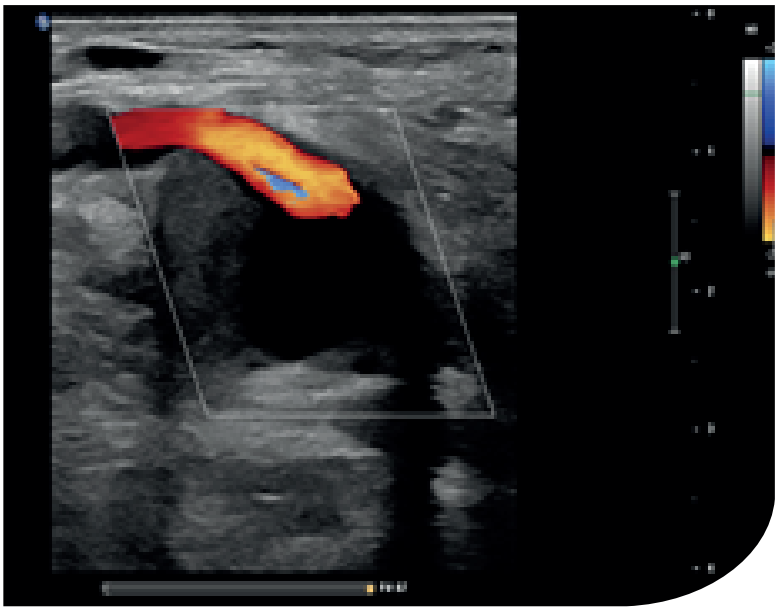
DOKUZ EYLÜL ÜNİVERSİTESİ
İZMİR-1982
DOKUZ EYLÜL ÜNİVERSİTESİ TIP FAKÜLTESİ

DEHM

Developments and Experiments in Health and Medicine

Volume:39 Issue:2 Year:2025
e-ISSN: 3062-2948



EDITORIAL BOARD

Publishing Coordinator:
Müjde UZHAN

Managerial Office:
Dokuz Eylül Üniversitesi Tıp Fakültesi Dekanlığı
35340 İnciraltı/Balçova - İZMİR /TÜRKİYE

Cover & layout design for this issue was kindly contributed by Prof. Dr. Çınla Şeker and Assist. Prof. Dr. Zehra ATABEY

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 Üniversitesi
Tıp Fakültesi Dekanlığı Yayın Kurulu
35340 İnciraltı / Balçova - İZMİR / TÜRKİYE

DEHM is indexed in Index Copernicus Master List, TÜBİTAK ULAKBİM Türk Tıp Dizini and TÜRKİYE ATIF DİZİNİ.

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, TÜBİTAK ULAKBİM TR Medical Index and Turkey 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 39/ Issue 2 / April

2025

Contents

Research Articles

Case Reports

KAPAK FOTOĞRAFI:

A Buerger's patient with brachial artery aneurysm

Brakial arter anevrizması gözlenen bir Buerger hastası

Onur Barış DAYANIR, Hüseyin SAYGIN, Erdem Erinç SİLİSTRELİ

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

RESEARCH ARTICLE

Sayfa:91-100

Determination of the predictive and prognostic value of the CONUT (Controlling Nutritional Status) score in the treatment process of metastatic colorectal cancer and its relationship with the clinicopathological features of the tumor

Metastatik kolorektal kanser tedavi sürecinde CONUT (Controlling Nutritional Status) skorunun prediktif ve prognostik değerinin belirlenmesi ve tümörün klinikopatolojik özellikleriyle olan ilişkisi

Merve KESKINKILIC[1,2]
Ozden OZER[3]
Hulya ELLIDOKUZ[4]
Isıl SOMALI[5]
Tuğba YAVUZSEN[1]

[1] Dokuz Eylul University Faculty of Medicine, Department of Internal Medicine, Division of Medical Oncology, Izmir, Türkiye
[2] Izmir Democracy University, Buca Seyfi Demirsoy Research and Training Hospital, Department of Medical Oncology, Izmir, Türkiye
[3] Denizli State Hospital, Denizli, Türkiye
[4] Dokuz Eylul University Oncology Institute, Department of Preventive Oncology, Izmir, Türkiye
[5] Private Egepol Hospital, Izmir, Türkiye

Metastatic Colorectal Cancer and CONUT Score

Received: 25.07.2024
Accepted: 14.04.2025
Doi:10.186614/dehm.1700161

Corresponding author
Merve KESKİNKILIÇ
ORCID ID: 0000-0002-3342-3144
mervekeskinkilic90@gmail.com

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

BACKGROUND
Studies have shown that the prognosis of various cancers is affected by factors such as inflammation, immunocompetence and nutrition, and the correlation between nutritional status and cancer prognosis is particularly striking. We aimed to evaluate the prognostic and predictive effect of The Controlling Nutritional Status (CONUT) score, calculated using serum albumin level (indicator of protein reserves), total cholesterol concentration (calorie consumption parameter) and total peripheral lymphocyte count (indicator of immunity), in patients with newly diagnosed metastatic colorectal cancer (mCRC).
METHODS
The prospectively designed study included 36 patients who were diagnosed with mCRC between June 2020 and December 2021 at the Department of Medical Oncology, Dokuz Eylül University Hospital, and were assessed according to the web-based software OpenEpi CONUT score was calculated using serum albumin level, total cholesterol concentration, and total peripheral lymphocyte count. Demographic, clinicopathological, and treatment-related characteristics of the patients, as well as CONUT values before treatment and at month 3, were recorded. The data obtained were analyzed in the SPSS statistical program according to appropriate analysis methods and the p value was <0. 05 considered statistically significant.
RESULTS
The median age of the study population was 67.09 (Range: 37.37-88.30 years) years and 66.7% (n=24) of the patients were male. The median follow-up period of the patients was 13.85 months (Range: 5.8-26.87 month) and 5.6% (n = 2) of the patients died during the follow-up period. The objective response rate (ORR) (complete and partial response) was higher in the group with low CONUT score than in the groups with medium and high CONUT scores (84.1% vs 73.3% vs 40%, respectively). When progression status was evaluated, the rate of patients progressing in the group with high CONUT score was higher than in the groups with medium and low CONUT scores (20% vs 13.3% vs 6.3% respectively). Patients with exitus were included in the CONUT high group, and the survival of these patients was shorter than in the CONUT low group. The median CONUT score value of the patients before treatment was 2 (0-11), and the median CONUT score at the 3rd month was 1 (0-10). When we looked at the correlation between the CONUT scores before treatment and at month 3, we saw that there was a statistically significant correlation between the baseline score and the 3rd month score (R: 0.36, p = 0.031).
CONCLUSION
Immunonutrition status is one of the factors affecting cancer prognosis, and the CONUT score, which reflects this status, has been shown to have a negative effect on prognosis if it is high at the beginning of treatment, as shown in our mCRC diagnosedpopulation of a small number of patients that we planned prospectively during the COVID period. In addition, it was thought that the decrease in the CONUT score was related to the increase in albumin values, which is a biomarker of improvement in nutritional status with systemic treatment.
KEYWORDS
CONUT score, immunonutritional status, metastatic colorectal cancer (mCRC), prognostic factor

AMAÇ
Kanserde prognozu etkileyen durumlara bakıldığında, çeşitli kanser türlerinde prognozun inflamasyon, immün yetmezlik ve beslenme gibi faktörlerden etkilendiği, beslenme durumu ile kanser prognozu arasındaki korelasyonun özellikle dikkat çekici olduğu yapılan çalışmalarla gösterilmiştir. Serum albümin düzeyi (protein rezervlerinin göstergesi), toplam kolesterol konsantrasyonu (kalori tüketim parametresi) ve toplam periferik lenfosit sayısı (bağışıklık göstergesi) kullanılarak hesaplanan Kontrollü Beslenme Durumu (CONUT) skorunun yeni teşhis edilen metastatik kolorektal kanserli (mKRK) hastalarda prognostik ve prediktif etkisini değerlendirmeyi amaçladık.
GEREÇ YÖNTEM
Prospektif olarak planlanan çalışmaya Dokuz Eylül Üniversitesi Hastanesi Tıbbi Onkoloji Kliniği'nde Haziran 2020-Aralık 2021 tarihleri arasında mKRK tanısı konulan ve OpenEpi web tabanlı yazılım programına göre belirlenen 36 hasta dahil edildi. CONUT Skoru serum albümin düzeyi, toplam kolesterol konsantrasyonu ve toplam periferik lenfosit sayısı kullanılarak hesaplandı. Hastaların demografik, klinikopatolojik, tedaviye bağlı özellikleri, tedavi öncesi ve 3. ay CONUT değerleri kaydedildi. Elde edilen veriler SPSS istatistik programında uygun analiz yöntemlerine göre analiz edildi ve p değeri <0. 05 olması istatistiksel olarak anlamlı kabul edildi.
BULGULAR
Çalışma popülasyonunun medyan yaşı 67,09 (Aralık: 37,37-88,30 yaş) idi ve hastaların %66,7'si (n=24) erkekti. Hastaların medyan takip süresi 13,85 ay (Aralık: 5,8-26,87 ay) idi ve hastaların %5,6'sı (n=2) takip süresi içerisinde öldü. Objektif yanıt oranı (ORR) (tam ve kısmi yanıt), düşük CONUT skorlu grupta, orta ve yüksek CONUT skorlu gruplara göre daha yüksekti (%84,1; %73,3; %40 sırasıyla). Progresyon durumu değerlendirildiğinde ise, yüksek CONUT skorlu grupta progresyon gösteren hastaların oranı, orta ve düşük CONUT skorlu gruplardan daha yüksekti (%20; %13,3; %6,3 sırasıyla). Ölen hastalar CONUT skoru yüksek gruba dahildi ve bu hastaların sağ kalım süreleri CONUT skoru düşük gruptan daha kısaydı. Hastaların tedavi öncesi median CONUT skor değeri 2 (0-11) ve 3. ayda median CONUT skoru 1 (0-10) idi. Tedavi öncesi ve tedavinin 3. ayında CONUT skorlarının korelasyonuna baktığımızda, başlangıç değeri ile 3. ay değeri arasında istatistiksel olarak anlamlı bir korelasyon olduğu görüldü (R: 0,36, p = 0,031).
SONUÇ
İmmünonütrisyon durumu kanser prognozunu etkileyen faktörlerden biri olup, bu durumu yansıtan CONUT skorunun, COVID döneminde prospektif olarak planladığımız az sayıda hastadan oluşan mKRK tanılı popülasyonumuzda gösterildiği üzere, tedavi başlangıcında yüksek değerde olması prognozu olumsuz etkilediği gösterilmiştir. Buna ek olarak sistemik tedaviyle beslenme durumundaki iyileşmenin biyobelirteci olan albümin değerlerindeki artışı ile de CONUT skorunda meydana gelen düşüşün ilişkili olduğu düşünülmüştür.
ANAHTAR KELİMELER
CONUT skoru, immunnutrisyonel durum, metastatik kolorektal kanser (KRK), prognostik faktör

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

According to GLOBOCAN data, colorectal cancer (CRC) is the third most commonly diagnosed cancer in men and the second most commonly diagnosed cancer in women, and although mortality rates have decreased since the 1980s, it is still the third most common cancer-related death in both women and men (1). It is believed that cancer screening programs, diagnosis at an early stage, development of surgical techniques, increased effectiveness of adjuvant treatments, use of molecular targeted treatments, and immunotherapies are effective in reducing CRC-related deaths and prolonging survival (2-3). Although the overall survival of patients with CRC are prolonged, recent studies have shown that the prognosis of various types of cancer is also influenced by patient-related factors such as inflammation, immune status and nutrition, in addition to clinicopathological and treatment-related features, and in particular the correlation between nutritional status and cancer prognosis (4). While good nutritional status has a positive effect on cancer prognosis and treatment response, immunosuppression and inflammation status have been shown to hurt cancer prognosis and treatment (5).

In this context, various indexes and biomarkers are used to assess the immunity, inflammation, and nutritional status of patients. Among these indexes, while neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and pan-immune inflammation value (PIV) are used to evaluate the immune-inflammation status, albumin-to-globulin ratio and prognostic nutritional index (PNI) are used to understand the immunonutritional status (5). In addition to these markers, the CONUT (Controlled Nutritional Status) score, a nutritional marker based on serum albumin, absolute lymphocyte count, and serum cholesterol levels, has been shown to have prognostic (predicting the course of the disease independently of treatment) and predictive (predicting the relationship with treatment response) value in studies conducted on many types of cancer (6-7).

Some of the retrospective studies conducted on the predictive and prognostic value of CONUT score in CRC include non-metastatic patient groups, some include patients of all stages, and some include only patient groups who underwent surgical procedures (8-14). Considering the results of all these studies and the meta-analyses conducted on this subject, it has been shown that although the cut-off value of the CONUT score (>2, >3, >4) varies in all studies, it is a biomarker that can be used prognostically and predictively, regardless of the stage (8-15). Since there is no prospectively designed study in the literature regarding the predictive and prognostic value of the CONUT score in CRC we aimed to determine the predictive and prognostic value of the CONUT score in patient groups diagnosed with mCRC.

Materials and Methods

Study design and population

This study was prospective and observational. The study evaluated patients with mCRC, who were diagnosed and whose treatment started between June 2020 and December 2021 at the Dokuz Eylul University Faculty of Medicine, Department of Medical Oncology. Study inclusion criteria were as follows: i) diagnosis of metastatic colorectal cancer, ii) treatment for at least 3 months, iii) ECOG PS being between 0-2, iv) having complete data, v) being male and female aged 18 years and over. The exclusion criteria of the study were determined as follows: i) having a secondary malignancy, ii) using a statin or lipid-lowering drug, ii) having proteinuria, iii) having protein-losing enteropathy, iv) using an intravenous parenteral nutrition product, v) using an enteral nutrition product.

At the time of diagnosis, the demographic characteristics, complete blood count, biochemical laboratory values, and clinicopathological characteristics of the patients were recorded through the hospital database. The Controlling Nutritional Status (CONUT) score was calculated using the patients' serum total cholesterol, serum albumin, and total absolute lymphocyte values before systemic treatment and in the 3rd month of treatment. The CONUT score ranges from 0 (normal nutritional status) to 12 (severe malnutrition), with a total score of 0-1 point: Normal, 2-4: Mild malnutrition, 5-8: Moderate malnutrition, 9-12: Severe malnutrition (Table 1).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

Table 1. Controlling Nutritional Status (CONUT) Score calculation

Parameter	Normal	Mild	Moderate	Severe
Serum albumin (g/dl)	≥3.5	3.0-3.49	2.5-2.9	<2.5
Score	0	2	4	6
Total Lymphocytes (ml)	>1.600	1.200-1.599	800-1.199	< 800
Score	0	1	2	3
Cholesterol (mg/dl)	>180	140-180	100-139	<100
Score	1	1	2	3
Total Score	0-1	2-4	5-8	9-12

Ethics committee approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Non-Invasive Research Ethics Committee of Dokuz Eylul University Faculty of Medicine (Date: 09.02.2022/No: 2022/05-09).

Systemic treatment

Patients diagnosed with metastatic colorectal cancer included in the study received anti-VEGF (bevacizumab) or anti-EGFR (cetuximab or panitumumab) treatment in combination with mFOLFOX chemotherapy as first-line treatment, depending on the RAS-BRAF mutation status.

Response and toxicity assessment

Tumors were staged according to the "Eighth Edition of the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) TNM stage classification" (25). Response assessments. They were made according to the "Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 guidelines" (26). Toxicity assessments were performed according to the National Cancer Institute Common Toxicity Criteria (NCI-CTC) (27).

Statistical analysis

Determining sample size

The sample size of the study was planned in 2020, when there was no similar study in the literature, and considering the presence of the COVID-19 pandemic in the same period, it was expected that approximately 6 patients would apply per month, and the study would be completed in 6 months. Considering that there were 36 patients in the specified time period, statistical power (1-β) was accepted as 80%, confidence interval (CI) as 95%, and accepted α margin of error of 5% was planned. As the frequency of malnutrition in these patients was expected to be 56% based on the studies literatüre review, it was calculated that at least 33 patients would be enrolled in the Openepi program.

Descriptive statistics and correlation analysis

Demographic characteristics, clinicopathological features, and blood sample results were collected from the hospital database. The suitability of the data for normal distribution was assessed using the Kolmogorov-Smirnov test, and it was found that the data were not normally distributed. Therefore, median values were used when reporting descriptive and survival data. In addition to descriptive statistics, the Chi-square test was used for categorical variables. Kruskal-Wallis tests were used to determine the differences between non-parametric variables as appropriate. The Pearson correlation test was used as a correlation test. The effect of CONUT score on treatment response and survival was analyzed with the Chi-square and Fisher's exact tests.

Survival Analysis

Progression-free survival (PFS) was defined as the time from the start of anti-EGFR or anti-VEGF combination chemotherapy to the date of progression; overall survival (OS) was defined as the time from the start of anti-EGFR or anti-VEGF combination chemotherapy to death/last follow-up. The Kaplan-Meier method and the Log-rank test were used for survival analysis. The median follow-up time in the study was calculated using the reverse Kaplan-Meier. IBM SPSS (Sciences

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

Statistical Package for the Social, version 24.0) package program was used to analyze all data. Statistical significance was defined as $p<0.05$.

Results

The median age of the 36 patients included in the study was 67.09 (range: 37.37-88.30 years) years, and 66.7% (n=24) of the patients were male. While 86.1% (n=31) had ECOG PS 0, 13.9% (n=5) had ECOG PS 1. Regarding comorbidities, 41.7% (n=15) of the population had hypertension, 27.8% (n=10) had type 2 diabetes mellitus, 11.1% (n=4) had coronary artery disease, 5.6% had chronic kidney disease, and 2.8% had COPD. Considering the habits of the patients, 2.8% (n=1) smoked, 33.3% (n=12) quit smoking, and 11.1% (n=4) consumed alcohol.

It was observed that the most common site of the tumor in the patients in the study population was the left colon, with a rate of 55.6% (n = 20). The most common sites of metastasis were the lymph nodes and liver, with a rate of 66.7% (n = 24). When patients were categorized by RAS mutation status, 44.4% (n=16) of the patients were RAS mutant. The clinicopathological characteristics of the patient population are shown in Table 2.

Table 2. Study population characteristics

Characteristics	% (n)
Tumor Location	
Left-sided colon	55.6 % (20)
Right-sided colon	19.4 % (7)
Rectum	16.7 % (6)
Transverse	5.6 % (2)
Pan-colon	2.8 % (1)
Histology	
Adenocarcinoma	38.9 % (14)
Low grade (well- differentiated)	33.3 % (12)
Low grade (moderately differentiated)	19.4 % (7)
High grade	5.6 % (2)
Poorly differentiated	2.8 % (1)
Ras Mutation Status	
Wild	55.6 % (20)
Mutant	44.4 % (16)
Metastasis Sites	
Lymph node	66.7 % (24)
Liver	66.7 % (24)
Lung	30.6 % (11)
Peritoneal	19.4 % (7)
Bone	5.6 % (2)
Brain	2.8 % (1)
Treatment Response Status	
Complete response	2.8 % (1)
Partial response	72.2 % (26)
Stable disease	13.9 % (5)
Progressive disease	11.1 % (4)

Fifty five percent of (n=20) of the 36 patients were RAS-wild, and these patients received folfox-anti EGFR (cetuximab or panitumumab) as first-line treatment. In 90% (n=18) of RAS wild patients, the tumor was located in the left colon, 5% (n=1) was in the transverse colon, and 5% (n=1) was in the right colon. RAS-mutant patients, which constituted 45% (n=16) of the patients, were given folfox-bevacizumab as first-line treatment. The tumor was located 62.5% (n=10) of these

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

patients, in the right colon in 31.25% (n=5) and in the transverse colon in 6.25% (n=1).

The median follow-up period of the patients was 13.85 months (Range: 5.80-26.87 months), and 5.6% of the population (n = 2) died during this period. In terms of best response, 2.8% (n=1) of the patients had a complete response, 72.2% (n=26) had a partial response, and 13.9% (n=5) had a stable disease. Disease progression occurred in 11.1% (n=4) of the patients. When patients were grouped in to low, medium, and high risk according to their CONUT score at the beginning of treatment, 47.1% (n = 16) of the patients were in the low-risk group, 44.1% (n = 15) were in the intermediate-risk group, and 8.8% (n = 3) were in the high-risk group.

When the response status was evaluated in the 3rd month of treatment, the only patient with a complete response was in the group with a low CONUT score, while 75% (n = 3) of the patients who progressed (11.1%, n = 4) were in the group with a medium and high CONUT score. In addition, objective response rate (ORR) (complete and partial response) was higher in the group with low CONUT score than in the groups with medium and high CONUT score (84.1% vs 73.3% vs 40%, respectively). When progression status was evaluated, the rate of patients progressing in the group with high CONUT score was higher than in the groups with medium and low CONUT scores (20%, 13.3%, and 6.3%, respectively) (Table 3).

Table 3. Relationship between CONUT score and treatment response

Response Status	**CONUT Score Low (Total n=16 / %)**	**CONUT Score Intermediate (Total n=15 / %)**	**CONUT Score High (Total n=5 / %)**	**Total Population (Total n= 36 / %)**
Complete response	1 (2.8%)	-	-	1 (2.8%)
Partial Response	13 (81.3%)	11 (73.3%)	2 (40%)	26 (72.2%)
Stable disease	1 (6.3%)	2 (13.3 %)	2 (40 %)	5 (13.9 %)
Progression	1 (6.3%)	2 (13.3%)	1 (20.0%)	4 (11.1%)

In the overall population, 5.6% (n=2) of the patients died during the follow-up period, the patients who died were in the group with a high CONUT score, and the overall survival time of these patients was also shorter (p=0.012) (Figure 1).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

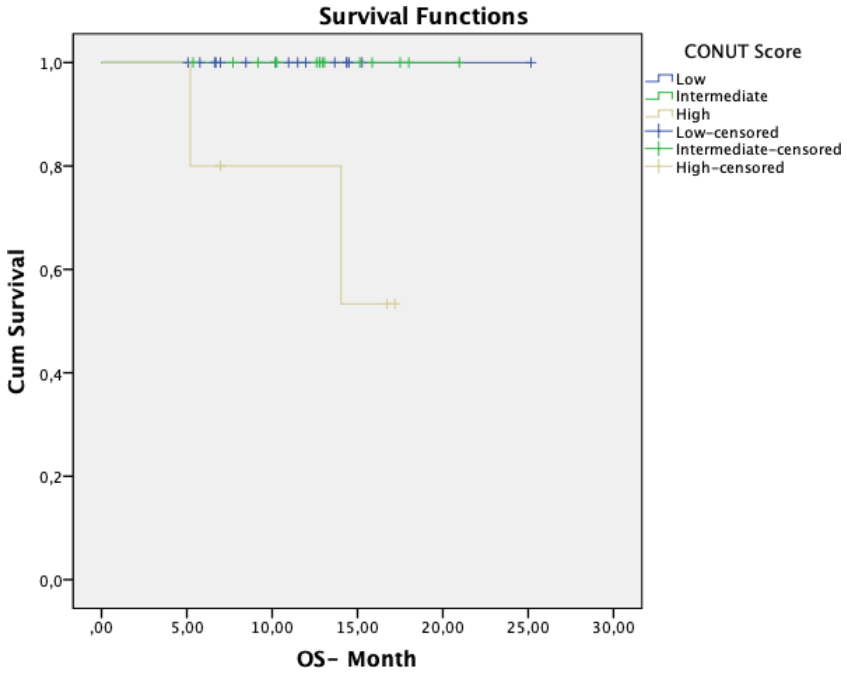


Figure 1. Survival analysis according to CONUT score (Kaplan Meier Curve)

While the median value of the patients' CONUT score at the beginning of treatment was 2 (0-11), the median value of the CONUT score at the 3rd month of treatment was 1 (0-10). When the correlation between the CONUT scores at baseline and at month 3 was evaluated, it was found that there was a statistically significant correlation between the baseline and month 3 scores (R: 0.36, p = 0.031).

