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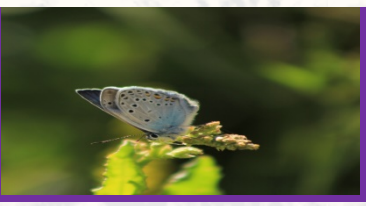

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Letter to the Editor

Positive and Negative Aspects of Artificial İntelligence in Psychiatry

Psikiyatride Yapay Zekanın Olumlu ve Olumsuz Yönleri

Okan IMRE[1]

[1]Department of Psychiatry, Karamanoglu Mehmetbey University, Faculty of Medicine, Karaman, Türkiye

Dear Editor.

The reason why I wrote this letter is to draw attention to the positive and negative aspects of increasingly developing artificial intelligence applications and machine learning in psychiatry and to start a discussion. As we know, psychiatric diseases worldwide have tended to increase in recent years. On the other hand, since the number of psychiatrists does not increase in correlation, the number of patients per psychiatrist is high(1). There is no doubt that the workload of psychiatric physicians will decrease with the introduction of artificial intelligence and machine learning applications(2). For example, artificial intelligence applications can make the psychiatrist think of a preliminary diagnosis about the patient before the examination by performing various survey-based tests(3). It can assist the physician in differential diagnosis in complex cases during the examination(4). Or, when prescribing medication after the examination, polypharmacy and drug interactions can be prevented with various artificial intelligence applications. When we think from the patient's perspective, artificial intelligence has many uses. For example, it may have positive aspects such as appointment time, reminding people to take their medications on time, and even making various psychotherapy suggestions. Another potential area of use of artificial intelligence applications and machine learning, which is not mentioned much in the literature, is that they can provide early intervention by detecting some of the precursor symptoms, such as insomnia and mobility, during the attack periods of some chronic diseases. As it is known, since manic and psychotic patients generally do not have insight, their relatives and psychiatrists may not notice the symptoms of the disease in the early period before they become fully evident. It is probable that patient-specific artificial intelligence applications will be beneficial in this regard. However, artificial intelligence applications and machine learning may also have some risks. For example, it may cause many legal problems by violating personal data(5). Artificial intelligence and machine learning may not be able to detect when some antisocial people involved in criminal offenses are lying. The probability of misdiagnosis is high in this case.

As a result, although some psychiatrists are worried that artificial intelligence and machine learning will replace humans and bring about the end of the profession, in my opinion, the physicians who will be least harmed by these applications in terms of job loss are psychiatrists. Because psychiatric patients require an emotional and empathetic approach that is not available in machines but is available in psychiatrists.

In summary, the right approach would be for psychiatrists to put aside all their prejudices, take into account the possible risks of artificial intelligence and machine learning, learn about these technologies, and turn them into an advantage. We are in the age of artificial intelligence and machine learning . We cannot remain indifferent.

Kind regards.

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Original article

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Long-term Exposure to 50 Hz Extremely Low Frequency Pulsed Electromagnetic Field Does not Alter the Electrocardiographic Parameters of Rats

50 Hz Aşırı Düşük Frekanslı Darbeli Elektromanyetik Alana Uzun Süre Maruz Kalmak, Sıçanların Elektrokardiyografik Parametrelerini Değiştirmez

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Abstract

Background: The heart is a contractile organ with the ability to generate its own signals. Because of the excitable nature of heart cells, they may be impacted by external impulses or stimuli. The purpose of this research is to use electrocardiogram (ECG) measurements to ascertain the effects of exposure to an extremely low frequency pulsed magnetic field (ELF-PEMF) at 1 milli Tesla (mT) and 5 mT intensity on the heart's electrical stimulation system.

Materials and Methods: Eighteen Wistar Albino rats, weighing 200-250g and aged 8 weeks, were randomly allocated into three groups, with six rats in each group: sham, 1 milli Tesla (1 mT), and 5 mT exposure groups. Rats were subjected to ELF-PEMF for 4-hours each day, 5-days per week for 8-weeks. The rats in the sham group were kept under the same condition, but the exposure system was turned off.

Results: The findings indicate that ELF-PEMF exposure at 1 mT and 5 mT intensities did not affect common ECG parameters used to evaluate cardiac rhythmic activity, including heart rate, P-wave amplitude, PR interval, QRS interval, R amplitude, and QT interval.

Conclusion: The 8-week exposure to ELF-PEMF at the 1 mT and 5 mT intensities didn't show any effect on ECG parameters in rats, at least according to the design applied in this study. The effects of these magnetic fields are also directly related to exposure durations and intensity. Therefore, more research is required to ascertain how varied application intensities and durations affect cardiac function.

Keywords: Heart function; Electrocardiogram (ECG); Extremely Low Frequency Pulsed Electromagnetic Fields (ELF-PEMF)

ÖZ

Amaç: Kalp, kendi sinyallerini üretebilen kasılabilir bir organdır. Kalp hücrelerinin uyarılabilir doğası nedeniyle, dış etkenler veya uyarıcılardan etkilenebilirler. Bu araştırmanın amacı, elektrokardiyogram (EKG) ölçümlerini kullanarak, 1 mili Tesla (mT) ve 5 mT şiddetindeki aşırı düşük frekanslı darbeli manyetik alanın (ELF-PEMF) maruziyetinin kalbin elektriksel uyarı sistemine etkilerini belirlemektir.

Gereç ve Yöntem: 200-250 g ağırlığında ve 8 haftalık 18 Wistar Albino sıçan, altışarlı üç gruba rastgele ayrıldı: sham, 1 mili Tesla (1 mT) ve 5 mT maruziyet grupları. Sıçanlar her gün 4 saat boyunca ELF-PEMF'ye maruz bırakıldı ve bu işlem haftada 5 gün, 8 hafta boyunca tekrarlandı. Sham grup sıçanları aynı koşullarda tutuldu, ancak maruziyet sistemi kapatıldı..

Bulgular: 1 mT ve 5 mT yoğunluğundaki ELF-PEMF maruziyeti, kalp hızı, P dalga genliği, PR aralığı, QRS aralığı, R genliği ve QT aralığı gibi kalp ritmik aktivitesinin değerlendirilmesinde yaygın olarak kullanılan EKG parametreleri üzerinde hiçbir etki göstermedi. **Sonuç:** Bu çalışmada uygulanan tasarıma göre, 1 mT ve 5 mT yoğunluğundaki ELF-PEMF'ye 8 haftalık maruziyet, sıçanlarda EKG parametreleri üzerinde herhangi bir etki göstermedi. Bu manyetik alanların etkileri aynı zamanda maruziyet süreleri ve şiddetleri ile doğrudan ilgilidir. Bu nedenle, farklı manyetik alan şiddetlerinin ve sürelerinin kalp fonksiyonunu nasıl etkilediğini belirlemek için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: Kalp Fonksiyonu, Elektrokardiyogram (EKG); Son Derece Düşük Frekanslı Darbeli Elektromanyetik Alanlar (ELF-PEMF)

Highlights

- 8-week exposure to 1mT and 5 mT did not affect rat cardiac electrical activity.
- Further studies are needed to explore effects of varying intensities and durations of ELF-PEMF on cardiac function.
- This study suggests that even at high intensities, ELF-PEMF exposure appears safe for the heart's electrical activity.

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Introduction

The exposure to electromagnetic fields is increasingly becoming prevalent in our daily lives' day by day. However, its effects on human health are highly debatable and draw attention to a controversial issue. A greater number of people have been exposed to weak electric or magnetic fields at home and at work due to a variety of electrical gadgets, industrial equipment, and household appliances. Extremely low-frequency electromagnetic fields (ELF-EMFs) are among the most prevalent components of the environment that can have an impact on biological systems. ELF part of the electromagnetic spectrum is often defined as 0 - 300 Hz (1). Magnetic fields produced by electrical or electronic devices used in our surroundings and electrical power lines have frequency ranges of 50 Hz in a large portion of the world and 60 Hz in North America (2). The biological effects of ELF-EMF and their harmful implications on human health have become a subject of intense discussion, according to the results obtained (3–5). The heart plays a crucial role in maintaining organismal homeostasis by pumping blood throughout the body. Any disruption in heart function can cause atherosclerosis, heart failure and sudden death (6,7).

Exposures to ELF-EMF are rising with the increasing use of electrical devices and technological products in our daily lives. However, it is noteworthy that there are very few studies showing the effects of these exposures on the cardiovascular system. A study conducted in 1999 showed that there was a parallel increase in the development of heart diseases as the duration of ELF-EMF exposure increased in electrical service workers (8). Long-term magnetic field (MF) treatment was demonstrated in another investigation to generate oxidative stress and, as a result, apoptosis and morphological abnormalities in rat cardiomyocytes (9). On the other hand, many studies have looked into the therapeutic benefits of extremely low frequency pulsed-magnetic field (ELF-PEMF) (10–12). Using a myocardial infarction model, Peng et al. demonstrated that pulsed magnetic field exposure, particularly at 30 Hz 3 milli Tesla (mT) intensity improved heart function in mice by inducing angiogenesis (13). In a different study, Wang et al. demonstrated that using a pulsed magnetic field in conjunction with adipose-derived stem cell treatment prevented cardiomyocyte death by controlling the miR-20a-5p/E2F1/p73 signaling pathway in a mouse model of myocardial infarction (14). Despite these findings, several other investigations have found that ELF-EMF exposure has no effect on heart function (15–17). In another study, Wang et al. showed that, short-term exposure to ELF-PEMF altered the RR interval slightly but had no influence on other intervals in human ECG measurements (18). In summary, it is noted that the duration, intensity, and waveform of applied ELF-EMF result in substantial variations.

PEMF is a form of collected electrical energy that is discharged in very short bursts (19). PEMF was first utilized for medicinal purposes in 1980, after it was licensed by the US Food and Drug Administration (20). Although the therapeutic properties of ELF-PEMF applications have been proven, more research is needed to show their potential impacts on the functioning of the heart. Additionally, to our best knowledge, the possible effects of long-term exposures of pulsed magnetic field on the electrical activity of the heart are not fully known. Thus, the effects of long-term (8-week) ELF-PEMF exposure at different strengths of 1 mT and 5 mT at a frequency of 50 Hz on rat electrocardiograms were investigated in that study.

Materials and Methods

Preparation of animals

For this study, 18 Wistar-Albino rats were employed. Rats were divided into three groups at random (each with 6-rats): sham, ELF-PEMF at 1mT and 5 mT intensities. Akdeniz University Local Ethics Committee's guidelines for the use of animals in experimentation were strictly adhered to (Date: 07.08.2023; Protocol Number: 1615/2023.08.001). A maximum of 3 animals were housed in each cage while the animals were maintained at 22±2 °C room temperature. Additionally, the experimental procedure was carried out on animals with free access to food and water and 12-second light/dark cycles.

Pulsed Magnetic Field Application

A pair of Helmholtz Bobin coils (copper wire with 120 turns, 2 mm2 cross-section area of each bobbin), each 50 cm in diameter, were placed in a Faraday cage along with a programmable signal generator power source (ILFA Electronics, Adana, Turkey) capable of adjusting the number of repeats, pulse frequency, pulse duration, and pulse number. **(Figure 1A)**.

In this investigation, a pulsed magnetic field of 1 mT or 5 mT magnitude was delivered to two experimental groups for 4 hours each day, five days a week, for eight weeks. The program consisted of 96 consecutive pulse trains, each lasting 2 minutes with a 30-second interval (**Figure 1B)**.

The coils generated magnetic fields peaking at 1 mT and 5 mT. The waveform of the magnetic field's time-varying component was quasi-triangular. Additionally, the device generated a horizontal homogeneous magnetic field in the desired way. A Gauss meter (Bell 5170, SYPRIS, USA) with a Hall effect probe was used to verify the appropriate magnetic field amplitude (in milliTesla) on each experimental day. The magnetic field in the magnetic field exposure area was found to be 95% homogeneous using the tesla meter as well.

Three rats were placed in a plexiglass container (40 x 15 x 20) for the administration of PMF. Magnetic field application was accomplished by positioning plexiglass in the center of the coils. PMF application was applied continuously at certain time intervals (9 am to 1 pm, for four hours each day, five days a week, for eight weeks) in order not to disturb the circadian rhythm of the animals. For the sham group, which differed from the 1 mT and 5 mT treatments, the rats were once more placed in plexiglass and left in the application area for 4 hours, but the power supply was left disconnected. Again, this routine was followed for 4 hours per day, 5 days per week, for a total of 8 weeks.

