopathy on physical examination or in an existing ultrasound report was sufficient for inclusion, all millimetric lymph node measurements used in the analyses were obtained from ultrasound reports. Short-axis diameters were abstracted from ultrasound imaging for all 99 evaluated children, ensuring a uniform measurement method across the cohort.

Parents were required to be able to communicate in Turkish, understand the study, and provide written informed consent. Children presenting for reasons other than lymphadenopathy, for whom lymph node enlargement was incidentally detected during examination, and for whom no follow-up was planned for this finding were excluded, as were parents who did not grant consent. In total, 99 consecutive parents were enrolled.

At the initial visit, data were obtained via a face-to-face structured interview using a standardized form. The first section captured child-level clinical information, including age, sex, the referring clinic or physician (e.g., general pediatrics, pediatric surgery, ear-nose-throat/otolaryngology) and the interval (weeks) since lymphadenopathy was first noticed. Laboratory results ordered as part of routine care, such as complete blood count, erythrocyte sedimentation rate, lactate dehydrogenase, uric acid, and, when available, Epstein–Barr virus serology, were abstracted from the medical records.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

Parents were also asked about systemic B symptoms (fever, night sweats, and unintentional weight loss).

For node-size analyses, the short-axis diameter was coded as a binary variable (≥10 mm vs. <10 mm), reflecting a commonly used clinical threshold that signals a "large" node to both clinicians and parents. For research purposes, size-derived measures based on the long and short axes, using equivalent diameter and elliptical area, were computed to better characterize node size; these derived metrics were used solely in the statistical analyses.

The second section of the data collection form captured psychosocial variables at the caregiver level. These included, as applicable, parental education level, any reported family history of malignant disease, whether the parent had searched the internet for information about the child's lymphadenopathy, and, if the internet was searched, how helpful or reassuring the parent had found the information to be. This section also assessed parental anxiety.

Parental anxiety was evaluated using the STAI. The reliability and validity of the Turkish version were established by Öner and Le Compte in 1985 (8). The STAI consists of two separate 20-item subscales. The state anxiety scale (STAI-State; referred to here as STAI-1) measures the respondent's immediate, situation-specific level of anxiety and was the primary outcome of interest in this study. The trait anxiety scale (STAI-Trait; STAI-2) reflects the respondent's general predisposition to anxiety and was treated as a potential confounding factor in the statistical models. Each item is rated on a four-point Likert-type scale, with higher total scores indicating higher levels of anxiety. Parents were asked to complete the questionnaire themselves; in cases where literacy was a concern, items were read aloud by a researcher in a neutral manner and responses were recorded verbatim.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 20. Continuous variables were summarized as mean ± standard deviation and/or median (minimum–maximum), whereas categorical variables were summarized as number and percentage. Distributional normality was assessed using the Shapiro–Wilk test. STAI-1 and STAI-2 data were available for 97 and 98 of the 99 parents, respectively, due to a small number of incomplete questionnaires. Analyses were performed using available-case (pairwise) deletion, and the effective sample size for each analysis is reported in tables.

Group differences were examined using the independent-samples t-test or the Mann–Whitney U test, depending on whether normality was confirmed, comparing parents who had searched the internet versus those who had not and parents of children with a lymph node short-axis diameter of ≥10 mm versus <10 mm. Associations between parental state anxiety and (i) the child's age, (ii) the duration of lymphadenopathy, and (iii) lymph node size were evaluated using Pearson or Spearman correlation coefficients as appropriate.

To identify independent correlates of acute parental anxiety, a multiple linear regression model was constructed with the STAI-1 score as the dependent variable. The following predictors were entered simultaneously: the child's age and sex, the duration of lymphadenopathy in weeks, the lymph node short-axis diameter in mm, whether or not the parent had sought information on the internet, and the parent's trait anxiety as reflected by the STAI-2 score. Model assumptions were checked, including approximate normality of residuals and multicollinearity (variance inflation factor). A two-sided value of $p < 0.05$ was considered statistically significant.

Ethics

The study protocol was approved by the İzmir Bakırçay University Ethics Committee (Approval No. 2302) and conducted in accordance with the Declaration of Helsinki and good clinical practice standards. Written informed consent was obtained from all legal guardians before participation.

Results

Patient and caregiver characteristics

A total of 99 children evaluated for lymphadenopathy, together with their accompanying caregivers, were included in the study. Of the children, 60.6% were male (n = 60). The mean age was 6.87 ± 4.33 years (median: 6.0 [3.0–9.0], range: 1.0–18.0). At presentation, lymphadenopathy had been present for a mean of 15.48 ± 18.20 weeks (median: 8.0 [1.25–21.0], range: 0.15–52.0). The mean short-axis diameter was 9.47 ± 3.67 mm (median: 10.0 [7.0–11.0], range: 2.0–25.0 mm) and the mean long-axis diameter

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

was 22.17 ± 7.37 mm (median: 22.0 [17.0–26.0], range: 5.0–40.0 mm). The mean equivalent diameter (√[L × S]) was 14.34 ± 4.63 mm and the mean elliptical area ([π/4] × L × S) was 178.23 ± 108.67 mm2.

Most referrals originated from general pediatrics (82.8%), followed by pediatric surgery (7.1%), otolaryngology/ear-nose-throat (6.1%), pediatric infectious diseases (3.0%), and family medicine (1.0%). Epstein–Barr virus serology was negative in 98.0% of cases (n = 97). Overall, 51.5% of the children (n = 51) had a short-axis diameter of at least 10 mm (Tables 1 and 2).

Table 1. Descriptive statistics for continuous variables.

Variable	n (valid)	Mean ± SD	Median [P25–P75]	Min–max
STAI-1 (state)	97	39.59 ± 9.99	38.0 [33.0–47.0]	20.0–64.0
STAI-2 (trait)	98	41.24 ± 8.52	41.0 [36.0–46.0]	21.0–65.0
Age (years)	99	6.87 ± 4.33	6.0 [3.0–9.0]	1.0–18.0
Lymphadenopathy duration (weeks)	99	15.48 ± 18.20	8.0 [1.25–21.0]	0.15–52.0
Short axis (mm)	99	9.47 ± 3.67	10.0 [7.0–11.0]	2.0–25.0
Long axis (mm)	99	22.17 ± 7.37	22.0 [17.0–26.0]	5.0–40.0
Equivalent diameter, √(L × S) (mm)	99	14.34 ± 4.63	14.70 [10.15–17.32]	3.16–25.75
Elliptical area, (π/4) × L × S (mm²)	99	178.23 ± 108.67	169.65 [80.90–235.62]	7.85–520.72

STAI, State–Trait Anxiety Inventory; SD, standard deviation; P25, 25th percentile; P75, 75th percentile

Table 2. Distribution of categorical variables.

Variable	Category	n	%
Sex	Male (1)	60	60.6
	Female (2)	39	39.4
Referring clinic	Pediatrics (1)	82	82.8
	Pediatric surgery (2)	7	7.1
	Otorhinolaryngology (3)	6	6.1
	Family medicine (4)	1	1.0
	Pediatric infectious disease	3	3.0
Internet searching status	Yes (1)	43	43.4
	No (2)	56	56.6
Online information's helpfulness	Helpful (1)	35	35.4
	Not helpful (2)	8	8.1
	Not applicable: did not search online (9)	56	56.6
Short-axis of ≥10 mm	No (0)	48	48.5
	Yes (1)	51	51.5

Total n = 99

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

Parental anxiety levels

The mean parental STAI-1 score was 39.59 ± 9.99 (median: 38.0 [33.0–47.0], range: 20.0–64.0). The mean STAI-2 score was 41.24 ± 8.52 (median: 41.0 [36.0–46.0], range: 21.0–65.0) (Table 1). The distributions of STAI-1 and STAI-2 scores did not deviate significantly from normality (Shapiro–Wilk, $p > 0.05$), and the homogeneity of variances was supported in between-group comparisons (Levene's test, $p > 0.05$ for all).

Internet information- seeking and anxiety

Overall, 43.4% (n = 43) of parents reported searching the internet for information about their child's lymphadenopathy, while 56.6% (n = 56) did not. Of those who searched, 81.4% (n = 35) found the information useful or helpful, whereas 18.6% (n = 8) did not find it useful (Table 2). No significant differences were observed when comparing parents who searched the internet (ISS = 1) with those who did not (ISS = 2). For STAI-1, the means were 40.05 ± 10.54 (n = 43) versus 39.22 ± 9.61 (n = 54); the mean difference was 0.82 points, which was not statistically significant ($t(95) = 0.40$, $p > 0.60$; Cohen's $d = 0.08$; 95% CI: –3.25 to 4.89). Similar results were obtained for STAI-2 (ISS = 1: 40.70 ± 8.76, n = 43; ISS = 2: 41.67 ± 8.39, n = 55; $t(96) = –0.56$, $p > 0.50$; $d = 0.11$; 95% CI: –4.43 to 2.48) (Table 3).

Lymph node size and anxiety

There was no significant difference in STAI-1 scores between parents of children with a lymph node short-axis diameter of ≥10 mm (n = 50) and those with a diameter <10 mm (n = 47) ($t(95) = 0.028$, $p = 0.978$; Cohen's $d = 0.006$; 95% CI: –3.99 to 4.11). Similarly, STAI-2 scores did not differ between the two groups ($t(96) = 0.532$, $p = 0.596$; $d = 0.108$; 95% CI: –2.51 to 4.35). Taken together, these results suggest that crossing the commonly used 10-mm short-axis threshold does not, by itself, meaningfully increase parental anxiety.

Correlation analyses

Using Pearson correlation coefficients, parental state anxiety as reflected by the STAI-1 was not significantly associated with the child's age ($r = 0.182$, $p = 0.075$) or sex ($r = 0.096$, $p = 0.348$). However, STAI-1 scores showed a weak but statistically significant inverse association with the duration of lymphadenopathy ($r = –0.204$, $p = 0.045$), indicating that longer duration was associated with lower state anxiety (Table 4).

No significant association was observed between STAI-1 scores and maternal education ($\rho = –0.096$, $p = 0.350$). Likewise, node size metrics, including equivalent diameter ($\rho = 0.125$, $p = 0.221$) and elliptical area ($\rho = 0.126$, $p = 0.218$), were not correlated with STAI-1.

Among parents who searched online and rated the information as helpful (internet information-seeking [ISS] = yes; online information's helpfulness [OIH] = helpful; n = 35), STAI-1 showed no significant correlations with child age, duration of lymphadenopathy, or node size ($p > 0.05$ for all). Among parents who searched online and rated the information as unhelpful (internet information-seeking [ISS] = yes; online information's helpfulness [OIH] = unhelpful; n = 8), STAI-1 showed a strong positive correlation with lymph node long-axis diameter ($\rho = 0.85$, $p = 0.007$). Consistent positive correlations were also observed with equivalent diameter and elliptical area ($\rho = 0.74$, $p = 0.037$ for both). Given the very small subgroup size, however, these findings should be interpreted with caution and regarded as exploratory.

Among parents who did not search online (ISS = no; n = 54), STAI-1 scores were significantly inversely correlated with the duration of lymphadenopathy ($\rho = –0.399$, $p = 0.003$), and there was a borderline positive trend with child age ($\rho = 0.263$, $p = 0.055$). No significant associations were observed with node size metrics in this subgroup ($p > 0.05$ for all) (Table 5).

Taken together, these subgroup analyses suggest that, among parents who did not search online, anxiety tended to decrease as the duration of lymphadenopathy increased, consistent with habituation and reduced uncertainty. In contrast, in the small subgroup that searched but did not find the information helpful, anxiety appeared to be more sensitive to the physical size of the lymph node.

A multiple linear regression model was then fitted with STAI-1 score as the dependent variable. The following predictors were entered simultaneously: the child's age and sex, the duration of lymphadenopathy in weeks, the lymph node short-axis diameter in mm, whether or not the parent had sought information online, and the parent's trait anxiety (STAI-2 score). Among the results (Table 6), lymphadenopathy

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

duration remained independently and inversely associated with STAI-1 (B = –0.150, β = –0.272, p = 0.002; 95% CI: –0.244 to –0.055). Short-axis diameter positively predicted STAI-1 (B = 0.562, β = 0.207, p = 0.019; 95% CI: 0.094 to 1.029). Age was independently and positively associated with STAI-1 (B = 0.660, β = 0.282, p = 0.002; 95% CI: 0.252 to 1.067). Trait anxiety (STAI-2) was a strong predictor (B = 0.554, β = 0.475, p < 0.001; 95% CI: 0.356 to 0.751). Finally, sex (p = 0.357) and internet information-seeking (p = 0.703) were not significant. Multicollinearity diagnostics indicated a stable model, with variance inflation factors of approximately 1.0–1.08 and condition index of ≤21.9. Even after adjustment for trait anxiety, the two clinical parameters of symptom duration and short-axis diameter were independently associated with acute parental anxiety. Specifically, a longer duration of lymphadenopathy was related to lower state anxiety, whereas a larger short-axis diameter was related to higher state anxiety.

Parental education level

The distribution of education levels was as follows: not literate, 1.0%; primary school, 24.2%; middle school, 15.2%; high school, 30.3%; associate degree, 13.1%; and bachelor's degree, 16.2%. There were no significant differences in parental state or trait anxiety across educational levels (STAI-1: H(5) = 5.42, p = 0.367, $\varepsilon^2 \approx 0.005$; STAI-2: H(5) = 6.71, p = 0.243, $\varepsilon^2 \approx 0.019$). Although mean rank scores suggested a tendency toward lower anxiety among parents with a bachelor's degree for both scales, this pattern did not reach statistical significance.

Table 3. STAI scores by internet searching status (t-test).

Scale	ISS = Yes (n)	Mean ± SD	ISS = No (n)	Mean ± SD	Mean diff. (Yes – No)	t (df)	p (two-tailed)	95% CI of diff.	Cohen's d
STAI-1	43	40.05 ± 10.54	54	39.22 ± 9.61	0.82	0.40 (95)	>0.60	–3.25 to 4.89	0.08
STAI-2	43	40.70 ± 8.76	55	41.67 ± 8.39	–0.98	–0.56 (96)	>0.50	–4.43 to 2.48	0.11

ISS, Internet searching status; SD, standard deviation; df, degrees of freedom; CI, confidence interval; STAI, State–Trait Anxiety Inventory

Table 4. Pearson correlations of STAI-1 with selected variables.

Independent variable	r	p	n
Age (years)	0.182	0.075	97
Lymphadenopathy duration (weeks)	–0.204*	0.045	97
Sex (0 = Female, 1 = Male)	0.096	0.348	97

STAI:,State–trait anxiety inventory; *, significant at p < 0.05

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

Table 5. Spearman correlations between STAI-1 and clinical variables by subgroup.