The relationship between CONUT score risk groups and clinicopathological features such as RAS status, tumor location, and tumor histology was evaluated. Accordingly, it was observed that the RAS mutation rate was higher in the group with a high CONUT score (13.8%, n = 5) (60%, n = 3). Another finding was that the rate of high-grade carcinoma was higher in the group with intermediate and high CONUT scores than in the group with low CONUT scores (13.3% (n=2) and 40% (n=2), respectively). When the relationship between tumor location and CONUT score was evaluated, tumors located in the left colon were most commonly seen in the group with a low CONUT score (81.2%, n = 13).

Discussion

This study prospectively evaluated the predictive and prognostic value of the CONUT score, used to assess immune-Nutritional status in patients diagnosed with de novo metastatic colorectal cancer. Consistent with retrospective and case-control studies in the literature, it was observed that overall survival was longer in the group with low CONUT scores, all deaths were in the group with high CONUT scores, and 75% of the patients who progressed during treatment were in the group with medium and high CONUT scores 15. In our study, where we used dynamic measurements, there was a decrease in the median CONUT score of the patients with treatment. Although more studies are needed on this topic, it was concluded that there was an improvement in the immunonutritional status with the treatment, and both measurements were correlated with each other. In addition, it was observed that the RAS mutant group, which is one of the poor prognostic clinicopathological features, had mostly had high CONUT scores, and that high-grade tumors, which are another badpoor prognostic factor, had medium and high CONUT scores, and tumors located in the left colon, which are good prognostic features, mostly had low CONUT scores. In line with all these results, we concluded that the CONUT score can be used as a predictive and prognostic marker in the treatment of metastatic colon cancer.

The CONUT (The Controlling Nutritional Status) score is a nutritional marker calculated from serum albumin value, which represents the nutritional status and is a non-

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

specific marker of inflammation, absolute lymphocyte count, which reflects the immune and nutritional status, and serum cholesterol levels, which indicate the caloric status (8-9). Low albumin level, an indicator of malnutrition and inflammation, one of the components of the CONUT score, has been shown to be a nutritional indicator associated with worse prognosis in various types of cancer (8-10). It has been reported that low serum cholesterol concentration, which occurs as a result of the uptake of the other component, cholesterol, by cancer cells is associated with increased cancer mortality and morbidity as a result of disruption of transmembrane signal transmission, since it is a vital compound in the cell membrane (10). Finally, the third component has been shown to have a poor prognostic value because low absolute lymphocyte count affects the immune response in various types of cancer and is associated with cancer progression (10). In line with these findings, the CONUT score, which is formed by combining these three nutritional and immunological parameters, reflects and evaluates the overall nutritional and immunological status more comprehensively and accurately than markers such as PNI and GPS, and explains why it can be used as a predictive and prognostic marker in patients diagnosed with cancer (8-10).

The prognostic and predictive value of the CONUT score has been investigated in colorectal cancer, as in various types of cancer (8). Studies have evaluated both patients with early-stage disease and those with advanced metastatic disease. Among the studies conducted on early-stage patients, a retrospective study by Pian G et al., which included Stage 1 (T1-2N0M0) colorectal cancer patients, found that those with a high CONUT score had worse OS and disease-free survival (DFS), whereas multivariate analysis showed that CONUT score was not an independent predictive factor associated with DFS and OS12. Contrary to this study, the study of Tokunaga R. et al., which included patients diagnosed with stage 1, 2, and 3 colorectal cancer who underwent curative surgery, found that a high CONUT score was an independent predictive factor related to OS. In addition, this study has also shown that a high CONUT score predicts serious postoperative complications (16). Iseki et al.'s retrospective study on patients diagnosed with stage 2 and 3 colorectal cancer who underwent curative surgery, they found that the group with a lower CONUT score had a longer 5-year cancer-specific survival (CSS), and multivariate analyses showed that the CONUT score was an independent risk factor for CSS a (17). In the retrospective study of Yang C. et al., which included patients diagnosed with stage 1, 2 and 3 colorectal cancer who underwent curative treatment, unlike their other studies, combined the CONUT score and circulating tumor cell (CTC) count, and in the group with a high CONUT-CTC score, it was observed that recurrence-free survival (RFS) and CSS were shorter than the other group, and in univariate-multivariate analysis, the CONUT-CTC score was an independent predictive factor for RFS and CSS (18). As a result of all these studies, we can say that the CONUT score can be used as a predictive marker in colorectal cancer that undergoing curative surgical treatment.

The CONUT score, which has been shown to have prognostic and predictive value in early-stage colorectal cancer, has also been shown to be a predictive and prognostic marker in studies of metastatic colorectal cancer patients. In fact, a retrospective study of metastatic colorectal cancer patients receiving first-line chemotherapy showed that the group with a higher CONUT score had shorter PFS and OS, correlation with our study. In addition, when the relationship between CONUT score and clinicopathological features was evaluated, it was shown that those with high CONUT scores were associated with a statistically significantly higher rate of metastasis (synchronous-metachronous) and a lower rate of primary tumor resection (19). Contrary to the fact that RAS mutant patients in our study were included in the group with numerically higher CONUT scores, no relationship was found between RAS status and CONUT score in this study (19). Contrary to other studies, in a study investigating the prediction of sarcopenia and the immune nutritional indexes CONUT score and geriatric nutritional risk index (GNRI) in patients with metastatic colorectal cancer, sarcopenia was seen at a higher rate in the group with a high CONUT score, while the median value in this group was also consistent with our study. OS was reported to be statistically significantly shorter (20). As a result, although there are no studies in the literature as in our study evaluating the relationship between CONUT score and treatment response in mCRC and the relationship between prospective and dynamic measurements before and after treatment, according to the results of retrospective studies in the literature and our study, as in early stage CRC patients who underwent curative surgery, In mCRC patients, the

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:91-100

CONUT score can be used as a prognostic and predictive immunonutrition marker.

On the other hand, in a meta-analysis that evaluated patients with CRC at all stages and included nine studies, it was stated that a high CONUT score was associated with poor OS, CSS, and RFS, and that the CONUT score could be a prognostic factor in CRC, supporting the above studies (15).

Studies that evaluated the prognostic and predictive value of the CONUT score, which reflects the immunonutritional status in metastatic colorectal cancer, and evaluated the importance of nutrition and systemic inflammation status with different nutritional indices (Nutritional Risk Index (NRI), Subjective Global Assessment (SGA)) in CRC also showed that chemotherapy toxicity was higher, postoperative hospital stays were longer, and overall survival was shorter in metastatic colorectal patients with poor nutritional status (21-22). As can be seen from these prospectively designed studies, the prognostic and predictive importance of nutritional and systemic inflammation status in patients diagnosed with metastatic colorectal cancer is increasing day by day, in addition to conventional clinicopathological prognostic and predictive factors such as histological subtype, metastasis site, stage, age, and comorbidity.

Our study had several limitations. First of all, our study was planned prospectively during the COVID-19 pandemic, so the number of patients was limited. Another limitation is that the results of our study included data from a single center, and it would be more appropriate to interpret survival analyses more carefully, especially since the number of deaths in our study was low. To eliminate these limitations, we believe that a multicenter, prospective study with a clearer sample size, including more patients, would increase the reliability of our results.

Conclusion

In conclusion, this study demonstrated that the dynamic measurement of CONUT score as an immune inflammation and nutritional marker in mCRC is prognostic and predictive. As shown in many studies, in addition to the traditionally used prognostic and predictive clinicopathological features in mCRC, systemic immune inflammation and nutritional status are considered as prognostic and predictive factors that are becoming increasingly important and should be considered for use in routine practice for every mCRC patient.

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. Global Cancer Observatory. International Agency for Research on Cancer. World Health Organization. Available at: https://gco.iarc.fr/ (Accessed on December 13, 2023).
2. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024 [published correction appears in CA Cancer J Clin. 2024 Mar-Apr;74(2):203. doi: 10.3322/caac.21830]. CA Cancer J Clin. 2024;74(1):12-49. doi:10.3322/caac.21820.
3. Cronin KA, Scott S, Firth AU, et al. Annual report to the nation on the status of cancer, part 1: National cancer statistics. Cancer. 2022;128(24):4251-4284. doi:10.1002/cncr.34479.
4. Yamamoto M, Saito H, Uejima C, et al. Prognostic Value of Combined Tumor Marker and Controlling Nutritional Status (CONUT) Score in Colorectal Cancer Patients. Yonago Acta Med. 2019;62(1):124-130. Published 2019 Mar 28. doi:10.33160/yam.2019.03.017
5. Li J, Zhu N, Wang C, et al. Preoperative albumin-to-globulin ratio and prognostic nutritional index predict the prognosis of colorectal cancer: a retrospective study. Sci Rep. 2023;13(1):17272. Published 2023 Oct 12. doi:10.1038/s41598-023-43391-5
6. Misevic V, Mitrovic M, Krstić M, et al. Significance of the CONUT Score in the Prognosis of Colorectal Cancer Patients. Chirurgia (Bucur). 2023;118(4):391-398. doi:10.21614/chirurgia.2023.v.118.i.4.p.391
7. Liang RF, Li JH, Li M, Yang Y, Liu YH. The prognostic role of controlling nutritional status scores in patients with solid tumors. Clin Chim Acta. 2017;474:155-158. doi:10.1016/j.cca.2017.09.021
8. Okamoto A, Furukawa K, Ohkuma M, et al. Clinical Significance of Controlling Nutritional Status (CONUT) Score in Patients With Colorectal Liver

Metastases After Hepatectomy. In Vivo. 2023;37(6):2678-2686. doi:10.21873/invivo.13377

9. Misevic V, Mitrovic M, Krstić M, et al. Significance of the CONUT Score in the Prognosis of Colorectal Cancer Patients. Chirurgia (Bucur). 2023;118(4):391-398. doi:10.21614/chirurgia.2023.v.118.i.4.p.391
10. Lu S, Chen Z, Peng R, et al. Prognostic effect of preoperative Controlling Nutritional Status score in patients with locally advanced rectal cancer: A two-center, retrospective study. Nutrition. 2023;112:112078. doi:10.1016/j.nut.2023.112078
11. Takamizawa Y, Shida D, Boku N, et al. Nutritional and inflammatory measures predict survival of patients with stage IV colorectal cancer. BMC Cancer. 2020;20(1):1092. Published 2020 Nov 11. doi:10.1186/s12885-020-07560-3
12. Pian G, Oh SY. Comparison of nutritional and immunological scoring systems predicting prognosis in T1-2N0 colorectal cancer. Int J Colorectal Dis. 2022;37(1):179-188. doi:10.1007/s00384-021-04043-0
13. Yamamoto M, Saito H, Uejima C, et al. Prognostic Value of Combined Tumor Marker and Controlling Nutritional Status (CONUT) Score in Colorectal Cancer Patients. Yonago Acta Med. 2019;62(1):124-130. Published 2019 Mar 28. doi:10.33160/yam.2019.03.017
14. Liu LX, Wang H, Gao B, et al. Preoperative controlling nutritional status as an optimal prognostic nutritional index to predict the outcome for colorectal cancer. World J Gastrointest Oncol. 2024;16(2):343-353. doi:10.4251/wjgo.v16.i2.343
15. Takagi K, Buettner S, Ijzermans JNM. Prognostic significance of the controlling nutritional status (CONUT) score in patients with colorectal cancer: A systematic review and meta-analysis. Int J Surg. 2020;78:91-96. doi:10.1016/j.ijsu.2020.04.046
16. Tokunaga R, Sakamoto Y, Nakagawa S, et al. CONUT: a novel independent predictive score for colorectal cancer patients undergoing potentially curative resection. Int J Colorectal Dis. 2017;32(1):99-106. doi:10.1007/s00384-016-2668-5
17. Iseki Y, Shibutani M, Maeda K, et al. Impact of the Preoperative Controlling Nutritional Status (CONUT) Score on the Survival after Curative Surgery for Colorectal Cancer. PLoS One. 2015;10(7):e0132488. Published 2015 Jul 6. doi:10.1371/journal.pone.0132488
18. Yang C, Wei C, Wang S, et al. Combined Features Based on Preoperative Controlling Nutritional Status Score and Circulating Tumour Cell Status Predict Prognosis for Colorectal Cancer Patients Treated with Curative Resection. Int J Biol Sci. 2019;15(6):1325-1335. Published 2019 May 12. doi:10.7150/ijbs.33671
19. Daitoku N, Miyamoto Y, Tokunaga R, et al. Controlling Nutritional Status (CONUT) Score Is a Prognostic Marker in Metastatic Colorectal Cancer Patients Receiving First-line Chemotherapy. Anticancer Res. 2018;38(8):4883-4888. doi:10.21873/anticanres.12802
20. 20- Güç ZG, Altay C, Özgül HA, Ellidokuz H, Yavuzşen T. GNRI And Conut Scores: Simple Predictors of Sarcopenia in Metastatic Colorectal Cancer Patients. Support Care Cancer. 2022;30(10):7845-7852. doi:10.1007/s00520-022-07218-9
21. Barret M, Malka D, Aparicio T, et al. Nutritional status affects treatment tolerability and survival in metastatic colorectal cancer patients: results of an AGEO prospective multicenter study. Oncology. 2011;81(5-6):395-402. doi:10.1159/000335478
22. Teraishi F, Yoshida Y, Shoji R, et al. Subjective global assessment for nutritional screening and its impact on surgical outcomes: A prospective study in older patients with colorectal cancer. Langenbecks Arch Surg. 2024;409(1):356. Published 2024 Nov 25. doi:10.1007/s00423-024-03548-wmedicine and critical appraisal. Medical Teacher. 2003 Jan;25(1):77-81.

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

RESEARCH ARTICLE

Sayfa:101-109

An evaluation of the small group study in the critical appraisal special study module

Eleştirel değer biçme özel çalışma modülünde küçük grup çalışmalarına dair bir değerlendirme

Serap KONAKCI [1]
Mualla Aylin ARICI[2]
Nevcivan GÜLDAŞ[3]
Başak BAYKARA[2]

[1] Dokuz Eylul University Faculty of Medicine, Department of Medical Education, Izmir, Türkiye
[2] Dokuz Eylul University Faculty of Medicine, Department of Pharmacology, Izmir, Türkiye
[3] Dokuz Eylül University ARLAB, Izmir, Türkiye
[4] Dokuz Eylul University Faculty of Medicine, Department of Histology and Embryology, Izmir, Türkiye

Received: 16.10.2024
Accepted: 27.02.2025

Doi:10.18614/dehm.1699428

Corresponding author
Serap KONAKCI
ORCID ID: 0000-0002-3325-6382
serapkonakci@yahoo.com

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

INTRODUCTION
Critical appraisal is one of the steps towards evidence-based medicine. Today, the production of new knowledge is quite rapid and its evaluation is becoming increasingly difficult. To overcome these difficulties, educational activities incorporating critical appraisal practices in medical education programmes have found a place in curricula around the world.
The aim of this study is to determine the opinions of trainers and students about the practice that is included in the Critical Appraisal Special Study Module (CA-SSM), which is carried out as a structured programme in Dokuz Eylül University Faculty of Medicine (DEUFM) and is carried out as a small group study.

METHOD
The population of the study consisted of 417 students who took CA-SSM in DEUFM Term 2 in the academic year 2023-2024 and 32 trainers who participated in the exercises. The opinions of the students and trainers were collected electronically using two different forms. They were asked to give a score between 0 and 5 for each item.
Percentage distributions, means and standard deviations were calculated for both groups. The Mann-Whitney U tests were used in the analyses. $p < 0.05$ was set as the statistical significance level. Thematic analysis was used for qualitative data.

RESULTS
The response rate for students was 51.8% and 62.5% for trainers. The mean for all items evaluated by both groups was above three points. The highest mean belongs to the item "level of preparation of trainers for practice" with 4.56 for the students and to the item "sufficiency of time allocated for practice" with 4.55 for the trainers. There was no statistically significant difference between the mean scores of the students according to their gender for any of the items ($p>0.05$ for all).
The most common theme in the written feedback was that the application was instructive and useful for the students, while for the trainers the placement of the application within the programme affected the students' performance.
There was no statistically significant difference between the students and the trainers in their evaluation of the articles used in the application. However, there was a statistically significant difference between the groups in terms of student participation and the evaluation of the adequacy of the time allocated for implementation (M-W U=1532,000 p=.023 and M-W U=1342,000 p=.003, respectively).

DISCUSSION
Students and trainers find the CA-SSM implementation valuable. Although the feedback from students and trainers on the CA practice is generally positive, it is important to make arrangements in line with the data obtained to increase the efficiency effectiveness of the practice. In order to enrich the programme and increase its educational impact, it would be appropriate to carry out studies to evaluate all its components.

KEYWORDS
Critical appraisal, evidence-based medicine, medical education, student feedback, trainer feedback

AMAÇ
Kanıta dayalı tıp uygulamalarına yönelik adımlardan biri eleştirel değer biçmedir. Yeni bilginin üretilmesi günümüzde oldukça hızlıdır ve değerlendirilmesi de giderek zorlaşmaktadır. Bu zorlukları aşmaya yönelik olarak tıp eğitimi programlarında eleştirel değerlendirme uygulamalarını içeren eğitsel etkinliklerin tüm dünyada müfredatlarda yer bulduğu görülmektedir. Bu araştırmanın amacı Dokuz Eylül Üniversitesi Tıp Fakültesi' nde (DEÜTF) yapılandırılmış bir program olarak sürdürülen Eleştirel Değer Biçme Özel Çalışma Modülü'de (EDB ÖÇM) yer alan ve küçük grup çalışması olarak sürdürülen uygulama hakkında eğitim yönlendiricileri ve öğrencilerin görüşlerinin belirlenmesidir.

YÖNTEM
Araştırmanın evrenini, 2023-2024 akademik yılında Dönem 2'de EDB ÖÇM' si alan 417 öğrenci ve uygulamalarda görev alan 32 öğretim görevlisi oluşturmaktadır. Öğrenci ve eğitim yönlendiricilerinin görüşlerine ait veriler, iki farklı form aracılığı ile elektronik ortamda toplanarak elde edilmiştir. Her bir madde için 0-5 arasında puanlama yapmaları istenmiştir. Her iki grup için yüzde dağılımlar, ortalama ve standart sapmalar hesaplanmıştır. Analizlerde ki-kare ve Mann – Whitney U testleri kullanılmıştır. $p < 0,05$, istatistiksel anlamlılık sınırı olarak alınmıştır. Nitel veriler için tema analizi yapılmıştır.

BULGULAR
Öğrenciler için ulaşma oranı %51,8; eğitim yönlendiricileri için %62,5'tir. Her iki grupda değerlendirdikleri tüm maddeler için ortalama üç puanın üstündedir. Öğrencilerde en yüksek ortalama 4,56 ile 'Eğiticinin uygulamaya hazırlık düzeyi' maddesine, eğitim yönlendiricilerinde 4,55 ile 'Uygulamaya ayrılan sürenin yeterliliği' maddesine aittir. Öğrencilerin cinsiyetlerine göre puan ortalamaları arasında hiçbir maddede istatistiksel olarak anlamlı bir farklılık saptanmamıştır (tümü için $p> 0,05$). Yazılı geri bildirimlerinde en sık karşılaşılan tema, öğrenciler açısından uygulamanın öğretici ve yararlı olması iken, eğitim yönlendiricileri için uygulamanın program içindeki yerinin öğrenci performansını etkilemesi olmuştur.
Uygulamada kullanılan makalelerin değerlendirilmesinde öğrenciler ve eğitim yönlendiricileri arasında istatistiksel olarak anlamlı bir fark saptanmamıştır ($p> 0,05$). Ancak öğrenci katılımı ve uygulamaya ayrılan sürenin yeterliliğinin değerlendirilmesi açısından gruplar arasında istatistiksel olarak anlamlı bir farklılık vardır (sırasıyla M-W U=1532.000 p= ,023 ve M-W U=1342.000 p= ,003).

TARTIŞMA
Öğrenciler ve eğitim yönlendiricileri, EDB ÖÇM uygulamasını değerli bulmaktadır. EBD uygulamaları için öğrenci ve eğitim yönlendiricilerinin geri bildirimleri genel olarak olumlu yönde olsa da ettiğimiz veriler doğrultusunda düzenlemeler yapılması uygulama verimliliğinin artırılması açısından önemlidir. Programın zenginleştirilmesi, eğitici etkisinin artırılabilmesi amacıyla tüm komponentlerinin değerlendirilmesine yönelik çalışmalar yapılması uygun olacaktır.

ANAHTAR KELİMELER
Eleştirel değer biçme, eğitici geri bildirimi, kanıta dayalı tıp, tıp eğitimi, öğrenci geri bildirimi

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

Healthcare services provided without the use evidence-based practices may result in missed opportunities to benefit patients and could potentially cause harm. The five steps of evidence-based medical practice were first described in 1992 (1). One of these steps the critical appraisal of evidence for validity, clinical relevance, and applicability (2).

For the critical appraisal process to be effective, health care providers must be able to acquire, evaluate, integrate and use new information in their decisions to meet current needs. However, the rapid production of new knowledge in the field of medicine today presents challenges. Access to the rapidly evolving literature has become increasingly difficult for users due to time constraints, inadequate in the presentation of findings, and the wide dispersion of the literature across numerous publications.

To address these challenges, many studies on effective reading and the critical appraisal of medical research literature have been conducted and discussed since the 1980's (3-4). Numerous guides have been published to assist in reading and critical appraisal of articles. The literature highlights the importance of organizing educational activities to develop the ability to critically assess evidence for validity and clinical significance (2).