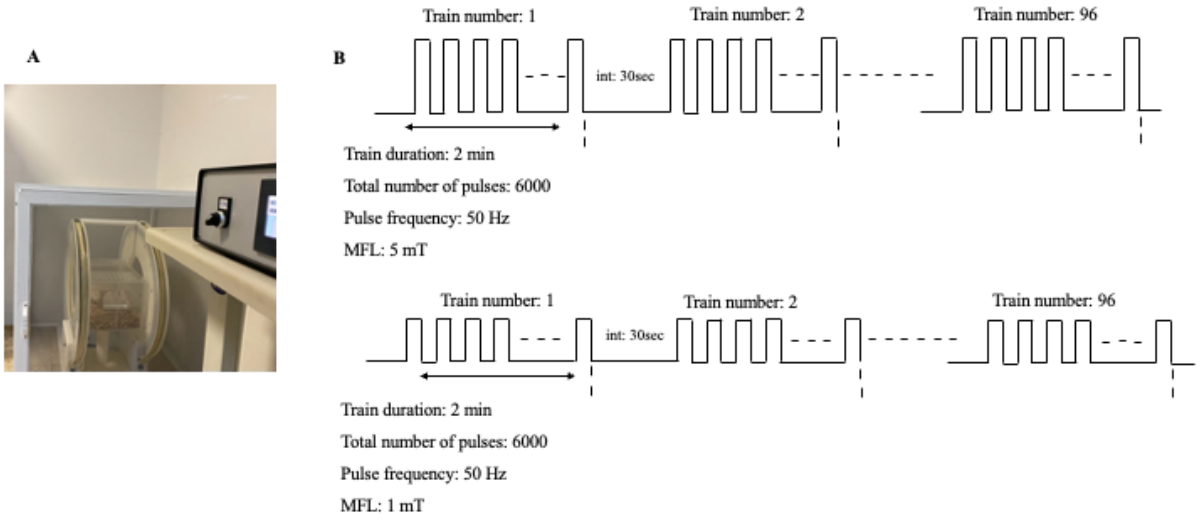

Figure 1: Pulsed magnetic field exposure system. (A) Signal generator and Helmhotz bobbin coils. **(B)** The pulse trains used in PMF application. Int: interval.

ECG Recordings

At the end of of the 8-week experiment, electrocardiographic measures were performed. To keep the anesthetic state, 10 mg/kg xylazine and 90 mg/kg ketamine were administered intramuscularly. All animals were given a 3-minute anesthetic before having their ECGs (lead II) measured. The MP150 (Biopac Systems) device was used to record changes in electrocardiographic activity. All data were shown as RR interval, heart rate (HR), PR interval, P duration, QRS interval, QT interval, corrected QT interval (QTc), P amplitude and R amplitude, which are commonly used ECG parameters. Lab Chart application was employed to analyze the ECG parameters. Relevant ECG recordings for each group are given in **Figure 2.**

Figure 2. Electrocardiogram recordings of rats from three groups: (**A**) Sham, (**B**) 1 mT, (**C**) 5 mT exposure.

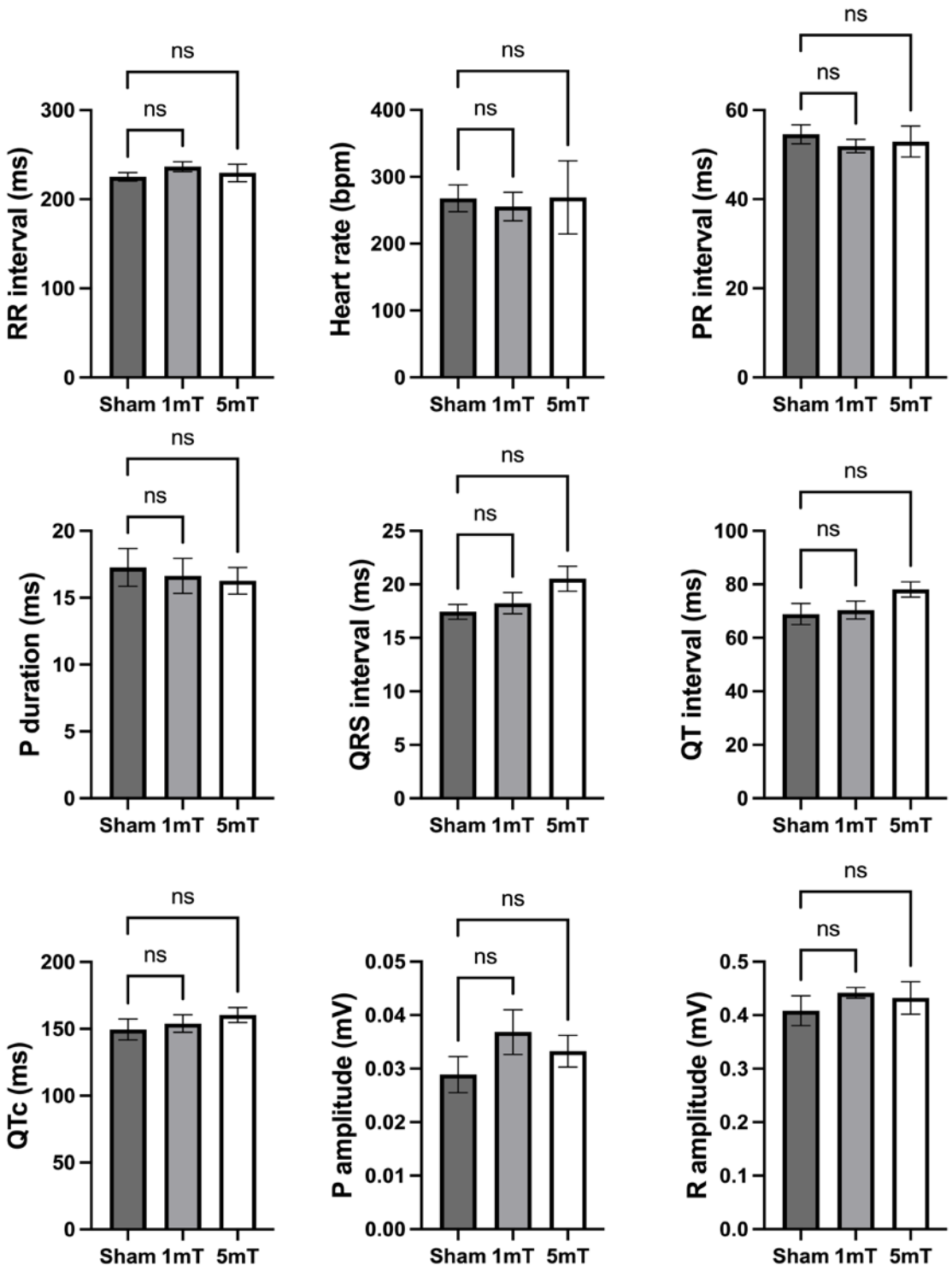

Figure 3. Graphs showing changes in ECG parameters following exposure.

Statistical analysis

The GraphPad Prism program was used to conduct the statistical analysis. All experimental results are shown as mean ± SEM. All parameters were compared via one way ANOVA followed by post hoc (Dunnett) test to determine the difference between groups. P values less than 0.05 was considered to be significant.

Results

The electrical activity of the heart, originating from the sinoatrial node, is crucial for normal cardiac function. The effects of ELF-PEMF at 1 mT and 5 mT intensities on cardiac electrical activity were examined utilizing electrocardiogram (ECG) measurements. As shown in Figure 3, ELF-PEMF exposure at 1mT and 5mT intensities had no effect on rat ECG values when compared to the sham group ($P > 0.05$).

Discussion

This study aimed to investigate the effects of 50-Hz PMF exposure at 1 mT and 5 mT intensities on rat ECG. We found that exposure to 1 mT and 5 mT for four hours per day, five days a week, for 8 weeks did not affect ECG parameters such as HR, P wave amplitude, PR interval, QRS interval, R amplitude and QT interval.

The effects of ELF-EMF exposure on cardiac function have been studied in other previous studies (21). In 1996, Korpinen and Partanen showed for the first time that ELF-EMF (1h exposure and < 6.6μT) had no effect on human systolic and diastolic blood pressure (22). Another investigation on humans found that exposure to ELF-EMF at 40 μT and 80 μT levels for 90 minutes had no effect on HR (23). Many other investigations have found that ELF-EMF exposure has no effect on heart functions (24,25). However, there are studies showing that ELF-EMF exposure has harmful effects on cardiovascular systems specifically on the HR (26,27). The reasons for these disparities in results may include differences in magnetic field exposure setup, intensity differences, and changes in the applied waveform. Especially in the results showing that ELF-EMF is effective on cardiac function, the magnitude of the applied field strength draws attention which are even above the occupational limit determined by the ICIRP (26). Although high ELF-PEMF field exposures of 1 mT and 5 mT were employed in this study, the major goal was to determine the probable effects of PEMF applications, particularly those used for therapy, on the rhythmic activity of the heart.

PEMF has been studied for its therapeutic effects in conditions such as insomnia, accelerated bone repair, and pain management. (10–12). However, relatively few research has been conducted to investigate the effects of PEMF applications on ECG parameters. According to the findings of this study, PEMF exposure at 1 mT and 5 mT had no effect on rat heart rate, P and R wave amplitude, PR and QRS time interval values, as well as corrected QT interval values.

On the other hand, the magnetic field intensity produced by the increasing number of electrical devices used in our daily lives is also increasing rapidly. As a result, it is critical to research the effects of high intensities and assess their potential effects. Furthermore, because it is a contractile organ, the heart can create its own electrical activity. This process, known as cardiac excitation-contraction coupling, involves the electrical activation of the myocyte followed by heart contraction (28). Because of its electrical characteristics, each cell alters its resting membrane potential during this process, allowing the entire heart to contract in a coordinated manner (29). The excitation-coupling system that results from this electrical activity of the heart might be influenced by both magnetic field exposure from the growing number of electronic devices around us and even by therapeutic devices. Although the negative or positive effects of the field intensities used in this study have been shown in other tissues and organs (30,31), it appears that they have no effect on the electrical activity of the heart. Interestingly, while studies demonstrate that short-term EMF exposure causes drops in heart rate, such effects vanish in prolonged exposure (32). This is due to the heart's ability to compensate for alterations generated by such exposures. The results obtained in this study need to be supported by different studies. Additionally, a magnetic field with a frequency of 50 Hz was selected in this study. Although similar intensities are used for therapeutic purposes, differences between the applied frequencies are noteworthy (12). Therefore, it is necessary to examine both the effects of ELF-PEMF at different frequencies and the effects of different exposure times. Moreover, it is thought that there may be different effects between PEMF and continuous EMF exposure applications. As a result, it is evident that more research is needed to properly understand whether ELF-EMF exposures are causal factors or therapeutic and diagnostic instruments in the development of disorders.

Study limitations

This experimental study has some limitations. The effects of ELF-PEMF exposure on rat cardiac functions were discussed through ECG evaluations. However, there is a need for the evaluation of the effects of pulsed magnetic field exposure on cardiac functions through histological and biochemical analyses as well.

Conclusion

The effects of long-term ELF-PEMF exposure of 1 mT and 5 mT on cardiac functions in rats were investigated using electrocardiogram (ECG) recordings in this study. Although such exposure has been shown to have both positive and negative effects on various tissues and organ systems, it has been found that it is ineffective against the heart's highly protected rhythmic electrical stimulation mechanism. Even if it has an effect, it is assumed that the body system can suppress it. However, special attention should be paid to long-term ELF-EMF exposures, whose effects on human health are still controversial. New studies evaluating the activities of ELF-PEMF, chronic or short-term exposures, under a range of situations, in conjunction with common real-life stressors, may aid in understanding their sincere biological consequences.

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Author Contributions: *Concept: YG. Literature Review: YG. Design: YG. Data acquisition: YG. Analysis and interpretation: YG. Writing manuscript: YG. Critical revision of manuscript: YG..*

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Evaluation of Self-Perception and Obesity Prejudice among Generation Z

Z Kuşağının Kendilik Algısı ve Obezite Önyargısının Değerlendirilmesi

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Abstract

Background: Obesity has arisen as an increasingly noteworthy public health issue worldwide, exerting its impact on nearly all countries. The objective of this study was to assess the self-perception and obesity prejudice among young individuals enrolled in health sciences programs and belonging to Generation Z.