Variable	ISS = Yes & OIH = Helpful	ISS = Yes & OIH = Not helpful	ISS = No
Age (years)	0.108 (0.535)	0.233 (0.578)	0.263 (0.055)
Lymphadenopathy duration (weeks)	–0.278 (0.106)	0.036 (0.933)	–0.399 (0.003)
Short axis (mm)	–0.053 (0.760)	0.528 (0.179)	0.086 (0.534)
Long axis (mm)	–0.045 (0.796)	0.850 (0.007)	0.104 (0.456)
Equivalent diameter, √(L × S) (mm)	–0.019 (0.915)	0.738 (0.037)	0.117 (0.398)
Elliptical area, (π/4) × L × S (mm²)	–0.017 (0.922)	0.738 (0.037)	0.118 (0.395)

ISS, Internet searching status; OIH , online information's helpfulness; cells show ϱ (p), two-tailed
Group sizes:,Helpful, n = 35; Not helpful, n = 8; Did not search, n = 54

Table 6. Multiple linear regression for STAI-1 (adjusted for STAI-2).

Predictor	B	SE	β (standardized)	t	p	95% CI (lower–upper)
Constant	12.669	6.708	–	1.889	0.062	–0.660 to 25.999
Lymphadenopathy duration (weeks)	–0.150	0.048	–0.272	–3.150	0.002	–0.244 to –0.055
Short axis (mm)	0.562	0.235	0.207	2.388	0.019	0.094 to 1.029
Age (years)	0.660	0.205	0.282	3.215	0.002	0.252 to 1.067
Sex (1 = Male, 2 = Female)	–1.646	1.777	–0.081	–0.927	0.357	–5.178 to 1.885
Internet searching (1 = Yes, 2 = No)	–0.663	1.736	–0.033	–0.382	0.703	–4.111 to 2.786
STAI-2 (trait)	0.554	0.099	0.475	5.578	<0.001	0.356 to 0.751

Dependent variable:,STAI-1 (state anxiety)
Collinearity diagnostics:,Variance inflation factor ≈ 1.0–1.08; condition index ≤ 21.9 (no problematic multicollinearity)

Discussion

This study examined parental anxiety at the time of referral to a pediatric hematology-oncology clinic for lymphadenopathy and explored factors associated with this anxiety. Overall, parents' STAI-1 scores fell within the mild-to-moderate range, and a history of seeking information on the internet was not associated with these scores. Although a short-axis diameter of ≥10 mm did not, by itself, produce a significant difference in anxiety, multivariable analysis

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

showed that a greater short-axis diameter and older age of the child were positively associated with STAI-1 scores, whereas a longer duration of lymphadenopathy was negatively associated. As expected, parental STAI-2 scores emerged as a strong predictor of state anxiety.

Most cervical lymphadenopathy in childhood is benign and self-limiting, typically reflecting a reactive response to infection, and contemporary clinical guidance generally favors observation when no red-flag features are present. Against this epidemiological backdrop, parental "cancer fear" may not align with medical reality and is often fueled by uncertainty. The anxiety levels observed in our cohort and the absence of a distinct effect at the 10-mm threshold are consistent with this framework.

The inverse association between lymphadenopathy duration and anxiety suggests two possible mechanisms: (i) many reactive nodes gradually regress over the course of several weeks, thereby reducing acute uncertainty, and (ii) families progressively reappraise the perceived threat as they gain information and experience (habituation/adaptation). This interpretation is consistent with the generally benign and self-limiting nature of pediatric lymphadenopathy.

The positive association between short-axis diameter as a continuous measure and anxiety is also notable: as morphologic "thickness" increases, parents may perceive the risk as higher. Conversely, the absence of a group difference at the 10-mm threshold suggests that parental risk perception is shaped less by a sharp threshold and more by graded, integrative cues (e.g., perceived firmness or tenderness, symptom duration, and accompanying features). The strong effect of trait anxiety is expected and underscores the importance of distinguishing between the state and trait components of the STAI when interpreting parental anxiety in clinical contexts (7).

An interesting finding of our multivariable model was that the child's age was an independent predictor of higher parental state anxiety, even after adjustment for trait anxiety and lymph node size. We speculate that parents may perceive lymphadenopathy in older children as less common and therefore more alarming. In addition, older children's greater awareness of and questions about serious illness may heighten parental worry. Further longitudinal research is required to clarify how age-related differences in risk perception and family communication influence this association.

The neutral overall association between internet information-seeking and anxiety in our cohort is consistent with the mixed findings in the literature. Online health information can exacerbate anxiety in some individuals, a situation known as "cyberchondria," particularly when the information is fragmented, alarmist, or poorly tailored to the clinical situation. In contrast, structured and trustworthy digital resources may promote understanding and provide reassurance, especially for parents with adequate e-health literacy. Although limited by small numbers, our subgroup findings suggest that the perceived usefulness of online information may be more important than the mere act of searching (9,10).

From a clinical standpoint, providing structured counseling at the initial consultation, together with a clear follow-up plan including red flags, return criteria, and review timings, may help reduce unnecessary investigations and clinician burnout while also lowering parental anxiety. Evidence from pediatric surgery and anesthesia shows that written or video-based information for parents can reduce anxiety as measured by the STAI; similar strategies could be adapted for lymphadenopathy clinics. In addition, standardized evaluation pathways incorporating history taking, physical examination, red-flag screening and, when indicated, ultrasound and targeted laboratory tests are likely to improve clinical efficiency as well as family satisfaction (11-13).

This study has several strengths, including the consecutive enrollment of participants, concurrent assessment of both state and trait anxiety, and the linkage of psychological outcomes to clinical parameters through multivariable modeling. However, its cross-sectional single-center design precludes causal inference and carries a risk of referral bias.

The anxiety measures relied on self-report; although the STAI is a valid and reliable instrument, scores may vary depending on the clinical context at the time of assessment. Lymph node measurements were obtained from ultrasound examinations and existing reports, which introduces potential variability in observer interpretation and imaging protocols.

The commonly used cut-off of a short-axis diameter of ≥10 mm is a pragmatic heuristic and may not fully capture biological continuity. While the total sample size was adequate

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

for the primary analyses, statistical power was limited for subgroup comparisons and for some parameters in the multivariable models, increasing the risk of type II error. In particular, subgroup analyses based on the perceived helpfulness of online information involved small numbers of individuals and should therefore be regarded as exploratory.

Furthermore, the absence of an external comparison group (e.g., parents of healthy children or those presenting with clearly reactive lymphadenopathy in primary care) restricts the interpretation of the relative magnitude of the STAI scores observed in this cohort. Information-seeking on the internet and its perceived helpfulness were based on subjective reports, and some subgroups were small, resulting in imprecise estimates. Without follow-up data, it was not possible to evaluate trajectories of anxiety over time or clinical outcomes (e.g., spontaneous resolution or the need for further testing/biopsy). Therefore, the findings should be interpreted in the context of a single-center cross-sectional cohort study and should ideally be confirmed in larger multicenter prospective studies with standardized imaging and communication protocols and, where feasible, external control groups.

Conclusion

Pediatric lymphadenopathy is most often benign, but it can elicit substantial parental anxiety. In our cohort, anxiety increased with greater short-axis diameter and older child age, but decreased as symptom duration lengthened, consistent with diminishing uncertainty. Internet searching was not an independent determinant. In clinical practice, structured counseling, guidance toward reliable information sources, and the integration of stepwise evaluation algorithms are recommended to enhance safety and improve the overall experience of families.

Acknowledgments

ChatGPT was used for language and grammar improvements in this manuscript.

Authorship contributions

Study conception and design: S.O.A., M.A.C.; data collection: S.O.A., M.A.C.; analysis and interpretation of results: S.O.A., M.A.C.; draft manuscript preparation: S.O.A., M.A.C. All authors reviewed the results and approved the final version of the article.

Funding

No funding to be declared.

Ethical committee approval

Informed consent was obtained from all patients' legal guardians prior to inclusion. The study protocol received approval from the Izmir Bakırçay University Ethics Committee (Approval No. 2302) and adhered to the principles of the Declaration of Helsinki and good clinical practice standards.

Conflict of interest

The authors report no conflict of interest.

References

1. Cameron, D., Stetson, A., Blase, J., & Weldon, C. Pediatric Lymphadenopathy. Advances in pediatrics. 2025; 72.
2. Pecora, F., Abate, L., Scavone, S., Petrucci, I., Costa, F., Caminiti, C., et al. Management of Infectious Lymphadenitis in Children.Children. 2021; 8.
3. Spielberger CD, Gorsuch RL, Lushene R. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1970.
4. Julian LJ. Measures of anxiety: State-Trait Anxiety Inventory (STAI), Beck Anxiety Inventory (BAI), and Hospital Anxiety and Depression Scale-Anxiety (HADS-A). Arthritis Care Res. 2011;63(S11):S467-S472.
5. Pai AL, Greenley RN, Lewandowski A, et al. A meta-analytic review of the influence of pediatric cancer on parent and family functioning. J Fam Psychol. 2007;21(3):407-15.
6. Mess E, Misiąg W, Klaszczyk T, Kryś K. Depressive and Anxiety Disorders of Parents of Children with Cancer. Journal of Clinical Medicine. 2022;11(19):5670.
7. Boutin-Foster C, Foster JC, Konopasek L. Viewpoint: Physician, know thyself: The professional culture of medicine as a framework for teaching cultural competence. Acad Med. 2008;83(1):106-111.
8. Öner N, Le Compte A. State-trait anxiety inventory handbook. 2nd ed İstanbul: Boğaziçi University Press; 1985.
9. Sansakorn P, Mushtaque I, Awais-E-Yazdan M, Dost MKB. The Relationship between Cyberchondria and Health Anxiety and the Moderating Role of Health Literacy among the Pakistani Public. Int J Environ Res Public Health. 2024 Sep 2;21(9):1168.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue:1
RESEARCH ARTICLE
Pages:111-121

10. Xiao P, Zhang Y, Wu Y. Exploring the relationship between multidimensional health information overload and cyberchondria: the mediating role of rumination". Online Information Review. 2025 Vol. 49 No. 6 pp. 1247–1264.
11. Luengo TD, Rivas AB, Loureido E, Vargas E. Reducing preoperative anxiety in parents of surgical patients. Heliyon. 2023 May 4;9(5):e15920.
12. Rudravaram S, Gupta A, Kalra B, Malhotra S, Gupta MK, Kamal G, Agarwal S, Parida R. Evaluation of parental anxiety following three methods of pre-anesthesia counseling: Video, brochure and verbal communication. Paediatr Anaesth. 2024 Jul;34(7):665-670.
13. Nytun KL, Moldestad IO, Snibsøer AK, Espehaug B. The effect of web-based preoperative information on parents of children who are going through elective ambulatory surgery: A systematic review and meta-analysis. Patient Educ Couns. 2022 Dec;105(12):3389-3397.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

Efficacy and safety of bleomycin–lipiodol transarterial chemoembolization in giant hepatic hemangiomas: Insights from a single-center experience

Dev hepatik hemanjiomların tedavisinde bleomisin–lipiodol transarteriyel kemoembolizasyonun etkinliği ve güvenliği: Tek merkez deneyimi

Halil Serdar ASLAN[1]
Kadir Han ALVER[1]
Mehmet ALPUA[2]
Sevda YILMAZ[3]

[1] Pamukkale University, Faculty of Medicine, Department of Radiology, Denizli, Türkiye
[2]Pamukkale University, Faculty of Medicine, Department of Gastroenterology, Denizli, Türkiye
[3]Pamukkale University, Faculty of Medicine, Department of General Surgery, Denizli, Türkiye

Bleomycin – Lipiodol TACE Results
Received: 05.11.2025
Accepted: 27.12.2025
DOI:10.18614/dehm.1873881

Corresponding author
Halil Serdar ASLAN
ORCID ID: 0000-0002-5255-8618
hsaslan@pau.edu.tr

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

ABSTRACT

BACKGROUND
This study aimed to evaluate the efficacy and safety of bleomycin–lipiodol transarterial chemoembolization in the treatment of giant hepatic hemangiomas based on data from our center and to assess volumetric changes in non-target hemangiomas, as well as the contribution of a coil-assisted superselective approach to procedural safety.

METHODS
Retrospective data from 23 patients who underwent bleomycin–lipiodol transarterial chemoembolization for the treatment of giant hepatic hemangiomas between October 2018 and December 2024 were analyzed. Target hemangioma volumes were calculated before the procedure and at 6 months of follow-up. Clinical success was defined as ≥ 50% volume reduction on ultrasonography at 6 months. Non-target hemangiomas were evaluated at mid- and long-term follow-up. Detachable mechanical coil embolization was performed for 4 patients to prevent reflux and vasospasm in the non-lesional parenchyma. Complications were classified according to Cardiovascular and Interventional Radiological Society of Europe standards.

RESULTS
The mean age of the patients was 51.2 ± 8.6 years, and 19 (82.6%) were female. No major complications or mortality were observed; minor complications occurred in 3 patients (13%). At 6 months, the mean volume reduction rate was 54.2 ± 11.3% ($p < 0.001$). Clinical success was achieved in 20 cases (87.0%). Volume reduction increased with longer follow-up, reaching 83% at 24 months and 94% at ≥ 36 months. Among 10 patients with multiple hemangiomas, non-target lesions demonstrated an average 85% reduction in volume in mid- to long-term follow-up evaluations.

CONCLUSION
Bleomycin–lipiodol transarterial chemoembolization is a safe and effective treatment for giant hepatic hemangiomas, achieving high efficacy with low morbidity. The treatment provides significant volume reduction not only in target lesions but also in non-target hemangiomas, suggesting a potential locoregional or diffuse pharmacological effect beyond the directly embolized area. Coil-assisted superselective embolization substantially enhances procedural safety.

KEYWORDS
Bleomycin, embolization, eemangioma, lipiodol, liver

ÖZ

AMAÇ
Dev hepatik hemanjiyom tedavisinde bleomisin-lipiodol transarteriyel kemoembolizasyonun etkinliğini ve güvenilirliğini merkezimizin verileri ışığında değerlendirmek; hedef dışı hemanjiyomlardaki hacimsel değişimleri ve ayrıca coil destekli süperselektif yaklaşımın işlem güvenliğine katkısını incelemektir.

GEREÇ YÖNTEM
Ekim 2018- Aralık 2024 tarihleri arasında kliniğimizde dev hepatik hemanjiyom tanısıyla bleomisin-lipiodol transarteriyel kemoembolizasyon uygulanan 23 hastanın retrospektif verileri analiz edildi. İşlem öncesi ve 6. ayda hedef hemanjiyom hacimleri hesaplandı. Klinik başarı, 6. ayda ultrasonografi ile %50 ve üzerinde hacim azalması olarak tanımlandı. Hedef dışı hemanjiyomlar orta ve uzun vadede değerlendirmeye alındı. Lezyon dışı parankime reflü ve vazospazmı engellemek amacıyla dört hastada mekanik ayrılabilir coil embolizasyon kullanıldı. Komplikasyonlar Avrupa Kardiyovasküler ve Girişimsel Radyoloji Derneği kılavuzlarına göre değerlendirildi.