Critical evaluation and evidence-based medicine are now widely incorporated into the curricula of undergraduate and postgraduate medical education programmes around the world. However, there are differing views in the literature about the impact of these programmes, which vary in implementation and level (5–11).

The aim of this study is to determine the opinions of training facilitators and students regarding the application of the Critical Appraisal Special Study Module (CA-SSM). This module is implemented as a structured programme at Dokuz Eylül University Faculty of Medicine (DEUFM) and conducted as a small group study.

Materials and Methods

CA-SSM is an educational programme that has been implemented in our faculty since the 2019–2020 academic year. It aims to equip students with the skills to research scientific literature and critically analyze the accessed literature in terms of design and methodology. Initially conducted online during the COVID-19 pandemic, the CA-SSM has resumed as a face to face programme after the pandemic.

Throughout the spring semester, second-year students receive various theoretical presentations within the CA-SSM. These presentations cover topics such as the concept of scientific research, types of research, and statistical analysis (Table 1).

Table 1. CA-SSM theoretical presentation titles

Basic concepts in scientific research
Data, information, and knowledge management in health
Types of research
Scan engines
Case control studies
Cohort studies
Research, technology, and publication ethics
Hypothesis tests
Types of articles and critical article reading
Introducing the critical article reading app
Basic biostatistics concepts
Biosafety training
Clinical studies
Sample size and sampling methods
CA-SSM application

Upon completion of the theoretical sessions, students are divided into groups of 11–12 and participate in two practical sessions. In these sessions, two research articles—one epidemiological and one experimental—are critically evaluated under the guidance of training facilitators.

Prior to the practical sessions, participants are provided with articles and evaluation guides prepared according to international guidelines to facilitate their evaluations. In addition, an introductory session is organized for the training facilitators to familiarize them with the articles and evaluation guides used during the sessions.

During the practical sessions, the groups are expected to discuss and critically evaluate the research articles based on the evaluation criteria provided, guided by the facilitators.

The assessment of the CA-SSM is conducted through an exam consisting of multiple-choice questions, held immediately following the practical sessions. The score of this exam contributes 5% to the student's overall grade at the end of the year.

The study population consisted of 417 students enrolled in Term 2 at Dokuz Eylül University Faculty of

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

Medicine during the 2023–2024 academic year, all of whom participated in the Critical Appraisal Special Study Module (CA-SSM), and 32 training facilitators who provided guidance during the CA-SSM sessions. No sampling was used; data were collected from all students and facilitators who voluntarily agreed to participate in the study. Only data from participants who completed the data collection forms completely and accurately were included in the analysis, and incomplete forms were excluded.

Two separate data collection forms were developed using Survey Monkey: one for the students and another for the training facilitators. These forms were distributed immediately after the second implementation session using QR codes and link-sharing methods. Data was collected anonymously in an electronic format.

For the students, data were collected on gender and their views on small group work, including the importance of acquiring critical appraisal skills for the medical profession, the compatibility of group work with theoretical courses within the CA-SSM framework, the adequacy of the application period, the appropriateness of the articles used for the purpose of the application, the trainers' level of preparation for the application, and the level of participation of the students in the group during the application. The students were asked to rate these aspects on a Likert-type scale: 0 for no opinion, 1 for very bad, 2 for bad, 3 for neither good nor bad, 4 for good, and 5 for very good. They were also asked an open-ended question to about their general opinions of the application.

For training facilitators, data were collected specialty, gender, training onin evidence-based medicine, institution where training in evidence-based medicine was received, experience with critical appraisal training, and their views on small group work. These views included the suitability of the articles used the appropriateness of appraisal forms the adequacy of the time allocated for the application, the students' preparation for the application, and the general level of student participation during the appraisal. Facilitators were also asked to ate these aspects on a Likert-type scale: 0 for no opinion, 1 for very bad, 2 for bad, 3 for neither good nor bad, 4 for good, and 5 for very good. They were also asked to give open-ended feedback on the application.

Statistical analysis

Frequency and percentage distributions, means, and standard deviations were calculated separately for both groups. The Mann-Whitney U Test was applied for comparisons between students and training facilitators. A p-value of < 0.05 was considered the threshold for statistical significance.

For the qualitative data collected through open-ended questions in both groups, theme analysis was conducted independently by two researchers from the research team. A consensus on the themes and theme expressions was reached through comparative evaluations performed collaboratively. All analyses were conducted using SPSS version 24.0 (IBM, Armonk, NY, United States).

Ethical approval

The study was conducted after receiving approval from the Dokuz Eylül University Faculty of Medicine Non-Interventional Studies Ethics Committee (DEÜ GOAEK, Decision No: 2024/18-16, Date: 22.05.2024).

Results

Student feedback

A total of 235 students completed the student questionnaire. However, 19 questionnaires were excluded from the analysis due to incomplete data, leaving 216 completed questionnaires for analysis. The student response rate was 51.8% (216/417). Of the respondents, 56.0% (121 students) were male.

The average group score for each item evaluating the application was above three points. The highest average score was for the item "Trainer's level of preparedness for application," with an average of 4.56 (Table 2). Additionally, 70.4% of the students (152 individuals) rated the trainers' level of preparedness for practice as "very good." The lowest mean score, 3.55, was for the item "Group study is compatible with the theoretical courses I have taken within the scope of CA-SSM" (Table 2).

For this item, 49.1% of the students (106 individuals) chose the "I agree" option (Table 3).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

Table 2. Average scores of the items for the evaluation of the application by the students (N=216)

	Average	SD
Acquiring critical appraisal skills is important for the medical profession*	3.91	1.16
Group study is compatible with the theoretical courses I have taken within the scope of CA-SSM*	3.55	1.21
Trainer's level of preparation for application **	4.56	.87
Participation of students in the group in the application**	4.01	1.02
The suitability of the articles used in the application for the purpose of the application**	3.86	1.08
Adequacy of time allocated for application **	3.81	1.22

Table 3. Distribution of student responses for the item 'Group work is compatible with the theoretical courses I have taken within the scope of the CA-SSM' (N=216)

	Number	%
No opinion	4	1.9
I totally disagree	14	6.5
I disagree	26	12.0
I neither agree nor disagree	27	12.5
I agree	106	49.1
I totally agree	39	18.1
Total	216	100.0

When the mean scores of the students were compared based by gender, no statistically significant difference was found between the scores of female and male students for any of the items ($p > 0.05$ for all items).

A total of 36.6% of the students (79 individuals) provided written feedback. Theme analysis of the written feedback identified 11 main themes. The most common theme was that the CA-SSM was an instructive and useful practice, as expressed by 46.8% (37 students). The second most common theme was criticism of scheduling of the practical on the same day as the theoretical exam for the CA-SSM, which was noted to have negative impact on participation in terms of both quantity and quality (Table 4).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

Table 4. Themes in student written feedback (N=79)

	Number	%
The order should be arranged with other SMs.	1	1.3
The physical environment is not suitable	1	1.3
Not practical	1	1.3
Statements related to theoretical presentations of the CA-SSM, not aimed at practice	2	2.5
Implementing applications that include methods to ensure more active participation of students in the application process.	2	2.5
The duration of the application is long	2	2.5
An unnecessary application	5	6.3
The number of applications should be increased	5	6.3
Good group harmony with the training facilitator and related satisfaction	6	7.6
Having the CA-SSM theoretical exam and the practical exam on the same day reduces participation both qualitatively and quantitatively.	17	21.5
CA-SSM application is an instructive and useful application.	37	46.8

Training facilitator feedback

Feedback from training facilitators showed a reach rate of 62.5% (20/32). Of the training facilitators who provided feedback, 65.0% were female, and 65.0% were employed in basic sciences (Table 5). In addition, 40% (8/20) of the facilitators were participating in this practice as trainers for the first time.

Table 5. Distribution of lecturers who gave feedback in the CA-SSM application according to their scientific fields and gender

		Number	%
Fields of science	Basic Sciences	13	65.0
	Internal Sciences	5	25.0
	Surgical Sciences	2	10.0
	Total	20	100.0
Gender	Woman	13	65.0
	Male	7	35.0
	Total	20	100.0

Of the training facilitators who responded to the survey, 75% (15/20) had previously received training in critical appraisal, and 66.7% of these 15 facilitators received their training at our faculty. The group average for each item scored for the evaluation of the application was above three points. The highest average score was for the item "Sufficiency of time allocated for application," with an average of 4.55 (Table 6). The lowest average score was for the item "Students' level of preparation for application," with an average of 3.55 (Table 6)

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

Table 6. Average scores of the items for the evaluation of the application by the training facilitators (N=20)

	Average	SD
The suitability of the articles used in the application for the purpose of the application*	4.25	.786
Suitability of evaluation forms for purpose*	4.50	.607
Adequacy of time allocated for application*	4.55	.686
Students' level of preparedness for practice*	3.55	.945
Participation of students in the group in the application*	4.00	1.076

Half of the training facilitators (50.0%, 10/20 individuals) provided written feedback. Theme analysis of this feedback revealed 5 main themes. The most common theme, cited by 40.0% (4/10) of the facilitators, was the low number and quality of participation due to the scheduling of the practice on the same day as the theoretical exam for the CA-SSM. The second most common theme, expressed by 30.0% (3/10) of the facilitators, was that the CA-SSM application is an instructive and useful practice (Table 7).

Table 7. Themes included in the written feedback from the training facilitator (N=10)

	Number	%
The application should be structured by presenting sample article referees.	1	10.0
The number of applications should be increased	1	10.0
The student's performance in the application should be reflected in the SM grade.	1	10.0
CA-SSM application is an instructive and useful application.	3	30.0
Having the CA-SSM theoretical exam and the practical exam on the same day reduces participation both qualitatively and quantitatively.	4	40.0

Among the parameters evaluated by the students and training facilitators, the student's participation in the practice, the appropriateness of the articles used in the practice for the purpose and the appropriateness of the duration of the practice were common parameters. When the scores given by the students and the training facilitators on these items were compared, no statistically significant difference was found between the groups in the evaluation of the appropriateness of the articles for the purpose. However, there is a statistically significant difference between the groups in terms of student participation and the assessment of the adequacy of the time allocated for implementation (M-W U=1532.000 p=.023 and M-W U=1342.000 p=.003, respectively).

Discusion

In our study, the coverage rate was 51.8% for students and 62.5% for training facilitators. The highest average score in the students' evaluations was for the item "The level of preparation of the trainer for the application," with a score of 4.56. In the evaluations by the training facilitators, the highest average score was for the item "Sufficiency of the time allocated for application," with a score of 4.55. When comparing the opinions on the parameters common to both groups, a statistically significant difference was found between the groups regarding student participation and the adequacy of the time allocated for the practice.

The thematic analysis revealed that the themes identified in both groups were similar, emphasizing the benefits of the implementation and the importance of proper time planning in the programme. Students have no prior knowledge or skills in critical appraisal from their previous educational experiences. For this reason, it is crucial that they

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:101-109

receive structured training in critical appraisal and reinforce it through practice, as noted by Gupta (12). CAS training activities are implemented in different ways worldwide (13–15). Introducing this practice at an early stage of training and structuring it throughout the curriculum is considered valuable.

Students who complete the CA-SSM develop the ability to plan, conduct, and report research as a team in the Research Skills SM programme, which is part of the third year curriculum. To be successful in this programme, students must demonstrate skills in literature review and critical appraisal. Inadequate training in the critical appraisal of scientific literature presents a significant barrier to the delivery of conducting the Research Skills SM programme (16).

Both training facilitators, and students, find the CA-SSM valuable. However, critical factor in the program success is its duration, an issue highlighted by both groups. The inclusion of the CA-SSM theoretical exam in the programme immediately after the second implementation session was found to have reduced participation both quantitatively and qualitatively. Nevertheless, the application provides an opportunity for a quick review of topics covered in the exam, such as type of research types, sample size, and research direction.

Low participation in the application process and exam anxiety among participants are likely to have affected the reach rate among students. In addition, although receiving feedback is often a challenging process (17), this alone does not fully explain the low response rate among training facilitators. Investigating the reasons for the low participation of faculty members in research processes and their reluctance to provide feedback could be a topic for future research.

When the responses to the common items were compared, a significant difference was observed between the training facilitators and students in terms of student participation and the assessment of the appropriateness of the time allocated for practice. This difference may be due to the fact that trainers tend to expect higher levels of student participation and may feel more pressure to use time due to multitasking.

Special Study Module (SM) programmes are important components that strengthen and enrich medical education curricula. However, this study did not aim to evaluate the CA-SSM programme as a whole. Instead, it focused solely on the application within the programme. To further improve the programme and maximize its educational impact, it would be beneficial to conduct comprehensive studies that evaluate all components together.

Although the student and training facilitators feedback on CAS practices generally scored three or above, it is important to make adjustments based on the findings of this research to improve the effectiveness of the practice in the next academic year. These improvements will help to ensure that the programme continues to meet its educational objectives effectively.

References

1. Cook DJ, Jaeschke R, Guyatt GH. Critical Appraisal of Therapeutic Interventions in the Intensive Care Unit: Human Monoclonal Antibody Treatment in Sepsis. Journal of Intensive Care Medicine. 1992;7(6):275-282. doi:10.1177/088506669200700601).
2. Dawes M, Summerskill W, Glasziou P, Cartabellotta A, Martin J, Hopayian K, et al. Sicily statement on evidence-based practice. BMC Med Educ. 2005 Dec;5(1)
3. Godwin M, Seguin R. Critical appraisal skills of family physicians in Ontario, Canada. BMC Med Educ. 2003 Dec 2;3(1)
4. HAYNES RB. How to Keep Up with the Medical Literature: I. Why Try to Keep Up and How to Get Started. Ann Intern Med. 1986 Jul 1;105(1):149.
5. Ibbotson T, Grimshaw J, Grant A. Evaluation of a programme of workshops for promoting the teaching of critical appraisal skills. Med Educ. 1998 Sep;32(5):486-91. doi: 10.1046/j.1365-2923.1998.00256.x. PMID: 10211289.
6. Taylor RS, Reeves BC, Ewings PE, Taylor RJ. Critical appraisal skills training for health care professionals: a randomized controlled trial [ISRCTN46272378]. BMC Med Educ. 2004 Dec;4(1)
7. Taylor R, Reeves B, Ewings P, Binns S, Keast J, Mears R. A systematic review of the effectiveness of critical appraisal skills training for clinicians. Med Educ. 2000 Feb;34(2):120-5. doi: 10.1046/j.1365-2923.2000.00574.x. PMID: 10652064.
8. Sasannia S, Amini M, Moosavi M, Askarinejad A, Moghadami M, Ziaee H, Vara F. Critical appraisal skills training to undergraduate medical students: A Randomized Control Study. J Adv Med Educ Prof. 2022 Oct;10(4):253-258. doi: 10.30476/JAMP.2022.94852.1610. PMID: 36310666; PMCID: PMC9589073.
9. Coomarasamy A, Taylor R, Khan K. A systematic review of postgraduate teaching in evidence-based medicine and critical appraisal. Medical Teacher. 2003 Jan;25(1):77-81.
10. Parkes J, Hyde C, Deeks J, Milne R. Teaching critical appraisal skills in health care settings. Cochrane

Database Syst Rev. 2001;3:CD001270. DOI: 10.1002/14651858.

11. Horsley T, Hyde C, Santesso N, Parkes J, Milne R, Stewart R. Teaching critical appraisal skills in healthcare settings. The Cochrane Database of Systematic Reviews 2011; Issue 11. Art. No.: CD001270. DOI: 10.1002/14651858.CD001270.pub2.
12. Gupta A. Importance of critical appraisal skills training in medical students. Natl Med J India 2022;35:370–1.
13. Hong B, Plugge E. Critical appraisal skills teaching in UK dental schools. Br Dent J. 2017 Feb 10;222(3):209-213. doi: 10.1038/sj.bdj.2017.126. PMID: 28184065.
14. Meats E, Heneghan C, Crilly M, Glasziou P. Evidence-based medicine teaching in UK medical schools. Med Teach. 2009 Apr;31(4):332-7. doi: 10.1080/01421590802572791. PMID: 19404893.
15. Daou D, Chakhtoura M, El-Yazbi A, Mukherji D, Sbaity E, Refaat MM, et al. Teaching critical appraisal to large classes of undergraduate medical students using team-based learning versus group discussions: a randomized controlled trial. BMC Med Educ. 2022 Dec;22(1).
16. Siemens DR, Punnen S, Wong J, Kanji N. A survey on the attitudes towards research in medical school. BMC medical education. 2010;10(1):4.
17. Constantinou C, Wijnen-Meijer M. Student evaluations of teaching and the development of a comprehensive measure of teaching effectiveness for medical schools. BMC Med Educ. 2022 Feb 19;22(1).

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

RESEARCH ARTICLE

Sayfa:111-126

Investigating the Ku70 (XRCC6) gene polymorphism in patients with gastric cancer

Mide kanseri olan hastalarda Ku70 gen polimorfizminin araştırılması

Sezin CANBEK[1]
Elçin BORA[2]
Seymen BORA[3]
Derya ERÇAL[2]

[1] Umraniye Research and Training Hospital, Medical Genetics Department, Istanbul, Türkiye [2] Dokuz Eylül University, Medical Genetics Department, Izmir, Türkiye
[3] Dokuz Eylül University, General Surgery Department, Izmir, Türkiye

Ku70 Gene Polymorphisms and Gastric Cancer Susceptibility

Received: 09.11.2024
Accepted: 28.01.2025

doi:10.18614/dehm.1699431

Corresponding author
Sezin CANBEK
ORCID ID: 0000-0001-9516-0047
sezin.canbek@ogr.iu.edu.tr

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

BACKGROUND
The DNA repair gene Ku70, a key component of the non-homologous end-joining repair pathway, plays a crucial role in the repair of DNA double strand breaks (DSBs). Deficiencies in DSB repair may result in permanent genomic instability. However, the association between polymorphic variations of Ku70 and susceptibility to gastric cancer remains unclear.

OBJECTIVE
This study aims to investigate the potential correlation between the Ku70 promoter G-57C (rs2267437) and intron 3 (rs132774) polymorphisms and the risk of developing gastric cancer in the Turkish population.

METHOD
A hospital-based case-control study was conducted, including 92 patients diagnosed with gastric cancer and 194 age- and gender-matched healthy controls. Genotyping of Ku70 promoter G-57C (rs2267437) and intron 3 (rs132774) polymorphisms was performed using real-time PCR at Dokuz Eylül University Hospital, Izmir.

RESULTS
No significant difference was observed in the distribution of genotype frequencies for either polymorphism between the gastric cancer patients and the control group. The Chi-Square test revealed no significant difference in the frequencies of the G-57C (rs2267437) polymorphism between the cancer group and the control group. The CC genotype was absent in the cancer group, while it was present in one in the control group. The GG genotype of intron 3 (rs132774) polymorphism was also absent in both groups. The Chi-Square test revealed no significant difference between the two groups.

CONCLUSION
The presence of the Ku70 promoter G-57C (rs2267437) and intron 3 (rs132774) polymorphisms does not appear to increase the risk of gastric cancer in the Turkish population.

KEY WORDS
Case-control study, DNA repair, gastric cancer, Ku70 gene, polymorphisms

ÖZ
Homolog olmayan uç birleştirme onarım yolunun önemli bir bileşeni olan DNA onarım geni Ku70, DNA çift sarmal kırıklarının (DSB'ler) onarımında önemli bir rol oynar. DSB onarımındaki eksiklikler kalıcı genomik instabiliteye neden olabilir. Ancak, Ku70'in polimorfik varyasyonları ile mide kanserine yatkınlık arasındaki ilişki hala belirsizliğini korumaktadır.

AMAÇ
Bu çalışma, Ku70 promotörü G-57C (rs2267437) ve intron 3 (rs132774) polimorfizmleri ile Türk popülasyonunda mide kanseri geliştirme riski arasındaki potansiyel korelasyonu araştırmayı amaçlamaktadır.

YÖNTEM
Mide kanseri tanısı konmuş 92 hasta ve yaş ve cinsiyete göre eşleştirilmiş 194 sağlıklı kontrol içeren hastane tabanlı bir vaka kontrol çalışması yürütülmüştür. Ku70 promoter G-57C (rs2267437) ve intron 3 (rs132774) polimorfizmlerinin genotiplendirilmesi, Dokuz Eylül Üniversitesi Hastanesi, İzmir'de gerçek zamanlı PCR kullanılarak gerçekleştirildi.

SONUÇ
Mide kanseri hastaları ve kontrol grubu arasında her iki polimorfizm için genotip frekanslarının dağılımında anlamlı bir fark gözlenmedi. Ku70 promoter G-57C (rs2267437) ve intron 3 (rs132774) polimorfizmlerinin varlığı, Türk popülasyonunda mide kanseri riskini artırmıyor gibi görünüyor.

ANAHTAR KELİMELER
Case-control study, DNA repair, gastric cancer, Ku70 geni, polymorphisms

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Gastric cancer, often known as GC, is the fourth most prevalent form of cancer globally, impacting around 900,000 individuals each year. The precise etiology is uncertain, however, Helicobacter pylori bacteria are implicated. Cancer genetics primarily concerns itself with the study of DNA repair mechanisms and the genes responsible for safeguarding the genome from both internal and external factors. The malfunctioning of these systems results in the development of cancer and aging, since mutations and deficiencies in DNA repair mechanisms contribute to the formation and progression of tumors. Recent research has shown a connection between genetic variants in the processes responsible for repairing DNA and the occurrence of stomach cancer (1, 2, 44).

Multiple environmental and genetic factors contribute to the development of stomach cancer, such as consuming excessive amounts of salt and smoked food, having low stomach acid levels (hypochlorhydria), being exposed to filthy environments, lacking sufficient vitamin C, being infected with Helicobacter pylori, having blood type A, experiencing atrophic gastritis, having gastric polyps, or undergoing stomach resection (3). The association between genetic and molecular alterations in GC cells and gastric cancer has been established since the 1990s. Chromosomes 3, 6, 8, trisomy, 11 (aberration in 11p13-p15), and marker chromosomes have both numerical and structural abnormalities in GC cells (6-13).

Disrupted DNA functioning may result in genetic and epigenetic alterations, ultimately leading to apoptosis and mortality. Cellular DNA repair mechanisms have the potential to restore the integrity of DNA. However, if DNA damage remains unrepaired throughout the process of replication, it may lead to mutations and instability in the genome. Genomic instability is a characteristic feature of both cancer and the aging process (14).

Conducting clinical research is necessary to determine the optimal treatment strategy based on genetic and epigenetic alterations. Analyzing the many combinations that might potentially indicate tumor development and the likelihood of developing cancer; will aid in prioritizing research on cancer drugs and enhancing our comprehension of the environmental elements involved in cancer prevention (13-15).