Materials and Methods: Irrespective of the magnitude of the sample, a collective of 787 individuals, including 450 undergraduate students and 337 associate degree students, were involved in the study. Researchers utilized a "Personal Information Form" created to measure students' attitudes towards obese individuals and gather information related to nutrition, with the second section employing the "Obesity Bias Scale for Health Sciences Students (GAMS 27-OB)" for data collection.

Results: It was determined that 68.7% of the students perceived themselves as normal/average weight, while 51.5% had perceived themselves as overweight at some point in their lives. The study revealed that a significant proportion of students, including 31.0% and 64.8% respectively, exhibited bias towards those who are obese.

Conclusion: The results of our study indicate that the younger individuals belonging to Generation Z exhibit views characterized by bias against individuals with obesity. Taking proactive measures to mitigate prejudice in the educational experiences of health sciences students prior to embarking on their professional endeavors has significant importance.

Keywords: Obesity, Self-Perception, Generation Z

ÖZ

Amaç: Obezite küresel ölçekte giderek önem kazanan bir halk sağlığı sorunu olarak ortaya çıkmış ve hemen hemen her ülkeyi etkilemektedir. Bu çalışma, sağlık bilimleri bölümlerinde öğrenim gören ve Z Kuşağı içerisinde yer alan gençlerin kendilik algısı ve obezite önyargılarının değerlendirilmesi amacıyla planlanmıştır.

Gereç ve Yöntem: Araştırmada örneklem büyüklüğüne bağlı kalmadan 450 lisans ve 337 ön lisans olmak üzere toplam 787 öğrenci katılmıştır. Öğrencilerin, obez bireylere karşı yaklaşımlarını ölçmek ve beslenmeyle ilgili bilgilerinin toplanmasına yönelik araştırmacılar tarafından oluşturulmuş "Kişisel Bilgi Formu", ikinci bölümde "Sağlık Bilimleri Öğrencileri için Obezite Önyargı Ölçeği (GAMS 27-OÖÖ)" kullanılmıştır.

Bulgular: Öğrencilerin %68.7'nin kendilerini normal/ortalama ağırlıkta gördüğünü, %51.5'inin ise daha önce hayatının herhangi bir döneminde kendini şişman olarak gördüğü belirlendi. Öğrencilerin %31.0'inin obeziteye karşı önyargı eğiliminde ve %64.8'inin obeziteye karşı önyargılı olduğu bulundu.

Sonuç: Bulgular, çalışmamızda yer alan Z Kuşağı içerisindeki gençlerin obezite önyargısı tutumlarına sahip olduğunu doğrulamaktadır. Sağlık bilimlerinde öğrenim gören öğrencilerin mesleklerine başlamadan önce eğitim hayatlarında bu önyargı düzeylerini azaltacak girişimlerde bulunulması önem arz etmektedir.

Anahtar Kelimeler: Obezite, Kendilik Algısı, Z Kuşağı

Highlights

- The study found that many health sciences students, particularly Generation Z, are biased toward obese people.
- Many students consider their weight normal or average, but over half were overweight before.
- Age was positively correlated with obesity prejudice.

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Introduction

The term "generation" refers to a cohort of individuals who were born within a roughly comparable time span (1). Generations are designated by naming distinct age groups, for instance Generation X, Y, and Z. The cohort of individuals born between 1965 and 1980, Generation X follows the baby boom generation (2). One of the defining attributes of Generation X is its membership comprise self-assured individuals who possess a high degree of practical adaptability and technological proficiency (3). Generation Y, comprising individuals born between 1980 and 2000, is frequently referred to as "millennials" (2). Its numerous distinguishing characteristics set it apart from previous generations. Among its general characteristics are the following: liberal ideology, intelligence, a strong affinity for technology, and proficient technology usage. However, they also desire the highest possible standard of living (3).

Generation Z, also referred to as IGen, Gen Wii, Post Gen, and Digital Natives, has been exposed to the entirety of digital comprehension development since infancy (4,5). Generation Z is the succeeding cohort following Generation Y and previous Generation Alpha. In broad terms, he designates the mid-to-late 1990s and the early 2010s as the initial and final years of his birth years, respectively. Economic crises, conflicts, terrorism, and unemployment are at their peak during Generation Z; digitalization is manifesting its influence in every field (4).

Despite being classified as youthful individuals based on their age range, Generation Z is confronted with significant health risks. Due to the proliferation of mobile phones, computers, and devices among this generation, there is an increased allocation of time towards online activities and social media platforms. Consequently, these individuals experience reduced sleep duration, physical activity levels, and social connections. Despite this circumstance, academic achievement declines and the prevalence of severe health conditions, including obesity and melancholy, rises (6).

A multitude of definitions pertaining to self-perception can be found throughout the literature. The notion of self-perception was explained by Mind in his publication "Self and Society" as follows: "The concept of the "self" is not inherent at birth; rather, it is developed over time through social interactions and activities. It distinguishes itself from the individual's psychological organism and plays a role in the language (speech) process, which facilitates interpersonal connections" (7). Concurrently, the self-concept serves as a comprehensive and methodical framework through which we endeavor to comprehend the emotions, cognitions, and actions of others (8).

Obesity has emerged as a progressively significant public health concern on a global scale, affecting nearly every nation. Since 1980, there has been an observed increase in obesity rates worldwide by more than twofold (9). Turkey exhibits a prevalence of obesity of 32.1%, as reported by the World Health Organization in 2018 (10). Obesity prejudice refers to adverse perceptions, conclusions, convictions, and choices made concerning the weight of individuals who are overweight or obese (11). When examining the prevalence of discrimination in the United States, weight-based discrimination against individuals ranks fourth (12). Obese individuals are stigmatized in social environments and the media. They are perceived as lacking success, motivation, initiative, self-control, and organization, and have a negative body image. This form of assessment leads members of society to internalize this perception, which subsequently results in prejudiced attitudes toward rotund individuals (13).

Materials and Methods

Study design

The cross-sectionally designed research group comprised students enrolled in the Vocational School Medical Services and Techniques Program (n = 357), as well as the Faculty of Health Sciences (n = 450), at a foundation university in Gaziantep.

Patient population

During the fall semester of 2022-2023, at a foundation university in Gaziantep, the Faculty of Health Sciences had the following student quotas: Nursing: 442, Nutrition and Dietetics: 299, Physiotherapy and Rehabilitation: 259. Additionally, within the Medical Services and Techniques Department of the Vocational School, there were a total of 1460 students, with 150 specializing in Dialysis, 150 in Anesthesia, and 160 in the Emergency Medical Services Program. As per the findings of power analysis, the number of samples required to calculate sample sizes for a significance level of 0.05 is 278 when the population size is 1000 (p = 0.5, q = 0.5). In the context of power analysis, the number of samples required to calculate sample sizes for a significance level of ∓ 0.05 is 217 when the population size is 500 (p = 0.5 q = 0.5). The study intends to involve a minimum of 278 undergraduates and 217 associate degree candidates, for a total of 495 participants. The research sample consists of 787 students, irrespective of the specific magnitude of the sample.

The researchers utilized a "Personal Information Form" in the initial phase to gather data for the study. Researchers utilized a "Personal Information Form" created to measure students' attitudes towards obese individuals and gather information related to nutrition, with the second section employing the "Obesity Bias Scale for Health Sciences Students (GAMS 27-OB)" for data collection. The personal information form comprises a total of fifteen inquiries that inquire about the participants' socio-demographic characteristics. GAMS-27 Obesity Prejudice Scale; The scale is a five-point Likert type. "Strongly disagree," "strongly agree," "undecided," and "strongly agree" comprise the scale. The scale for positive items is from 5 to 1, with the option "strongly agree" serving as the starting point; the scale for negative items is from 1 to 5, with the option "strongly agree." The rating scale for positive items (2, 4, 7, 10, 11, 14, 15, 17, 20, 22, 25, 27) is from 1 to 5, with "strongly agree" representing the highest score; for negative items (1, 3, 5, 6, 8, 9, 12, 13, 16, 18, 19, 21, 23, 24, 26), the scale is from 5 to 1, with "strongly agree" representing the lowest score. The scale provides the opportunity to attain a maximum score of 135 and a minimum score of 27. It was determined that the scale had a mean score of 76.394 and a median score of 76. Upon examining the percentiles of the scores, it is determined that the 5th percentile corresponds to a score of 58, the 25th percentile to 68, the 50th percentile to 76, and the 75th percentile to 84. The score that corresponds to the 95th percentile is 96. Upon analyzing the scores in relation to positive and negative items, it was ascertained that individuals held unprejudiced views regarding obesity as their score decreased, whereas they held prejudiced views regarding obesity as their score increased. The classification of the scale score was determined by considering both the scores associated with the percentiles and the scale score's normal distribution curve The reliability coefficient (Cronbach's alpha) of the scale is 0.847. In our study, however, the Cronbach's alpha coefficient was found to be 0.888 (14).

Evaluation of GAMS-27 Obesity Prejudice Scale score

Score Range	Obesity Bias Status
Below 68.00 (Below 25th percentile)	Unbiased
68.01 - 84.99 (25th-75th percentile)	Inclined towards bias
85.00 and above (Above 75th percentile)	Biased

The independent variables of the study include gender, age, field of study, self-identification of students, whether they have experienced a period in their lives when they perceived themselves as overweight, and how they perceive obese individuals. The dependent variable is the "Obesity Bias Scale for Health Sciences Students (GAMS 27-OÖÖ)." Students were provided with information that included online links to the Personal Information Form and GAMS 27 OOO via their class representatives. The study exclusively recruited students whose birth years fell within the period from 1997 to 2004.

This study was approved by The Hasan Kalyoncu University Faculty of Health Sciences Non-Interventional Research Ethics Committee. (Date: 25.07.2023; Protocol Number: 2023/57). In addition, all participants were provided with an online explanation of the study's objectives and were required to provide informed consent by volunteering to participate.

Statistical Analysis

Utilizing Statistical Package for the Social Sciences (SPSS) 25.0, the research data were analyzed. The data were presented in the form of means (Mean) and standard deviations (SD) for continuous variables, and numbers (n) and percentages (%) for categorical variables. The Kolmogorov-Smirnov normality test yielded insignificant results ($p>0.05$) regarding the normality distribution of continuous dependent variables. The study does not focus on validation; hence, detailed discussion regarding skewness and kurtosis is unnecessary. It suffices to state that the skewness and kurtosis values fall within the acceptable range of ±1. Additionally, normality checks, such as the bell-shaped histogram and the Normal Q-Q plot, confirm the data's adherence to normal distribution assumptions. As the aforementioned characteristics are predominantly supplied by continuous variables, parametric tests were employed. The one-way ANOVA test was utilized for variables with three or more groups, while the independent sample t test was applied to variables with two groups. When the variances exhibited non-uniform distribution, the Welch test (Robust test of equality of means) was applied as a more reliable alternative to non-parametric tests. To assess the relationship between categorical variables, the Chi-Square test was employed. The statistical significance level utilized in all conducted tests was $p<0.05$.

Results

With 787 participants in total, the mean age of the group was 20.94±1.44 years. It was determined that the mean Body Mass Index (BMI) of the participants was 22.31±3.78 kg/m2. 68.5% of the students were of normal weight, 28.8% were 21 years old, 82.2% were female, 32.0% were nursing students, and 51.0% were in their

first year. The literacy rate of the mothers of 54.3% of the pupils was ascertained, while the educational attainment of the fathers of 51.0% was limited to primary school. It was ascertained that a majority of the students (68.7%) regarded their weight as normal or average, slightly more than half (51.5%) had previously perceived themselves as overweight, and 56.9% were dissatisfied with their physical appearance but did not withdraw from society. 64.4 percent of respondents consider obese individuals to be harmful, 68.1 percent say they consume more food when they are in a good mood, and 31.3 percent say they consume grains. A total of 92.9% of the students were found to be free from chronic diseases, 78.7% abstained from smoking, and 92.5% abstained from alcohol consumption (Table 1).