BULGULAR
Hastaların ortalama yaşı 51,2 ± 8,6 olup, 19 hasta (% 82,6) kadındı. Majör komplikasyon veya mortalite gözlenmedi; minör komplikasyon üç hastada (%13) gelişti. 6. ayda ortalama hacim azalması % 54,2 ± 11,3 olarak hesaplandı ($p < 0,001$). Klinik başarı oranı 20 olguda (%87,0) elde edildi. Takip süresi uzadıkça hacimsel küçülmenin arttığı (24. ayda %83, 36. ay ve üzerinde %94) saptandı. Multipl hepatik hemanjiyomlu 10 hastada hedef dışı lezyonlarda orta/uzun dönem takipte ortalama %85 hacim azalması gözlendi.

SONUÇ
Bleomisin-lipiodol transarteriyel kemoembolizasyon, dev hepatik hemanjiyomların tedavisinde yüksek etkinlik ve düşük morbidite oranı ile güvenli bir yöntemdir. Tedavi, yalnızca hedef lezyonda değil, aynı zamanda hedef dışı hemanjiyomlarda da anlamlı hacim azalması sağlayarak ilacın lokal-bölgesel etkinin ötesinde bir etkiye sahip olabileceğine işaret etmektedir. Koil destekli süperselektif embolizasyon, işlem güvenliğini önemli ölçüde artırmaktadır.

ANAHTAR KELİMELER
Bleomisin, embolizasyon, hemanjiyom, karaciğer, lipiodol

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

Hepatic hemangiomas (HHs) are benign tumors of mesodermal origin that are supplied by the hepatic arterial system and composed of blood-filled vascular spaces lined by a single layer of flattened endothelial cells (1). They are approximately 5–6 times more common in women than in men (2). Most HHs are incidentally detected during radiological examinations and may appear as solitary or multiple lesions. Lesions are generally confined to a single lobe; however, in some cases, they may involve the entire liver. Based on size, they are classified as small or, when larger than 5 cm, as giant hepatic hemangiomas (GHHs); sizes ranging from 1 mm to 50 cm have been reported in the literature (3,4). The vast majority of HHs are asymptomatic and incidentally detected. However, some patients may develop symptoms such as abdominal distension, pain, nausea, or hemorrhage, often necessitating interventional treatment (5). In particular, symptomatic GHHs pose significant clinical challenges due to potential complications, and therapeutic options should be carefully evaluated in these cases (6).

Until the 2010s, surgical management was widely accepted as the primary treatment for symptomatic GHHs (7). However, in the early 2000s, transarterial chemoembolization (TACE) emerged as an alternative therapeutic modality. This technique is based on selective catheterization of the artery supplying the lesion, followed by the administration of chemotherapeutic agents such as bleomycin or pingyangmycin mixed with lipiodol to achieve sinusoidal opacification and embolization of the lesion. In addition, the use of an ethyl alcohol–lipiodol mixture solely as an embolic agent has also been described as an alternative treatment approach (8,9). Numerous studies have shown that TACE is both effective and safe in the treatment of GHHs (10,11). These favorable outcomes have led to its increasing adoption as a primary therapy for GHHs. In recent years, multiple reports on TACE using a bleomycin–lipiodol mixture have further encouraged the use of this locoregional therapy as a first-line option (12–15). Moreover, a recent study made a noteworthy contribution by demonstrating the volumetric shrinkage of non-target HHs located in liver segments not supplied by the embolized hepatic artery branch during follow-up in patients with multiple HHs after superselective bleomycin–lipiodol TACE of the target lesion (16).

The aim of this study was to evaluate, using data from our center, the efficacy of bleomycin–lipiodol TACE, an increasingly utilized method in the treatment of GHHs. In this context, we analyzed volumetric changes in target hemangiomas at the 6-month follow-up according to ultrasonography (USG) as well as volumetric changes of lesions, including non-target HHs, according to cross-sectional imaging [computed tomography (CT) and magnetic resonance imaging (MRI)] performed for mid-term (24-month) and long-term (36-month) follow-up. In addition, we aimed to contribute to the literature by emphasizing the value of coil-assisted bleomycin–lipiodol TACE in preventing non-target embolization.

Materials and Methods

This retrospective study was approved by the Pamukkale University Ethics Committee (Pamukkale University Non-Interventional Clinical Research Ethics Committee, 18/02/2025, file number: E-60116787-020-657768). Informed consent was obtained from all patients prior to the procedure. This study retrospectively reviewed the medical records and archived radiological images of patients diagnosed with GHH by dynamic CT or MRI and treated with bleomycin–lipiodol TACE at the Pamukkale University Faculty of Medicine Hospital between October 2018 and December 2024. The cohort included all patients treated with this method since its implementation at our institution. Twenty-six patients who underwent bleomycin–lipiodol TACE were identified in our hospital's archives. Data from 23 followed patients, including those with GHHs and non-target HHs, as well as those who underwent coil embolization to prevent non-target embolization, were included in the analysis.

Patients included in this study were those diagnosed with GHH, with or without multiple HHs, in cross-sectional examinations such as dynamic CT (Ingenuity 128, Philips Medical Systems, the Netherlands) or dynamic MRI (Ingenia, Philips Healthcare, the Netherlands). All HH volumes were calculated in cubic centimeters using the ellipsoid formula during USG (Aplio XG, Toshiba Medical Systems Corp., Japan; Acuson Sequoia, Siemens Healthineers, USA). Volume measurements were performed by the interventional

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

radiologist who conducted the procedures. Lesion location was categorized as right lobe, left lobe, or bilobar. In addition, the absence of contraindications such as uncorrectable coagulopathy, platelet count of < 50,000/mm^3, or active infection was confirmed.

Owing to the retrospective nature of the study, all procedures had been performed by a single interventional radiologist (H.S.A.) with approximately 20 years of experience in vascular interventions, using a C-arm angiography system (Artis Zee, Siemens Healthineers, Germany). After establishing sterile conditions prior to TACE, femoral artery puncture was performed under local anesthesia with an 18-G Seldinger needle (Egemen International, Türkiye). Following the placement of a 5-F introducer sheath, the abdominal aorta was imaged and vascular anatomy and feeder arteries were identified using a 5-F pigtail catheter. With selective angiography of the celiac and superior mesenteric arteries, hepatic arterial variants and the feeder artery of the GHH were determined using diagnostic Simmons 1 or Cobra catheters (TaHa Biomedical, Türkiye). The feeder arteries were then superselectively catheterized with a 2.7-F microcatheter and a microwire (Renegade HIFLO, Boston Scientific Corp., USA).

Embolization of the target hemangioma was performed selectively via the feeder arteries. Bleomycin sulfate (Blemisin 15 mg, Koçak Farma, Türkiye) was dissolved in 5 mL of normal saline and then 10 mL of ethiodized oil (Lipiodol Ultra-Fluid, Guerbet, France) was added; using the three-way stopcock technique and 20-mL syringes, the mixture was agitated at least 20 times until a homogeneous emulsion was achieved. A total of 15 mL of the mixture was selectively infused through the microcatheter. For hemangiomas larger than 10 cm in diameter, doses of up to a maximum of 30 mg of bleomycin and 20 mL of ethiodized oil were administered, reaching a maximum total volume of 30 mL. The endpoint of embolization was defined as complete opacification of the GHH sinusoids by the mixture, with the goal of achieving complete stasis in the feeder artery. If complete stasis was not achieved after infusion of the mixture, polyvinyl alcohol (PVA) particles of 300–500 μm (Embosoft Microspheres, Scitech Medical, Brazil) were used to obtain full stasis. Avoiding reflux is critical to prevent exposure of non-target parenchyma to bleomycin. Therefore, in cases where the lesion's feeder artery shared a common origin with a branch supplying normal parenchyma, or where a branch supplying normal parenchyma originated from the GHH feeder and distal caliber reduction led to vasospasm and reflux in the normal parenchyma, coil embolization with mechanically detachable coils (2–3 × 40 mm) sized to the vessel diameter (Concerto Detachable Coil System, Medtronic, USA) was performed for some patients prior to infusion of the mixture (Figure 1).

All procedures were performed in a single session. Technical success was defined as successful catheterization of the vessel feeding the GHH and infusion of the mixture without reflux. Postprocedural major and minor complications were evaluated according to Cardiovascular and Interventional Radiological Society of Europe guidelines (17). Minor complications included groin access-site hematoma, pseudoaneurysm, transient elevation of liver function tests, and postembolization syndrome (PES). PES was defined and recorded as abdominal pain, nausea, vomiting, and fever. The postprocedural hospital stay was 1 day for patients without PES; patients who developed PES were discharged after an additional 2 or 3 days of supportive care. Major complications were defined as hepatic failure and death.

In our clinic, routine USG follow-up is recommended at 6 and 12 months after the procedure for short-term assessment. All patients attended the 6-month USG follow-up appointment, and due to low adherence at 12 months, only the 6-month USG data were included in the analysis. Short-term clinical success was defined as a ≥ 50% reduction in target lesion volume measured by USG at 6 months by the interventional radiologist who had performed the procedure. In contrast, mid-term (24-month) and long-term (36-month) volumetric evaluations were not part of a predefined routine follow-up protocol but were performed using cross-sectional imaging studies (CT or MRI) conducted at our institution for other clinical indications. In these assessments, volumetric changes in GHHs and non-target HHs were analyzed by comparison with preprocedural cross-sectional imaging.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 25.0 (IBM Corp., USA). Continuous variables were expressed as mean ± standard deviation, median (minimum–maximum), and interquartile range; categorical variables were summarized as number and percentage (%) values. Normality was assessed with the Shapiro–Wilk test. For continuous variables not normally distributed, the Wilcoxon signed-rank test was used to evaluate the significance of differences between pre- and postprocedural volumes. The volume

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

reduction rate (%) was calculated as (preprocedural volume − postprocedural volume) / preprocedural volume × 100. Relationships between the volume reduction rate and baseline volume and follow-up duration were examined using Spearman rank correlation analysis. Values of $p < 0.05$ were considered statistically significant for all tests.

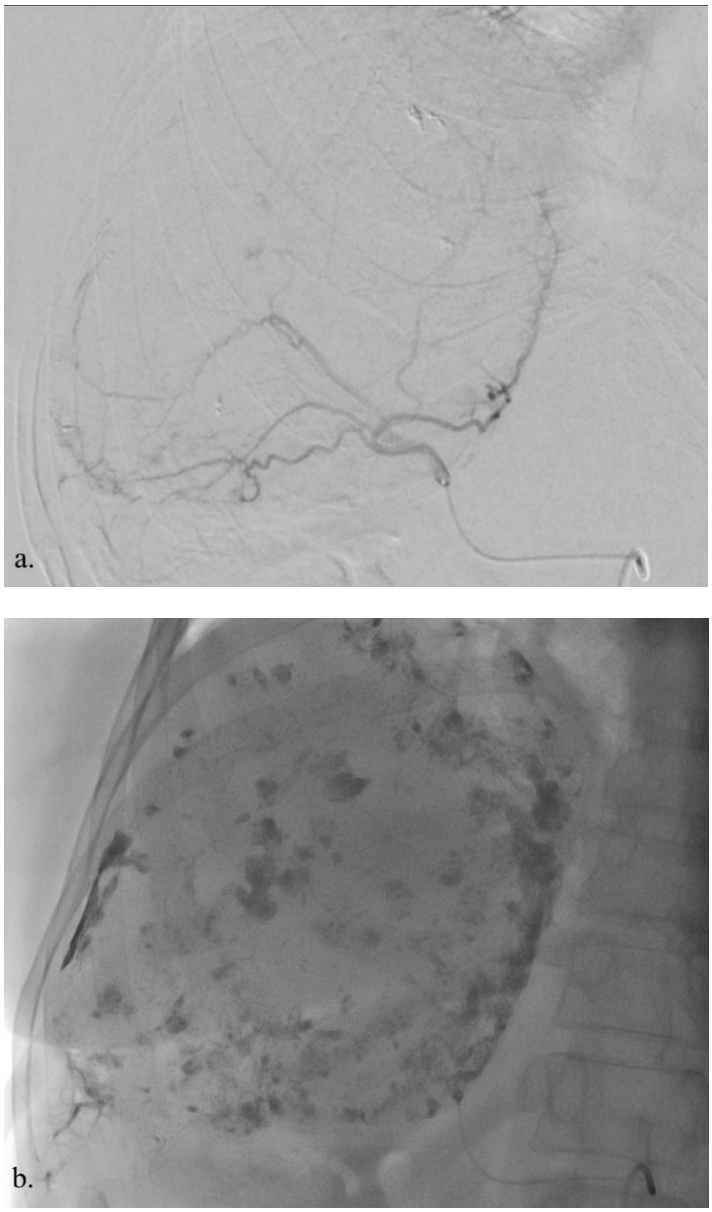


Figure 1. (a) Angiographic image obtained via a microcatheter advanced into the right hepatic artery in a 45-year-old female patient presenting with right upper quadrant pain and fullness, demonstrating a giant hemangioma in the right hepatic lobe. (b) Post-treatment angiographic image following transarterial administration of a bleomycin–lipiodol combination, showing extensive lipiodol retention throughout the lesion with markedly reduced tumoral vascularity.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

Results

A total of 26 patients who underwent bleomycin–lipiodol TACE were identified from our institutional archival records. However, three of these patients were excluded from the study because they had not completed the 6-month USG follow-up required by the study's inclusion criteria (Figure 2). The demographic characteristics and procedural details of the remaining 23 patients included in the analysis are summarized in Table 1. The mean age of the patients was 51.2 ± 8.6 years and the majority were female (82.6%). Regarding anatomical distribution, right lobe involvement was predominant (65.2%), and approximately half of the patients (43.5%) had multiple HHs.