DNA repair genes have a role in signal transduction and the control of DNA repair, including mismatch repair, base excision repair, and nucleotide excision repair. Uninterrupted monitoring is essential to remove and substitute impaired nucleotides during replication in order to avoid mutations. Several DNA repair techniques including direct repair or reversal of damage, excision repair, repair by recombination, SOS repair, and DNA double-strand break repair (15, 16).

DNA double-strand breaks (DSBs) are very hazardous types of DNA damage that pose a significant risk to the integrity of the genome. They may lead to mutations, neoplastic transformation, or cell death. Cells use many strategies to deal with double-strand breaks (DSBs), such as activating checkpoints, repairing DNA, and modifying gene transcription. The DNA damage checkpoint encompasses sensor, transducer, and effector proteins that identify and react to DNA damage (2, 13-16).

The KU70 (XRCC6) (NM_001469.5) gene generates a heterodimer that binds to DNA ends that have been damaged and engages DNA-dependent protein kinase (DNA-PK) as the first sensor in non-homologous end joining (NHEJ) repair. The Non-Homologous End Joining (NHEJ) mechanism is less intricate but prone to errors, as it may connect DNA ends without the need for homologous sequences. On the other hand, Homologous Recombination (HR) is a more intricate and error-free process, as it utilizes homologous sequences to carry out DNA repair (2, 17-20).

Genetic variables that increase the likelihood of developing cancer include hereditary genetic mutations, differences in the activity of enzymes involved for processing cancer-causing substances, and changes in DNA repair pathways caused by genetic variances. Errors during DNA replication give rise to polymorphisms, which make up 0.1% of the genetic variety in humans. Among these polymorphisms, single nucleotide polymorphisms (SNPs) account for 90% of the overall genetic variance (21-36).

Gaining knowledge about the genetic foundation of gastric cancer and the processes involved in DNA repair, specifically the role of the Ku protein, is essential for the advancement of focused treatments and the enhancement of patient results. The presence of genetic variations and the effectiveness of DNA repair mechanisms have a substantial impact on the likelihood and advancement of cancer (37-38).

Materials and Methods

We used archival DNAs extracted from peripheral blood or normal tissue samples collected from 92 patients, who were diagnosed with stomach cancer between 2006 and 2008 at Dokuz Eylül University Hospital General Surgery Service. A control group consisting of 194 healthy persons, matched in terms of age and gender with the sick group, was established. The participants in the control group provided their assent using a voluntary consent form.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Extraction of DNA from Peripheral Blood

In our retrospective analysis, patient DNA samples were accessible from our laboratory's DNA repository and were collected using the salt precipitation technique (36).

Following the completion of our research design, blood samples were collected from participants who did not have a family history of cancer, were in good health, and were similar to the patient group in terms of gender and age. This was done by having them fill out a permission form and providing their signatures.

DNA was extracted from 4cc of peripheral blood collected from the control group using a DNA extraction kit. The Bioneer DNA extraction kit - AccuPrep®Genomic DNA Extraction Kit contains the following components: Proteinase K (25 mg, lyophilized), Binding buffer (25 ml), Washing buffer 1 (40 ml), Washing buffer 2 (20 ml), Elution buffer (30 ml), Binding tubes, Filtration tubes (2ml), Elution tubes (1.5 ml), and Supplementary Materials List. The DNA extraction process involves the use of pure ethanol, pure isopropanol, a table-top microcentrifuge, an incubator, a vortex mixer, Eppendorf tubes (1.5 ml), and PBS (Phosphate buffer saline).

Following the technique, an initial volume of 20 µl of Proteinase K was poured into a 1.5 ml Eppendorf tube. Subsequently, 200 µl of peripheral blood was added to the Eppendorf tube holding the Proteinase K. 200 µl of binding buffer, also known as binding solution, was introduced to the Eppendorf tube that contained proteinase K and blood. The solution in the Eppendorf tube was subjected to incubation in the incubator at a temperature of 60 degrees Celsius for a minimum duration of 10 minutes. A volume of 100 µl of isopropanol was added to the tube retrieved from the incubator and pipetted. The solution in the Eppendorf tube was transferred to 2 ml connecting tubes. The sample was subjected to centrifugation in a microcentrifuge equipment at a speed of 8000 revolutions per minute for a duration of 1 minute. The connecting tube was replaced with a new tube by removing the liquid that had gathered at the bottom. Next, 500 µl of washing solution was introduced and subjected to centrifugation at a speed of 8000 revolutions per minute for a duration of 1 minute. The liquid that collected at the bottom was removed. Then, 500 µl of washing solution number 2 was added and the mixture was centrifuged at a speed of 8000 rpm for a duration of 1 minute. A second round of centrifugation was performed at a speed of 12,000 revolutions per minute for a duration of 1 minute in order to fully eliminate the ethanol present in the tube. The coupling tube was moved to 1.5 ml Eppendorf tubes, and 200 µl of elution buffer was introduced. The sample was subjected to centrifugation in a microcentrifuge equipment at a speed of 8000 revolutions per minute for a duration of 1 minute. The DNA that was transferred to the Eppendorf tube is now prepared for either storage or further analysis. The DNAs collected were quantified using the Nano Drop DNA spectrophotometer. The DNAs that were recovered were diluted with distilled water to a concentration of 10 ng in a volume of 11.25 µl. Once the DNAs were acquired, they were preserved at a temperature of +4°C if they were intended for immediate examination, and at a temperature of -20°C if they were intended for future study.

Genotyping of target sequences by RealTime-PCR

The allelic discrimination approach was used using the ABI 7300 Real Time PCR apparatus from Applied Biosystems. The TaqMan Universal PCR Master Mix Without AmpErase UNG from Invitrogen was utilised, along with the 40 x SNP Genotyping Assay from Invitrogen. The reagents used included Ku70... promoter G-57C (rs2267437) and Ku70... intron3 (rs132774). In accordance with the procedure, the mixture was made at the prescribed rate shown in the table and thereafter dispersed to the wells. A volume of 5 µl of DNA was added to each sample. (Table 1).

(Archive EnsEMBL release 54 - May 2009 © WTSI / EBI))

Table 1. Study protocol

Added material	Quantity
TaqMan Univ. PCR Master Mix	12.50 µl
20 x SNP Genotyping Assay	1.25 µl
DNA	11.25 µl

Primer Sequences Used to Amplify Ku70 Promotor Regions

Context Sequence [VIC/FAM]; rs 132774:

F:5'TTTTTGTTAAAATTTGATATTTATG[C/G]CCATTACTT TCACTGATTCATTACC-3'

Context Sequence [VIC/FAM]; rs 2267437:

R:5'GCCCAAGTCTCCCCACCTCGGCCAG[C/G]CGCCACC CTCTGGCCTGGCTCCCGC-3'

Real Time PCR Conditions

(Table 2).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Table 2. PCR steps

PCR steps	Temperature (°C)	Duration	
Denaturation	96	10 min	
Annealing	92	15 sec	40 loops
Elongation	60	60 sec	

The PCR technique, which was invented in 1985 by Henry A. Erlich, Kary Mullis, and Randall K. Saiki while working at the Cetus corporation in the United States, relies on the amplification of nucleic acids under controlled laboratory circumstances. Kary Mullis received the 1993 Nobel Prize in Chemistry for his contributions to the creation of PCR, a technique that has significant implications in scientific research and clinical laboratory diagnostics. Polymerase Chain Reaction (PCR) is a method of replicating DNA in a laboratory setting.

Real Time PCR is a technique that involves the integration of the traditional PCR technology with gene analysis. Fluorescently labelled probes and dyes are used in this amplification technique to enable visualisation and monitoring of PCR amplification. The fluorescence intensity is directly proportional to the amount of DNA produced.

The Real Time PCR TaqMan technology employs a probe that is labelled with fluorochrome compounds at both the 5' and 3' ends. The probe has a reporter fluorochrome, 6-carboxyfluorescein (6-FAM), at its 5' end, and a quencher fluorochrome, 6-carboxy-tetramethyl-rhodamine (TAMRA), at its 3' end. The probe attaches to the area between the binding sites of the primers on the single-stranded target molecule. The ongoing hybridization between the probe and the target molecule hinders the generation of a signal by the reporter fluorochrome material due to the presence of the suppressor fluorochrome at the 3rd end. Once the primers bind to the target nucleic acid and the primer extension begins, the Taq DNA polymerase enzyme starts to degrade the probe from its 5' end utilising its 5'→3' nuclease activity. This allows the synthesis to proceed. Therefore, the reporter fluorochrome is liberated and generates a signal. The signal strength correlates directly with the quantity of amplicon generated in each cycle (39).

Real-time PCR may provide quantitative findings rapidly. Given that the diagnostic is conducted without the need to physically access the tubes, the likelihood of contamination is minimal. Multiplication may get results without using electrophoresis. Furthermore, the presence of alterations in the specific nucleic acid may be identified by the use of fluorescent probes (39).

Results

The DNA samples from both the patients and the control group were prepared and completed by using the real-time multiplex PCR technique. The assessment was conducted using the photos shown below. During the research, two variations in the genetic code were observed for each person, resulting in three distinct genotypes.

Due to allelic discrimination, individuals were categorised into three groups based on their CC/CG/GG genotypes (Figure 1).

The interpretation of the analytical findings for each example was based on the significant curves they produced. If a real-time polymerase chain reaction produces a single substantial green (VIC) curve, it is classified as the CC genotype, as shown in the example below (Figure 2).

The analysis results of the cases with heterozygous genotype were evaluated as FAM/VIC; that is, if two curves in dark blue and green colors were found together, it was evaluated as CG (Figure 3).

The study identified subjects withhomozygous GG genotype by seeing a single FAM-dark blue colour fluorescence and a single curve in the analysis (Figure 4).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

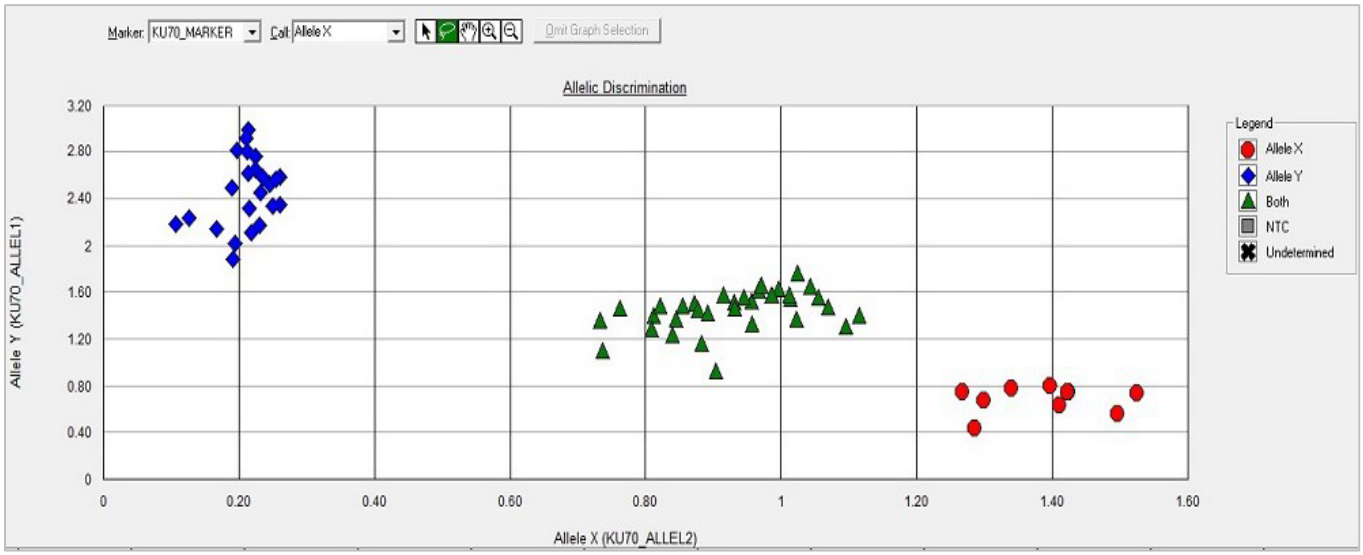


Figure 1. Results of allelic discrimination analysis

Figure 2. The melting RealTime PCR profiles showing CC Genotype (Arrow)

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Figure 3. An example of a result with a heterozygous genotype

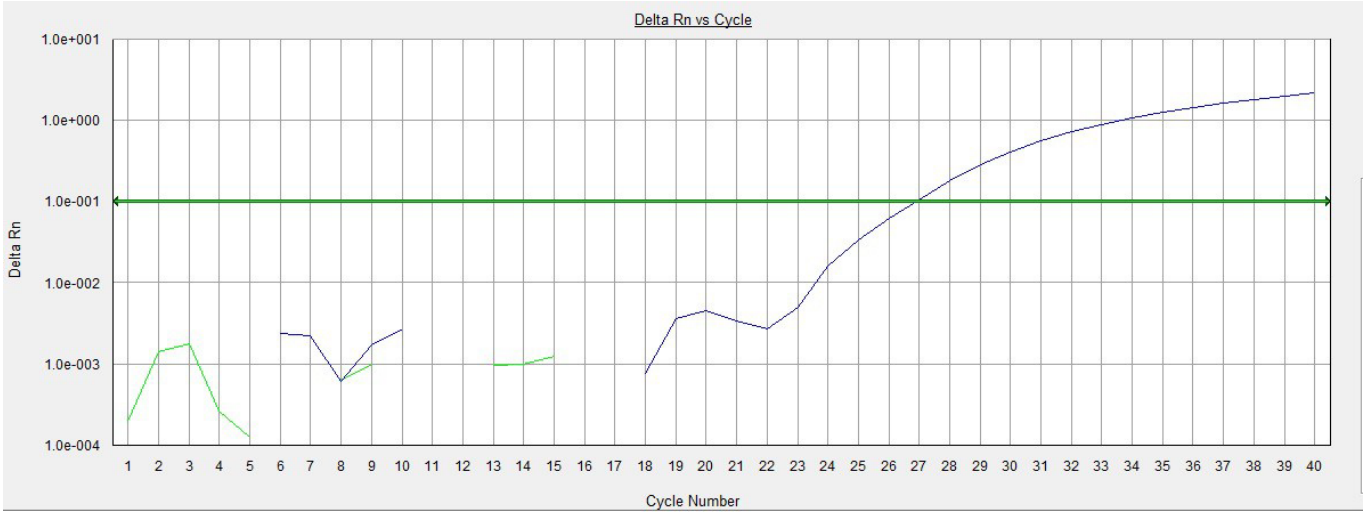


Figure 4. An example of a result in the GG genotype

The analytical findings of both the case and control groups were uploaded to the SPSS programme. The findings were assessed using the Chi-Square test. Each participant in the investigation was evaluated for three potential genotypes in relation to the intron 3 (rs132774) and G-57C (rs2267437) polymorphisms of the Ku70 gene. The demographic information of people was ascertained based on their age and gender. The data were compared and summarised using tables, which included numbers and percentages.

When comparing the cases and control groups, it was observed that the frequencies of the GG genotype of the G-57C (rs2267437) polymorphism were equal in both healthy individuals and cancer patients (Table 3).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Table 3. Chi-Square Test for rs2267437 GG polymorphism

rs2267437 polymorphism	Cases (%)	Controls (%)	Total (%)
GG ones	15 (28.3)	38 (71.7)	53 (100)
Non-GG (Non-GG means others that are not in the GG genotype.)	77 (33,0)	156 (67.0)	233 (100)
Total	92 (32.2)	194 (67.8)	286 (100)
Chi-Square p > 0.5			

When comparing the cases and control groups in relation to the rs2267437 polymorphism GC genotype, there was no significant difference found in terms of its frequency in both the control group and the cases (Table 4).

Table 4. Chi-Square Test for rs2267437 GC polymorphism

rs2267437 polymorphism	Cases (%)	Controls (%)	Total (%)
GC ones	77 (33.2)	155 (66.8)	232 (100)
Non-GC (Non-GC means others that are not in the GC genotype.)	15 (27.8)	39 (72.2)	54 (100)
Total	92 (32.2)	194 (67.8)	286 (100)
Chi-Square p > 0.5			

Upon comparing the patients and control groups in relation to the G-57C (rs2267437) polymorphism and CC genotype, it was noted that the CC genotype was completely absent in the cases. However, it was seen in just one individual in the control group (Table 5).

Table 5. Chi-Square Test for rs2267437 CC polymorphism

rs2267437 polymorphism	Cases (%)	Controls (%)	Total (%)
CC ones	0 (0.00)	1 (100)	1 (100)
Non-CC (Non-CC means others that are not in the CC genotype.)	92 (32.3)	193 (67.7)	285 (100)
Total	92 (32.2)	194 (67.8)	286 (100)
Chi-Square p > 0.5			

When comparing the patients and control groups in relation to the intron 3 (rs132774) polymorphism GG genotype, no statistically significant difference was seen between them (Table 6).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Table 6. Chi-Square Test for rs132774 GG polymorphism

rs132774 polymorphism	Cases (%)	Controls (%)	Total (%)
GG ones	47 (30.5)	107 (69.5)	154 (100)
Non-GG (Non-GG means others that are not in the GG genotype.)	45 (34.1)	87 (65.9)	132 (100)
Total	92 (32.2)	194 (67.8)	286 (100)
Chi-Square p > 0.5			

Upon comparing the cases and control groups, it was observed that the frequencies of rs132774 polymorphism GC genotype were comparable in both cancer patients and the control group (Table 7).

Table 7. Chi-Square Test for rs132774 GC polymorphism

rs132774 polymorphism	Cases (%)	Controls (%)	Total (%)
GC ones	37 (32.7)	76 (67.3)	113 (100.0)
Non-GC (Non-GC means others that are not in the GC genotype.)	55 (31.8)	118 (68.2)	173 (100.0)
Total	92 (32.2)	194 (67.8)	286 (100.0)
Chi-Square p > 0.5			

The CC genotype for the intron 3 (rs132774) polymorphism, which was the focus of our study, was uncommon in both the patients and control group. Furthermore, the Chi-Square test revealed that there was no significant difference between the two groups, as shown in (Table 8).

Table 8. Chi-Square Test for rs132774 CC polymorphism

rs132774 polymorphism	Cases (%)	Controls (%)	Total (%)
CC ones	8 (42.1)	11 (57.9)	19 (100.0)
Non-CC(Non-CC means others that are not in the CC genotype.)	84 (31.5)	183 (68.5)	267 (100.0)
Total	92 (32.2)	194 (67.8)	286 (100.0)
Chi-Square p > 0.5			

The research comprised a total of 92 patients with stomach cancer, including 63 men and 29 women. The control group, as shown in (Table 9), consisted of 134 men and 60 women.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

Table 9. Case and control groups and genders

Gender	Cases (%)	Controls (%)	Total (%)
Male	63 (68.5)	134 (69.1)	197 (100.0)
Female	29 (31.5)	60 (30.9)	89 (100.0)
Total	92 (32.2)	194 (67.8)	286 (100.0)

Upon splitting the cases and controls into two age groups, namely those over and under the age of 55, it was seen that the occurrence of stomach cancer was much greater in persons over the age of 55 (Table 10).

Table 10. Age-based case distribution

Over- and under-55s	Cases (%)	Controls (%)	Total (%)
55years<	18 (19.6)	66 (34.0)	84 (29.4)
55years>	74 (80.4)	128 (66.0)	202 (70.6)
Total	92 (100.0)	194 (100.0)	286 (100.0)
Chi-Square $p < 0.5$			

Upon comparing the incidence rates of the genotypes associated with the studied SNPs between the cases and control group, using the GG genotypes as the baseline, we observed no significant variation in terms of stomach cancer risk across the genotypes (Table 11).

Table 11. Polymorphisms and gastric cancer risk; Adjusted OR: Adjusted ratio

	Cases	Controls	Adjusted OR	p value
rs2267437 polymorphism				
GG genotype	15	38	1.00(ref)	0.782
GC genotype	77	155	1.291	0.483
CC genotype	0	1	0.000	1.000
rs132774 polymorphism				
GG genotype	47	107	1.00(ref)	0.523
GC genotype	37	76	1.086	0.774
CC genotype	8	11	1.808	0.255

This research aimed to determine the potential correlation between gastric cancer and polymorphisms of the Ku70 gene. The Real Time PCR method was used to determine the alleles and genotypes of Ku70 rs132774 and rs2267437 polymorphisms. DNA samples were obtained from peripheral blood and normal tissues of 92 patients diagnosed with Stomach Cancer at Dokuz Eylül University Hospital's Department of General Surgery.

The research had a cohort of 29 female and 63 male participants, with an average age of 60.2 years. The Ku70 genotypes were analysed for allele frequencies and statistically analysed using the Chi-Square Test in the SPSS programme. The results are shown in (Figure 5).

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

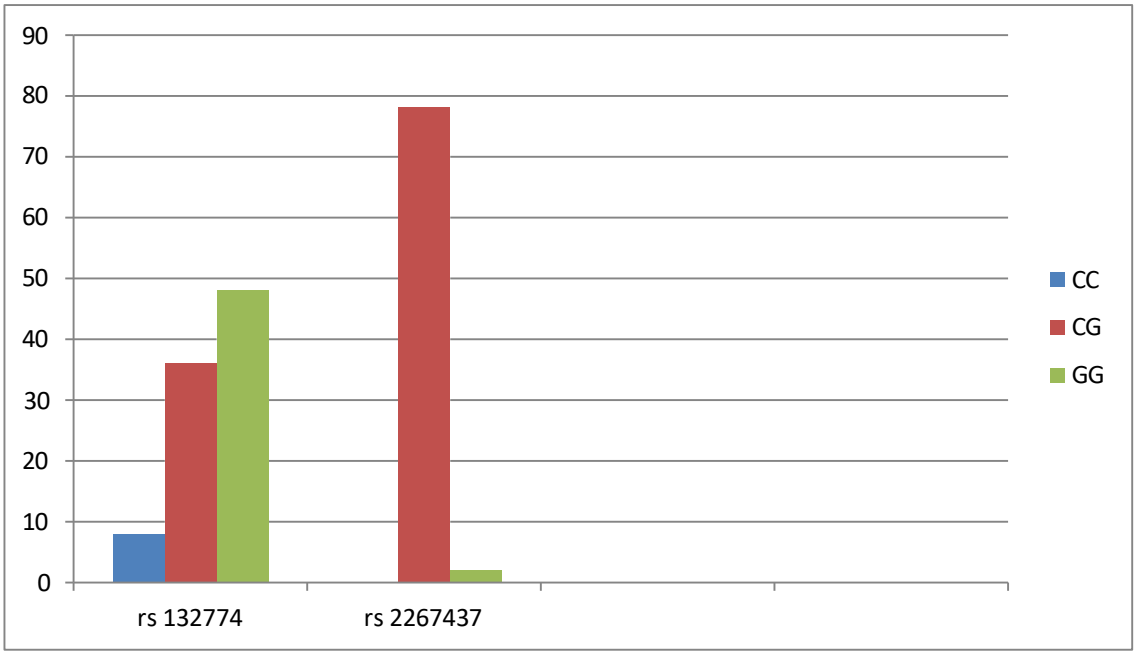


Figure 5. Genotype rates of cases

A control group consisting of 194 cancer-free people, matched with the patient group in terms of age and gender, was included in the research. The compatibility of the allele ratios in the control group with those in the sick group was assessed and documented in (Figure 6).