Table 1. Distribution of Socio-demographic Characteristics of Students (n=787)

Variables	**Mean ± SD**	**Min. – Max.**
Age (years)	20.94 ± 1.44	18-26
BMI (kg/m²)	22.31 ± 3.78	15.62-39.25
Variables and Subgroups	**Number (n)**	**Percentage (%)**
Age		
18-19 years	125	15.9
20 years	198	25.2
21 years	227	28.8
22 years	237	30.1
Gender		
Female	647	82.2
Male	140	17.8
Department		
Nursing	252	32.0
Nutrition and Dietetics	96	12.2
Physical Therapy and Rehabilitation	102	13.0
Dialysis	133	16.9
Anesthesia	146	18.6
First Aid	58	7.4
BMI		
Underweight	104	13.2
Normal Weight	539	68.5
Owerweight	114	14.5
Obese	30	3.8
Self-perceived Weight		
Underweight	170	21.6
Normal/average Weight	541	68.7
Overweight	76	9.7

Abbreviations: Mean: Mean, **SD:** Standard Deviation, **Min.:** Minimum value, **Max.:** Maximum value

The participants obtained an average GAMS-27 score of 90.49±14.07. The minimal score achieved was 54, while the maximum score reached 132 **(Table 2).**

Table 2. Distribution of GAMS-27 Scale Scores

Scales and Sub-dimensions	**Number of Items**	**Expected Min-Max**	**Observed Min-Max**	**Mean ± SD**	**Median (IQR)**
GAMS-27	27	27-135	54-132	90.49±14.07	88 (96-82)

Abbreviations: Mean: Mean, **SD:** Standard Deviation, **Min.:** Minimum value, **Max.:** Maximum value, **IQR:** Interquartile Range, **Q3:** 75th Percentile, **Q1:** 25th Percentil, **GAMS-27:** Weight Bias Scale

Upon assessing the students based on predetermined thresholds, the results indicated that 4.2% lacked prejudice against obesity, 31.0% exhibited a tendency toward prejudice, and 64.8% harbored prejudice against obesity.

An analysis was conducted to compare the rates of prejudice among students with those of their socio-demographic characteristics, including the following: "age," "class," "BMI," "education level of mother," "education level of father," "self-evaluation regarding weight," "isolation from society due to appearance," and "eating in accordance with mood" within the groups. A statistically insignificant relationship was found to

exist between the variables "alcohol use," "diet," and "chronic disease status" (p>0.05). Conversely, a statistically significant correlation was found between the following group variables: "smoking status," "gender," "department," "previously perceiving oneself as fat," and "identifying obese individuals" (p<0.05) **(Table 3)**.

Table 3. Comparison of Prejudice Status Rates and Socio-demographic Characteristics of Students

Varaiables	**Non-prejudiced**	**Tendency toward Prejudice**	**Prejudiced**	**Total**
	n (%)	n (%)	n (%)	n (%)
Gender				
Female	32 (97.0)	204(83.6)	411(80.6)	647(82.2)
Male	1(3.0)	40(16.4)	99(19.4)	140 (17.8)
Total	33(100.0)	244 (100)	510 (100)	787(100)
Test	**χ^2=6.158, p=0.046**			
Department				
Nursing	14 (42.4)	91 (37.3)	147(28.8)	252(32)
Nutrition and Dietetics	5 (15.2)	28 (11.5)	63(12.4)	96(12.2)
Physical Therapy and Rehabilitation	0(0)	40 (16.4)	62(12.2)	102(13)
Dialysis	4 (12.1)	22 (9)	107(21.0)	133(16.9)
Anesthesia	8 (24.2)	48 (19.7)	90(17.6)	146(18.6)
First Aid	2 (6.1)	15 (6.1)	41(8.0)	58 (7.4)
Total	33 (100)	244(100)	510(100)	787(100)
Test	**χ^2=28.255, p=0.002**			
Have you ever perceived yourself as overweight?				
Yes	23 (69.7)	113(46.3)	269(52.7)	405(51.5)
No	10(30.3)	131(53.7)	241(47.3)	382(48.5)
Total	33(100)	244(100)	510(100)	787(100)
Test	**χ^2=7.320, p=0.026**			
How do you describe obese people?				
Normal	14 (42.4)	96(39.3)	128(25.1)	238(30.2)
Bad	2(6.1)	8(3.3)	32(6.3)	42(5.3)
Unhealthy	17(51.5)	140(57.4)	350(68.6)	507(64.4)
Total	33(100)	244(100)	510(100)	787(100)
Test	**χ^2=19.709, p=0.001**			
Smoking status				
Yes	7 (21.2)	39(16)	122(23.9)	168(21.3)
No	26(78.8)	205(84)	388(76.1)	619(78.7)
Total	33(100)	244(100)	510(100)	787(100)
Test	**χ^2=6.194. p=0.045**			

Abbreviations: n: *Number*, **%:** *Percentage*, **Test (χ^2):** *Pearson Chi-Square test*

When comparing the rates of prejudiced attitudes among students with their socio-demographic characteristics, it was observed that there were no statistically significant relationships (p>0.05) between the variables of "age," "grade," "BMI," "mother's education level," "father's education level," "self-assessment regarding weight," "tendency to isolate oneself from society based on appearance," "eating habits based on mood," "chronic illness status," "dietary habits," and "alcohol consumption status". On the other hand,

statistically significant relationships were found (p<0.05) between the variables of "gender," "department," "previous self-perception of being overweight," "perception of obese individuals," and "smoking status" **(Table 4).**

Table 4. Comparison of GAMS-27 Scale Average Scores According to Socio-demographic Characteristics of Students (n=787)

Variables	**GAMS-27 Scale**	**Statistical Evaluation**		
	Mean ± SD	**test**	**p**	**Post Hoc***
Gender Female[1] n= 647	89.56 ± 13.90	**t=-3.488**	**0.001**	2>1
Male[2] n=140	94.10 ± 14.30			
Department				
Nursing[1] n=252	88.07 ± 13.41	**F=4.019**	**0.001**	4>1
Nutrition and Dietetics[2] n=96	89.31 ± 13.59			
Physical Therapy and Rehabilitation[3] n=102	90.24 ± 12.69			
Dialysis[4] n=133	94.47 ± 14.69			
Anesthesia[5] n=146	90.61 ± 15.20			
First Aid[6] n=58	92.31 ± 13.75			
How do you describe obese people?				
Normal[1] n=238	86.82 ± 12.94	**W=14.652**	**<0.001**	2>1-3
Bad[2] n=42	98.19 ± 16.66			3>1
Unhealthy[3] n=507	91.38 ± 13.95			
Smoking status Yes[1] n=168	92.95 ± 15.07	**t=2.697**	**0.007**	1>2
No[2] n=619	89.66 ± 13.72			

Abbreviations: n: Number**, Avg.:** Average, **SS:** Standard deviation, **1-2-3-4-5-6:** Representation of differences between groups ***Post Hoc:** Bonferroni correction, **W:** Welch test (Robust test of equality of means), **F:** One-way ANOVA test, **t:** Independent samples t-test

According to the findings, a statistically significant, weak positive correlation (r=0.097) was found between age and GAMS-27 (p=0.006). However, it should be noted that a positive correlation does not necessarily imply causation; rather, it indicates that as age increases, there is a tendency for GAMS-27 scores to increase or decrease, albeit modestly. On the other hand, a weak positive correlation (r=0.060) was observed between GAMS-27 and students' BMI, although this correlation did not reach statistical significance (p=0.090). **(Table 5).**

Table 5: Correlation Between Sociodemographic Variables and GAMS-27 Scale

Sociodemographic Variables	**GAMS-27 Scale (n=787)**	
	r	p
Age (years)	**0.097**	**0.006**
BMI (kg/m²)	0.060	0.090

Abbreviations: r: *represents the Pearson Product-Moment Correlation Coefficient.* r values between 0.1 and <0.3 indicate a weak correlation. r values between 0.3 and <0.7 indicate a moderate correlation. r values between 0.7 and <1.0 indicate a high level of correlation. p values are provided for each correlation coefficient to assess the statistical significance of the correlations.

Discussion

Ensuring proper nutrition is critical for individuals to maintain optimal health and mitigate the risk of developing chronic illnesses. (15). The literature indicates that complications associated with malnutrition are comparatively less frequent than complications related to obesity. (16).

It is critical to maintain a Body Mass Index (BMI) within the acceptable ranges during adolescence and youth (17). This is when nutritional behaviors become particularly influential. (18). Overweight and obesity have increased among members of Generation Z, a cohort that spends a great deal of time with technological devices, due to their preference for online food applications, fast food orders, and global coffee chains (19).

The average body mass index (BMI) of the participants in our research remained within the normal range as established by the World Health Organization (WHO) (20). The increasing use of contemporary technology has led to a rise in the consumption of conveniently prepared, high-calorie foods and a concomitant obesity epidemic among members of Generation Z. This demographic predominantly engages with electronic devices such as computers and mobile phones (21). Furthermore, we did not observe any statistically significant correlation between BMI and prejudice against obesity. According to the findings of Aydin et al. (2020) and Balaban et al. (2022), the majority of students enrolled in the health program were at an ideal weight (11, 22). This result may have been attributable to the fact that over half of the participants in our study had a body mass index of normal or average. Further, the composition of the research group, consisting of students pursuing degrees in health disciplines, might have contributed to this outcome. The exemplary behavior of these individuals, who will soon be health professionals, will serve as a model for overweight or obese patients who utilize their services, given that their BMI values are within normal ranges.

Our research revealed that students consumed more food when they were joyful. Adults frequently perceive food consumption and eating as a pleasant reward in circumstances where their interests and activities are restricted (23). Due to the fact that students' mobility is partially restricted during the academic year, dining can become a pastime. Generation Z exhibits a preference for consuming food that provides them with increased delight and enjoyment. As the food diversity spectrum continues to expand, they are exposed to a wider variety of novel and distinct foods, which can elicit happiness and subsequently influence their eating habits (18, 24).

Our research findings revealed that marginally more than half of the participants identified as overweight at some juncture. Furthermore, we found that over half of the participants expressed contentment with their physical appearance and did not withdraw from social interactions. Particularly during adolescence and youth, when body image is prominent and significant, how individuals perceive their own bodies and even minor flaws becomes problematic; therefore, even a slight weight gain is crucial.

Obesity, apart from being a significant contributor to health decline, presents a propensity for numerous other ailments, particularly those of the metabolic and cardiovascular varieties (25). Due to the fact that health department students are cognizant of this, over fifty percent of the participants in our study consider obese individuals to be hazardous.

One critical factor that impacts individuals' well-being is the quantity and composition of their food intake (26). According to research, Generation Z places a greater emphasis on weight management and associates it with maintaining good health. Additionally, despite not enjoying them, Generation Z prefers nutritious foods, according to observations (27). An examination of the students' dietary patterns reveals that they consume cereals predominately, followed by fast food and a meat-based diet. The environmental conditions have a substantial impact on decisions pertaining to food consumption (28, 29). The prevalence of grain and meat-based diets may vary depending on the geographical region in which one resides. Furthermore, it is hypothesized that the research group's student status contributes to the widespread consumption of fast food nutrition.

More than half of the participants exhibited prejudice towards obesity. Prior research has yielded results that are comparable to those of our study (30). It is crucial to address the significant degree of prejudice present in the research group, as they will be exposed to overweight and obese individuals on a regular basis as a result of their chosen profession. Efforts should be made to mitigate this prejudice during the students' academic years, prior to commencing their professional careers.

The variables included in our research were the following: age, class, BMI, educational attainment of the mother and father, self-perceived overweight status, tendency to isolate oneself from social interactions due to appearance, occurrence of cravings for food, chronic illness, dietary habits, smoking status, and alcohol consumption. Nevertheless, no statistically significant correlation was found between prejudice against obesity and $p>0.05$. A statistically significant relationship ($p<0.05$) was observed between the variables of gender, department, past self-perceived fatness, evaluation of obese individuals, and prejudice against obesity. The research conducted by Sayın Kasar et al. (2019), Sert et al. (2019), and Usta et al. (2015) identified a correlation between prejudice against obesity and the following variables: age, grade level, BMI, educational status of both parents (both mothers and fathers), smoking, and alcohol use. is not present (31). In contrast, certain studies have identified a correlation between age, BMI, and prejudice against obesity (32). The relationship between age, grade level, body mass index, and prejudice against obesity is shaped by individuals' lifelong experiences, perceptions, and societal norms, often resulting from comparisons related to body image, social interactions, and external appearances.