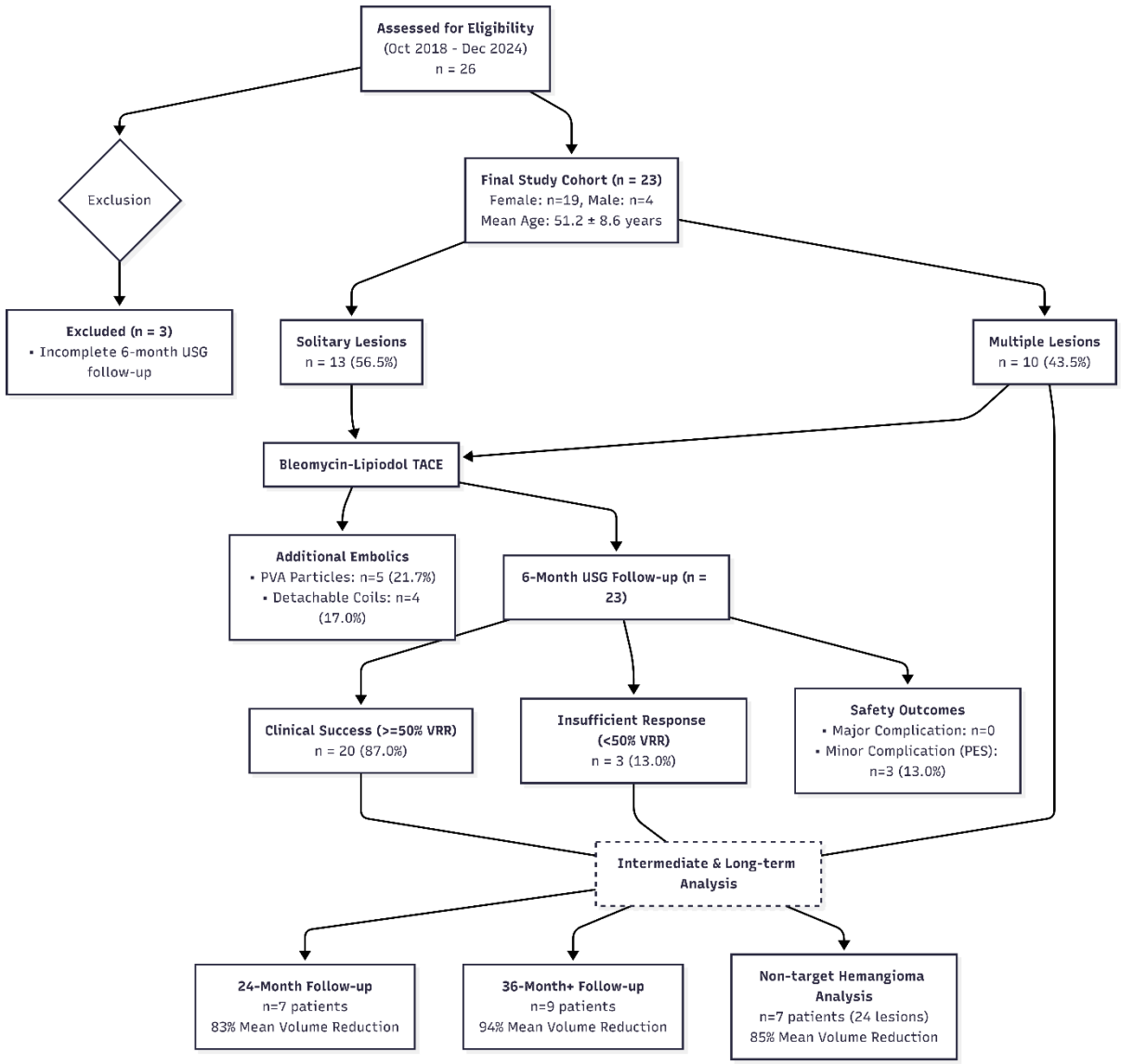


Figure 2. Flowchart of the study population, procedural details, and clinical outcomes
TACE, Transarterial chemoembolization; USG, ultrasonography; PVA, polyvinyl alcohol; PES, postembolization syndrome; VRR, volume reduction rate

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

Table 1. Demographic, clinical, and procedural characteristics

Characteristic	Subcategory	Value
Number of Patients	Total (n)	23
Age	Mean ± SD (years) Range (years)	51.2 ± 8.6 36 – 71
Sex	Female (n, %) Male (n, %)	19 (82.6%) 4 (17.4%)
Lesion number	Solitary (n, %) Multiple (n, %)	13 (56.5%) 10 (43.5%)
Location	Right Lobe (n, %) Left Lobe (n, %) Bilobar (n, %)	15 (65.2%) 7 (26.1%) 1 (8.7%)
Symptoms	Present (n, %) Absent (n, %)	11 (47.8%) 12 (52.2%)
Supportive technique	Coil (n, %) PVA particle (n, %)	4 (17%) 5 (21.7%)
Success	Technical (n, %) Clinical (n, %)	23 (100%) 20 (87%)
Complications	Major (n) Minor (n, %)	0 3 (13%)

SD, Standard deviation.

Technical success was achieved in all patients (100%), with superselective catheterization of the feeding artery of the GHH. In 4 cases (17%), mechanical detachable coil embolization was successfully performed to prevent vasospasm and reflux in the normal hepatic parenchyma.

In USG evaluations performed at the 6-month follow-up, a statistically significant reduction in target GHH volumes was observed compared to preprocedural measurements ($p < 0.001$). The mean volumetric reduction rate at 6 months was 54.2%, resulting in clinical success in 20 of the 23 patients (87.0%). Even in the 3 patients who did not meet the clinical success criteria at 6 months, volumetric reduction continued during follow-up, reaching volume loss of 78% to 85% in the long term (Figure 3).

A significant positive correlation was identified between follow-up duration and the degree of volume reduction ($p = 0.007$), indicating that the therapeutic effect increased over time. Mid-term (24-month) and long-term (36-month and beyond) results obtained using CT or MRI demonstrated mean volumetric reduction rates of 83.0% and 94.1%, respectively (Table 2).

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

In patients with multiple HHs, evaluation of non-target lesions revealed a marked volumetric reduction, with a mean decrease of approximately 85% observed during mid- and long-term follow-up (Figure 4).

No procedure-related major complications or mortality occurred. Minor complications were observed in 3 patients (13%) in the form of PES and all of these patients were successfully managed with supportive treatment and discharged without sequelae. During the follow-up period, no radiological recurrence was observed in the treated target lesions and none of the patients required repeat bleomycin–lipiodol TACE or surgical intervention. Among the 11 patients (47.8%) who presented with symptoms, marked clinical improvement in pain and abdominal fullness was achieved at the 6-month follow-up. No non-target embolization or related complications were observed in patients who underwent coil-assisted embolization.

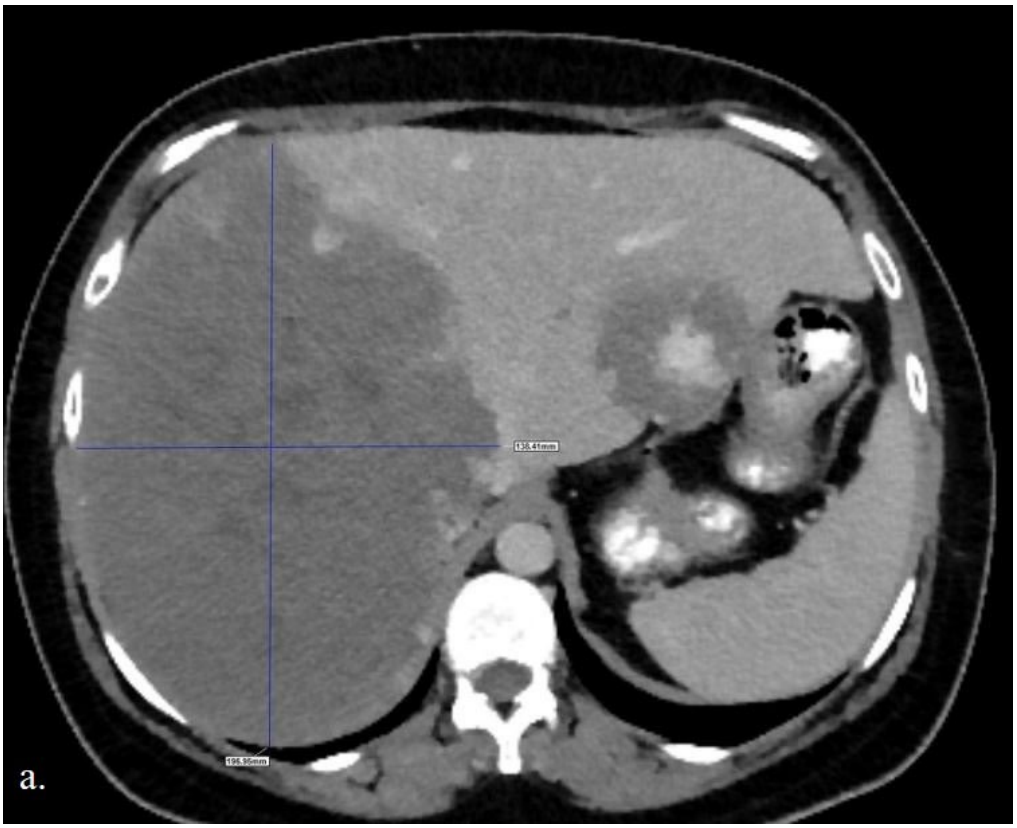


Figure 3. (a) Preprocedural contrast-enhanced upper abdominal computed tomography (CT) image demonstrating a large hypodense lesion in the right hepatic lobe, measuring approximately 196.95 × 138.41 mm, nearly occupying the entire right lobe and causing diffuse enlargement of the liver. (b) Contrast-enhanced upper abdominal CT obtained 24 months after treatment showing a marked reduction in lesion volume, now measuring approximately 74.79 × 79.82 mm, consistent with significant postprocedural involution of the hemangioma.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

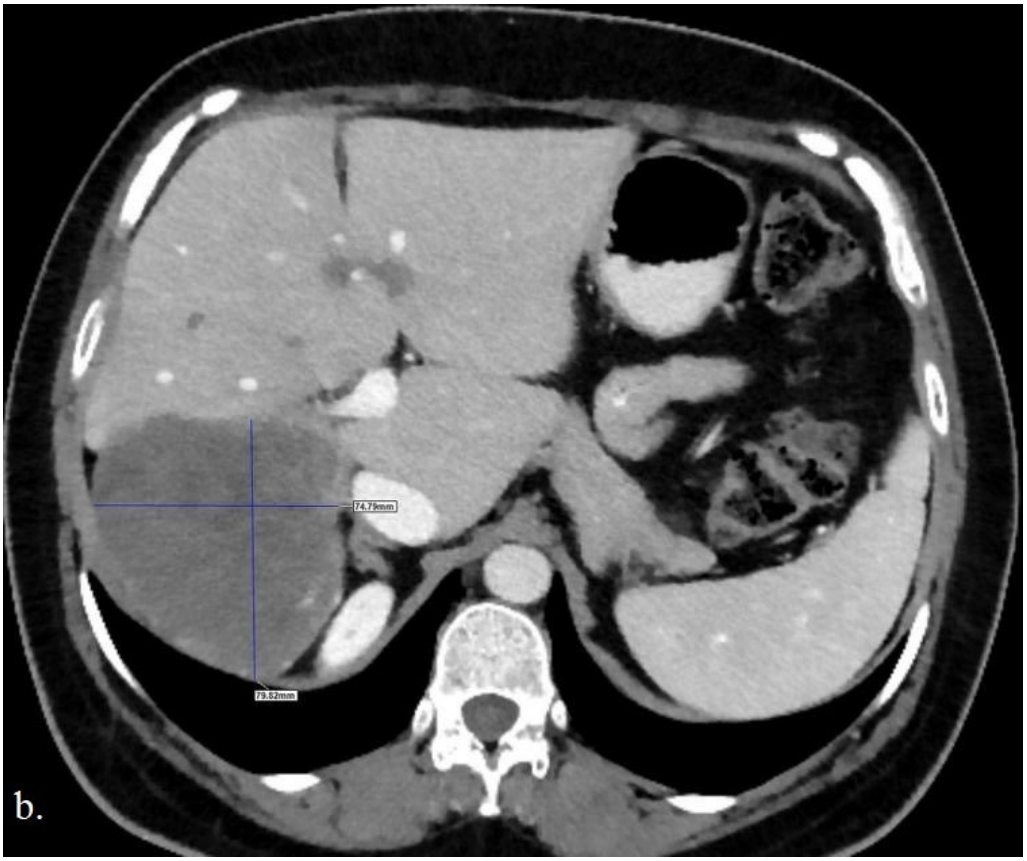


Table 2. Volumetric outcomes of target and non-target hepatic hemangiomas at different follow-up intervals

		n (patients)	Preprocedural volume (cm³), mean ± SD (min-max)	Postprocedural volume (cm³), mean ± SD (min-max)	Volume reduction ratio (%)
Target	6-month control with USG	23	464.2 ± 733.5 (52 – 3452)	189.8 ± 245.2 (25 – 1100)	54.2%
	24-month control with CT/MRI	7	835.1 ± 1190.8 (163 – 3452)	138.4 ± 106 (11 – 293)	83.0%
	36-month control with CT/MRI	9	765 ± 263.7 (138 – 1004)	45.2 ± 84.7 (3 – 273)	94.1%
Non-target	24- or 36-month control with CT/MRI	7	31.4 ± 27.4 (18 – 155)	4.7 ± 4.1 (1 – 25)	85.0%

SD, Standard deviation; USG, ultrasonography; CT, computed tomography; MRI, magnetic resonance imaging

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

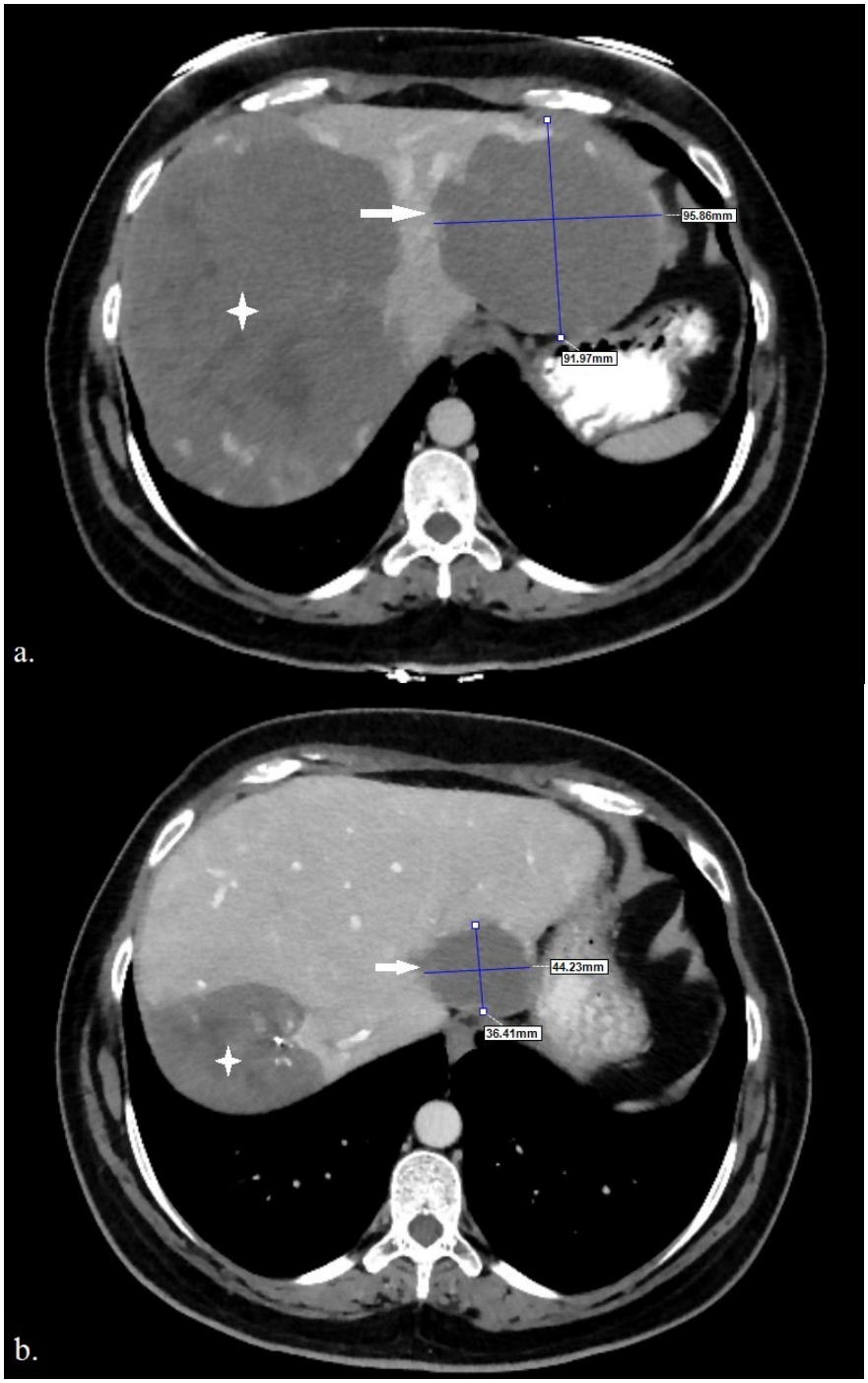


Figure 4. (a) Preprocedural contrast-enhanced abdominal computed tomography (CT) image of a 42-year-old female patient presenting with right upper quadrant fullness and dyspepsia, demonstrating both a target hepatic hemangioma (quadrilateral star) and a concomitant non-target hemangioma (white arrow). (b) Contrast-enhanced CT image obtained 36 months after treatment, demonstrating marked volumetric reduction of both the target lesion (quadrilateral star) and the non-target hemangioma (white arrow) following bleomycin–lipiodol transarterial chemoembolization.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