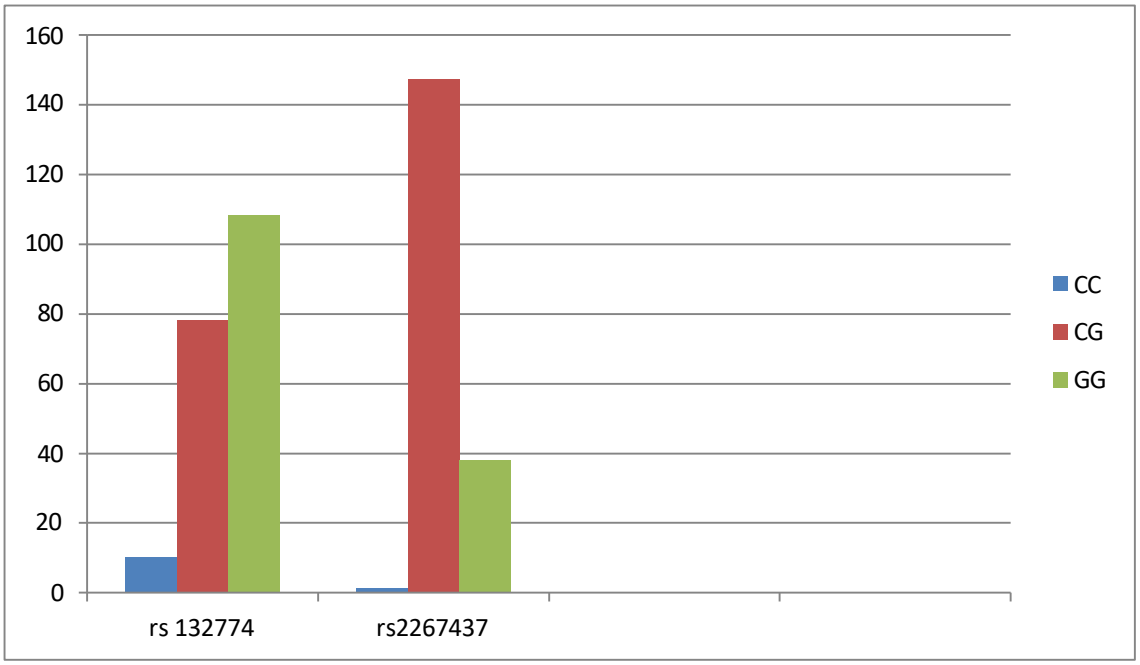


Figure 6. Polymorphism results of the control group

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICL
Sayfa:111-126

Discussion

Gastric cancer is a complex illness influenced by several variables, including both genetic and environmental influences. Despite a decline in the occurrence and fatality rates of stomach cancer over the last ten years, it remains the fourth most prevalent form of cancer and the second leading cause of death globally.

The prevalence of gastric cancer differs between males and females. According to the research, the occurrence of stomach tumours is twice as prevalent in males (1, 40). No reports have been made about the impact of gender differences on survival rates in stomach cancer. The Male/Female ratio reveals a notable surplus in favour of males, with a ratio of 1.87. The median age at which stomach cancer is often diagnosed is 56. The average age in our study group is similar when compared to the foreign sources. Although it is most commonly seen in the 70s in Western societies, the average age in our country is ten years younger. A research conducted by the Turkish oncology group in 2008 examined 840 patients and found that the average age at which stomach cancer was detected was 57 years, with the age range spanning from 19 to 85 years. This information was reported by 140 individuals. The research group included 92 patients, with an average age of 60.2 years (ranging from 33 to 89 years old). The disparity may be attributed to the limited patient population. DNA repair is a crucial concern in the field of cancer genetics. Polymorphisms in DNA repair genes result in alterations in the amino acid sequence and impair the ability to repair DNA, leading to the development of different types of malignancies. Multiple mechanisms exist for repairing DNA damage, including the involvement of various proteins (37, 38, 40).

Genetic variations in the DNA repair system may result in variations in the ability to repair DNA and can, to some extent, alter the susceptibility of cells to substances that damage DNA, leading to their transformation into cancer cells (38). According to previous reports, DNA repair systems are responsible for fixing DNA damage produced by substances that cause cancer and drugs used to treat cancer. Insufficient or defective DNA repair mechanisms increase the chance of developing different types of cancer. So far, several variations have been discovered in genes that play a role in DNA repair (2, 40). Despite several investigations, the precise correlation between polymorphisms of DNA repair genes and the risk of stomach cancer remains inconclusive (1-2). The Ku protein investigated in our work has a crucial function in the repair of DNA double-strand breaks in mammalian cells.

In a research conducted by Bau et al. in 2008, 380 patients who had been diagnosed with oral cancer between 1998 and 2007 were examined. They had also included an equal number of healthy controls who were matched to the patient group in terms of age and gender. The analysis revealed the presence of Ku70 T-991C, C-57G, and A-31G polymorphisms. They examined the correlation between oral cancer and these polymorphisms. Research has shown that those with the C allele (T/C and C/C) had a 2.14-fold increased risk of developing oral cancer compared to those with the T/T (wild) genotype. The study found that there was no significant difference in the link between the frequency of the C-57G and A-31G polymorphisms with the occurrence of oral cancer in both the patients and control groups (1-3).

He and his colleagues conducted a research to examine the correlation between the Ku70 -1310C/G polymorphism and breast cancer. The research conducted on 293 breast cancer patients and 301 control groups found that those with CG and GG allele frequencies had a significantly increased risk compared to those with the CC homozygous allele ($p = 0.038$).

In a study conducted by Willems et al. (2009), the researchers examined the connection between non-familial breast cancer and a specific genetic variation called C-1310G single nucleotide polymorphism. They focused on the Ku70 promoter region. The study group consisted of 206 patients and 171 control individuals. The results revealed a significant increase in the CG allele in the breast cancer patient group with elevated levels of endogenous oestrogen. The Ku70 gene polymorphisms indicated are potential subjects for further research to better understand the processes behind cancer formation (1-5, 41).

Yang et al. (2011) conducted a study in Taiwan to investigate four variations of the Ku70 gene in both gastric cancer patients and healthy control groups. The research comprised 136 individuals with stomach cancer and 560 individuals in the control group. Research has shown that those with TC and CC genotypes had a much higher susceptibility to stomach cancer in comparison to those with TT genotypes. The study indicated that the Ku70 promoter T-991C (rs5751129) polymorphism was significant in male patients over 55 years of age. It was proposed that this polymorphism might serve as a possible biomarker in gastric cancer patients.

We conducted a research to investigate the correlation between gastric cancer and variations in the Ku70 gene. Our nation has not yet completed a research on Ku70 polymorphisms for stomach cancer (2). Fu et al. (2003) discovered an association between breast cancer and the Ku70 promoter G-57C (rs2267437) polymorphism among the ones we examined. Due to its location in the promoter region of stomach tissue, the presence of Ku70 G-57C (rs2267437) is

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:111-126

believed to potentially result in varying levels of gene expression depending on the various genotypes.

The examined variants in the Ku70 G-57C (rs2267437) and Ku70 intron 3 (rs132774) polymorphisms have a significant impact on the expression levels of the Ku70 protein, DNA repair capability, whole genome stability, and eventually contribute to the development of cancer. Previous research has been conducted on the processes of carcinogenesis. For instance, in a research done by Hu et al. in 2010, they proposed that the expression levels of proteins such as Ku70, TRF, TERT, and BRCA may be linked to the shortening of telomere length and the development of cancer (42-43).

Over the last two decades, researchers have undertaken tests on mice and studies on patients to investigate the role of Ku70 and Ku80 proteins in the non-homologous end joining (NHEJ) process of DNA repair. The first investigations were mostly focused on connective tissue disorders, namely Systemic Lupus Erythematosus. Subsequently, genetic differences pertaining to these repair genes were examined in several forms of cancer, such as bilateral pterygium pathology, mouth malignancies, cutaneous cancers, and hepatic cancers. These cancer studies include the selection of large control groups to conduct the research (41-44).

The research we did in partnership with the Department of Medical Genetics and Department of General Surgery at Dokuz Eylül University Hospital included 92 individuals diagnosed with gastric cancer and 194 individuals who volunteered as controls. The findings were assessed using the Chi-Square test. No statistically significant difference was seen when comparing the analysed SNPs and samples from patients with gastric cancer and those from a healthy control group. When comparing the patients and control groups, it was observed that the frequencies of the GG genotype of the G-57C (rs2267437) polymorphism were equal in both categories. When comparing the cases and control groups in relation to the G-57C (rs2267437) polymorphism GC genotype, no statistically significant difference in incidence was found between the two groups. Upon comparing the patients and control groups in relation to the G-57C (rs2267437) polymorphism and CC genotype, it was seen that the CC genotype was completely absent in the cases. Conversely, it was discovered to be present in just one individual within the control group. while comparing the cases and control groups in relation to the GG genotype of intron 3 (rs132774) polymorphism, no significant difference was seen between them. Similarly, while comparing them in terms of the GC genotype, equal rates were reported in both groups. The CC genotype for the intron 3 (rs132774) polymorphism was seldom detected in both the cancer group and the control group in our study. Furthermore, the Chi-Square test revealed that there was no significant difference between the two groups. Our investigation did not find any significant correlation between gastric cancer and the Ku70 gene intron 3 (rs132774) and G-57C (rs2267437) polymorphisms. Nevertheless, it is unfeasible to form a definitive assessment. Genetic expression discrepancies vary between populations. In our research, we included a total of 92 patients with stomach cancer, of whom 63 were male and 29 were female. The control group, on the other hand, included 134 males and 60 females. Future research should aim to guarantee uniformity in age and gender between cases and controls, and to increase the number of cases included in the study. Upon categorising the cases and controls into two age groups, namely those above and below the age of 55, a notable disparity in the occurrence of stomach cancer was identified. Specifically, persons aged 55 and above exhibited a considerably greater incidence of stomach cancer. This information aligns with the existing body of evidence. It is unsurprising that the likelihood of developing cancer rises as one gets older.

Continuing our investigation with the same patient population and including other DNA repair gene variants that are expected to increase the susceptibility to cancer might be beneficial. An additional research endeavour might be identifying a genetic biomarker that indicates a predisposition to stomach cancer. This would enable the acquisition of meaningful personal data for patients with a family history of stomach cancer or those who are highly susceptible to environmental variables.

Conclusions

The subject of our investigation was gastric cancer, a complex illness with several contributing factors. In the field of aetiology, there are both unalterable elements, such as age and gender, and modifiable ones, such as food habits and environmental influences, that contribute to the development of a condition. Additionally, genetic predisposition also plays a role in this process. An essential aspect of studying stomach cancer patients is to analyse the genetic aspects, particularly the variations in the Ku70 genes that play a crucial role in DNA repair. This investigation is significant as it helps to uncover the causes and origins of cancer. A research done in Taiwan previously shown a correlation between stomach cancer patients and variations in the Ku70 gene. As far as we know, there has been no research conducted in Turkey on the relationship between stomach cancer patients and the Ku70 gene. While the current patient population is adequate for a study on individuals with stomach cancer, it is crucial to have a bigger sample size for future research, since the development

of cancer is influenced by several variables. When selecting the control group for our research, we made sure to include people who were in good health and had no personal or familial history of cancer. In order to enhance the value of future research, it is crucial to include a bigger control group. To enhance our research, which was done utilising archival records, we may augment the number of stomach cancer patients and include other SNPs into the analysis.

Acknowledgments

We would like to express our sincere gratitude to the staff of the Medical Genetics Department and the General Surgery Department at Dokuz Eylül University Hospital for their valuable assistance throughout the study. Special thanks to the patients and healthy volunteers who participated in the study for their contribution. We also appreciate the efforts of the laboratory personnel who performed the genotyping and supported the data collection.

Ethical Approval and Consent

This study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Dokuz Eylül University Ethics Committee (Project No: 2012254). All participants provided informed consent before their inclusion in the study. For patients diagnosed with gastric cancer, as well as healthy controls, written informed consent was obtained to collect and use their blood or tissue samples for genotyping. The confidentiality and anonymity of the participants were strictly maintained throughout the research process.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Funding

This research was supported by the Dokuz Eylül University Research Fund under Project No: 2012254.

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author, [Sezin Canbek], upon reasonable request. Due to ethical concerns and privacy policies, individual patient data cannot be made publicly available. Aggregated and anonymized data sets, however, may be provided to qualified researchers who meet the criteria for access to confidential data, in compliance with the approved ethical guidelines.

Author Contributions

Sezin Canbek conceived and designed the study, performed the,0 genetic analysis, and drafted the manuscript. Elçin Bora contributed to the study design, data interpretation, and critically revised the manuscript. Seymen Bora participated in patient recruitment and clinical data collection. Derya Erçal contributed to data analysis and manuscript preparation. All authors read and approved the final version of the manuscript.

References

1. Forman D, Plummer M. Gastric cancer: epidemiology and risk factors. Gastroenterology Clinics of North America. 2013 Jun;42(2):219-40.
2. Yang MD, Wang HC, Chang WS, Tsai CW, Bau DT. Genetic polymorphisms of DNA double strand break gene Ku70 and gastric cancer in Taiwan. BMC Cancer. 2011;11:174. PubMed PMID: 21575261.
3. Chiu CF, Wang CH, Wang CL, Lin CC, Hsu NY, Weng JR, et al. A novel single nucleotide polymorphism in XRCC4 gene is associated with gastric cancer susceptibility in Taiwan. Annals of Surgical Oncology. 2008 Feb;15(2):514-8.
4. Yamamoto S. Cancer statistics Digest. Trends of all cancer in Japan [News]. Japanese Journal of Clinical Oncology. 2001 Jun;31(6):294-6.
5. Kelley JR, Duggan JM. Gastric cancer epidemiology and risk factors. Journal of Clinical Epidemiology. 2003 Jan;56(1):1-9.
6. Torres J, Correa P, Ferreccio C, Hernandez-Suarez G, Herrero R, Cavazza-Porro M, et al. Gastric cancer incidence and mortality is associated with altitude in the mountainous regions of Pacific Latin America. Cancer Causes & Control. 2013 Feb;24(2):249-56.
7. Washington K. 7th edition of the AJCC cancer staging manual: stomach. Annals of Surgical Oncology. 2010 Dec;17(12):3077-9.
8. Guggenheim DE, Shah MA. Gastric cancer epidemiology and risk factors. Journal of Surgical Oncology. 2013 Mar;107(3):230-6.
9. Bonequi P, Meneses-Gonzalez F, Correa P, Rabkin CS, Camargo MC. Risk factors for gastric cancer in Latin America: a meta-analysis. Cancer Causes & Control. 2013 Feb;24(2):217-31.
10. Mizuno S, Miki I, Ishida T, Yoshida M, Onoyama M, Azuma T, et al. Prescreening of a high-risk group for gastric cancer by serologically determined Helicobacter pylori infection and atrophic gastritis.

Digestive Diseases and Sciences. 2010 Nov;55(11):3132-7.
11. Kang Y, Zhang J, Sun P, Shang J. Circulating cell-free human telomerase reverse transcriptase mRNA in plasma and its potential diagnostic and prognostic value for gastric cancer. International Journal of Clinical Oncology / Japan Society of Clinical Oncology. 2012 Apr 12.
12. Ito H, Inoue H, Sando N, Kimura S, Gohda K, Sato J, et al. Prognostic impact of detecting viable circulating tumour cells in gastric cancer patients using a telomerase-specific viral agent: a prospective study. BMC Cancer. 2012;12:346.
13. Zhang JF, Zhang JG, Kuai XL, Zhang H, Jiang W, Ding WF, et al. Reactivation of the homeotic tumor suppressor gene CDX2 by 5-aza-2'-deoxycytidine-induced demethylation inhibits cell proliferation and induces caspase-independent apoptosis in gastric cancer cells. Experimental and Therapeutic Medicine. 2013 Mar;5(3):735-41.
14. Corso G, Carvalho J, Marrelli D, Vindigni C, Carvalho B, Seruca R, et al. Somatic mutations and deletions of the e-cadherin gene predict poor survival of patients with gastric cancer. Journal of Clinical Oncology. 2013 Mar 1;31(7):868-75.
15. Furgason JM, Bahassi el M. Targeting DNA repair mechanisms in cancer. Pharmacology & Therapeutics. 2013 Mar;137(3):298-308.
16. Mondal P, Datta S, Maiti GP, Baral A, Jha GN, Panda CK, et al. Comprehensive SNP scan of DNA repair and DNA damage response genes reveal multiple susceptibility loci conferring risk to tobacco associated leukoplakia and oral cancer. PloS One. 2013;8(2):e56952.
17. Kutuzov MM, Khodyreva SN, Ame JC, Ilina ES, Sukhanova MV, Schreiber V, et al. Interaction of PARP-2 with DNA structures mimicking DNA repair intermediates and consequences on activity of base excision repair proteins. Biochimie. 2013 Jan 26.
18. Maria Berra C, Santos de Oliveira C, Carriao Machado Garcia C, Ribeiro Reily Rocha C, Koch Lerner L, Carmo de Andrade Lima L, et al. Nucleotide excision repair activity on DNA damage induced by photoactivated methylene blue. Free Radical Biology & Medicine. 2013 Apr 5.
19. Hardy PO, Chaconas G. The nucleotide excision repair system of B. burgdorferi is the sole pathway involved in repair of DNA damage by UV light. Journal of Bacteriology. 2013 Mar 8.
20. Budden T, Bowden NA. The Role of Altered Nucleotide Excision Repair and UVB-Induced DNA Damage in Melanomagenesis. International Journal of Molecular Sciences. 2013;14(1):1132-51.
21. McKinney JS, Sethi S, Tripp JD, Nguyen TN, Sanderson BA, Westmoreland JW, et al. A multistep genomic screen identifies new genes required for repair of DNA double-strand breaks in Saccharomyces cerevisiae. BMC Genomics. 2013 Apr 15;14(1):251.
22. Ghodke I, Muniyappa K. Processing of DNA double-strand breaks and intermediates of recombination and repair by Saccharomyces cerevisiae Mre11 and its stimulation by Rad50, Xrs2 and Sae2 proteins. The Journal of Biological Chemistry. 2013 Feb 26.
23. Dehennaut V, Loison I, Dubuissez M, Nassour J, Abbadie C, Leprince D. DNA Double-strand Breaks Lead to Activation of Hypermethylated in Cancer 1 (HIC1) by SUMOylation to Regulate DNA Repair. The Journal of Biological Chemistry. 2013 Apr 12;288(15):10254-64.
24. Taleei R, Nikjoo H. The Non-homologous End-Joining (NHEJ) Pathway for the Repair of DNA Double-Strand Breaks: I. A Mathematical Model. Radiation Research. 2013 Apr 5.
25. Fujita M, Sasanuma H, Yamamoto KN, Harada H, Kurosawa A, Adachi N, et al. Interference in DNA replication can cause mitotic chromosomal breakage unassociated with double-strand breaks. PloS One. 2013;8(4):e60043.
26. Prodosmo A, De Amicis A, Nistico C, Gabriele M, Di Rocco G, Monteonofrio L, et al. p53 centrosomal localization diagnoses ataxia-telangiectasia homozygotes and heterozygotes. The Journal of Clinical Investigation. 2013 Mar 1;123(3):1335-42.
27. Lawrence J, Karpuzoglu E, Vance A, Vandenplas M, Saba C, Turek M, et al. Changes in gamma-H2AX expression in irradiated feline sarcoma cells: An indicator of double strand DNA breaks. Research in Veterinary Science. 2013 Jun;94(3):545-8.
28. Kuefner MA, Brand M, Engert C, Kappey H, Uder M, Distel LV. The effect of calyculin A on the dephosphorylation of the histone gamma-H2AX after formation of X-ray-induced DNA double-strand breaks in human blood lymphocytes. International Journal of Radiation Biology. 2013 Feb 19.
29. Somyajit K, Basavaraju S, Scully R, Nagaraju G. ATM- and ATR-Mediated Phosphorylation of XRCC3 Regulates DNA Double-Strand Break-Induced

Checkpoint Activation and Repair. Molecular and Cellular Biology. 2013 May;33(9):1830-44.
30. Peter D Turnpenny BSc MB ChB FRCP FRCPCH SEB. Emery's Elements of Medical Genetics. 14th ed. 2011: 27-41
31. Fernandez-Capetillo AJL-CaO. Protein phosphorylation in human health. Biochemistry, Genetics and Molecular Biology. 2012 Sept 6; under CC BY 3.0 license.
32. Mazina OM, Rossi MJ, Deakyne JS, Huang F, Mazin AV. Polarity and bypass of DNA heterology during branch migration of Holliday junctions by human RAD54, BLM, and RECQ1 proteins. The Journal of Biological Chemistry. 2012 Apr 6;287(15):11820-32.
33. Wechsler T, Newman S, West SC. Aberrant chromosome morphology in human cells defective for Holliday junction resolution. Nature. 2011 Mar 31;471(7340):642-6.
34. Rosenberg M, Fan AX, Lin IJ, Liang SY, Bungert J. Cell-cycle specific association of transcription factors and RNA polymerase II with the human beta-globin gene locus. Journal of Cellular Biochemistry. 2013 Mar 20.
35. Deng B, Melnik S, Cook PR. Transcription factories, chromatin loops, and the dysregulation of gene expression in malignancy. Seminars in Cancer Biology. 2013 Apr;23(2):65-71.
36. Hong CP, Choe MK, Roh TY. Characterization of Chromatin Structure-associated Histone Modifications in Breast Cancer Cells. Genomics & Informatics. 2012 Sep;10(3):145-52.
37. Canbay E, Kahraman OT, Bugra D, Caykara B, Seyhan MF, Bulut T, et al. Increased Gastric Cancer Risk with PTEN IVS4 Polymorphism in a Turkish Population. Genetic Testing and Molecular Biomarkers. 2013 Mar;17(3):249-53.
38. Xue H, Ni P, Lin B, Xu H, Huang G. X-ray repair cross-complementing group 1 (XRCC1) genetic polymorphisms and gastric cancer risk: A HuGE review and meta-analysis. American Journal of Epidemiology. 2011 Feb 15;173(4):363-75.
39. Schikorski D, Renault T, Paillard C, Bidault-Toffin A, Tourbiez D, Saulnier D. Development of TaqMan real-time PCR assays for monitoring Vibrio harveyi infection and a plasmid harbored by virulent strains in European abalone Haliotis tuberculata aquaculture. Aquaculture. 2013 May 10;392:106-12.
40. Brenner H, Rothenbacher D, Arndt V. Epidemiology of stomach cancer. Methods in Molecular Biology. 2009;472:467-77.
41. Xu L, Ju XB, Li P, Wang J, Shi ZM, Zheng MJ, et al. Association between the Ku70-1310C/G promoter polymorphism and cancer risk: a meta-analysis. Asian Pacific Journal of Cancer Prevention: APJCP. 2012;13(2):683-7.
42. Fu YP, Yu JC, Cheng TC, Lou MA, Hsu GC, Wu CY, Chen ST, Wu HS, Wu PE, Shen CY: Breast cancer risk associated with genotypic polymorphism ofthe nonhomologous end-joining genes: a multigenic study on cancersusceptibility. Cancer Res 2003, 63:2440-2446.
43. Hu H, Zhang Y, Zou M, Yang S, Liang XQ: Expression of TRF1, TRF2, TIN2,TERT, KU70, and BRCA1 proteins is associated with telomere shorteningand may contribute to multistage carcinogenesis of gastric cancer. JCancer Res Clin Oncol 2010, 136:1407-1414.
44. Fan HN, Chen W, Peng SQ, Chen XY, Zhang R, Liang R, et al. Sanguinarine inhibits the tumorigenesis of gastric cancer by regulating the TOX/DNA-PKcs/KU70/80 pathway. Pathol Res Pract. 2019;215(11):152677.2022 Oct;10(4):253-258. doi: 10.30476/JAMP.2022.94852.1610. PMID: 36310666; PMCID: PMC9589073.