Our research revealed a positive correlation between age and prejudice against obesity. Analogous findings to the present investigation were observed in the scientific inquiries of Işık et al. (2019) and Phelan et al. (2014) (33). The connection between age and increasing prejudice against obesity can be explained by the deepening of individuals' acquired biases and negative perceptions within society as they age.

As a rule, women are more likely than men to experience dissatisfaction with the physical alterations that occur to them (34). The issue of obesity becomes more pronounced among women as a result of their apprehension regarding weight gain and the potential loss of their aesthetic appeal. This may result in a more pessimistic perception of obese individuals among women (38 35). In our investigation, however, the exact opposite occurs. Men have been observed to be more prejudiced than women regarding obesity. In contrast to the findings of our study, Mengi Çelik et al. (2022) discovered that women held more prejudices against obesity than men did, and that their awareness of these biases was substantial (16). The reason why men exhibit higher levels of prejudice towards obesity compared to women may stem from various factors such as societal gender norms, media influence, cultural stereotypes, and individual experiences.

An observation was made that students enrolled in the dialysis program held more extreme prejudices against obesity than students enrolled in other programs. Due to the lack of a direct study comparing students enrolled in the dialysis program and those enrolled in the health department, the existing body of research has yielded inconsistent findings across programs. Research has indicated that prejudice has a tendency to increase among health department students, occasionally among midwives, nurses, or students from other programs (36,37). The study's findings revealed that students who characterized the situation of obese individuals as undesirable scored higher on the average obesity prejudice scale, whereas those who characterized the situation as normal and unhealthy displayed lower scores but were more prejudiced against obesity.

Study limitations

The findings may be limited by the study's foundation university setting. Study participants may not reflect other countries or areas due to demography and culture.

Conclusions

More than half of the participants exhibited prejudice towards obesity. Additional studies and methodologies should be made available to undergraduate and associate degree students in order to enhance their understanding of diet and physical activity, hence mitigating adverse alterations in body composition. Additionally, it should prioritize the development of treatments aimed at mitigating students' prejudices.

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Is Cystic Duct Anastomosis a Suitable Option in the Presence of Double Bile Ducts in Living Donor Liver Transplantation?

Canlı Vericili Karaciğer Naklinde Çift Safra Kanalı Varlığında Sistik Kanal Anastomozu Uygun Bir Opsiyon Olabilir mi?

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Abstract

Background: The biliary duct anastomosis performed during living donor liver transplantation (LDLT) surgery is a critical surgical procedure that significantly influences postoperative patient mortality and morbidity. The aim of the present study was to evaluate the feasibility of utilizing the recipient's cystic duct along with the common bile duct in situations where biliary duct anastomosis becomes necessary.

Materials and Methods: In 16 of 49 liver transplants performed at Harran University Faculty of Medicine Organ Transplant Clinic between 2018 and 2021, the donor graft had double bile duct orifice. For the anastomosis of these bile ducts, the cystic duct was used along with the common bile duct in 9 patients, whereas in 7 patients, reconstruction was completed using various techniques without utilizing the cystic duct. Patients who underwent anastomosis to the cystic duct and those who underwent alternative techniques were evaluated in terms of difficulty and complications.

Results: Of the 16 patients included in the study, 7 (44%) were female and 9 (56%) were male. The mean age was 51.18 (±12.77) years. Anastomosis was performed to the cystic duct in nine patients. Regarding postoperative complications, among patients who underwent anastomosis to the cystic duct, only one developed bile leakage, which was treated with endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous drainage. Complications developed in 3 of 7 patients in the other group. The two cases of bile duct strictures were treated with ERCP, while the bile leakage in one patient was conservatively monitored, and the leakage resolved spontaneously.

Conclusion: The utilization of the cystic duct in bile duct anastomosis in LDLT may offer advantages, especially in grafts with multiple and distant bile ducts. When preparing donors for LDLT, when multiple bile ducts are detected in the donor liver preoperatively or intraoperatively, it should be kept in mind that in cases with a narrow donor pool, the cystic duct can also be used in the anastomosis.

Keywords: Living donor liver transplantation, biliary anastomosis, biliary anastomosis to cystic duct

ÖZ

Amaç: Canlı vericili karaciğer nakli (CVKN) ameliyatı sırasında yapılan safra yolu anastomozu postoperatif hasta mortalite ve morbiditesini etkileyen kritik öneme sahip cerrahi bir işlemdir. Bu çalışmanın amacı; safra yolu anastomozu için mecbur kalınan durumlarda koledok ile birlikte alıcı sistik kanalının da kullanılabilirliğini değerlendirmektir.

Gereç ve Yöntem: Harran Üniversitesi Tıp Fakültesi Organ Nakli Kliniği'nde 2018-2021 yılları arasında gerçekleştirilen 49 karaciğer naklinden 16'sında donör greftinde çift safra yolu ağzı mevcuttu. Bu safra yollarının anastomozları için, 9 hastada koledok ile birlikte sistik kanal kullanılırken, 7 hastada ise sistik kanal kullanılmadan farklı tekniklerle rekonstrüksiyon tamamlandı. Sistik kanala anastomoz yapılanlar ve diğer teknikler, zorluk ve komplikasyon açısından değerlendirildi..

Bulgular: Çalışmaya dahil edilen 16 hastanın 7 (% 44)'si kadın, 9 (% 56)'u erkekti. Yaş ortalaması 51.18 (±12,77) idi. Dokuz hastada anastomozda sistik kanal kullanıldı. Postoperatif komplikasyonlar açısından sistik kanala anastomoz yapılan hastaların sadece 1 tanesinde safra kaçağı gelişti, bu hasta endoskopik retrograd kolanjiopankreatografi (ERCP) ve perkütan drenaj ile tedavi edildi. Diğer gruptaki 7 hastanın ise 3'ünde komplikasyon gelişti. Oluşan 2 safra yolu darlığı ERCP ile tedavi edilirken, 1 hastada ki safra kaçağı ise konservatif olarak takip edildi ve kaçak kendiliğinden durdu.

Sonuç: CVKN'de safra yolu anastomozunda sistik kanal kullanımı, çoklu ve birbirinden uzak safra yolu olan greftlerde avantaj sağlayabilir. CVKN için donör hazırlanırken donör havuzunun dar olduğu hastalarda, donör karaciğerinde preoperatif veya intraoperatif çoklu safra yolu tespit edildiğinde anastomozda sistik kanalın da kullanılabileceği akılda tutulmalıdır.

Anahtar Kelimeler: Canlı vericili karaciğer nakli, safra yolu anastomozu, sistik kanala safra anastomozu

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Highlights

- Bile duct anastomosis is of critical importance in liver transplantation.
- Bile anastomosis to the cystic duct can be performed in cases where it is necessary.
- Bile complications can be managed with minimally invasive treatments.

Introduction

Biliary anastomosis in LDLT continues to maintain its critical importance due to its high potential for complications. Biliary complications not only delay postoperative recovery but also significantly impact the quality of life and may reduce graft survival (1).

The presence of multiple distant bile ducts in the donor graft may make anastomosis to the right and left bile ducts of the recipient impossible. Although multiple ducts can be obtained with a high hilar division of the recipient bile ducts, the technical difficulty it poses during anastomosis and the vascularization pattern of the bile ducts, which tends to be from bottom to top, make the proximal bile ducts more prone to ischemia. Therefore, this procedure is generally not recommended. In such cases, various techniques such as hepaticojejunostomy (HJ), multiple anastomoses to the common bile duct, and anastomosis to the cystic duct are attempted to address the issue (1, 2).

Following HJ performed for biliary drainage in the recipient, there may be some disadvantages such as the potential development of enteric leaks, limitations for endobiliary interventions in case of biliary complications, and delayed enteral nutrition. Additionally, edema developing in the intestinal wall due to portal hypertension and portal vein thrombosis presents another challenge from a technical perspective for the anastomosis (3). Furthermore, performing anastomosis to the bile ducts from a very proximal level in the recipient may lead to a swan-neck deformity. Despite a technically correct anastomosis, the presence of a long bile duct can lead to angulation and result in functional obstruction. This can make therapeutic ERCP very difficult.

Due to such circumstances, performing anastomosis to the cystic duct can be a viable solution in biliary reconstruction (2, 14, 15).

The aim of the present study was to investigate whether the cystic duct may be a viable option for biliary anastomosis in LDLT, in grafts with multiple bile ducts and particularly in anatomically challenging cases.

Materials and Methods

Ethical approval was obtained from the Harran University Ethics Committee with decision number HRÜ/23.25.07 dated 28.12.2023 and was implemented in accordance with the rules of the Declaration of Helsinki. Informed consent was obtained from all patients.

The data of 49 patients who underwent liver transplantation in our clinic between June 2018 and May 2021 were retrospectively reviewed. Cadaveric liver transplantation was performed in 11 of 49 patients (22%). The remaining 38 patients (78%) all underwent living donor right lobe liver transplantation. Among the 38 patients, 22 (58%) had a single bile duct, while 16 (42%) had double bile ducts. Patients with double bile ducts were divided into two groups: those in whom one bile duct was anastomosed to the cystic duct, and those in whom other techniques were used to complete the bile duct anastomoses.

Patients' age, gender, primary diagnosis, technique used for biliary anastomosis, use of internal stent, feeding, postoperative biliary complications, and graft weight were recorded. Additionally, the preoperative Model for End-Stage Liver Disease (MELD) scores, operative times, durations of intensive care unit (ICU) stay, and total follow-up periods of these patients were also noted.

Patients who underwent living donor right lobe liver transplantation and developed double bile ducts when the biliary tree was divided during surgery were included in the study. Patients who underwent cadaveric liver transplantation and patients with single bile duct were excluded from the study.

In patients undergoing anastomosis to the cystic duct, the anastomosis was performed using 5/0 or 6/0 polydioxanone (PDS) sutures, depending on tissue thickness. The posterior aspect of the anastomosis was sutured continuously with PDS sutures, while the anterior aspect was individually sutured with PDS sutures as well. The same technique was applied for the second anastomosis made to the main hepatic duct. In both anastomoses, once suturing of the posterior aspect was completed, an appropriately sized internal stent was passed into the lumen, followed by completion of suturing of the anterior aspect (Figure 1).

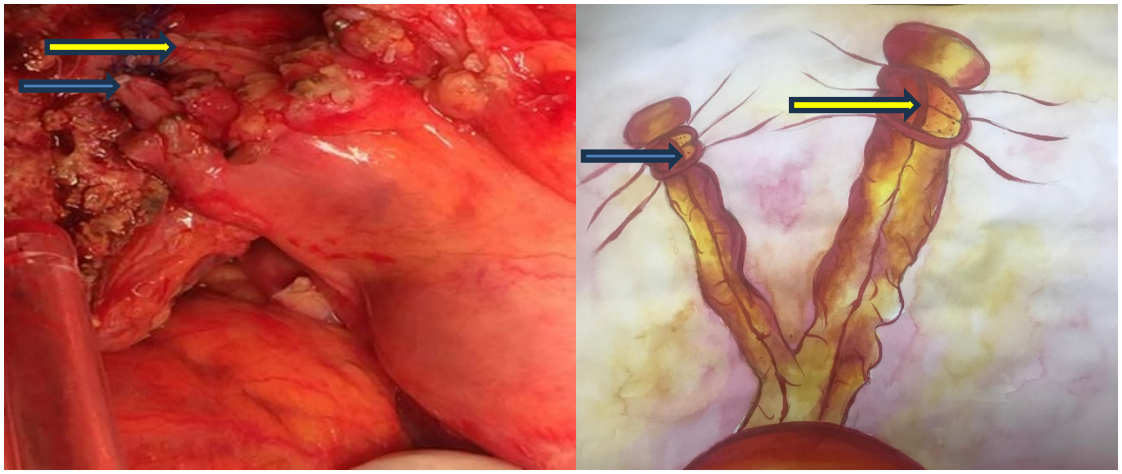

Figure 1: Blue arrow cystic duct anastomosis, yellow arrow main hepatic duct anastomosis and illustration of the cystic duct and common hepatic duct

Statistical Analysis

All statistical analyses were performed using SPSS version 21.0 (SPSS Inc, Chicago, IL) software package. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test the conformity of continuous variables to normal distribution. All continuous variables were presented as mean ± standard deviation and median (max - min). For normally distributed variables, the Student's t-test was used to compare differences between two independent groups. For non-normally distributed variables, the Mann-Whitney U test was used. ANOVA test was used to compare normally distributed variables between more than two groups, whereas Kruskal-Wallis test was used for non-normally distributed variables. Categorical variables were analyzed using the Chi-square test. A p value of <0.05 was considered statistically significant in all analyses.