Discussion

This study evaluated the effectiveness of bleomycin–lipiodol TACE in the treatment of GHHs. The findings demonstrated an average 54% reduction in target lesion volume 6 months after the procedure, with clinical success achieved in the majority of cases (87%). Results from a large series of 241 patients reported by Yuan et al. support our findings; in that study, the proportion of GHHs exhibiting >50% reduction in maximum diameter at 6 months after TACE was 88.1%, indicating a high rate of early success (10). We also observed continued gradual shrinkage beyond 6 months, and the strong positive correlation between follow-up duration and volume reduction underscores the increasing effectiveness of the treatment over time. Collectively, these results show that bleomycin–lipiodol TACE yields meaningful and durable volumetric reductions in the treatment of GHHs. These outcomes are consistent with prior reports indicating that bleomycin–lipiodol TACE is an effective and safe option for GHHs (10–15). Furthermore, the absence of major complications again highlights the feasibility of this method with low morbidity.

The findings of our study are consistent with recent meta-analyses evaluating the efficacy and safety of TACE in the treatment of GHHs. In a meta-analysis including 2617 patients, Günkan et al. reported an approximately 100% technical success rate, a clinical success rate of 99.9%, and a radiological success rate of 81.9% for TACE (18). Similarly, Elek et al. reported a clinical success rate of 99.9% in the TACE group (19), supporting the high clinical success (87%) and significant volumetric reduction observed in our series. From a safety perspective, the incidence of severe adverse events related to TACE has been reported to range between 0.2% and 0.26%, which is markedly lower than the major complication rates for thermal ablation techniques (1.99%–2.08%) (18, 20). The absence of major complications or mortality in our study is consistent with these findings. Furthermore, while the pooled incidence of PES has been reported as 45.5% (19), the substantially lower rate observed in our cohort (13%) suggests a potential contribution of the superselective approach and adjunctive coil embolization in reducing ischemic burden and systemic adverse effects.

In our study, the occurrence of PES being limited to mild-to-moderate and self-limiting clinical manifestations supports the favorable safety and tolerability profile of bleomycin–lipiodol TACE. Clinical presentations were predominantly confined to transient abdominal pain, low-grade fever, and nausea, with symptoms resolving within a short period of time. Successful management of all cases with conservative supportive measures alone, including analgesics, antipyretics, antiemetics, and intravenous hydration when necessary, without the need for additional invasive interventions or prolonged hospitalization indicates that the procedure offers a manageable postprocedural response profile. Taken together with the absence of major complications, these findings suggest that bleomycin–lipiodol TACE can be safely implemented in clinical practice with low morbidity for the treatment of GHHs, and our results are consistent with the PES profile reported in the literature to date (13, 14, 21).

Regarding bleomycin dosing, Kirnap et al. described tumor size-based dosing strategies in the literature, recommending a maximum bleomycin dose of 30 mg for lesions larger than 10 cm (13). Similarly, Akhlaghpoor et al. proposed doses of up to 45 IU (approximately 45 mg) for hemangiomas exceeding 10 cm, suggesting that a bleomycin dose of 30 mg falls within a reasonable and therapeutic range for giant lesions (22). The most serious safety concern associated with bleomycin administration is cumulative dose-related pulmonary fibrosis; however, the literature indicates that this risk typically emerges when the cumulative dose exceeds 400–450 mg (23). In this context, the bleomycin doses used in the present study were well below the reported toxicity thresholds, indicating that the observed therapeutic efficacy was achieved within a safe dosing range.

Several studies in the literature have reported the volumetric reduction of HHs following the systemic use of bleomycin for the treatment of various malignancies. It has been suggested that the BEP regimen (bleomycin, etoposide, and cisplatin), administered for germ cell tumors, may contribute to the regression observed in non-target HHs through a pharmacological “remote effect.” This is thought to be associated with the sclerosing effects of bleomycin, which induce endothelial cell pyknosis and microthrombus formation, as well as the antiangiogenic response mediated by

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

vascular endothelial growth factor (VEGF) inhibition. The observation of clinical responses even in estrogen receptor-negative cases suggests that direct microvascular injury caused by cytotoxic agents, rather than hormonal suppression, may constitute the dominant mechanism underlying hemangioma regression. Nevertheless, further studies at the pharmacodynamic and microcirculatory levels are required to elucidate the precise pathophysiological mechanisms involved (24–26). A distinctive aspect of our study is the demonstration of significant long-term volumetric shrinkage in non-target lesions among patients with multiple hemangiomas after locoregional therapy. As also described by Kutlu et al., this observation suggests that the bleomycin–lipiodol mixture may exert a systemic effect within the vascular architecture (16). The mean 85% reduction observed in non-target HHs in mid-term and long-term follow-up evaluations in our cohort supports the possibility that local microcirculatory alterations after embolization may produce therapeutic effects. This implies that the bleomycin–lipiodol mixture could act as a diffusely effective agent not limited to the target arterial bed but also active within surrounding vascular areas.

In addition, using a coil-assisted approach to reduce the risk of reflux and non-target embolization during the procedure contributed meaningfully to patient safety in this study. To the best of our knowledge, although data exist regarding coil use in bleomycin–lipiodol TACE for GHH, coil embolization is more commonly employed in daily practice during transarterial radioembolization, another treatment option for primary or metastatic liver disease, to prevent reflux into the gallbladder or gastroduodenal artery (27). We believe this technique offers a protective barrier, particularly in cases where the feeder artery has a common origin with branches supplying normal parenchyma. Moreover, in scenarios where vasospasm is anticipated in small-caliber parent arteries, coil embolization enables more proximal embolization. In our study, the use of mechanically detachable coils for 4 patients proved to be a practical, reliable, and feasible strategy.

Our observations also align with the conclusion that the volumetric reduction achieved after effective TACE procedures in GHH persists into mid-term and long-term follow-up. This suggests that routine radiological surveillance may be adequately limited to 6- and 12-month assessments. Additionally, USG during this period is sufficiently sensitive to monitor changes in lesion volume. This approach maintains an appropriate balance between patient safety and healthcare sustainability by avoiding unnecessary ionizing radiation exposure and preventing additional financial burden on the social security system.

This study has several limitations that should be considered while interpreting the results. The retrospective single-center design inherently limits the generalizability and introduces the potential for selection and information bias. In addition, all procedures were performed by a single operator, which, while ensuring technical consistency, may restrict the external validity of the findings. Another important limitation concerns follow-up imaging: short-term volumetric assessment of target GHHs was uniformly performed using USG, whereas mid- and long-term volumetric measurements, particularly for non-target HHs, were available only for a subgroup of patients and were derived from CT or MRI examinations performed for various other clinical indications. The absence of a standardized long-term imaging protocol and the use of different imaging modalities may have contributed to measurement variability. Furthermore, the use of additional embolic materials such as PVA particles and coils in selected cases, although intended to enhance procedural safety, may have reduced cohort homogeneity and should be acknowledged as a potential confounder. Despite these limitations, the observed clinical outcomes and complication rates are in line with previously published data, supporting the overall reliability of our results.

Future research would benefit from prospective study designs with standardized imaging protocols to ensure uniform volumetric assessment across follow-up intervals. The inclusion of validated symptom scoring systems could allow a more objective evaluation of clinical outcomes alongside radiological responses. Additionally, clearly defined criteria for coil utilization during TACE procedures would facilitate a more systematic assessment of its contribution to procedural safety and efficacy. These methodological refinements would strengthen the evidence base and enhance the interpretability and generalizability of future studies.

Our study has shown that bleomycin–lipiodol TACE can induce volumetric reduction not only in target lesions but also in concomitant multiple HHs and that coil-assisted superselective embolization is a complementary technique that

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
RESEARCH ARTICLE
Pages:123-136

enhances procedural safety. These findings make valuable contributions to clinical practice in terms of efficacy and safety, in addition to the personalization of embolization protocols for GHH.

Conclusion

TACE performed with a bleomycin–lipiodol mixture is a safe method with high efficacy and low complication rates in the treatment of GHHs. Although short-term follow-up was a primary focus of this study, volumetric reductions of ≥90% were observed for GHHs during long-term follow-up. In addition, by highlighting significant volume reduction in non-target hemangiomas and the role of a coil-assisted approach in improving procedural safety, this study contributes to the literature.

Conflicts of interest and source of funding

No conflict of interest was declared by the authors. This study was conducted without any funding or financial support from external institutions. The authors did not receive support from any organization for the submitted work.

Acknowledgements

None

References

1. Ishak KG, Rabin L. Benign tumors of the liver. Med Clin North Am 1975; 59: 995-1013 [PMID: 167242 DOI: 10.1016/s0025-7125(16)31998-8]
2. Choi BY, Nguyen MH. The diagnosis and management of benign hepatic tumors. J Clin Gastroenterol. 2005;39:401-12.
3. Yang Z, Tan H, Liu X, Sun Y. Extremely Giant Liver Hemangioma (50 cm) with Kasabach-Merritt Syndrome. J Gastrointest Surg. 2017; 21: 1748-1749 [PMID: 28424986 DOI: 10.1007/s11605-017-3429-7]
4. Adam YG, Huvos AG, Fortner JG. Giant hemangiomas of the liver. Ann Surg. 1970; 172: 239-245 [PMID: 5433290 DOI: 10.1097/00000658-197008000-00010]
5. Choi BY, Nguyen MH. The diagnosis and management of benign hepatic tumors. J Clin Gastroenterol. 2005;39:401–12.
6. Paradis V. Benign liver tumors: an update. Clin Liver Dis. 2010;14:719–29.
7. Abdel Wahab M, El Nakeeb A, Ali MA, Mahdy Y, Shehta A, Abdulrazek M at al. Surgical Management of Giant Hepatic Hemangioma: Single Center's Experience with 144 Patients. J Gastrointest Surg. 2018 May;22(5):849-858. doi: 10.1007/s11605-018-3696-y. Epub 2018 Feb 27. PMID: 29488123.
8. Bozkaya H, Cinar C, Besir FH, Parıldar M, Oran I. Minimally invasive treatment of giant haemangiomas of the liver: embolisation with bleomycin. Cardiovasc Intervent Radiol. 2014 Feb;37(1):101-7. doi: 10.1007/s00270-013-0618-y. Epub 2013 Apr 12. PMID: 23580121.
9. Shaha S, Rodrigues D, Mitragotri S. Locoregional drug delivery for cancer therapy: Preclinical progress and clinical translation. J Control Release. 2024 Mar;367:737-767. doi: 10.1016/j.jconrel.2024.01.072. Epub 2024 Feb 14. PMID: 38325716.
10. Yuan B, Zhang JL, Duan F, Wang MQ. Medium and Long-Term Outcome of Superselective Transcatheter Arterial Embolization with Lipiodol-Bleomycin Emulsion for Giant Hepatic Hemangiomas: Results in 241 Patients. J Clin Med. 2022 Aug 15;11(16):4762. doi: 10.3390/jcm11164762. PMID: 36013000; PMCID: PMC9409947.
11. Torkian P, Li J, Kaufman JA, Jahangiri Y. Effectiveness of transarterial embolization in treatment of symptomatic hepatic hemangiomas: systematic review and meta-analysis. Cardiovasc Intervent Radiol. 2020. https://doi.org/10.1007/s00270-020-02611 5.
12. Furumaya A, van Rosmalen BV, Takkenberg RB, van Delden OM, Dejong CHC, Verheij J, et al. Transarterial (chemo)embolization and lipiodolization for hepatic haemangioma. Car diovasc Intervent Radiol. 2019;42(6):800–11. https://doi.org/10. 1007/s00270-019-02169-x (Epub 2019 Feb 19).
13. Kirnap M, Boyvat F, Boyacioglu S, Hilmioglu F, Moray G, Haberal M. Effect of Bleomycin Embolization on Symptomatic Improvement and Hemangioma Size among Patients with Symptomatic Giant Liver Hemangiomas. Journal of the American College of Surgeons. 2018 Oct; 227(4), e36.
14. Pehlivan UA, Ballı HT, Aikimbaev K. Safety and efficacy of chemoembolization with mixture of bleomycin and lipiodol in the treatment of giant liver hemangiomas. Cukurova Med J. 2022;47(1):310-321. DOI: 10.17826/cumj.1035544