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

RESEARCH ARTICLE
Sayfa:127-135

Suicide news reporting in Türkiye: Compliance with World Health Organization guidelines

Türkiye'de intihar haberi raporlamasının Dünya Sağlık Örgütü kılavuzlarına uygunluğu

Buğra GÜLLE[1]
Büşra TOZDUMAN[2]

[1] Izmir Provincial Health Directorate, Türkiye
[2] Dokuz Eylul University Faculty of Medicine, Izmir, Türkiye

Suicide Reporting In Türkiye

Received: 08.12.2024
Accepted: 16.04.2025
doi:10.18614dehm.1699935

Corresponding author **Büşra TOZDUMAN**
ORCID ID: 0000-0003-0372-6280
busratoz@yandex.com

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

OBJECTIVE(S)
Purpose: Suicide is a significant public health problem worlwide and in Turkey, where more than 4,000 people die by suicide each year. Responsible media reporting is a critical component of suicide prevention, as outlined in the World Health Organization (WHO) guidelines. These guidelines discourage sensationalism, the inclusion of explicit details, and personal disclosures, while promoting the dissemination of help-seeking resources. This study evaluates the adherence of Turkish media to these guidelines through a content analysis of suicide-related news published between 2022 and 2024.

METHODS
The study employed a cross-sectional content analysis, using Google News to collect 467 eligible reports from an initial pool of 600 articles. A coding framework based on WHO recommendations assessed adherence to criteria such as sensational language, explicit method details, and the inclusion of supportive resources. Two independent coders reviewed the reports to ensure objectivity and reliability.

RESULTS
The results show widespread non-compliance with WHO guidelines. Sensationalist language was tcommon in headlines, and 57.6% of the reports analyzed were murder-suicide cases. The method of suicide was mentioned in 87.3% of the reports, and all reports provided detailed information about the location. Personal information, such as names (67.6%) and ages (55.8%), was often given. Notably, only one report included information on how to get help, and none included expert opinions or references to scientific research

DISCUSSION
These findings underscore the urgent need for reform in Turkish media practices. Recommendations include integrating ethical reporting training into journalism curricula, adopting internal guidelines, and reinstating a national suicide hotline to support vulnerable populations and mitigate public health risks associated with sensational reporting.

KEYWORDS
media, reporting, suicide, Türkiye, WHO guideline

AMAÇ
İntihar, hem dünya genelinde hem de Türkiye'de önemli bir halk sağlığı sorunudur. Türkiye'de her yıl 4.000'den fazla kişi intihar nedeniyle yaşamını yitirmektedir. Dünya Sağlık Örgütü (DSÖ) rehberlerinde vurgulanan sorumlu medya haberciliği, intiharı önleme çalışmalarının kritik bir bileşenidir. Bu rehberler, sansasyonel içerikten, ayrıntılı yöntem açıklamalarından ve kişisel bilgilerin ifşasından kaçınılmasını, bunun yerine yardım arama kaynaklarının yaygınlaştırılmasını önermektedir. Bu çalışma, 2022-2024 yılları arasında yayımlanan intihar içerikli haberlerin içerik analizi yoluyla Türk medyasının bu rehberlere uyumunu değerlendirmektedir.

YÖNTEM
Çalışma, kesitsel bir içerik analizidir. Google Haberler aracılığıyla 600 haberden oluşan bir havuzdan 467 uygun rapor toplanmıştır. DSÖ tavsiyelerine dayalı bir kodlama çerçevesi kullanılarak sansasyonel dil, yöntem ayrıntıları ve destekleyici kaynakların dahil edilmesi gibi kriterlere uyum değerlendirilmiştir. Raporların objektifliğini ve güvenilirliğini sağlamak için iki bağımsız kodlayıcı tarafından incelenmiştir.

BULGULAR
Bulgular, DSÖ rehberlerine uyumda yaygın bir eksiklik olduğunu ortaya koymaktadır. Başlıklarda sansasyonel dil yaygındır ve analiz edilen raporların %57,6'sı cinayet-intihar vakalarını içermektedir. Haberlerin %87,3'ünde intihar yöntemi belirtilmiş ve tüm raporlarda olay yerinin ayrıntılı bilgileri verilmiştir. Kişisel bilgiler, örneğin isimler (%67,6) ve yaşlar (%55,8), sıklıkla ifşa edilmiştir. Dikkate değer bir şekilde, yalnızca bir raporda yardım arama bilgileri verilmiş ve hiçbir haberde uzman görüşü veya bilimsel araştırma referansı yer almamıştır.

SONUÇ
Bu sonuçlar, Türk medyasındaki uygulamalarda acil reform gerekliliğini vurgulamaktadır. Öneriler arasında etik habercilik eğitimlerinin gazetecilik müfredatına dahil edilmesi, kurum içi yönergelerin benimsenmesi ve sansasyonel habercilikle ilişkili halk sağlığı risklerini azaltmak için ulusal bir intihar yardım hattının yeniden oluşturulması yer almaktadır.

ANAHTAR KELİMELER
Dünya Sağlık Örgütü kılavuzu, haber, intihar, medya, Türkiye

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

Suicide is a significant global public health problem, with more than 700,000 people dying by suicide each year [1]. Suicide is the fourth leading cause of death among people aged 15–29 years worldwide, underscoring its profound impact on younger populations (1). In Türkiye alone, more than 4,000 people die by suicide each year, further highlighting the scale of the problem at a national level (2). In addition to the individual loss, each suicide has far-reaching social, emotional, and economic consequences, affecting families, communities, and health systems (1).

The World Health Organization (WHO) emphasizes that suicide is preventable through coordinated efforts that include early mental health intervention, reducing access to means of suicide, and promoting responsible media reporting to minimize the risks of imitation and stigma. Holistic approaches to suicide prevention require a combination of public health strategies, community support, and awareness initiatives (1).

There is considerable evidence of both the harmful and beneficial effects of the media on suicide prevention. Irresponsible reporting of suicides, whether celebrity or non-celebrity, has the potential to contribute to an increase in suicide rates. This phenomenon is known as the "Werther effect" (3). Sensationalized coverage of suicide, particularly when it includes explicit details of the method used, increases the risk of imitation, especially among vulnerable groups (4- 5). This risk is further increased by repeated and prominent reporting, which can contribute to a contagion effect within communities (6).

Conversely, studies of the "Papageno effect" demonstrate that stories emphasizing hope and resilience can reduce suicide rates (7). In Austria, the implementation of media guidelines led to a 75% reduction in subway suicides and a 20% reduction in the overall suicide rate [8]. Campaigns featuring stories of recovery have also been associated with increased help-seeking behavior (9), while positive discussions in digital media offer additional protective effects (10).

Various national guidelines on responsible suicide reporting exist, such as the Mindframe guidelines (Australia), the Samaritans media guidance (UK), and the Reporting on Suicide recommendations (USA). Although valuable, these are often tailored to specific national contexts (11–13). The WHO guidelines on responsible suicide reporting are among the most frequently cited resources in this area (14). The guidelines, last updated in 2023, provide comprehensive recommendations for media professionals on how to report on suicide in a way that minimizes the risk of imitation and promotes public awareness of suicide prevention. The WHO resource places particular emphasis on key practices, including the avoiding of sensationalism, the avoiding specific details regardingof methods and locations, and the includingsion of information on how individuals can access mental health support or psychiatric services. This resource, developed in collaboration with the International Association for Suicide Prevention, addresses the complex and nuanced impact of media coverage on public perceptions of suicide and provides detailed guidance for both traditional and new media platforms (14). This study aims to determine the opinions of training facilitators and students regarding the application of the Critical Appraisal Special Study Module (CA-SSM). This module is implemented as a structured programme at Dokuz Eylül University Faculty of Medicine (DEUFM) and conducted as a small group study.

Several studies conducted in different countries have assessed the extent to which suicide news coverage is consistent with WHO media guidelines (15–30). These studies examine the extent to which media coverage is consistent with WHO recommendations for responsible reporting. Although research has previously examined the compliance of suicide reporting with the media guidelines in Turkey, there is currently no comprehensive and up-to-date evaluation based on the latest WHO guidelines (31–34).

This study aims to evaluate the extent to which suicide-related news in the Turkish media adheres to WHO's guidelines for responsible reporting. By identifying areas of compliance and gaps, this research seeks to support more responsible media practices in Turkey and ultimately contribute to suicide prevention efforts.

Materials and Methods

Study design

This study is a cross-sectional content analysis designed to assess the extent to which Turkish media follow the WHO guidelines for reporting on suicide. Content analysis was chosen as the optimal method for a systematic review and categorization of the media's approach to suicide-related news, facilitating a comprehensive evaluation of their alignment with the WHO's recommendations (11).

Data collection

Data for this study was collected through Google News searches, as it is one of the most widely used search engines, allowing for comprehensive access to relevant news sources. The keywords used for searches included "took their own life" and "died by suicide" in Turkish. The data collection

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

was carried out in October and November 2024 and focused on news articles published within the last three years.

To ensure the relevance and focus of the analysis, certain types of articles were excluded. These included videos, articles not related to Turkey, cases involving euthanasia, suicides related to terrorist attacks, and editorial content such as opinion columns and analytical pieces that did not present a specific incident in a news reporting format. The aim was to focus on news reporting directly related to suicide cases specific to the Turkish context.

Checklist and coding criteria

The coding framework developed for this study was based on WHO guidelines for responsible reporting of suicide. The aim was to reduce the risk of imitation and promote suicide prevention. Key recommendations included avoiding sensationalism, omitting explicit details of the method or location, and including information about sources of help.

Based on these guidelines, a checklist was developed to assess the degree of compliance with the to WHO recommendations. The checklist included criteria such as the presence of help-seeking information, expert opinions, scientific events, and specific elements such as the use of sensational language, method details, and location. In addition, the framework allowed for the coding of identifiable information (e.g., name, age) and visual elements (e.g., personal photographs or scene images). This approach facilitated a structured assessment of compliance with WHO standards.

Data analysis

To ensure objectivity and reliability, the coding process was carried out by two independent coders. Any discrepancies between the two coders were reviewed and discussed until a consensus was reached. Data analysis was primarily descriptive, using Excel to summarize the level of adherence to WHO guidelines across the coded items.

Ethical considerations

This study is based solely on publicly available news articles, and no personal data were collected from individuals. Given the public nature of the data sources, no formal ethical approval was sought for this research. Furthermore, the content of this study was carefully curated to exclude any personal or potentially identifiable information about individuals involved in suicide cases. All analyses and discussions in this article are conducted in a manner that respects the privacy and dignity of individuals, adhering to the ethical standards set for the reporting on sensitive topics such as suicide.

Results

The study initially identified 600 reports, which were then screened to determine eligibility for inclusion. After initial screening, 115 reports were excluded because they did not meet the pre-established inclusion criteria. These included reports that were not related to suicide, duplicates, or articles that lacked substantial textual content. As a result, 485 reports were analyzed in detail. Furthermore, 18 reports were then excluded from further analysis. Six of these were duplicates, ten contained only videos, and two described accidental shootings. In total, 467 reports were included in the final analysis, as detailed in Table 1.

Table 1. Key characteristics of suicide reports in the Turkish media

Key Characteristics of Suicidal Reports	**N (Total=467)**	**%**
Suicidal behaviour		
Completed Suicide	427	91.4
Attempt	40	8.6
Murder related with suicide	269	57.6
Celebrity suicide	22	4.7
Identity of the person		
Name stated	316	67.6
Initials stated	139	29.7
Age stated	261	55.8
Gender stated	435	93.1
Occupation mentioned	188	40.2

The reports covered three years. The dataset includes 424 reports from 2024, 41 from 2023, and two from 2022. Figure 1 illustrates the distribution of reports published in 2024.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

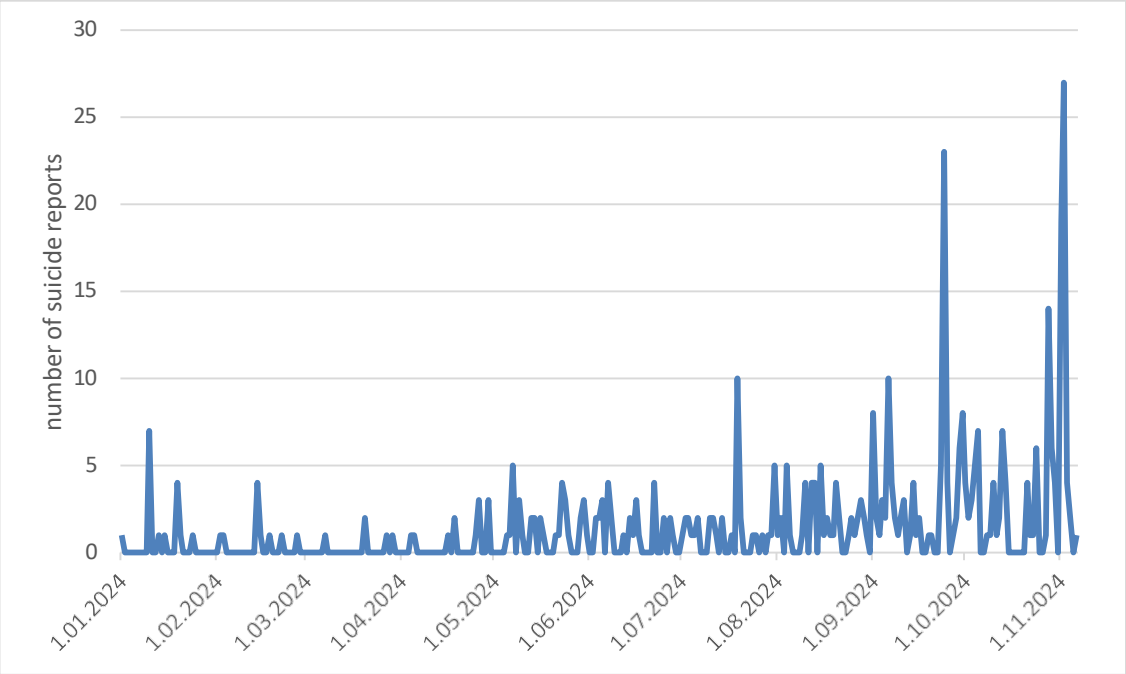


Figure 1. Number of suicide reports by time

Characteristics of reported suicides

The vast majority of reports (91.4%) described completed suicides, of which 57.6% were suicide-related homicides. A total of 4.7% of the reports were of celebrity suicides. The disclosure of personal details about the people involved was a common occurrence. Full names were given in 67.6% of the reports, while initials were used in 29.7% of the reports, initials were used. Age was given in 55.8% of the reports, gender in 93.1%, and occupation in 40.2%. Table 1 illustrates the disclosure of various personal details in the reports.

One report provided information on the availability of mental health support by directing the reader to a website of a medical association offering psychological counseling services. Only two reports included educational content. The perspectives of family members were mentioned in 21 reports, but none of these included the perspective of children. In addition, no reports included expert opinions, references to scientific research, or suggestions for coping mechanisms related to suicide prevention (Table 2).

Visual and content analysis

Each report included at least one photograph, with half of which were of the person who died by suicide or the scene of the suicide. The method of suicide was mentioned in 87.3% of the reports, and all reports provided detailed information about the location. Suicide notes were mentioned in 14.3% of the reports, of which 11.1% contained direct quotations from the notes. In addition, 15.4% of the reports gave an oversimplified account of the reasons for suicides. Of the reports, 15.6% (n=73) did not mention any life event as a reason for the suicide. In addition, 31 (6.6%) reports described suicides that occurred in institutions such as prisons, courts, dormitories, or schools (Table 2) exam contributes 5% to the student's overall grade at the end of the year.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

Table 2. Quality assessment of adherence to WHO guidelines

Quality Assessment Indicators	n	%
Information about where and how to seek help for suicidal thoughts	1	0.2
Education with the facts about suicide and suicide prevention	2	0.4
Stories of how to cope with life stressors	0	0
Expert opinion	0	0
Research findings	0	0
Perspectives of the bereaved family	21	4.4
Followed a cautionary approach when reporting celebrity suicides	0	0
No life event was specified as a reason for the suicide	73	15.6
Photo		
Any photo	467	100
Photo of the victim	237	50.7
Photo of the scene	246	52.6
Description of method	408	87.3
Details about the site/location	467	100
Information on the institutional setting of suicide	31	6.6
Suicide note		
Present	67	14.3
Citation from note	52	11.1
Oversimplifying the reason for suicide	72	15.4
Headline		
Suicide in the headline	308	65.9
Reason for suicide in the headline	33	7.0
Suicide note	32	6.8
Method in headline or sub-headline	323	69.1

Headline analysis

The term "suicide" was present in 65.9% of headlines, and 6.8% of headlines referred to either suicide notes or reasons, with phrases such as "committed suicide due to depression" or "Doctor divorced from spouse committed suicide with a farewell message." The use of sensational language was widespread, with examples such as "Horror in the hospital garden! Spouse killed and committed suicide" or "The suicide that shook Izmir...". The method of suicide was mentioned in 69.1% of headlines or sub-headlines, such as "Horrific event! Suicide with a gun on the balcony" (Table 2).

Discussion

The results of this study illustrate a widespread failure by the Turkish media to follow guidelines for reporting on suicide. Of the 467 reports analyzed, only one included information about help-seeking resources, a critical element in suicide prevention. In contrast, prohibited practices were widespread: sensational language was often used in headlines, explicit details about suicide methods were included in 87.3% of reports, and all reports described the site or location of the

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

incident. In addition, personal details, including full names (67.6%) and ages (55.8%), were often published.

These patterns of non-compliance are consistent with findings from countries such as Pakistan, Ghana, Bangladesh, Nigeria, and Indonesia, where similar lapses in responsible reporting practices have been observed (13,17,18,20,24). However, the level of non-compliance observed in the Turkish media appears to be more severe compared to countries such as Australia and Ireland, where media practices reflect a more ethical approach to suicide reporting (19-30). This study also corroborates previous research in Türkiye that found high levels of guideline violations in suicide-related news articles (26,27,31).

The phenomenon of "suicide contagion," whereby exposure to sensational or explicit reporting increases the likelihood of similar behaviors, is well-documented in the literature (35-36). This risk is particularly pronounced among vulnerable populations, including adolescents, those with mental health problems, and those facing socio-economic challenges (37). Furthermore, the oversimplification of suicide motives in 15.4% of reports not only trivializes the complex factors behind suicides but also risks fostering harmful narratives that could influence vulnerable individuals. (38). Such sensationalist headlines risk normalizing suicide and trivializing its complex causes, particularly among vulnerable populations (38). Based on the patterns observed, there appears to be a need for improved media practices in Türkiye, particularly in the reporting of suicide cases, to help minimize the associated public health risks.

Adherence to suicide reporting guidelines could make a significant contribution to public health efforts. Responsible reporting, which avoids sensationalism and includes information on how to seek help, could discourage suicide as a perceived solution and encourage those in distress to seek help. For example, the consistent inclusion of a national suicide prevention hotline in news articles could provide a vital resource for those at risk (32). However, such a hotline has not existed in Türkiye since 2008, representing a critical gap in the suicide prevention infrastructure. Targeted interventions are needed to address these issues. Media organizations should establish internal policies in line with international guidelines, and a regulatory body should monitor media compliance to ensure accountability. In addition, the reintroduction of a national suicide hotline, promoted alongside suicide-related news coverage, could serve as a vital safety net for those at risk.

Compared to previous studies conducted in Türkiye (31–34, 39), which often focused on limited time frames or specific types of media outlets, this study provides a more comprehensive and up-to-date analysis by systematically applying the 2023 version of the WHO guidelines. In addition, the larger sample size and broader range of news sources analyzed allow for more generalizable conclusions. By incorporating the most recent international standards, the study adds new insights to the national literature and addresses previously unmet needs for assessing media compliance in Türkiye.

Further research at the national level is necessary to explore how media coverage influences suicidal behavior in Türkiye. Understanding the impact of specific reporting practices could inform both media reforms and public health interventions aimed at reducing preventable suicide-related deaths.

This study was limited to articles available on Google News and focused on text-based reporting over three years. Future research should explore broader media formats and assess the direct public health impact of reporting practices.

Conclusion

This study highlights a notable lack of adherence to suicide reporting guidelines in the Turkish media. The pervasive use of sensational language, explicit details of suicide methods, and the lack of information about help-seeking resources highlight the need for improved media practices. While the precise impact of such reporting on suicide rates in Türkiye remains unclear, evidence suggests that responsible reporting could play a pivotal role in suicide prevention, particularly among vulnerable groups.