Results

Between June 2018 and May 2021, a total of 49 patients underwent liver transplantation at our clinic. Of these patients, 11 received cadaveric liver transplants and 38 underwent living donor liver transplantation. In living donor transplants, 22 patients had a single bile duct and 16 patients had double bile ducts (Table 1). Of the 16 patients with double bile ducts, 9 (56%) were male and 7 (44%) were female. The mean age of the patients was 51.18 (±12.77) years.

In cadaveric liver transplants, only 1 (9%) patient developed complications during postoperative follow-up. Biliary stricture developed in this patient, and was resolved after endoscopic retrograde cholangiopancreatography (ERCP). Among the 22 patients who underwent living donor right lobe liver transplantation and had a single bile duct, complications were encountered in 5 (23%) cases. Biliary stricture in three patients was resolved by ERCP and bile leakage in two patients was resolved by ERCP and percutaneous drainage.

Table 1: Distribution of patients according to the number of bile ducts

Variables		Female	Male	Total
Bile Duct Anastomosis	Single Bile Duct	12	21	33
	Double bile duct and no anastomosis to the cystic duct	2	5	7
	Double bile duct and anastomosis to the cystic duct	5	4	9
Total		19	30	49

Of the 16 living donor liver transplant patients with double bile ducts, the cystic duct was used for anastomosis of one of the bile ducts during biliary reconstruction in 9 patients. In 5 of the remaining 7 patients, reconstructions were performed in different localizations of the common bile ducts, and additional HJ reconstructions were performed in 2 patients. In patients with double bile ducts, the anterior sector of the transplanted right lobe graft was draining as a separate bile duct, while the posterior sector was also draining as a separate bile duct. A separate anastomosis was performed for each sector of the bile duct. Table 2 presents the demographic data of the patients and information regarding which anatomical structure the biliary anastomoses were performed on.

In patients who underwent anastomosis to the cystic duct, biliary complications occurred in only one patient (11%). The bile leakage that occurred in this patient was brought under control with ERCP and percutaneous drainage. In the other group, biliary complications developed in 3 of 7 patients (42%). Of these three patients, two developed biliary stricture and one developed bile leakage. Biliary strictures in two patients were treated with ERCP, while bile leakage in one patient resolved spontaneously with conservative follow-up (Table 2).

The mean follow-up period of our patients was 492.18 (±279.10) days. The mean MELD score was 17.68 (±5.88). The median graft weight was 700 (500-1150) g and the mean operative time was 12.5 (8-15) hours. The median duration of ICU follow-up was 5 (2-17) days (Table 3).

The patients with double bile ducts who underwent biliary anastomosis to the cystic duct and those who did not were statistically compared in terms of certain parameters. There was no significant difference in terms of mean age, MELD score, and graft weight (Table 3).

When comparing the operative times to assess the technical difficulty of biliary anastomosis, no significant difference was found between the two patient groups (p=0.231, Table 3).

Similarly, when comparing the two patient groups in terms of ICU stay, no significant difference was found (p=0.340, Table 3). The mean follow-up durations after discharge were significantly lower for patients who underwent anastomosis to the cystic duct compared to those who did not (p=0.008, Table 3).

Table 2: Demographic information of patients with double bile ducts and data regarding anastomoses

N	Primary Disease	Age	Sex	Graft Weight	Number of Bile Ducts	Internal Stent	Feeding Catheter	Anterior Sector	Posterior Sector	Bile-related Complication
1	HBV	58	M	580	2	+	-	Right	Left	-
2	HCV	67	F	700	2	+	-	Choledoch	Cystic Duct	Bile Leak, ERCP, Percutaneous Drainage
3	PSC	63	M	730	2	+	-	HJ	Choledoch	Bile Leak, Conservative Follow-up
4	HBV	21	M	705	2	+	-	Right	Choledoch	Bile Duct Stenosis, ERCP
5	Cryptogenic	38	F	630	2	+	-	Right	Left	Bile Duct Stenosis, ERCP
6	HBV	59	M	600	2	+	-	Right	Choledoch	
7	HBV	56	M	620	2	+	-	Choledoch	Cystic Duct	
8	HBV	60	M	770	2	+	-	Choledoch	Right	
9	Secondary Biliary Cirrhosis	53	F	690	2	+	-	HJ	Choledoch	
10	HBV, HCV	46	F	500	2	+	-	Cystic Duct	Left	
11	Cryptogenic	57	F	970	2	+	-	Choledoch	Cystic Duct	
12	HBV	56	M	810	2	+	-	Cystic Duct	Choledoch	
13	Cryptogenic	31	M	1150	2	+	-	Cystic Duct	Choledoch	
14	HBV	53	F	905	2	+	-	Cystic Duct	Choledoch	
15	HBV	39	M	890	2	+	-	Cystic Duct	Choledoch	
16	Cryptogenic	62	F	640	2	+	-	Choledoch	Cystic Duct	

Abbreviations: N: Patient Number ERCP: Endoscopic retrograde cholangiopancreatography, HBV: Hepatitis B, HCV: Hepatitis C, HJ: Hepaticojejunostomy, PSC: Primary Sclerosing Cholangitis,

Table 3: Comparative data according to the number of bile ducts

Type of Anastomosis		**Double bile duct and no anastomosis to the cystic duct**	**Double bile duct and anastomosis to the cystic duct**	**Total**	***p*-value**
Number of patients		7 (% 44)	9 (% 56)	16	
Mean age (year)		50.29 ± 15.32	51.89 ± 11.34	51.18 ± 12.77	0.813
Sex	Male	5	4	9	
	Female	2	5	7	
Mean follow-up (day)		686.29 ± 137.96	341.22 ± 270.53	492.18 ± 279.10	0.008*
Mean MELD score		17.57 ± 4.28	17.78 ± 7.16	17.68 ± 5.88	0.947
Graft weight		690 (580-770)	810 (500-1150)	700 (500-1150)	0.140
Operative time (hours)		12 (8-15)	13 (11-15)	12.5 (8-15)	0.231
Postoperative intensive care unit stay (day)		5 (2-6)	5 (2-17)	5 (2-17)	0.340

Abbreviations: MELD: Model for end stage liver disease

Discussion

Biliary complications in LDLT are reported in the literature with a wide range. ranging from 0.4% to 67%. and they continue to be the leading cause of postoperative morbidity (4. 12. 13). Secondary to biliary complications. delayed healing. decreased graft survival. and decreased quality of life may be observed. As a result of these complications. the patient remains hospitalized for a long time and cannot be discharged. The risk of biliary complications may increase due to factors such as having smaller and multiple bile ducts and devascularization during hilar dissection (5). Increased donor age also leads to an increase in biliary morbidities (1). In the present study. none of the biliary complications experienced in patients with single or double bile ducts resulted in a reduction of graft survival or mortality in the patients. Biliary complications were managed with rapid interventions. and necessary interventional procedures were promptly implemented. No patient required reoperation or experienced mortality due to this reason.

In their study. Pamecha et al. found that the number of bile ducts and the number of anastomoses were independent risk factors for the development of biliary complications in adults. In this study. biliary reconstruction with HJ was frequently performed in patients with multiple bile ducts (6). In the present study. the rate of biliary complications in cadaveric liver transplants with choledochocholedochostomy remained at 9%. In LDLT. however. the complication rate increased and exceeded 20%. independent of the number of bile ducts (single or double). In fact. this result alone shows that the most optimal option in liver transplantation is cadaveric liver transplantation and that countries should put more effort into cadaveric organ donation.

In a meta-analysis. Chok et al. identified factors determining the type of biliary reconstruction in liver transplantations as the type of liver disease. graft size. width and number of bile ducts in the donor and the recipient. presence of known bile duct disease. history of abdominal trauma or surgery. and presence of inflammatory bowel disease (7). In the present study. we did not differentiate patient groups based on the primary diagnosis. In other words. we did not exclude any diagnostic group from the study. Furthermore. statistical analysis showed that there was no significant difference in graft weight among the compared groups ($p=0.060$. Table 3). In larger patient groups. the preferred biliary anastomosis technique can be determined according to the patient's primary diagnosis and the results can be compared. Since our number of patients is not large enough to allow such a study. centers with larger patient groups can conduct such studies and interesting results can be obtained.

Although there are numerous studies in the literature on the overall incidence of biliary complications in liver transplantation. the number of studies focusing on anastomoses performed in the presence of multiple bile ducts is limited (1. 4. 8. 9). Therefore. it continues to be a topic of discussion in LDLT. The main limitation of the present study was the small number of patients. which restricted us from making definitive statements on this issue. In a series of 5 patients in whom cystic duct anastomosis was performed end-to-end and end-side-to-side in LDLT patients with multiple bile ducts. Malago et al. yielded promising results. They emphasized the prerequisite of having a sufficiently long and vascularized cystic duct for this procedure (10). In addition. the study by Salvalaggio et al. demonstrated that the presence of multiple bile ducts is a risk factor for biliary complications. especially in pediatric patients (11). Our patient group consisted only of adult patients. Since growth and development continue in pediatric patients. the most effective technique for biliary anastomosis may vary in these patients. Studies on this subject with a large number of patients will shed light on finding the most effective technique in the pediatric patient group. In the study by Muhammed et al. it was found that complications in LDLT patients with multiple bile ducts were similar to those in patients with single bile duct (4). In two recent studies by Kollmann and Arıkan. it was stated that the number of bile ducts and the type of anastomosis did not alter the outcomes in LDLT (1. 8). In their meta-analysis. Zhang et al. stated that although anastomosis to the cystic duct for biliary reconstruction is never the first choice. it can be used in the presence of multiple bile ducts if there is a reasonably wide cystic duct (9). In the present study. biliary complications were observed in only 1 out of 9 patients. which is encouraging regarding the feasibility of using the cystic duct for biliary anastomosis.

Study limitations

The retrospective nature of our study. its single-center design. and the limited number of cases can be considered as limiting factors.

Conclusion

In conclusion. despite all the advancements in surgery. biliary complications continue to be a significant problem in LDLT. Despite the conflicting data in studies with a limited number of cases in the literature. in our experience. the postoperative outcomes of cases with cystic duct anastomosis are certainly not poor. Even if biliary complications develop. endoscopic management is possible. We believe that cystic duct anastomoses performed with good surgical technique may have similar or even better postoperative outcomes compared to other types of anastomoses. However. large prospective series with longer

postoperative follow-up are needed to evaluate the effectiveness of cystic duct anastomosis in biliary reconstruction.

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Anxiety and depression levels of patients undergoing external dacryocystorhinostomy for tear duct obstruction

Gözyaşı kanalı tıkanıklığı nedeniyle eksternal dakriyosistorinostomi yapılan hastaların anksiyete ve depresyon düzeyleri

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Abstract

Background: The purpose of this study was to evaluate the impact of treatment on psychological well-being by looking at changes in anxiety and depression levels in patients receiving treatment for tear duct obstruction.

Materials and Methods: Forty patients who had been diagnosed with tear duct obstruction and receiving dacryocystorhinostomy (DSR) were included in our prospective cohort study. The Beck Anxiety and Depression Inventory, two standardized psychometric measures, were used to measure the individuals' levels of anxiety and depression both before and after DSR treatment.

Results: The study comprised 40 patients in total, 16 (40%) of whom were male and 24 (60%) of whom were female. The number of patients in the "minimal anxiety" class climbed to 37 (92.5%) after DSR, compared to 22 (55%) patients in the class prior to DSR, based on the patients' anxiety levels. There was a significant change ($p<0.001$) in the median Beck anxiety scores before and after DSR. The median was 0 after it was 6.5 previously. There was a significant change ($p<0.001$) between the median Beck depression ratings before and after DSR. The median after was 13, compared to the prior median of 14. The results indicate that the scores for anxiety and depression decreased in a way that was statistically significant.

Conclusion: In summary, this study represented a significant advancement in our understanding of the anxiety and sadness experienced by patients having DSR for tear duct obstruction. The study's noteworthy reduction in the levels of depression and anxiety implies that DSR might be beneficial for psychological as well as physical health.