15. Küsbeci M, Elek A, Oztürk E, Bozkaya H, Cınar C, Parıldar M at al. Long-Term Outcomes of Transarterial Chemoembolization of Giant Liver Hemangiomas with Lipiodol-Bleomycin Emulsion. Cardiovasc Intervent Radiol. 2024 Nov;47(11):1506-1514. doi: 10.1007/s00270-024-03876-w. Epub 2024 Oct 15. PMID: 39406873.
16. Kutlu R, Dag N, Saparbekov E, Yagin FH. Nontarget Hemangioma Size Reduction after Bleomycin-Ethiodized Oil Embolization of Primary Hepatic Hemangioma. J Vasc Interv Radiol. 2025 May;36(5):787-794. DOI: 10.1016/j.jvir.2025.01.042. Epub 2025 Jan 28. PMID: 39884351.
17. Flippiadis DK, Binkert C, Pellerin O, Hoffmann RT, Krajina A, Pereira PL. Cirse quality assurance document and standards for classification of complications: The Cirse classification system. Cardiovasc Intervent Radiol. 2017;40:1141-1146.
18. Günkan A, Elek A, Ohannesian VA, Mendes LL, Pehlivan UA, Fouad MEM, Shafeea MS, Loffroy R, Hannallah J, Woodhead G, Young S. Safety and Effectiveness of Image-Guided Therapies for Giant Hepatic Hemangiomas: A Systematic Review and Meta-Analysis of 2,617 Patients. J Vasc Interv Radiol. 2025 Oct;36(10):1502-1512.e18. DOI: 10.1016/j.jvir.2025.06.025. Epub 2025 Jul 7. PMID: 40633757.
19. Elek A, Günkan A, Ohannesian VA, Lima Mendes L, Albayrak E, Cam I, Oran I, et al. Percutaneous Sclerotherapy Versus Transarterial Chemoembolization for Giant Hepatic Hemangiomas: A Systematic Review and Meta-analysis. Cardiovasc Intervent Radiol. 2025 Nov;48(11):1549-1561. DOI: 10.1007/s00270-025-04198-1. Epub 2025 Sep 21. PMID: 40976792.
20. Elek A, Günkan A, Ohannesian VA, Chadli N, Oran I. Thermal Ablation for Giant Hepatic Hemangiomas: A Meta-Analysis with Subgroup Analysis of Microwave and Radiofrequency Ablation Techniques. Cardiovasc Intervent Radiol. 2025 Aug 29. DOI: 10.1007/s00270-025-04172-x. Epub ahead of print. PMID: 40883579.
21. Zhao D, Xie L, Makamure J, Liu Z, Zhang L, Li Q, et al. Transcatheter Arterial Embolization with Bleomycin-Lipiodol of Hepatic Hemangiomas: Safety, Efficacy and Predictors of Response. Cardiovasc Intervent Radiol. 2024 Jul;47(7):931-942. DOI: 10.1007/s00270-024-03690-4. Epub 2024 Mar 20. PMID: 38509337.
22. Akhlaghpoor S, Torkian P, Golzarian J. Transarterial bleomycin-lipiodol embolization (B/LE) for symptomatic giant hepatic hemangioma. Cardiovasc Intervent Radiol. 2018;41(11):1674–82. https://doi.org/10.1007/s00270-018-2010-4.
23. Y,20 Bennett JM, Reich SD. Drugs five years later: bleomycin. Ann Intern Med. 1979;90(6):945–8.
24. Hashimoto M, Sugawara M, Ishiyama K, Sato T, Yamamoto Y, Nanjo H. Reduction in the size of a hepatic haemangioma after chemotherapy. Liver Int 2008; 28:1043–1044.
25. Bekci T, Özdemir M, Mehmet Selim N, Danacı M. Chemoresponsive liver hemangioma in a patient with metastatic malignant teratoma. Clin Res Hepatol Gastroenterol 2015; 39:1–2.
26. Arévalo N, Méndez R, Manzano A. Chemotherapy-induced response of liver hemangiomas in a patient with a germ cell tumor: a case report. Radiologia (Engl Ed) 2018; 60:441–445.
27. Keane G, Lam M, Braat A, Bruijnen R, Kaufmann N, de Jong H, et al. Transarterial Radioembolization (TARE) Global Practice Patterns: An International Survey by the Cardiovascular and Interventional Radiology Society of Europe (CIRSE). Cardiovasc Intervent Radiol. 2024 Sep;47(9):1224-1236. DOI: 10.1007/s00270-024-03768-z. Epub 2024 Jun 24. PMID: 38914769; PMCID: PMC11379766.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
CASE REPORT
Pages:137-142

Non-infectious, caseous necrosis involving constrictive pericarditis treated with pericardiectomy: A case report

Perikardiyektomi ile tedavi edilen non-enfeksiyöz, kazeifikasyon nekrozu içeren konstriktif perikardit hastası: Vaka raporu

Barış AVŞAR[1]
Onur Barış DAYANIR[1]
Osman Nejat SARIOSMANOĞLU[1]

[1] Dokuz Eylül University, Faculty of Medicine, Cardiovascular Surgery, İzmir, Türkiye

The Patient with Non-infectious, Caseous Necrosis İnvolving Constrictive Pericarditis Treated with Pericardiectomy: A Case Report.
Received: 23.01.2025
Accepted: 03.07.2025
DOI: 10.18614/dehm.1873891

Corresponding author
Barış AVŞAR
ORCID ID: 0009-0006-4938-2777
brs.avsr1905@gmail.com

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
CASE REPORT
Pages:137-142

ABTSTRACT
In constrictive pericarditis, pericardial inflammation causes the parietal and visceral pericardial layers to adhere to each other and become scarred, resulting in the loss of pericardial elasticity. This condition impedes ventricular filling during diastole. The fibrotic pericardium, by preventing the heart from filling during diastole, leads to a decrease in venous return to the heart. A reduction in venous return secondary to this results in a decrease in cardiac output. This clinical condition is associated with constrictive pericarditis. This case report presents a 61-year-old male patient who was diagnosed with constrictive pericarditis, and has experienced orthopnea and edema in his lower extremities for the past month. An elective transthoracic echocardiogram demonstrated increased pressure on the right ventricle, with a left ventricular ejection fraction of 50%. Contrast-enhanced thorax magnetic resonance imaging revealed intensity changes consistent with pericardium, showing calcified areas between the pericardial layers. Thorax tomography imaging showed dense calcification that extended from the anterior surface of the right atrium and ventricle toward the apex. This patient was diagnosed with constrictive pericarditis, and a pericardiectomy was planned as treatment.

KEYWORDS
Calcification, necrosis, pericarditis, pericardiectomy

ÖZ
Konstriktif perikardit hastalığında perikardiyal enflamasyon nedeniyle parietal ve visseral perikard yaprakları birbirine yapışarak skarlaşır ve perikard elastikiyetini kaybeder. Bu durum diyastolde ventriküllerin doluşunu engeller. Fibrotik perikardın, kalbin diyastolde doluşunu engellemesi sonucunda kalbe olan venöz dönüş azalır. Venöz dönüşün azalmasına sekonder olarak kalp debisi düşer. Bu durum konstriktif perikarditi akla getirir. Gelişmekte olan ülkelerde konstriktif perikarditin en yaygın nedeni tüberküloz enfeksiyonudur. Bu vaka raporunda 1 aydır ortopne ve alt ekstremitelerde ödem şikayeti olan 61 yaşındaki konstriktif perikardit tanısı alan erkek hastanın vakası sunulmaktadır. Hastaya elektif şartlarda yapılan transtorasik ekokardiyografide sağ ventriküle bası olduğu ve sol ventrikül ejeksiyyon fraksiyonu %50 olduğu değerlendirildi. Kontrastlı toraks manyetik rezonans görüntülemede perikard yaprakları arasında kalsiyum sütü ile uyumlu intensite değişiklikleri izlendi. Toraks BT görüntülemelerinde sağ atrium ve sağ ventrikülün ön yüzünden apekse kadar çevreleyen kalsifikasyon görüldü. Konstriktif perikardit tanısıyla perikardiyektomi planlandı.

ANAHTAR KELİMELER
Kalsifikasyon, nekroz, perikardit, perikardiyektomi

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
CASE REPORT
Pages:137-142

In cases of constrictive pericarditis, common clinical findings include shortness of breath, chest pain, edema, fatigue, weight loss, hepatosplenomegaly, and syncope. Additionally, among the classic findings, a reduction in heart sounds, jugular venous distension, and pericardial friction rub may also be present in many patients.

Pericarditis is a condition caused by inflammation of the pericardial membrane. It is usually triggered by viral infections, bacterial infections, rheumatological diseases, or trauma. Autoimmune diseases, malignancies, and drug reactions can also provoke pericarditis. Constrictive pericarditis, on the other hand, is a condition that develops as a result of thickening, stiffening, and calcification of the pericardial membrane. This leads to a loss of pericardial elasticity and impaired cardiac pumping function. The condition most often occurs after inflammatory pericarditis (1). Symptoms of this condition may include syncope, shortness of breath, fatigue, pretibial edema, hepatic congestion, nausea, and anorexia. Diagnostic imaging methods, such as echocardiography, computed tomography (CT), magnetic resonance imaging (MRI), and invasive cardiac catheterization, can be used for diagnosis. Treatment typically requires surgical intervention, such as pericardiectomy or pericardiotomy.

According to the literature, most cases of constrictive pericarditis are reported in regions like Asia and Africa, where tuberculosis is common. Additionally, it is known to occur more frequently in males than females, with an average age range of 50 to 70 years (2). Epidemiological data show that the incidence is low, and there is limited data in the literature. However, recent studies suggest an increasing trend in the number of cases (3). Infections, such as tuberculosis, radiotherapy, and uremia, are common causes of the condition (4).

The diagnosis of constrictive pericarditis is usually made based on clinical findings, radiological images, and laboratory tests. Echocardiography can reveal changes, such as thickening and calcification of the pericardium. Additionally, thorax CT or MRI can provide a clearer assessment of pericardial thickening and calcification. Diagnosis can also be supported by invasive cardiac catheterization (5).

Laboratory findings that may assist in the diagnosis of constrictive pericarditis include elevated acute-phase reactants, such as C-reactive protein and erythrocyte sedimentation rate, increased white blood cell count, and elevated total protein levels and white blood cell count in pericardial fluid analysis (6).

Case presentation

A 61 years old male patient presented to the cardiology department with complaints of shortness of breath and edema in his lower extremities, which had been present for one month. Transthoracic echocardiography revealed calcification of the pericardium, and signs of pressure on the right ventricle. Pericardiectomy was planned due to an unsuccessful attempt at pericardiocentesis performed under echocardiographic guidance. Thorax CT imaging showed calcified pericardium, and the accumulation that compressing the right ventricle (Figure 1). Contrast-enhanced chest MRI demonstrated intensity changes consistent with pericardial calcification between the pericardial layers (Figure 2).

A sternotomy was performed, revealing severe and widespread pericardial calcification (Figure 3). The pericardial adhesions were carefully dissected. During the opening of the pericardium, purulent, and non-malodorous fluid was drained (Figure 4). The heart was freed from the pericardium. Tissue samples were obtained from the pericardial tissue, and sent for pathological examination and culture. A sub-atmospheric drainage tube system was placed into the mediastinum, and the tissue layers were closed anatomically. The patient was followed up in the cardiothoracic intensive care unit for two days and was discharged on the seventh postoperative day.

The pathology examination of the patient revealed hyalinized fibrotic lesions with central necrosis, calcification, cholesterol clefts, and fibrin. No basil structures were observed on acid-fast staining. The samples taken for aerobic and anaerobic culture studies showed no growth. The absence of growth in the mycobacterial culture ruled out tuberculous pericarditis. During postoperative follow-up, the patient reporterd no symptoms of shortness of breath or lower extremity edema.

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
CASE REPORT
Pages:137-142

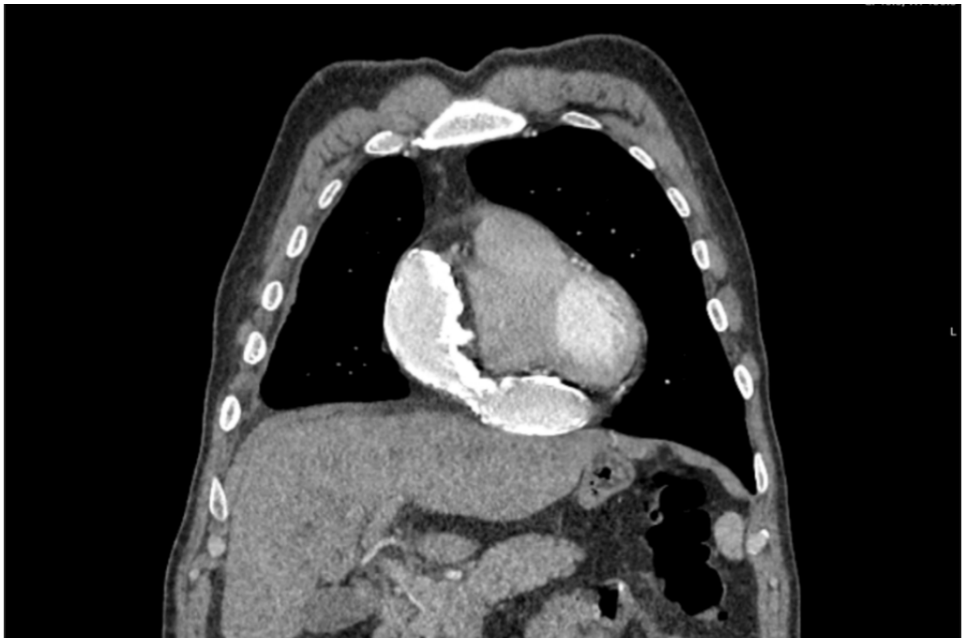


Figure 1. Thorax CT pericardial calcification

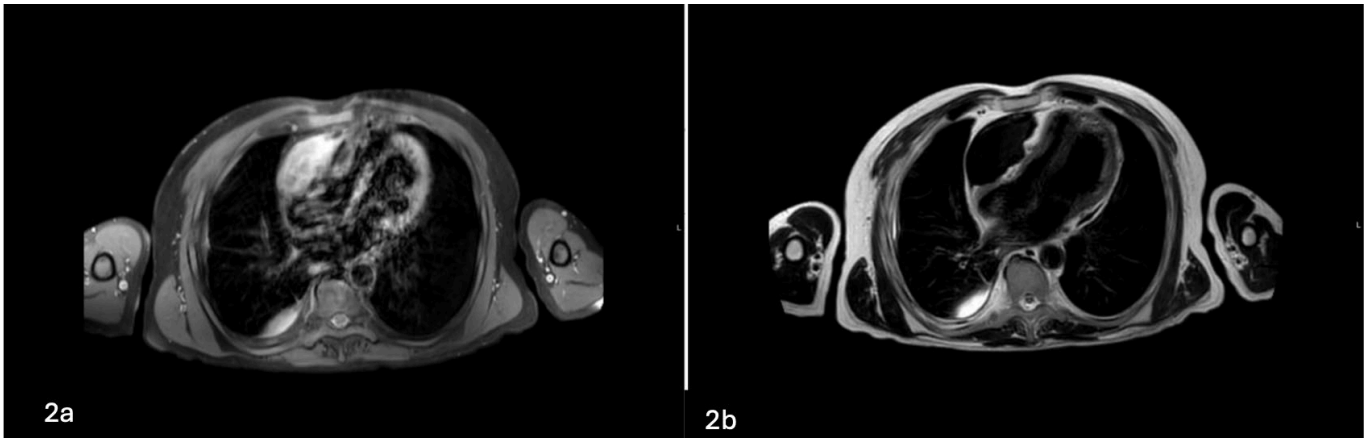


Figure 2a. MRI T1 sequence examination

Figure 2b. MRI T2 sequence examination. Pericardial fluid that compressing the right ventricle