Targeted interventions are needed to address these issues, including media training, the development of internal guidelines, and the reintroduction of a national suicide hotline. By adopting responsible reporting practices, the Turkish media can contribute to public health efforts aimed at reducing suicide rates and promoting a more informed and supportive approach to mental health.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

References

1. World Health Organization. Suicide prevention. 2024(https://www.who.int/health-topics/suicide#tab=tab_1). Accessed 18 November 2024.
2. Türkiye İstatistik Kurumu. İntihar sayısı ve kaba intihar hızı, 1975-2023. 2024.
3. Phillips DP. The Influence of Suggestion on Suicide: Substantive and Theoretical Implications of the Werther Effect. American Sociological Review 1974; 39: 340.
4. Stack S. A reanalysis of the impact of non celebrity suicides: A research note. Social Psychiatry and Psychiatric Epidemiology 1990; 25: 269–273.
5. Pirkis JE, et al. The relationship between media reporting of suicide and actual suicide in Australia. Social Science & Medicine 2006; 62: 2874–2886.
6. Gould MS, et al. Newspaper coverage of suicide and initiation of suicide clusters in teenagers in the USA, 1988–96: a retrospective, population-based, case-control study. The Lancet Psychiatry 2014; 1: 34–43.
7. Niederkrotenthaler T, et al. Role of media reports in completed and prevented suicide: Werther v. Papageno effects. British Journal of Psychiatry 2010; 197: 234–243.
8. Sonneck G, Etzersdorfer E, Nagel-Kuess S. Imitative suicide on the Viennese subway. Social Science & Medicine 1994; 38: 453–457.
9. King KE, et al. Can a documentary increase help-seeking intentions in men? A randomised controlled trial. Journal of Epidemiology and Community Health 2018; 72: 92–98.
10. Sinyor M, et al. The association between Twitter content and suicide. Australian & New Zealand Journal of Psychiatry 2021; 55: 268–276.
11. World Health Organization. Preventing Suicide: a Resource for Media Professionals, 2023 Update. 1st ed. Geneva: World Health Organization, 2023.
12. Arafat SMY, et al. Quality of media reporting of suicide in Iraq. International Journal of Social Psychiatry 2022; 68: 443–448.
13. Arafat SMY, Mali B, Akter H. Quality of online news reporting of suicidal behavior in Bangladesh against World Health Organization guidelines. Asian Journal of Psychiatry 2019; 40: 126–129.
14. Arafat SMY, et al. Quality of media reporting of suicidal behaviors in South-East Asia. Neurology, Psychiatry and Brain Research 2020; 37: 21–26.
15. Menon V, et al. Do Tamil newspapers educate the public about suicide? Content analysis from a high suicide Union Territory in India. International Journal of Social Psychiatry 2020; 66: 785–791.
16. Menon V, et al. Quality of media reporting following a celebrity suicide in India. Journal of Public Health 2022; 44: e133–e140.
17. Oyetunji TP, et al. News reporting of suicidal behaviour in Nigeria: Adherence assessment to World Health Organization guidelines. International Journal of Social Psychiatry 2021; 67: 448–452.
18. Quarshie EN-B, et al. Online media reporting of suicidal behaviour in Ghana: Analysis of adherence to the WHO guidelines. International Journal of Social Psychiatry 2021; 67: 251–259.
19. McTernan N, et al. Media reporting of suicide and adherence to media guidelines. International Journal of Social Psychiatry 2018; 64: 536–544.
20. Nisa N, et al. Indonesian online newspaper reporting of suicidal behavior: Compliance with World Health Organization media guidelines. International Journal of Social Psychiatry 2020; 66: 259–262.
21. Chandra PS, et al. Do newspaper reports of suicides comply with standard suicide reporting guidelines? A study from Bangalore, India. International Journal of Social Psychiatry 2014; 60: 687–694.
22. Chu X, et al. Assessing the Use of Media Reporting Recommendations by the World Health Organization in Suicide News Published in the Most Influential Media Sources in China, 2003–2015. International Journal of Environmental Research and Public Health 2018; 15: 451.
23. Armstrong G, et al. Assessing the quality of media reporting of suicide news in India against World Health Organization guidelines: A content analysis study of nine major newspapers in Tamil Nadu. Australian & New Zealand Journal of Psychiatry 2018; 52: 856–863.
24. Ayub M, et al. Assessing the quality of media reporting of suicide deaths in Pakistan against international guidelines. International Journal of Social Psychiatry 2023; 69: 406–411.
25. Wu C-Y, et al. Adherence to World Health Organization guideline on suicide reporting by media in Taiwan: A surveillance study from 2010 to 2018. Journal of the Formosan Medical Association 2021; 120: 609–620.
26. İlhan RS. İntiharla ilgili internet haberlerinin Türkiye' de sunum şekli ile ilgili bir ön çalışma. 2018; 26Published online: 2018.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:127-135

27. İlhan RS, AğtaşErtan E, Kızılpınar SÇ. İntihar Haberlerinin Türkiye'deki Sunum Şekli: İnternetteki İntihar Haberleri Üzerine Bir İçerik Analizi. 2019; 27: 4–11.
28. Baysan Arabaci L, et al. Examination Of Suicide News Presentation On Print Media Between 2018-2019. Fenerbahçe Üniversitesi Sağlık Bilimleri Dergisi 2022; 2: 601–612.
29. Köseoğlu A. İntihar Haberlerinin Sunumu: Posta.com.tr Üzerine Bir İnceleme. Bitlis Eren Üniversitesi Sosyal Bilimler Dergisi 2023; 12: 64–82.
30. Blood RW, Pirkis J, Holland K. Media Reporting of Suicide Methods: An Australian Perspective. Crisis 2007; 28: 64–69.
31. Aydogdu HI, Balci Y. Physician Suicides Reported By Media In The Last Decade In Turkey. Archives of Neuropsychiatry 2021; Published online: 2021.doi:10.29399/npa.27792.
32. World Health Organization. Preventing suicide: a resource for establishing a crisis line. Geneva: World Health Organization, 2018.

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

RESEARCH ARTICLE

Sayfa:137-144

The impact of COVID-19 ischemic stroke in the emergency department

Acil serviste COVID-19'un iskemik inme üzerindeki etkisi

Ertug ORHAN[1]
Sedat YANTURALI[2]
Rıdvan ATİLLA[2]
Eren BAL[2]
Berat ŞEN[2]

[1] Department of Emergency Medicine, Kocaeli State Hospital, Kocaeli, Türkiye
[2] Dokuz Eylul University Faculty of Medicine, Department of Emergency Medicine, Izmir, Türkiye

The Impact of Pandemic on Ischemic Stroke
Received: 28.02.2025
Accepted: 22.04.2025

doi:10.18614/dehm.1699943

Corresponding author
Ertug ORHAN
ORCID ID: 0000-0001-8982-0096
ertugorhan@gmail.com

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

RESEARCH ARTICLE

Sayfa:137-144

OBJEKTIVE(S)
The aim of this study is to investigate the number and characteristics of ischemic stroke patients admitted to the emergency department before and during the COVID-19 pandemic, to determine the impact of the pandemic on a disease with high mortality and morbidity, and to support the development of preventif strategies.

METHODS
This single-center, retrospective cohort study, included patients diagnosed with ischemic stroke and transient ischemic attack who presented to the emergency department between March 2018 and March 2022. We classified patients into two groups, pre-pandemic and pandemic, each covering a two-year periods. We compared the numbers, admission characteristics and outcomes of the patients.

RESULTS
A total of 1,632 patients were included in the study, including 915 patients in the pre-pandemic period and 717 patients in the pandemic period. During the pandemic period, there was a 21.6% decrease in the number of stroke cases (n:915 vs. n:717). The median National Institutes of Health Stroke Scale at admission was similar (4 vs. 4, p = 0.071). The rate of thrombectomy was higher in the pandemic group (p <0.001). The rate of hospitalization was lower in the pandemic group (p <0.001), but there was no difference in 28-day mortality (p = 0.100).

DISCUSSION
During the COVID-19 pandemic, we observed a decline in the number of strokes, as a result of people in seeking medical care. The implementation of health policies and educational campaigns is essential to ensure timely access to health care and minimize morbidity and mortality in future pandemic.

KEYWORDS
COVID-19, Emergency Department, ischemic stroke, thrombectomy

AMAÇ
Bu çalışmanın amacı, pandeminin yüksek mortalite ve morbiditeye sahip hastalıklar üzerindeki etkisini belirlemek ve önleyici stratejilerin geliştirilmesini sağlamak amacıyla COVID-19 pandemisi öncesinde ve sırasında acil servise başvuran iskemik inme hastalarının sayısını ve özelliklerini araştırmaktır.

YÖNTEM
Bu tek merkezli, retrospektif kohort çalışmasına Mart 2018 ile Mart 2022 arasında acil servise başvuran iskemik inme ve geçici iskemik atak tanısı almış hastalar dahil edildi. Hastaları ikişer yıllık dönemleri kapsayan pandemi öncesi ve pandemi dönemi olmak üzere iki gruba ayırdık. Hastaların sayıları, başvuru özellikleri ve sonuçlarını karşılaştırdık.

BULGULAR
Çalışmaya pandemi öncesi dönemde 915 hasta ve pandemi döneminde 717 hasta olmak üzere, 1632 hasta dahil edildi. Pandemi döneminde inme olgularının sayısında %21,6 oranında azalma görüldü (n:915 vs. n:717). Hastaların Ulusal Sağlık İnme Ölçeği ortanca değerleri benzerdi (4 vs. 4, p = 0,071). Trombektomi oranı pandemi döneminde daha yüksekti (p <0,001). Hastaneye yatış oranı pandemi döneminde daha düşüktü (p <0,001), ancak 28 günlük mortalitede bir farklılık yoktu (p = 0,100).

SONUÇ
COVİD-19 pandemisi döneminde, hastaların tıbbi bakım alma konusundaki tereddütleri nedeniyle inme sayılarında ciddi bir azalma saptandı. İleride yaşanabilecek pandemilere yönelik hazırlanacak sağlık politikaları ve eğitim kampanyalarının uygulanması sağlık hizmetine erişimi sağlamak, morbidite ve mortaliteyi en aza indirmek için oldukça önemlidir.

ANAHTAR KELİMELER
Acil Servis, COVİD-19, iskemik inme, trombektomi

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:137-144

The COVID-19 disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) originated from Wuhan, China, and led to a global health crisis (1). According to the World Health Organization (WHO), there have been approximately 768 million confirmed cases, and 6.9 million deaths due to COVID-19 (2). Numerous studies have been published indicating that COVID-19 significantly increases the number of thromboembolic events, which have a significant impact on mortality (3–5). This has been attributed to inflammation and endothelial damage caused by the virus, resulting in a procoagulant state (6-7). It is now known that the devastating effects of COVID-19 are not solely due to a viral infection, but rather to a systemic procoagulant process triggered by endothelial damage (8-9). Venous thromboembolism, particularly pulmonary embolism, accounts for the majority of these thromboembolic complications (10-11). In addition, studies have shown the development of arterial thrombotic complications such as ischemic stroke and myocardial infarction (5,12).

Stroke is one of the leading causes of disability worldwide (13). Approximately 12 million people worldwide experience their first stroke attack each year (14). In Türkiye, the annual incidence of ischemic stroke has been reported to be 93.2-108.6 per 100,000 population (15). The majority of ischemic strokes are caused by thromboembolic processes such as large artery atherosclerosis, cardioembolic and small artery occlusion (16). Despite the studies showing an increase in thromboembolic complications associated with COVID-19, several studies have been published showing a decrease in ischemic strokes and transient ischemic attacks (TIAs) during the pandemic (17–19). However, large-scale studies on this topic in Türkiye are lacking. In this study, our primary objective is to determine the impact of the COVID-19 pandemic on the number of cases of ischemic stroke and transient ischemic attack (TIA) presenting to the emergency department by comparing the pre-pandemic and pandemic periods. Our secondary objectives are to assess the impact on time to presentation, hospitalization rates, and mortality rates.

Materials and Methods

This retrospective cohort study included cases presenting with stroke to the emergency department (ED) of our university hospital between March 2018 and March 2022. Our ED is a stroke center located in Izmir, the third largest city in Türkiye. Cases diagnosed with ischemic stroke or TIA based on clinical findings and radiological imaging were included. Patients with hemorrhagic stroke or missing demographic and clinical data were excluded.

Patients were categorized into pre-pandemic and pandemic groups based on the date of the first confirmed COVID-19 case in Türkiye (March 11th, 2020). The study compared differences in the number of admissions clinical severity at admission, time from symptom onset to presentation and treatments administered. Demographic data, comorbidities, risk factors for ischemic stroke, admission dates, time from symptom onset to presentation to the ED, National Institutes of Health Stroke Scale (NIHSS) scores at admission, radiological findings, treatments administered, patient outcomes (discharge, admission to stroke unit, death) and 28-day mortality data were obtained from electronic patient records in the hospital information management system. Patients diagnosed with TIAs were recorded as having a, NIHSS score of "0" on admission. For ischemic strokes, patients with admission NIHSS score <5 were classified as having a mild strokes, while patients with an NIHSS score ≥5 were classified as having a moderate and severe strokes. When comparing admission times, patients were divided into two groups based on the target thrombolysis time of 4.5 hours, categorized as early and late admissions.

Statistical analysis

Data were analyzed by using SPSS Statistics for Windows, Version 29.0 (IBM SPSS Statistics for Windows, Version 29.0. Armonk, NY: IBM Corp). The normal distribution of the variables was tested using the Kolmogorov-Smirnov test. Numerical data that conformed to the normal distribution were presented as mean and standard deviation, while those that did not conform to the normal distribution were presented as median and interquartile range. The Mann-Whitney U test was used to compare non-parametric numerical data. Chi-square and Fisher's exact tests were used to compare categorical data. Data was analyzed with a 95% confidence interval, and $p < 0.05$ was considered statistically significant.

Results

In total, 2006 patients with stroke were admitted to the ED. Of these them, 228 (11.3%) patients were excluded because of hemorrhagic stroke and 146 (7.2%) patients were excluded because of missing data. A total of 1632 patients with ischemic stroke were included in the analysis. Of those patients, 934 (%57.2) were male and the median age was 72 years. The distribution of stroke subtypes among these patients over different time periods is shown in Figure 1.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:137-144

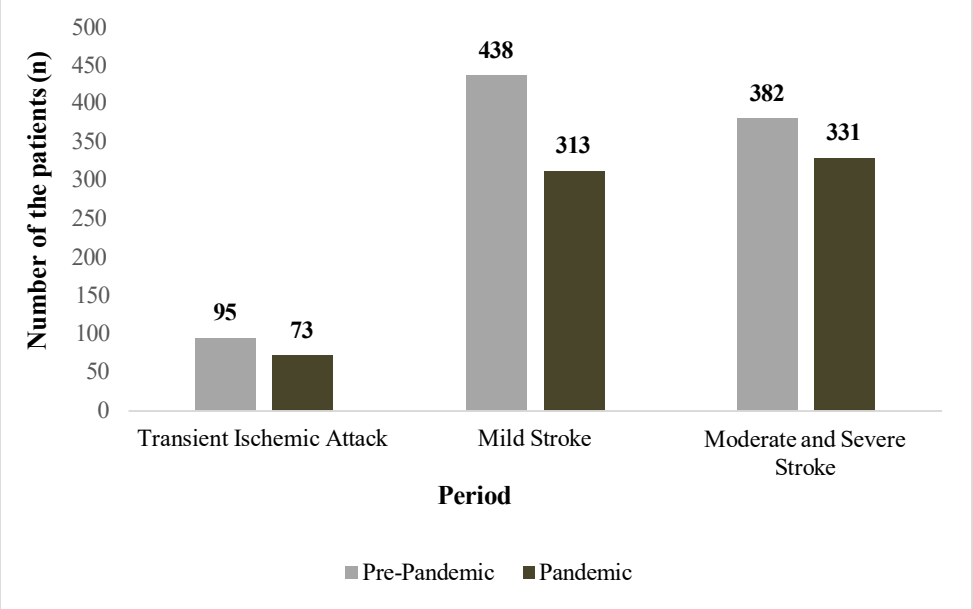


Figure 1. Distribution of patients according to stroke subgroups in different periods

The total number of patients admitted to the ED in the pre-pandemic period was 263,000 with 915 ischemic strokes (0.34%), whereas the total number of patients in the pandemic period was 161,000 with 717 ischemic strokes (0.44%). There was a 38.8% reduction in the total number of patients presenting to the ED, and a 21.6% reduction in the number of stroke cases.

The demographics characteristics and risk factors of the patients were shown in Table 1.

Table 1. Demographic characteristics and risk factors of patients with ischemic stroke.

Demographic characteristics	**Total**	**Pre-Pandemic**	**Pandemic**	***p***
Age (Median, IQR)	72 (62-80)	73 (64-81)	71 (61-78)	**<0.001**
Sex (Male)	937 (57.4)	518 (56.6)	419 (58.4)	0.459
Risk Factors	***n* (%)**	***n* (%)**	***n* (%)**	
Hypertension	1002 (61.4)	551 (60.2)	451 (62.9)	0.269
Diabetes	496 (30.4)	239 (26.1)	257 (35.8)	**<0.001**
Hyperlipidemia	121 (7.4)	71 (7.8)	50 (7.0)	0.547
Malignancy	91 (5.6)	45 (4.9)	46 (6.4)	0.191
Smoking	221 (13.5)	86 (9.4)	135 (18.8)	**<0.001**
Atrial Fibrillation	269 (16.5)	158 (17.3)	111 (15.5)	0.334
Coronary Artery Disease	515 (31.6)	256 (28.0)	259 (36.1)	**<0.001**
History of Stroke	286 (17.5)	168 (18.4)	118 (16.5)	0.316

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:137-144

The gender distribution (male) did not differ between pre-pandemic and pandemic groups (p = 0.459). However, the data showed that the pandemic group was younger (73 vs.71 years, p <0.001, respectively). Smoking (p <0.001), presence of diabetes mellitus (p <0.001) and coronary artery disease (p <0.001) were also higher patients in the pandemic group.

The clinical stroke characteristics of the patients are shown in Table 2.

Table 2. Clinical characteristics of patients with ischemic stroke.

Clinical characteristics	Total *n* (%)	Pre-Pandemic *n* (%)	Pandemic *n* (%)	*p*
Transient ischemic attacks	168 (10.3)	95 (10.4)	73 (10.2)	
Mild Stroke	751 (46.0)	438 (47.9)	313 (43.7)	0.186
Moderate and Severe Stroke	713 (43.7)	382 (41.7)	331 (46.2)	
Onset-to-door time, ≤4,5h	612 (37.5)	324 (39.4)	288 (43.8)	0.083
	Median (IQR 25-75)	**Median (IQR 25-75)**	**Median (IQR 25-75)**	
Onset-to-door time, h	6 (2.5-17.5)	6.5 (2.5-19.0)	5.5 (2.5-14.0)	0.112
NIHSS* on admission	4 (2-8)	4 (2-7)	5 (3-9)	0.071
NIHSS* at discharge/7th day	3 (1-6)	3 (1-5)	4 (2-8)	**<0.001**

*National Institutes of Health Stroke Scale

There was no significant difference in the distribution of stroke subgroups between groups. Although the median admission NIHSS scores were similar in both periods (p = 0.071), the discharge/7th-day NIHSS score was higher in the pre-pandemic group (p <0.001). The median time from symptom onset to ED admission was similar (6.5 vs. 5.5 hours, p = 0.112).

There was no difference in intravenous thrombolysis, but endovascular treatment was used more frequently in during the pandemic group. Comparing patient outcomes, the hospitalization rate for treatment was lower during the pandemic compared to the pre-pandemic group (p <0.001). Mortality rates were similar in both periods (Table 3).

Table 3. Treatments and outcomes of patients with ischemic stroke.

Treatment and Outcomes	Total *n* (%)	Pre-Pandemic *n* (%)	Pandemic *n* (%)	*p*
Intravenous thrombolysis	266 (16.3)	139 (15.2)	127 (17.7)	0.177
Mechanical thrombectomy	120 (7.4)	49 (5.4)	71 (9.9)	**<0.001**
Hospitalization rate	1386 (85.1)	830 (90.9)	556 (77.7)	**<0.001**
28-day mortality	92 (5.6)	44 (4.8)	48 (6.7)	0.100

Discussion

During the pandemic, many articles have been written about the reduction in ischemic stroke admissions the delayed admissions worldwide. However, no comprehensive study that conducted in our country. To the best of our knowledge, this is the most comprehensive study conducted in a tertiary stroke center in one of the largest cities in our country. In our study, we found a decrease in the number of ischemic strokes, but we found an increase in the frequency of ischemic strokes due to the decrease in the total number of patients admitted to the ED. Furthermore, we did not find a delay in the time from symptom onset to admission to the ED in ischemic stroke patients. We found an absolute increase in the use of mechanical thrombectomy, but we found a significant decrease in hospitalization rates.

Several studies have investigated the impact of the COVID-19 pandemic on stroke, and the majority of these studies reported a decrease in the number and incidence of strokes during the pandemic period (20–22). One of the most significant findings of our study is the 21.6% decrease in the number of stroke cases presenting to the ED. Although the total number of stroke cases has decreased, the proportion of stroke

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:137-144

cases among all patients presenting to the ED has increased. This finding could be attributed to two main factors. First, when analyzing patient numbers, it is possible that the restrictions imposed by COVID-19 and the fear of infection led to a reduction in the number of stroke patients presenting to the ED. However, the more pronounced decrease in ED admissions for non-stroke conditions may explain the relative increase in the proportion of stroke cases. Secondly, despite the significant decrease in the total number of patients presenting to the ED, the increased thromboembolic complications due to from endothelial dysfunction caused by COVID-19 may have contributed to this relative increase.

In our study, similar to the current literature, there was no difference in patients' NIHSS scores on admission between the pre-pandemic and pandemic groups (20,23,24). However, NIHSS scores at discharge were higher in the pandemic group. Several parameters such as age at admission, comorbidities, infarct area size, time from symptom onset to admission to the ED, and treatments administered influence the clinical outcome of stroke patients. In our study, the higher prevalence of risk factors in stroke patients in the pandemic group combined with the shorter duration of hospitalization during the pandemic group may have contributed to this result.

The time from symptom onset to ED admission, defined as the last well-known time, plays a crucial role in the treatment planning for ischemic stroke. In our study, there was no significant difference in the time from symptom onset to admission to the ED between the two periods. Balucani et al. and Tanaka et al. reported that patients in the pandemic group in their study had late ED admission (21-25). However, there are also studies reporting the contrary (20,24,26).

While rates of intravenous thrombolysis were similar in both periods in our study, the use of mechanical thrombectomy was higher in the pandemic period. This increase may not be due to the impact of COVID-19, but rather to the global trend towards increased use of endovascular procedures in stroke patients, coupled with a limited number of centers capable of performing such procedures. Other studies have supported similar findings showing that the use of mechanical thrombectomy has not decreased despite a decrease in the number of patients (17,21,26). Our study also found that patient hospitalization rates decreased, similar to other studies on this topic (17,22). To reduce hospital transmission of COVID-19, fewer hospital admissions can be managed as outpatients cases, such as TIAs and mild strokes, which may explain this finding.