Keywords: Dacryocystorhinostomy, Anxiety, Depression

ÖZ

Amaç: Bu çalışmanın amacı, gözyaşı kanalı tıkanıklığı nedeniyle tedavi gören hastalarda anksiyete ve depresyon düzeylerindeki değişikliklere bakarak tedavinin psikolojik iyi oluş üzerindeki etkisini değerlendirmektir.

Gereç ve Yöntem: Prospektif kohort çalışmamıza gözyaşı kanalı tıkanıklığı tanısı konan ve dakriyosistorinostomi (DSR) uygulanan 40 hasta dahil edildi. DSR tedavisi öncesinde ve sonrasında bireylerin anksiyete ve depresyon düzeylerini ölçmek için iki standardize psikometrik ölçüm olan Beck Anksiyete ve Depresyon Envanteri kullanıldı.

Bulgular: Çalışmaya 16'sı (%40) erkek ve 24'ü (%60) kadın olmak üzere toplam 40 hasta dahil edilmiştir. Hastaların anksiyete düzeylerine göre DSR öncesinde "minimal anksiyete" sınıfında yer alan 22 (%55) hasta varken, DSR sonrasında bu sayı 37'ye (%92,5) yükselmiştir. DSR öncesi ve sonrası Beck anksiyete skorlarının medyanında anlamlı bir değişiklik ($p<0.001$) olmuştur. Daha önce 6,5 olan medyan 0'a düşmüştür. DSR öncesi ve sonrası ortanca Beck depresyon puanları arasında anlamlı bir değişiklik ($p<0,001$) vardı. Önceki medyan 14 iken, DSR sonrası medyan 13 olmuştur.

Sonuç: Özetle, bu çalışma gözyaşı kanalı tıkanıklığı nedeniyle DSR uygulanan hastaların yaşadığı kaygı ve üzüntüyü anlamamızda önemli bir ilerlemeyi temsil etmektedir. Çalışmanın depresyon ve anksiyete düzeylerinde kayda değer bir azalma sağlaması, DSR'nin fiziksel sağlık için olduğu kadar psikolojik sağlık için de faydalı olabileceğine işaret etmektedir.

Anahtar Kelimeler: Dakriyosistorinostomi, Anksiyete, Depresyon

Highlights

- Investigates the association between anxiety and depression and external DSR surgery for tear duct obstruction.
- Findings can inform patient counseling and perioperative management for DSR by understanding the emotional well-being of patients undergoing this procedure.

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Introduction

The state of one's eyes greatly affects their quality of life. In addition to resulting in vision loss, eye illnesses and disorders can also have psychological repercussions. The anxiety and depression levels of patients receiving treatment for tear duct obstruction (DSR - Dacryocystorhinostomy) will be the main topic of this essay. DSR is a surgical technique used to rectify tear flow, and research has demonstrated how positively this treatment affects psychological outcomes (1, 2).

The problem known as a plugged tear duct stops tears from draining normally. Patients may have discomfort, wetness, edema, and an increased risk of infection in their eyes as a result of this. DSR is a surgical procedure that is utilized to clear this obstruction and provide symptom relief for patients (2–5).

Physical health issues are frequently linked to depression and anxiety. These psychiatric disorders may be more common in people with eye illnesses, particularly those that are persistent. Additionally, social isolation and a lower quality of life are two characteristics that may be brought on by eye disorders and increase the likelihood of anxiety and depression (1, 2, 5, 6). This study looked into how individuals receiving DSR for tear duct obstruction changed in terms of their feelings of anxiety and depression.

Materials and Methods

The ophthalmology department gave standardized psychometric measures (the Beck Anxiety Inventory and Beck Depression Inventory) to patients who were scheduled for DSR in order to quantify their anxiety and depression both before and after the procedure. A period before and after DSR was established, with a minimum of one week and a maximum of one month. Excluded patients were those with patients diagnosed with any psychiatric disease or using psychiatric medication, those whose data on the scales used were inconsistent or missing, and those who declined to participate in the study without providing written informed consent. Evaluations of the disparities between the classes and the scale scores were also used to make classifications. Before beginning the study, ethical approval was acquired from the clinical research ethics committee of Adana City Training and Research Hospital (Meeting number: 126, Date: 11.05.2023, Decision no: 2553). and was implemented in accordance with the rules of the Declaration of Helsinki.

Informed consent was obtained from all patients.

The Beck Anxiety Inventory (BAI) is a scale of evaluation created by Beck and associates that is used to ascertain how frequently a person experiences anxiety symptoms (7). It is a 21-item Likert-type scale with a score range of 0 to 3. There are four categories for anxiety: minimum (0–7 points), mild (8–15 points), moderate (16–25 points), and severe (26–63 points). Ulusoy et al. conducted a validity and reliability assessment in Turkey, and they discovered that the internal consistency coefficient was 0.93 (8).

The Beck Depression Inventory (BDI) was created by Beck and colleagues. This depression rating scale consists of 21 questions in total, with each response's ratings between 0 and 3 added together to form the total (8). The scale is rated as minimal depression between 0 and 9, mild mood disturbance between 10 and 16, moderate depression between 17 and 29, and severe depression between 30 and 63, in accordance with the relevant score ranges. Hisli conducted a study on the validity and reliability of the scale in Turkey, and the results showed that the internal consistency coefficient was 0.74 (10).

Statistical Analysis

Data analysis was done using IBM SPSS V23. The Kolmogorov-Smirnov test was used to determine if the data conformed to a normal distribution. When comparing data from paired groups that did not have a normal distribution, the Wilcoxon test was employed. The chi-square test was employed to compare patients who were categorized based on the scales. The findings of the analysis were displayed as mean ± standard deviation, median (minimum - maximum) for quantitative variables, and frequency (%) for categorical variables. A significance threshold of $p<0.05$ was used.

Results

The study included 40 patients in all, 16 (40%) males and 24 (60%) females. 45.03 ± 17.92 years was the mean age, and 46.5 (18-88) was the median. Table 1 displays frequency data along with descriptive information.

Based on the patients' anxiety scores, the "minimal anxiety" class comprised 22 (55%) individuals prior to DSR administration; however, after DSR, the number of individuals in this class rose to 37 (92.5%). With regard to the patient classification based on their depression scores, the proportion of individuals in the "minimal depression" class rose from 12 (30%) to 14 (35%) following the use of DSR. When the values for the anxiety and depression classifications were compared before and after the DSR, a statistically significant association was discovered (p values 0.008, <0.001, respectively) (Table 2). Figure 1 displays the number changes of the anxiety and depression score classes.

Table 1. Descriptive statistics

	Frequency (n)	Percentage (%)
Gender		
Male	16	40
Female	24	60
Marital Status		
Married	27	67.5
Single	13	32.5
Education Status		
Illiterate	5	12.5
Primary education	12	30
Secondary education	3	7.5
High School	8	20
University and above	12	30

Table 2. Comparing the scale values based on their categories before and after the DSR

	Before DSR n (%)	After DSR n (%)	p*
Beck Anxiety Classification			
Minimal anxiety (0-7 points)	22 (55)	37 (92.5)	
Mild anxiety (8-15 points)	8 (20)	3 (7.5)	**0.008**
Moderate anxiety (16-25 points)	10 (25)	0 (0)	
Severe anxiety (26-63 points)	0 (0)	0 (0)	
Beck Depression Classification			
Minimal depression (0-9 points)	12 (30)	14 (35)	
Mild depression (10-16 points)	14 (35)	17 (42.5)	**<0.001**
Moderate depression (17-29 points)	12 (30)	8 (20)	
Severe depression (30-63 points)	2 (5)	1 (2.5)	

Abbreviations: *Chi-square test

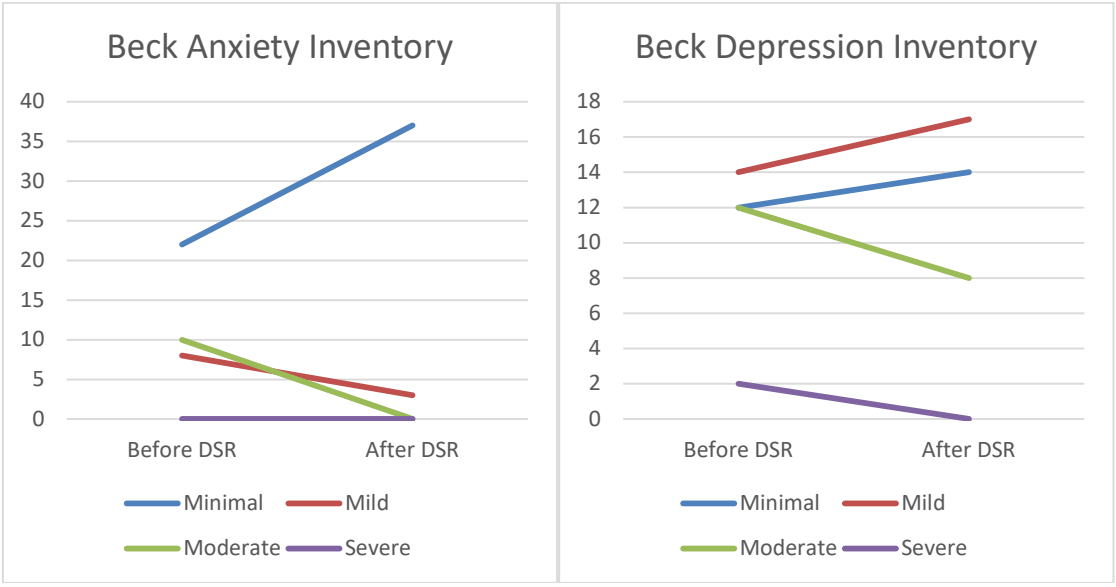

Figure 1. Before and after the DSR treatment, the curves of the scale score groups

There was a significant change ($p<0.001$) in the median Beck anxiety scores before and after DSR. The median was 0 after it was 6.5 previously. There was a significant change ($p<0.001$) between the median Beck depression ratings before and after DSR. Table 3 shows that the median after was 13, compared to the prior median of 14. The results indicate that the scores for anxiety and depression decreased in a way that was statistically significant.

Table 3. Scale-based comparison of results prior to and following DSR

	Mean ± SD	Mean (Min-Max)	Test Statistic	p*
Beck Anxiety score Before DSR	8.95 ± 7.48	6.5 (0 - 24)	-4.940	**<0.001**
Beck Anxiety score After DSR	1.60 ± 2.53	0 (0 - 9)		
Beck Depression score Before DSR	14.08 ± 8.97	14 (0 - 40)	-3.958	**<0.001**
Beck Depression score After DSR	12.40 ± 8.27	13 (0- 40)		

Abbreviations: *Wilcoxon test

Discussion

This study assessed the anxiety and depression levels of individuals undergoing DSR for blocked tear duct both prior to and after the procedure. According to the study, patients who had DSR had a considerable reduction in their symptoms of anxiety and depression. These results imply that psychological issues like anxiety and depression may be exacerbated by or caused by DSR.

The congestion caused by the blocked tear duct may lead to symptoms such as watering, redness and stinging in the eye. These symptoms may negatively affect the quality of life of patients and lead to psychological problems (1-3). The findings of the study suggest that DSR may be beneficial for psychological problems caused by blocked tear duct. DSR reduces ocular symptoms by relieving the congestion caused by blocked tear duct. This improves the quality of life of patients and helps to reduce psychological problems.

Lemaitre et al. (11) observed a similar drop in anxiety levels in patients following DSR, based on various means of reducing anxiety that occur prior to DSR. The study's conclusions also align with those of previous investigations. The prevalence and severity of anxiety and depression in people with dry eye were investigated by Wan et al. in a meta-analysis of 22 research involving about 3 million patients. The importance of ophthalmologists being aware of potential psychiatric comorbidities was underlined (12). Our study's results highlight the fact that applying DSR will lower anxiety and depressive symptoms. DSR has been demonstrated in the study by Luo et al. to improve quality of life in patients with acute dacryocystitis, reduce pain intensity, soothe negative emotions, and enhance postoperative self-care abilities (13).

The incidence of depression and anxiety disorders was found to be higher in patients with nasolacrimal duct obstruction than in the general population in a study by Guo et al. highlighting the significance of depression and anxiety screening and psychosocial support that can improve the quality of life and patients' compliance with medical appointments. According to the study, 13.1% of patients experienced mild-to-severe depression and 63.4% of patients had severe anxiety (5). There were no patients with severe anxiety in our study, and the proportion of patients with mild depression rose from 35% to 42.5% following DSR. This suggests that the number of people with depression may have decreased. Congruent with our research findings, a significant reviews article by Seo et al. demonstrated that numerous studies concluded that the treatment of DSR decreased anxiety and depression levels by raising quality of life (14). Our research has certain shortcomings. The study's sample was narrowly focused and limited. Larger sample sizes and multicenter investigations should thereby validate the results.