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
CASE REPORT
Pages:137-142

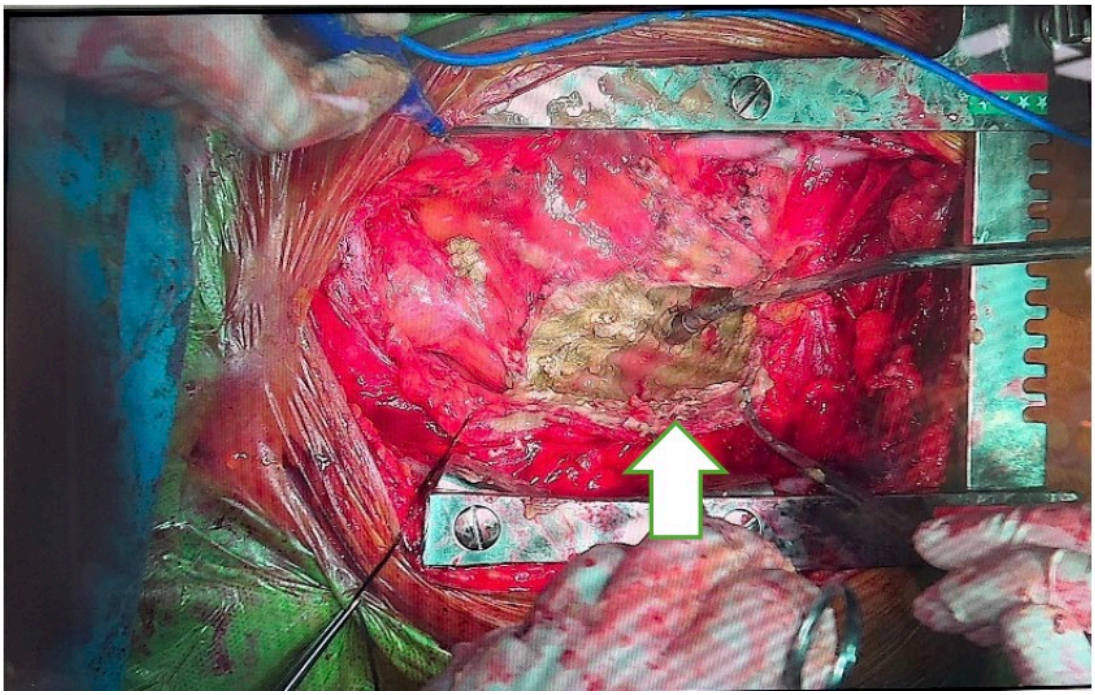


Figure 3. Pericardial calcification

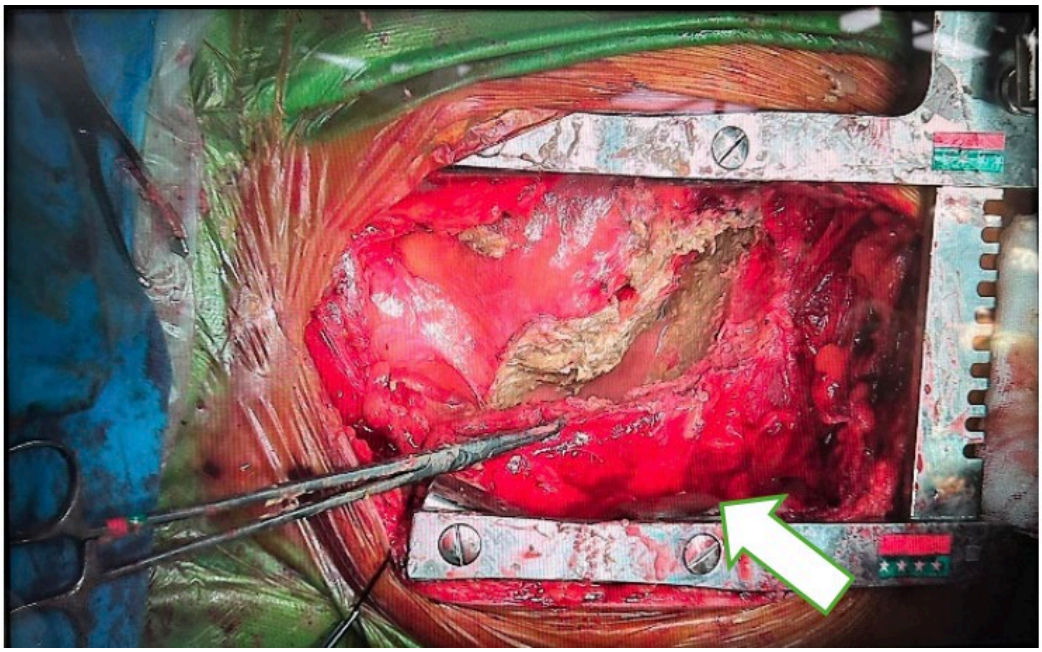


Figure 4. Calcified purulent material

Developments and Experiments in Health and Medicine
Year: 2026
Volume: 40
Issue: 1
CASE REPORT
Pages:137-142

Discussion

Constrictive pericarditis currently presents with nonspecific symptoms that can also be seen in many other diseases. Common reasons for patient referral to clinics include shortness of breath, fatigue, easy fatigability, and swelling in the legs.

The most common cause of the condition in developing countries is tuberculous pericarditis (7,8). This case demonstrates that caseous necrosis, associated with chronic inflammatory processes in pericarditis, can occur in a non-infectious context, without tuberculosis being the cause.

Constrictive pericarditis should always be considered in the differential diagnosis, particularly for patients with chronic right heart failure, persistent recurrent lung infections, and pleural effusion.

References

1. Ismail TF. Acutepericarditis: update on diagnosisandmanagement. ClinicalMedicine. 2020.
2. Çavuşoğlu Y, Çelik A, Altay H, Nalbantgil S, Özden Ö, Temizhan A, Ural D, Ünlü S, Yılmaz MB, Zoghi M. Düşük Ejeksiyon Fraksiyon Dışı Kalp Yetersizliği: Epidemiyoloji, Patofizyoloji, Fenotipler, Tanı ve Tedavi Yaklaşımları. Türk Kardiyoloji Derneği Arşivi. 2022; 2:50.
3. Garipoğlu C. Sistemik skleroz hastalarında epikardiyal yağ volümü ile parankim bulgularının karşılaştırılması. 2023.
4. Karima T, Nesrine BZ, Hatem L, Skander BO, Raouf D, Selim C. Constrictivepericarditis: 21 years' experienceandreview of literature. PanAfricanMedicalJournal. 2021; 8:38(1).
5. Fadl SA, Nasrullah A, Harris A, Edwards R, Kicska G. Comprehensivereview of pericardialdiseasesusingdifferentimagingmodalities. The International Journal of CardiovascularImaging. 2020; 36(5):947-69.
6. Andreis A, Imazio M, Casula M, Avondo S, Brucato A. Recurrentpericarditis: an update on diagnosisandmanagement. InternalandEmergencyMedicine. 2021; 16:551-8.
7. Çelebi S, Bostan Ö, Hacımustafaoğlu M, Aygün FD. Konstriktif Perikardit Tanısı Konulan Bir Tüberküloz Vakası. Journal of Child, 2012; 12(1); 43-46.
8. Keleşoğlu Ş, Akpek M, Doğdu O, Ardıç İ. Kalsifik konstriktif perikardit Calcific constrictive pericarditis. Turk Kardiyol Dern Ars. 2011; 39(4): 345-345.

Manuscript Submission Overview

Types of Publications

Developments and Experiments in Health and Medicine requires that authors publish all experimental controls and make full datasets available where possible (see the guidelines on Supplementary Materials and references to unpublished data).

Manuscripts submitted to Developments and Experiments in Health and Medicine should neither be published previously nor be under consideration for publication in another journal.

Developments and Experiments in Health and Medicine accepts to use the "Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication" standards prepared by the International Committee of Medical Journal Editors-ICMJE (http://www.icmje.org/recommendations).

Authors are advised to follow the CONSORT guidelines for randomized trials, STROBE for observational studies, STARD for diagnostic/prognostic studies, PRISMA for systematic reviews and meta-analyses, ARRIVE for preclinical studies with experimental animals,TREND for non-randomized behavioral and community health interventional studies, and CARE guidelines for case reports. These reporting guidelines are available on the EQUATOR network (www.equator-network.org/home/) and on the National Library of Medicine-NLM "Research Reporting Guidelines and Initiatives" website (www.nlm.nih.gov/services/research_report_guide.html).

The main article types are listed below. Requirements for different types of articles are as follows:

- Research article: These are original research manuscripts. The work should provide a substantial amount of new information. Full experimental details must be provided so that the results can be reproduced. The structure should include a structured abstract, introduction, materials and methods, results, discussion, conclusion(s) (if appreciated), acknowledgement (if applicable), and references sections. The abstract should be structured as follows: objective(s), methods, results, conclusion(s). The length of the article should not exceed 3750 (250 abstract + 3500 body) words excluding the references, figures and tables. The article should include the most recent and relevant references in the field. Up to 45 references can be stated.

- Case reports: Should contain a non-structured abstract and three to five keywords both in Turkish and English, introduction, case presentation, discussion, conclusion(s) (if

appreciated), acknowledgment (if applicable), and references sections. The length of the article should not exceed 1650 words (150 abstract + 1500 body) excluding the references, figures and tables. Case reports should optimally be accompanied by relevant figures to document findings. Up to 20 references can be provided. Informed consent should be obtained from the patients to report their cases. The Journal keeps the right to ask for original signed informed consents.

- Review articles: These manuscripts will only be considered when invited by the Editorial Board. Reviews should critically assess the current knowledge of the field. A non-structured abstract both in Turkish and English is needed. The length of the article should not exceed 5250 words (250 abstract + 5000 body) excluding the references, figures and tables. Up to 100 references can be provided.
- Letters to the Editor: Letters should be less than 750 words. No abstract is required for articles to be evaluated under this title. Three to five keywords both in Turkish and English should be provided. Up to 5 references should be stated. If the submitted letter is discussing an article published in the Developments and Experiments in Health and Medicine, it should be submitted at most within 4 months after the publication of the main article. Letters will also undergo peer review.
- Insights and Images: Submissions to the Insights and Images section should be of high-quality clinical pictures, radiology or surgical images that provide insight to the diagnosis or pathophysiology of a clinical problem or a solution. Text should be a succinct short clinical vignette or description and a brief discussion of the most relevant new information, such as a differential diagnosis, management, pathophysiology, or genetic basis. A non-structured abstract both in Turkish and English is needed. The length of the article should not exceed 1750 words (250 abstract + 1500 body) excluding the references, abstract, figures and tables. Up to 20 references can be provided. Informed consent should be obtained from the patients to report their cases. The Journal keeps the right to ask for original signed informed consents.

Submission Process

Manuscripts should be sent through the online submission system:
(https://dergipark.org.tr/tr/pub/@tipdergisi)
The submitting author, who is generally the corresponding author, is responsible for the manuscript during the submission and peer review process. The submitting author must ensure that all eligible co-authors have been included in the author list (read the criteria to qualify for authorship) and that they have all read and approved the submitted version of the manuscript.
To submit your manuscript, register and login to the submission website. All co-authors can see the manuscript details in the submission system, if they register and log in using the e-mail address provided at the time of manuscript submission.
Developments and Experiments in Health and Medicine follows a double-blind reviewing procedure which means the author will remain anonymous to the reviewers throughout peer review. It is the responsibility of the author to anonymize the manuscript and any associated materials. Author names, affiliations and any other potentially identifying information should be removed from the manuscript text and any accompanying files (such as figures of supplementary material). Authors should avoid citing their own work in a way that could reveal their identity.
Although not mandatory, the Journal's editorial board welcomes reviewer suggestions who are
expert in the relevant field with. Developments and Experiments in Health and Medicine also enables the authors to exclude reviewers. The names of proposed and excluded reviewers should be provided in the submission system, not in the cover letter.
All articles sent to the journal are evaluated by the Editorial Board in terms of their conformity with the scope of the journal and the writing rules. Editors may decide to reject the article or send it back to the author(s) for correction before sending it to the advisor's evaluation.

Revisions

Developments and Experiments in Health and Medicine is a double-blind journal and articles are sent to at least two expert advisors on the relevant subject. Developments and Experiments in Health and Medicine aims to inform the author(s) about the evaluation result within 6-8 weeks after the article is sent to the journal. The editor may request revision of the article,

considering the advisors' suggestions. Revision should be completed within 30 days. If the

revised version of the article is not sent to the journal on time, the article will be evaluated as a new application.

When your manuscript reaches the revision stage, you will be requested to format the manuscript according to the journal guidelines. When submitting a revised version of a paper, the author must submit a detailed “Response to reviewers” that states point by point how each issue raised by the reviewers has been covered and where it can be found (each reviewer's comment followed by the author’s reply) as well as a clear copy of the main document. The authors are required to copy the changes they make in the main text and other components of the article into the response letter.

Revised manuscripts must be submitted within 30 days from the date of the decision letter. If the submitting author(s) believe that additional time is required, they should request an extension before the initial 30-day period is over.

The final decision (acceptance/rejection) regarding the article is notified to the author by the editor. All authors accept the editor's corrections without changing the basic meaning.

Ethical Principles and Publication Policy

Research and Publication Ethics

Developments and Experiments in Health and Medicine publishes articles that comply with ethical and scientific standards. The Editorial Board examines all submitted articles for plagiarism and republishing. If an ethical problem is detected, the Committee on Publication Ethics-COPE (https://publicationethics.org/guidance/guidelines) guidelines are followed.

For clinical research, approval from the relevant Ethics Committee must be obtained in accordance with the “WMA Declaration of Helsinki-Ethical Principles for Medical Research Involving Human Subjects” (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/), for studies involving experimental animals, the “International Guiding Principles for Biomedical Research Involving Animals” (http://iclas.org/wp-content/uploads/2013/03/CIOMS-ICLAS-Principles-Final.pdf) and the “Guide for the Care and Use of Laboratory Animals” (https://grants.nih.gov/grants/olaw/guide-for-the-care-and-use-of-laboratory-animals.pdf).

In the preparation of case reports; Care should be taken to protect the patient's privacy. Identifying information and photographs of patients, hospital registration numbers and dates should not be used. For case reports, "Informed Consent" should be obtained. Information on ethics committee approval and informed consent should be provided within the Methods section of the main text.

In experimental animal studies, procedures performed to minimize pain, and discomfort should be explained in the text.

Copyright and Authorship

All local and international publication rights of the manuscript sent to Developments and Experiments in Health and Medicine are transferred to Developments and Experiments in Health and Medicines with the “The DEHM Assignment Form” (available in the Forms tab of the website). A wet signature and scanning are not obligatory for signing the form; electronic signatures made through Adobe Acrobat (using the ‘Fill & Sign’ module in newer versions or

the signature function in older versions of Acrobat Reader) are accepted as well.