Study limitations

As there was no information on whether the stroke patients in our study had previously had COVID-19, it is difficult to draw definite conclusions about the exact cause of the relative increase in stroke incidence. Due to the retrospective nature of the study, unavailable data is an important limitation. In addition, the generalizability of the results is not given because the study was conducted at a single center and the population was limited.

Conclusion

During the COVID-19 pandemic, a decrease in the total number of patients and the number of stroke cases presenting to the ED was observed. There was no significant difference in the admission NIHSS scores and the time from symptom onset to admission. Mortality rate did not change although the rate of mechanical thrombectomy increased during the pandemic period.

Although several factors may have contributed to the decline in stroke cases, the most important factor appears to have been the reluctance to seek medical care the pandemic. For diseases with high morbidity and mortality, such as stroke, the benefits of access to healthcare outweigh the risks of infection. Therefore, health policies should be developed to address potential pandemic periods, and education campaigns for the public and healthcare worker should be implemented..

Acknowledgements

Thanks to Associate Professor Sevilay VURAL for her contributions to writing, language help and structural arrangements.

Conflict of interest

Authors declare no conflict of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
RESEARCH ARTICLE
Sayfa:137-144

References

1. Kumar A, Singh R, Kaur J, Pandey S, Sharma V, Thakur L, et al. Wuhan to World: The COVID-19 Pandemic. Front Cell Infect Microbiol 2021;11.
2. COVID-19 cases | WHO COVID-19 dashboard n.d. Available from:URL: https://data.who.int/dashboards/covid19/cases?n=c (accessed January 15, 2024).
3. Malas MB, Naazie IN, Elsayed N, Mathlouthi A, Marmor R, Clary B. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: A systematic review and meta-analysis. EClinicalMedicine 2020;29–30.
4. Bikdeli B, Madhavan MV, Jimenez D, Chuich T, Dreyfus I, Driggin E, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol 2020;75:2950–2973.
5. Klok FA, Kruip MJHA, van der Meer NJM, Arbous MS, Gommers DAMPJ, Kant KM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020;191:145–147.
6. Loo J, Spittle DA, Newnham M. COVID-19, immunothrombosis and venous thromboembolism: biological mechanisms. Thorax 2021;76:412–420.
7. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. New England Journal of Medicine 2020;383:120–128.
8. Zhang J, Tecson KM, McCullough PA. Endothelial dysfunction contributes to COVID-19-associated vascular inflammation and coagulopathy. Rev Cardiovasc Med 2020;21:315–319.
9. Kunutsor SK, Laukkanen JA. Incidence of venous and arterial thromboembolic complications in COVID-19: A systematic review and meta-analysis. Thromb Res 2020;196:27–30.
10. Gąsecka A, Borovac JA, Rui &, Guerreiro A, Giustozzi M, Parker W. Thrombotic Complications in Patients with COVID-19: Pathophysiological Mechanisms, Diagnosis, and Treatment. Cardiovasc Drugs Ther. 2021;35:215-229
11. Al-Ani F, Chehade S, Lazo-Langner A. Thrombosis risk associated with COVID-19 infection. A scoping review. Thromb Res 2020;192:152–160.
12. Abou-Ismail MY, Diamond A, Kapoor S, Arafah Y, Nayak L. The hypercoagulable state in COVID-19: Incidence, pathophysiology, and management. Thromb Res 2020;194:101–115.
13. Feigin VL, Forouzanfar MH, Krishnamurthi R, Mensah GA, Connor M, Bennett DA, et al. Global and regional burden of stroke during 1990-2010: Findings from the Global Burden of Disease Study 2010. The Lancet 2014;383:245–255.
14. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. International Journal of Stroke 2022;17:18–29.
15. Topcuoglu MA, Ozdemir AO. Acute stroke management in Turkey: Current situation and future projection. Eur Stroke J 2023;8:16–20.
16. Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, et al. Classification of Subtype of Acute Ischemic Stroke Definitions for Use in a Multicenter Clinical Trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke. 1993;24(1):35-41.
17. Richter D, Eyding J, Weber R, Bartig D, Grau A, Hacke W, et al. Analysis of Nationwide Stroke Patient Care in Times of COVID-19 Pandemic in Germany. Stroke 2021;52:716–721.
18. Clodfelder C, Cooper S, Edwards J, Kraemer J, Ryznar R, LaPorta A, et al. Delayed care in myocardial infarction and ischemic stroke patients during the COVID-19 pandemic. American Journal of Emergency Medicine 2022;54:326.e1-326.e4.
19. Bersano A, Kraemer M, Touzé E, Weber R, Alamowitch S, Sibon I, et al. Stroke care during the COVID-19 pandemic: experience from three large European countries. Eur J Neurol 2020;27:1794–1800.
20. Diegoli H, Magalhães PSC, Martins SCO, Moro CHC, França PHC, Safanelli J, et al. Decrease in Hospital Admissions for Transient Ischemic Attack, Mild, and Moderate Stroke during the COVID-19 Era. Stroke 2020;51:2315–2321.
21. Balucani C, Carhuapoma JR, Canner JK, Faigle R, Johnson B, Aycock A, et al. Exploring the Collateral Damage of the COVID-19 Pandemic on Stroke Care: A Statewide Analysis. Stroke 2021;52:1822–1825.
22. Nogueira RG, Abdalkader M, Qureshi MM, Frankel MR, Mansour OY, Yamagami H, et al. Global impact of COVID-19 on stroke care. International Journal of Stroke 2021;16:573–584.
23. Rinkel LA, Prick JCM, Slot RER, Sombroek NMA, Burggraaff J, Groot AE, et al. Impact of the COVID-19

outbreak on acute stroke care. J Neurol 2021;268:403–408.

24. Bhatia R, Sylaja PN, Srivastava MVP, Komakula S, Iype T, Parthasarathy R, et al. Clinical profile and outcome of non-COVID strokes during pandemic and the pre pandemic period: COVID-Stroke Study Group (CSSG) India. J Neurol Sci 2021;428:117583.

25. Tanaka K, Matsumoto S, Nakazawa Y, Yamada T, Sonoda K, Nagano S, et al. Delays in Presentation Time Under the COVID-19 Epidemic in Patients With Transient Ischemic Attack and Mild Stroke: A Retrospective Study of Three Hospitals in a Japanese Prefecture. Front Neurol 2021;12: 748316.

26. John S, Hussain SI, Piechowski-Jozwiak B, Dibu J, Kesav P, Bayrlee A, et al. Clinical characteristics and admission patterns of stroke patients during the COVID 19 pandemic: A single center retrospective, observational study from the Abu Dhabi, United Arab Emirates. Clin Neurol Neurosurg 2020;199:106227.

Developments and Experiments in Health and Medicine

Year: 2025
Volume: 39
Issue: 2

CASE REPORT

Sayfa:145-150

A Buerger's patient with brachial artery aneurysm

Brakial arter anevrizması gözlenen bir Buerger hastası

Onur Barış DAYANIR[1]
Hüseyin SAYGIN[1]
Erdem Erinç SİLİSTRELİ[1]

[1] Dokuz Eylul University, Faculty of Medicine, Department of Cardiovascular Surgery, Izmir, Türkiye

A Buerger's patient with brachial artery aneurysm

Received: 16.01.2025
Accepted: 07.04.2025
doi:10.18614/dehm.1699943

Corresponding author
Onur Barış DAYANIR
ORCID ID: 0000-0003-1293-3898
onurbarisdayanir95@gmail.com

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
CASE REPORT
Sayfa:145-150

ABTSTRACT
Thromboangiitis obliterans (TAO) is a vasculopathy that presents with non-atherosclerotic segmental involvement in small and medium-sized arteries, usually in the upper and lower extremities. Brachial Artery Aneurysm (BAA) is not one of the classic findings of TAO and has no example in the literature. In this report, we described a TAO patient who underwent an aneurysmectomy due to a BAA.

KEYWORDS
Arteritis, brachial artery aneurysm, smoking, thromboangiitis obliterans

ÖZ
Buerger hastalığı (tromboanjitis obliterans); genellikle üst ve alt ekstremitelerde, küçük ve orta büyüklükteki arterlerde aterosklerotik olmayan segmental tutulumla seyreden bir vaskülopatidir. Brakial arter anevrizması, Buerger hastalığının klasik bulgularından biri değildir ve literatürde Buerger ve brakial arter anevrizması koinsidansının bir örneği yoktur. Bu raporda, brakial arter anevrizması nedeniyle anevrizmektomi geçiren bir Buerger hastasını sunduk.

ANAHTAR KELİMELER
Arterit, Buerger hastalığı, brakial arter anevriması, sigara

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
CASE REPORT
Sayfa:145-150

Buerger's disease is a chronic, inflammatory, and thrombotic vascular disease associated with tobacco use (1). This disease affects the small and medium-sized arteries of the upper and lower extremities causing non-atherosclerotic segmental occlusion and is frequently seen in men aged 20-40 years (2). It is common in Turkey and its frequency is increasing in women (3). The characteristic pathophysiological changes of Buerger's disease are the deterioration of microvascular regulation due to multiple arterial obstructions at the onset of the disease and then the development of critical ischemia in the extremities. Ischemic symptoms and trophic lesions usually occur in the distal regions of the extremities (4). Recurrent and migratory superficial thrombophlebitis of the extremities (phlebitis saltans/migran thrombophlebitis) may be seen as an early finding in 16-65% of patients (5). The annual incidence of Buerger's disease is estimated to be 5-12 per 100,000 people worldwide. In addition, approximately 7,000 cases of Buerger's disease were reported between 2014 and 2017:(6). Brachial artery aneurysm is extremely rare in Buerger's disease and only one case with radial artery aneurysm has been reported in the literature (7). This case report, describes a patient with a Buerger's disease with a brachial artery aneurysm. Pathological examination of the aneurysmatic brachial artery excised from the right arm revealed thromboangiitis obliterans.

Case Report

A 49-year-old male patient presented with swelling and pain in his right arm. In 2021, he was diagnosed with Buerger's disease due to rest pain in the left lower extremity, digital ulcers, a history of smoking, and occlusive lesions below the knee. Therefore, peripheral percutaneous transluminal angioplasty (atherectomy and balloon dilatation of the left popliteal artery) and thoracic sympathectomy operations were performed. In addition, he underwent a cystectomy due to a pulmonary hydatid cyst and a varicocelectomy due to a varicocele. He was using acetylsalicylic acid and cilostazol. On physical examination, a pulsatile mass extending from the antecubital region to the proximal radial artery tract was palpated in the right arm (Figure1).

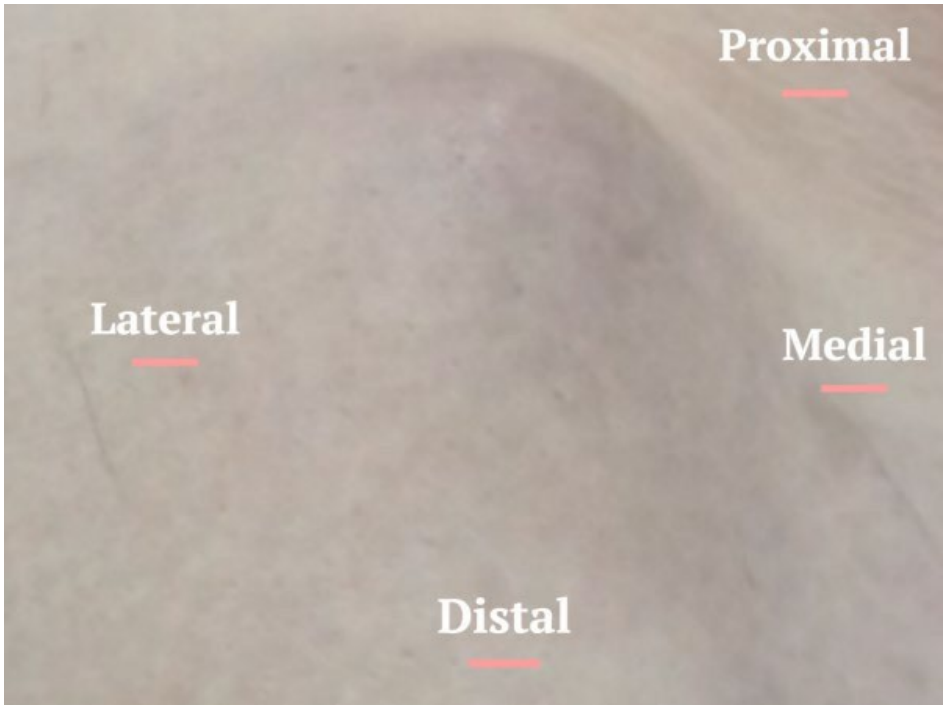


Figure 1. Inspection of the antecubital region

Forearm flexion was limited and painful. Radial and ulnar pulses were absent. Arterial and venous Doppler ultrasonography of the upper extremity revealed aneurysmatic enlargement and a mural thrombus reaching 15x25 mm in diameter in a segment of approximately 4 cm at the level of the brachial artery-radial artery junction in the right antecubital

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
CASE REPORT
Sayfa:145-150

region. Edema and thickening of the soft tissues were observed around the aneurysm (Figure2). Low-amplitude flow was seen in the right radial ulnar arteries.

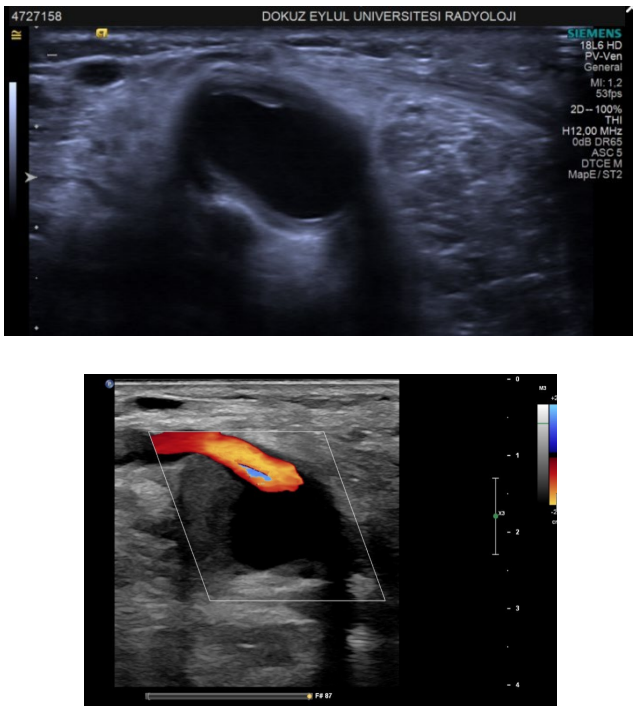


Figure 2. Aneurysmatic enlargement reaching a diameter of 15x25 mm in a segment of approximately 4 cm at the level of the brachial artery-radial artery junction in the right antecubital region

Operation

An elective brachial aneurysmectomy was planned. General anaesthesia was given in the operation room. The brachial and radial artery aneurysms were marked by ultrasonography. The brachial artery and cephalic vein were accessed through a right antecubital incision. The branches of the cephalic vein were ligated and prepared as grafts. The aneurysm was explored and measured to be 5x2x1.5 cm at the brachioradial junction. The ulnar artery was explored. A dose of 100 units/kg of heparin was administered. After clamping the distal and proximal segments, aneurysmectomy was performed. The excised aneurysmal artery was prepared for pathological examination. Strong antegrade flow was observed from the brachial artery and weak retrograde flow from the radial artery. The ulnar artery was completely occluded. Embolectomy of the ulnar was attended with a 3 F Fogarty catheter but was unsuccessful. The ulnar artery was ligated. The cephalic vein, prepared as a graft, was placed between the brachial artery and the radial arteriesy. Brachial artery, interposed graft, and radial artery flows were evaluated perioperatively by ultrasonography. There were no flow problems. A hemovac drain was placed, and the skin was closed with matrees sutures.

Pathology

There were no postoperative complications. The patient was discharged on the second day. Macroscopic pathological examination revealed a lumen structure with a diameter of 1.3 cm at the widest part of the gray-white tissue. Occlusive gray content was seen in this lumen structure. Microscopic examination revealed granulomatous inflammation with giant cells in the thrombus formation and tunica intima. It was considered as compatible with Buerger' disease. After three months, the patient had no symptoms or ischemic signs at follow-up. disease. After three months, the patient had no symptoms or ischemic signs at follow-up

Developments and Experiments in Health and Medicine
Year: 2025
Volume: 39
Issue: 2
CASE REPORT
Sayfa:145-150

Discussion

Buerger's disease is a vasculopathy that presents with non-atherosclerotic segmental involvement of small and medium-sized arteries, usually in the upper and lower extremities (8). Von Winiwarter first described the disease in 1879, but it was Leo Buerger who published a detailed description of the pathological findings in amputated limbs and gave the disease its name in 1908 (9). The pathological feature of this disease is the presence of an inflammatory thrombus in the affected arteries and veins. It may present with symptoms such as coldness, paraesthesia, skin colour changes, intermittent claudication, rest pain, ulcers, gangrene and migratory superficial thrombophlebitis. Magnetic resonance angiography, contrast three-dimensional computed tomography (3D-CT) and conventional angiography may be used for vascular imaging (10). Medical treatment includes smoking cessation, lifestyle changes, antiplatelet drugs, prostaglandin inhibitors and pain control (11). Surgical treatment may include vascular bypass surgery or endovascular methods for revascularization. Sympathectomy may be considered in patients for whom revascularization is not possible. Since Leo Buerger's 1908 article, progress in understanding the cause, pathophysiology, and optimal treatment of thromboangiitis obliterans has been limited (12). Therefore, case reports such as ours can guide further research.

Our report describes a brachial artery aneurysm in a patient with Buerger's disease that we successfully treated surgically. Brachial artery aneurysms usually occur due to arteriovenous fistula, post-trauma, or idiopathic causes (13). In this case, the observation of Buerger's disease-specific findings in the pathological examination of the aneurysmectomy material is a rare etiopathogenesis for brachial artery aneurysm. Furthermore, brachial artery aneurysm may contain pathological findings specific for Buerger's disease, and this may be considered an atypical clinical presentation.

Conclusion

Non-atherosclerotic occlusive lesions in Buerger's disease expected to cause ischemic findings. However, brachial artery aneurysms is very rare in patients with Buerger's disease. It is also rare for an aneurysm to be symptomatic prior to ischaemic findings in the limb affected by Buerger's disease. The active smoking observed in this case may be a common factor in the etiology of brachial artery aneurysm and Buerger's disease.

References

1. Akar AR, Inan M. Buerger's Disease. In: Sidawy AN, Perler BA, editors. Rutherford's Vascular Surgery and Endovascular Therapy. Philadelphia: Elsevier, 2019. p. 1809-26.
2. Olin JW. Thromboangiitis obliterans (Buerger's disease). N Engl J Med. 2000 Sep 21; 343(12):864-9. doi: 10.1056/NEJM200009213431207. PMID: 10995867.
3. Shionoya S, Ban I, Nakata Y, Matsubara J, Shinjo K. Diagnosis, pathology, and treatment of Buerger's disease. Surgery. 1974 May; 75(5):695-700. PMID: 4824428.
4. Piazza G, Creager MA. Thromboangiitis obliterans. Circulation. 2010 Apr 27; 121(16):1858-61. doi: 10.1161/CIRCULATIONAHA.110.942383. PMID: 20421527; PMCID: PMC2880529.
5. Fazeli B, Modaghegh H, Ravrai H, Kazemzadeh G. Thrombophlebitis migrans as a footprint of Buerger's disease: a prospective-descriptive study in north-east of Iran. Clin Rheumatol. 2008 Jan; 27(1):55-7. doi: 10.1007/s10067-007-0652-8. Epub 2007 Jun 7. PMID: 17554578.
6. Isobe M, Amano K, Arimura Y, Ishizu A, Ito S, Kaname S, Kobayashi S, Komagata Y, Komuro I, Komori K, Takahashi K, Tanemoto K, Hasegawa H, Harigai M, Fujimoto S, Miyazaki T, Miyata T, Yamada H, Yoshida A, Wada T, Inoue Y, Uchida HA, Ota H, Okazaki T, Onimaru M, Kawakami T, Kinouchi R, Kurata A, Kosuge H, Sada KE, Shigematsu K, Suematsu E, Sueyoshi E, Sugihara T, Sugiyama H, Takeno M, Tamura N, Tsutsumino M, Dobashi H, Nakaoka Y, Nagasaka K, Maejima Y, Yoshifuji H, Watanabe Y, Ozaki S, Kimura T, Shigematsu H, Yamauchi-Takihara K, Murohara T, Momomura SI; JCS Joint Working Group. JCS 2017 Guideline on Management of Vasculitis Syndrome - Digest Version. Circ J. 2020 Jan 24; 84(2):299-359. doi: 10.1253/circj. CJ-19-0773. Epub 2020 Jan 18. PMID: 31956163.
7. Giler S, Zelikovski A, Goren G, Urca I. Aneurysm of the radial artery in a patient with Buerger's disease. Vasa. 1979; 8(2):147-9. PMID: 463287.
8. Cacione DG, Baptista-Silva JC, Macedo CR. Pharmacological treatment for Buerger's disease. Cochrane Database Syst Rev. 2016 Feb 1; 2:CD011033. doi: 10.1002/14651858.CD011033.pub2. Update in: Cochrane Database Syst Rev. 2016 Mar 11;

3:CD011033. doi: 10.1002/14651858.CD011033.pub3. PMID: 26828199.

9. BUERGER L. Thrombo-angitis obliterans; a study of the vascular lesions leading to presenile spontaneous gangrene. Am J Med. 1952 Nov; 13(5):526-32. doi: 10.1016/0002-9343(52)90015-6. PMID: 12996526.
10. Sakaguchi S, Mishima Y. Report of Angiographic Findings. Buerger Disease. Ministry of Health and Welfare Specific Diseases Systematic Study Group on Vascular Lesions Subcommittee Report 1976. 1977: 1–38
11. Mills JL Sr. Buerger's disease in the 21st century: diagnosis, clinical features, and therapy. Semin Vasc Surg. 2003 Sep; 16(3):179-89. doi: 10.1016/s0895-7967(03)00023-1. PMID: 12975757.
12. Olin JW. Thromboangiitis Obliterans: 110 Years Old and Little Progress Made. J Am Heart Assoc. 2018 Dec 4; 7(23):e011214. doi: 10.1161/JAHA.118.011214. PMID: 30571606; PMCID: PMC6405560.
13. Hammad Alam SM, Moin S, Gilani R, Jawad N, Abbas K, Ellahi A. True brachial artery aneurysm: A systematic review. J Pak Med Assoc. 2024 Feb; 74(2):341-365. doi: 10.47391/JPMA.9042. PMID: 38419237.

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