The contribution of each author to the manuscript must be clearly stated on the form. After the manuscript is sent to the journal, it will not be possible to add or remove author names or change the order of authors. The journal’s practices in this regard comply with the rules of the International Committee of Medical Journal Editors–ICMJE (http://www.icmje.org) and the Council of Science Editors-CSE (https://www.councilscienceeditors.org).

Your article will not be published unless you warrant that “This article is an original work, has not been published before, and is not being considered for publication elsewhere in its final form either in printed or electronic form”. The DEHM Assignment form should be signed and dated by all authors and sent along with the manuscript during the submission process.

If a manuscript contains any previous published image or text, it is the responsibility of the author to obtain authorization from copyright holders. The author is required to obtain and submit the written original permission letters for all copyrighted material used in his/her manuscript.

Conflict of Interest

All authors and reviewers must inform us about any kinds of "Conflict of Interest" (such as financial, personal, political, or academic) that would potentially affect their judgment.

Financial Disclosure

General institutional support for an author's time on the work should be distinguished from

direct overall funding of the work. "The DEHM Assignment Form" available through the link below must be filled in and uploaded by the corresponding author at the time of submission for disclosure. An appropriate funding statement might be: "This study was funded by A; Dr. F's time on the work was supported by B.

Acknowledgment Permission

Author(s) should inform the editor about all forms of support including any financial support, donations or commercial connections they have received from official or private institutions related to the research from which the article originates and should indicate this in the acknowledgments section.

Plagiarism

Authors are not allowed to utilize verbatim text of previously published papers or manuscripts submitted elsewhere. All submitted manuscripts will be checked for possible similarity in any part of the work by iThenticate or Turnitin plagiarism checker. Based on the amount of plagiarism detected in a manuscript, it will be passed to the authors and ask them to rephrase copied phrases or include as direct quotations with references. COPE's flowcharts and guidelines are approached in cases in which plagiarism is detected.

Data Fabrication/Falsification

Falsification is the practice of omitting or altering research materials, data, or processes so that the results of the research are no longer accurately reflected. Fabrication is the practice of inventing data or results and reporting them in research. Both of these misconducts are fraudulent and seriously alter the integrity of the research. Therefore, articles must be written based on original data and the use of falsified or fabricated data is strongly prohibited. In

confronting cases with fabricated or falsified data COPE's flowcharts and guidelines are followed.

Researchers who perform randomized controlled or clinical trials (RCTs) are advised to keep their original data at hand. The Journal keeps the right to ask for raw data even after publication.

Image Manipulation

Developments and Experiments in Health and Medicine encourages authors to send their original images. No specific feature within an image may be enhanced, obscured, moved, removed, or introduced. Adjustments of brightness, contrast, or color balance are acceptable as long as they are applied to the entire image and do not misrepresent any information present in the original, including the background.

Open Access Policy

This journal provides immediate open access to its content on the principle that making research freely available to the public supports a greater global exchange of knowledge.

Manuscript Preparation

Accepted Formats

During the preliminary evaluation of the articles, it is checked whether they comply with the determined journal writing rules. Articles that do not comply with the spelling, reference and bibliography rules are sent back to the authors and the article is requested to be prepared according to the spelling rules and sent to the Journal.

Articles should be written in Microsoft Word format (doc or docx extension) in Times New Roman font, 12 points and 1.5 line spacing. Footnotes should be written in 9 points and single line spacing.

Manuscript pages should be numbered consecutively, beginning with the abstract page.

Abbreviations should be standard and used just in necessary cases, after complete explanations in the first usage. Avoid abbreviations in the title and abstract.

Footnotes should be indicated with numbers and should be placed at the end of the page.

Headings;

• The main title of the article should be in capital letters and bold,

• Subheadings should be in bold and only the first letter should be capitalized,

• Section headings should be in italics, only the first letter should be capitalized.

• All headings should be left-justified and unnumbered.

Paragraphs should be adjacent to each other and indented 1 tab.

Quotations, if short, should be in double quotation marks within the text; if 40 words or more, they should be in blocks and indented 1 tab from the right and left. In quotations, the font, point size and line spacing used in the main text are valid. In block quotations, the line spacing should be 1.

Single-digit numbers should be indicated with letters, and larger numbers with numbers.

In additions to abbreviations made in lower case letters, the pronunciation of the word should be considered; in additions to abbreviations made in upper case letters, the pronunciation of the last letter of the abbreviation should be considered.

Dates should be indicated with numbers, and an apostrophe should be used for the additions they receive. (For example, 1990s, 2003)

In texts, explanatory notes should be given as footnotes, not endnotes.

The editorial office reserves the right to edit the submitted manuscripts in order to comply with the Journal's style. In any case, the authors are responsible for the published material.

All submitted manuscripts must be "spell checked" and "grammar checked." The manuscripts

should be written in proper English (American or British usage is acceptable, but not a mixture of both). Concerning manuscripts that are in the acceptance process, if the Journal feels the submitted manuscript has major grammatical and spelling errors, the Editor may request the author(s) to improve the English of their work to minimize potential grammatical or spelling errors while still conforming to accurate scientific English standards. Therefore, to continue with the article process, the authors should use / employ the English Language Editing service and provide a valid certificate.

Cover Letter

A cover letter must be included with all manuscripts. This letter may be used to emphasize the importance of study and its contributions to existing knowledge.

Any prior submissions of the manuscript to Developments and Experiments in Health and Medicine must be acknowledged. If this is the case, it is strongly recommended that the previous manuscript ID is provided in the submission system, which will ease your current submission process.

All cover letters are required to include the following statements:

1. We confirm that neither the manuscript nor any parts of its content are currently under consideration for publication with or published in another journal.
2. All authors have approved the manuscript and agree with its submission to Developments and Experiments in Health and Medicine.
3. In the case of acceptance of the manuscript, the copyright will be transferred to the Developments and Experiments in Health and Medicine.

The names of proposed and excluded reviewers should be provided in the submission system, not in the cover letter.

Potential Reviewers

To assist with a prompt, fair review process, authors are encouraged to enter the names, departments, institutions, and e-mail addresses (institutional e-mail accounts, not gmail, yahoo, hotmail, etc.) of 5 potential reviewers in Notes to Editor section. Potential reviewers must have the appropriate expertise to evaluate the manuscript, be outside the authors' institution(s), and have no known potential conflicts of interest. It is recommended that at least one of the reviewers be a foreign reviewer. Ultimately, the editors reserve the right to choose reviewers.

Title Page

A separate Title Page should be submitted, containing the following:

1. A concise and informative title of the article in Turkish and English
2. A running title of no more than 45 characters (including spaces) in Turkish and English
3. The name(s) and affiliation(s) of the author(s)
4. Complete mailing address, telephone number, and e-mail address of the corresponding author
5. If available, the 16-digit ORCID of the author(s)
6. Any conflict of interest and sources of funding should be included on the title page of the manuscript with the heading “Conflicts of Interest and Source of Funding:”. If there is no conflict of interest, this should also be explicitly stated as none declared.

7. Acknowledge all forms of support, with the heading “Acknowledgements:”. If there are no acknowledgements, this should also be explicitly stated as none declared.

Author Affiliation: All authors should list their current affiliation and the affiliation where most research was carried out for the preparation of their manuscript. We recommend adding as primary the affiliation where most of the research was conducted or supported. It is very important that author names and affiliations are correct. Incorrect information can mean a lack of proper attribution or incorrect citation and can even lead to problems with promotion or funding. After the publication of an article, updates or corrections to the author’s address or affiliation may not be permitted.

Independent Researcher: If one or all the authors are not currently affiliated with a university, institution or company, or have not been during the development of the manuscript, they should list themselves as an “Independent Researcher”.

Abstract and keywords

Abstract should be structured for Research articles providing the objective of the study, methods, results, and conclusion(s). Case Reports, Review articles, Insights and Images should include an abstract summarizing the content in a single paragraph. Letters to Editors do not require an abstract. Structured or non-structured abstracts should be both in Turkish and English. Preferably, abbreviations should not be mentioned in the abstract. Number this page as page 1.

Keywords are used for indexing purposes; each article should provide three to five keywords both in Turkish and English. English keywords should be selected from the Medical Subject Headings (MeSH).

Introduction

The introduction should provide a short background to previous studies and possible gaps in the literature. The purpose of the study, its place in literature, and the research question should be clearly stated.

Materials and methods

How the research was conducted, the methods used, and the data collection techniques should

be explained in detail (including: controls, inclusion and exclusion criteria, etc.) and may be separated into subsections. Repeating the details of standard techniques is best avoided. The software used for statistical analyses and description of the actual method should be mentioned. Authors who used AI technology to conduct the study should describe its use in the methods section in sufficient detail to enable replication of the approach, including the tool used, version, and prompts where applicable.

Information on ethics committee approval and informed consent should be provided within the Methods section of the main text.

Results

The results of the study should be presented clearly based on your own findings and supported with tables and figures. The results should be organized according to their importance.

Discussion

Discussion should challenge the findings of the study with other available evidence in the literature. It should emphasize the new and important aspects of the study and the conclusions that follow them. Possible mechanisms or explanations for these findings should be explored. The limitations, drawbacks, or shortcomings of the study and the implications of the findings for future research or clinical practice should be explored.

Conclusion(s)

Conclusion(s) should state the main result(s) of the study and recommendation that the author(s) has (have) reached. Such results and recommendations should be derived from the researcher's own study and the results of other studies should not be stated in this section.

Tables and Figures

Tables, figures and graphics must be cited in the order in which they appear in the text, using Arabic numerals as Table1, Table2 and Figure1, Figure2.

Tables: Tables should be simple and should not duplicate information in the text of the paper. They should be uploaded as a separate file. A descriptive title should be provided for all tables and the titles should be placed above the tables. Abbreviations used in the tables should be defined below by footnotes (even if they are defined within the main text). The font of the

table abbreviations should be "Times New Roman" with a size of "10". Tables should be

created using the “insert table” command of the word processing software.

Figures: Figures and figure legends should be submitted separately from the main document. Each of them should have its own legend and description. Type legends and descriptions for figures on a separate page at the end of the manuscript. When there are figure subunits, the subunits should not be merged to form a single image. In the subunits of the image, the image name should be numbered as 'a, b, c' and should not be located on the figure. Like the rest of

the submission, the figures too should be blind. Any information within the images that may indicate the institution, or the patient should be removed. Markings on images such as arrows and circles should be put in place for specific sections of the pathology figures and radiographs.

For radiographic films, scans, and other diagnostic images, as well as pictures of pathological specimens or photomicrographs, send high resolution figures in JPEG or .TIFF format with a resolution of at least 300 dpi. Line art (forest plots, graphs, etc) should be submitted in TIFF or PNG format at a resolution of at least 600 dpi.

Supplementary materials

Supplementary materials such as movie clips, questionnaires, etc. may be any format, but it is recommended that you use common, non-proprietary formats where possible.

Acknowledgment

If there are any technical, general, financial, and material support or contributions that need acknowledging but do not justify authorship, they can be cited at the end of the text before references as Acknowledgment. Use of AI for writing assistance should be reported in the acknowledgment section.

References

References should be numbered consecutively in the order they are referred to within the main text in Vancouver style. Alphabetical order is not required. References should be indicated in parentheses at the end of the sentence. There should be no inconsistency between the list of references and their inclusion in the text. The author(s) are responsible for the

accuracy of the references. All sources should be indicated in the text. The abbreviation of journal names should be in accordance with Index Medicus. A journal not indexed in Index Medicus should be written without abbreviation.

For the references credited to more than six authors please provide the name of the first six authors and represent the remaining authors by the phrase “et al.”

The numbers of references should preferably not exceed 45 for research articles, 100 for reviews, 20 for case reports, and 5 for letters to editor.

References should be shown as in the following examples.

Journal Article: Pugazhennthi S, Khandelwai RL. Insulin-like effects of vanadate on hepatic glycogen metabolism in nondiabetic and straptozotocin-induced diabetic rats. Diabetes 1990;39:821-827.

Journal article in electronic form: Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis [serial online] 1995 Jan-Mar [cited 1996 Jun 5];1(1):[24 screens]. Available from: URL: http://www.cdc.gov/ncidod/EID/eid.htm

Monograph in electronic form: CDI, clinical dermatology illustrated [monograph on CD-ROM]. Reeves JRT, Maibach H. CMEA Multimedia Group, producers. 2nd ed. Version 2.0. San Diego: CMEA; 1995.

Complete Book: Ravel R. Clinical Laboratory Medicine. Fourth Edition. Chicago: Yearbook Medical Publishers Inc, 1984; 265-281.

Turkish Book: Yazıcı O. İki uçlu duygudurum bozuklukları ve diğer duygudurum bozuklukları.Psikiyatri Temel Kitabı (ı) içinde Ed: C Güleç, E Köroğlu, Hekimler Yayın Birliği, Ankara 1997; 429-448.

Compilation Book: Elevitch FR, Hicks GP, Microprocessors and computers in the clinical laboratory, In:Tietz NW, ed. Fundamental of clinical chemistry, third edition. Philadelphia: W.B.Saunders, 1987; 254-265.

Chapter in Book: Phillips SJ, Whisnant JP. Hypertension and stroke. In: Laragh JH, Brenner BM, editors. Hypertension: pathophysiology, diagnosis and management. 2nd ed. New York: Raven Press; 1995. p. 465-478.

If the author is an organization: The Cardiac Society of Australia and New Zealand. Clinical

exercise testing. Safety and performance guidelines. Medl Aust 1996; 164-228.

If no author is specified: Cancer in South Africa (editorial). S Afr Med 1994; 84-115

Web page: http://www.wma.net/e/policy/b3.htm (Erişim tarihi 26 Haziran 2010).

Not: Referencing AI-generated material as the primary source is not acceptable.

Correction of Errata

The Journal will publish an erratum when a factual error in a published item has been documented.

Journal Archiving

To guarantee long-term digital preservation, all articles published in the MHMS are archived by the DergiPark in ULAKBİM Dergi Sistemleri (UDS), the free digital repository of biomedical and life science scholarly publications. In this context, all articles published in the MHMS are open to access at MEDIAJ DergiPARK and mediajdergi.com.

Article Withdraw

The author has the right to withdraw the article while it is in new submission status. If the article is in lower roles or has at least 1 reviewer review, the author can request a withdraw with the approval of the editor. If the editor does not respond to the request within 15 days, the article will be automatically withdrawn.

During the production process, the author will only be able to send request, and the 15-day period will not apply. With this feature, a withdraw card has also been added to the editor panel. Withdraw requests can be viewed from this card.

For further information, please contact the Editorial Office

Contact Information of the Editorial Office

Developments and Experiments in Health and Medicine Editorial Office

Address: Mithatpaşa Cad. No: 1606 Dokuz Eylül University Faculty of Medicine Dean Office 35340 İnciraltı-Balçova/İZMİR

Phone: +90 232 4122290

Publication Coordinator Müjde UZHAN

E-mail: dehm@deu.edu.tr

Forms

Copyright Agreement and Declaration Form

Title Page Template

Submission Checklist