In this study, the pre- and post-operative anxiety and depression levels of patients undergoing DSR for ocular duct obstruction were assessed. The study's findings indicate that patients who had DSR had far lower levels of anxiety and depression. These findings imply that SCT may exacerbate pre-existing psychological issues or cause new ones to arise.

The IOL's congestion might result in symptoms such eye watering, redness, and stinging. Patients may experience psychological issues and a decline in their quality of life as a result of these symptoms (1-3). According to our research, DSR may help with the psychological issues brought on by blocked tear duct. By reducing the blockage brought on by blocked tear duct, DSR lessens ocular discomfort, enhancing patient quality of life and lowering psychological issues. In fact, this psychological improvement is likely to be due to improved scoring of more objective data, such as eye acuity and intraocular pressure, derived from scales or examination data, and should be kept in mind.

Lemaitre et al. conducted studies to lessen pre-existing anxiety prior to DSR. In this study, patients' anxiety levels decreased following DSR (11). These results concur with those of other research. Wan et al. discovered significant data about the frequency and severity of anxiety and depression in individuals with dry eye conditions using a meta-analysis of 22 studies involving 3 million patients (12). These studies provide evidence that DSR may lower anxiety and depressive symptoms. Furthermore, DSR may improve quality of life in patients with acute dacryocystitis, lessen pain intensity, lessen negative emotional reactions, and raise patients' satisfaction with nursing care, according to the study by Luo et al (13).

Furthermore, compared to the general population, patients with nasolacrimal duct obstruction had greater frequencies of depression and anxiety disorders, according to the Guo et al. study. According to this study, 13.1% of patients had mild-to-severe depression and 63.4% of patients had severe anxiety (5). However, our investigation did not reveal any patients with severe anxiety, and the percentage of patients with mild-to-

severe depression rose from 35% prior to DSR to 42.5% following DSR. As a result of the decrease in "moderate" and "severe" anxiety levels after surgical intervention; it is possible that an increase in "minimal" and "mild" anxiety levels may occur. These findings imply that depression scores might be declining. According to the paper by Seo et al., which is based on extensive reviews, there are several research that suggest DSR may raise anxiety and depressive symptoms by enhancing quality of life (14).

Study limitations

However, this study has some limitations. Our study did not examine the relationship between dry eyes, anxiety and depression. However, there are a limited number of studies suggesting that eye surgery can reduce anxiety and depression levels, thus limiting the number of articles discussed. The use of self-report scales (beck depression and anxiety scale) in the study is also one of the limitations. It would have been more appropriate to use more objective methods. Comparison of clinical objective data to confirm the decrease in anxiety and depression levels with improvement of tear obstruction symptoms will provide more reliable results. There was only one facility and a tiny sample size. Consequently, bigger sample sizes and multi-center investigations are required to validate the findings.

Conclusions

The study's findings suggest that the DSR process has the ability to lower anxiety and depressive symptoms. DSR helps patients experience a better quality of life by reducing eye discomfort by clearing the obstruction in the tear duct. Tear duct obstruction can cause symptoms like redness, stinging, and watery eyes. Patients may experience psychological issues and a decline in their quality of life as a result of these symptoms. The study's findings highlight the possibility that DSR can help with psychological issues brought on by tear duct constriction.

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Original Article

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Identification of clinical features and prognosis of children hospitalized with first afebrile seizure: A single-center study

İlk afebril konvülziyon nedeniyle hastaneye yatırılan olguların klinik özelliklerinin ve prognozlarının araştırılması: Tek merkezli bir araştırma

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Abstract

Background: It is aimed to evaluate the risk of recurrence of the first afebrile seizure according to the use of antiepileptics.

Materials and Methods: One year follow up of children hospitalized with first afebrile convulsion were investigated retrospectively. Age, gender, history, neurological findings, electroencephalogram, neuroradiological imaging were evaluated for seizure recurrence considering antiepileptic treatment use.

Results: Antiepileptic was started in 45.2% (33 out of 73) of patients. Seizure recurrence was 39.4% (13 out of 33) under treatment. No recurrence was observed in 92.5% (37 out of 40) of untreated patients (p=0.001).

Conclusions: After the first afebrile seizure, antiepileptic treatment could lower but could not remove recurrence risk totally. Seizure did not recur in most of children followed-up without treatment, therefore decision to start antiepileptic after the first unprovoked seizure should be carefully evaluated.

Keywords: Seizure; Anticonvulsant; Electroencephalogram; Neuroimaging

ÖZ

Amaç: İlk afebril nöbetin tekrarlama riskinin, antiepileptik kullanımına göre değerlendirilmesi amaçlanmıştır**.**

Gereç ve Yöntemler: İlk afebril konvülziyon nedeniyle hastaneye yatırılan çocukların bir yıllık takipleri retrospektif incelendi. Yaş, cinsiyet, özgeçmiş, nörolojik bulgular, elektroensefalogram, nöroradyolojik görüntüleme, nöbet tekrarı açısından antiepileptik tedavi kullanımı dikkate alınarak değerlendirildi.

Bulgular: Hastaların %45,2'sine (33/73) antiepileptik başlandı. Tedavi altında nöbet tekrarı %39,4 (13/33) idi. Tedavi almayan hastaların %92,5'inde (37/40) nöbet tekrarı görülmedi (p=0.001).

Sonuç: İlk afebril konvülziyon sonrası, verilen tedavinin nöbet nüksünü azalttığı ama tamamen ortadan kaldırmadığı görülmüştür. İlk afebril konvülziyon sonrası antiepileptik tedavi verilmeden izlenen olguların çoğunda nöbet tekrarlamamıştır, bu nedenle ilk afebril konvülziyon sonrası antiepileptik başlanma kararı dikkatli değerlendirilmelidir.

Anahtar Kelimeler: Konvülziyon; Antiepileptik; Elektroensefalogram; Nörogörüntüleme

Highlights

- After the first seizure of a child, if the recurrence risk is high, antiepileptic treatment is started.
- If the recurrence risk is not high, seizure recurrence may not occur in the followed up without antiepileptic treatment.
- The decision to initiate treatment after the first seizure should be individualized according to risk of recurrence.

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Introduction

In children, the prevalence of seizures is 4-10%, and seizures are 1% of pediatric emergency admissions (1). Brain infections, head injury, metabolic disorders may trigger seizures, but in the unprovoked seizure an immediate, clearly documented underlying cause could not be identified (1-4).

The most important and yet difficult point in the approach to the first unprovoked seizure, is to predict whether the seizure will recur (5-7). Epilepsy diagnosis is made according to the recurrence risk of the seizure, and this risk of recurrence is crucial for initiating antiepileptic therapy (AET) at the first seizure (1,4-6). The recurrence of first seizure is the most common in the following 1-2 years (14–65%) (5).

Focal type of seizure, head injury history, parental consanguinity, epilepsy diagnosis in family (genetic inheritance), specific findings on neurologic examination, epileptic electroencephalogram (EEG) and pathological cranial (CR) magnetic resonance imaging (MRI) evaluations are high risk factors for seizure recurrence (1-3,6-9). If EEG and CR images are normal, AET is debatable and usually AET is initiated after a second attack or at the first attack with the presence of high recurrence risk (3,10).

The guidelines underline that if a comprehensive evaluation of the recurrence risks of first seizure is desired, it should be taken into consideration that the most important determinant is treatment (6). There are few studies in the literature investigating whether starting AET at the first seizure affects recurrence (4,11).

We undertook a study with pediatric first afebrile seizure and aimed to assess the recurrence risk. While evaluating the risk factors of seizure recurrence, we wanted to research the effect of treatment on recurrence. We examined the patients with their determinants such as descriptive data, EEG and neuroimaging for seizure recurrence in 1 year follow-up by comparing whether they were under treatment or not. Our study is one of the few studies that conducted to determine whether recurrence is influenced by treatment.

Materials and Methods

Characteristics of Patients

This was a study of children aged 1 month to 16 years who were hospitalized for a first afebrile seizure between January 2009 to December 2009 at the pediatric emergency department of University of Health Sciences Turkey Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital. Syncope, chorea, tic, tremor, migraine and febrile seizures were excluded. Status epilepticus was included.

Data collection

This study was designed as a retrospective study. The data were collected from patient files. Characteristics like age, gender, previous history (febrile convulsion, mental motor retardation), family histories (consanguineous marriage, febrile convulsion, epilepsy), neurologic examination findings at emergency department were noted. Results of EEG taken during hospitalization at emergency department (early EEG) were obtained. The decision to start or not to start AET at discharge from hospital was stated. Children were separated in two different categories according to the decision whether to start AET or not. They were followed for 1 year at pediatric neurology outpatient clinic for seizure recurrence. Late EEG and CR MRI results taken during follow-up in the pediatric neurology outpatient clinic after discharge were obtained. The relationships between patients' descriptive data, AET decision at discharge from hospital, and seizure recurrence at 1 year follow-up were investigated.

Ethics committee approval

This article is derived from thesis published in 2011 and ethics committee approval was obtained from Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Ethics Committee (Number: B-10-4-ISM-4-35-65-72 Date:28.04.2011). This study complied with the principles stated in the Declaration of Helsinki that developed by the World Medical Association. Since this study was retrospective, informed patient consent statement was not collected.

Statistical Analysis

Data were statistically evaluated. Descriptive findings were presented as numbers, percentages for categorical variables. Chi-square test and Fisher's exact test were used for assessing associations between variables of categorical data. A p-value less than 0.05 (≤0.05) was considered statistically significant.

Results

Our study conducted with 73 patients. At discharge from hospital AET was initiated in 45.2% (33 out of 73) of patients. At 1-year follow-up seizure recurrence was observed in 39.4% (13 out of 33) of the treated group and no recurrence was observed in 92.5% (37 out of 40) of the untreated group. The relationship between the decision to start AET at discharge and seizure recurrence was found to be statistically significant (p=0.001) (Table 1).

There were 32 (43.8%) girls and 41 (56.2%) boys. The median age was 34.7 months. History of mental motor retardation was found in 2 (2.7%) patients. Six (8.2%) patients had complex febrile convulsion history. Seven (9.6%) consanguineous marriages, 10 (13.7%) febrile seizures, 11 (15.1%) epilepsy were detected in family history (Table 2). Nineteen (26%) patients had neurological deficits (Table 3).

Early EEG was performed during hospitalization in 49 (67.1%) patients and 40.8% (20 out of 49) were pathological. Antiepileptic was initiated in 60% (12 out of 20) of patients with pathological EEG. In patients with pathological early EEG, seizure recurrence was 33.3% (4 out of 12) under treatment and 12.5% (1 out of 8) without treatment (Table 4). Late EEG was obtained in 64 (87.7%) patients after discharge at neurology outpatient clinic and 40.6% (26 out of 64) were pathological. Antiepileptic was initiated in 57.7% (15 out of 26) of patients with pathological EEG. In patients with pathological late EEG, seizure recurrence was 46.7% (7 out of 15) under treatment and no recurrence was observed without treatment (Table 4).

CR MRI was performed in 57 (78.1%) patients after discharge and 19.3% (11 out of 57) were pathological. Antiepileptic was initiated in 45.5% (5 out of 11) of patients with pathological CR MRI. In patients with pathological CR MRI, seizure recurrence was 60% (3 out of 5) under treatment and 16.7% (1 out of 6) without treatment (Table 4).

Table 1. Decision to start antiepileptic therapy at discharge from hospital and seizure recurrence

Anti-epileptic treatment	**Total patients**	**Seizure recurrence**		***P***
		Yes	No	
Started, n (%)	33(45.2)	13(39.4)	20(60.6)	0.001
Not started, n (%)	40(54.8)	3(7.5)	37(92.5)	

Table 2. Patient characteristics, antiepileptic treatment initiation at discharge and seizure recurrence

Category	**Total**	**Anti-epileptic initiation**	**Total**	**Seizure recurrence**	
				Yes	No
Gender	32(43.8)	Yes	16(50)	6(37.5)	10(62.5)
Girl, n (%)		No	16(50)	1(6.3)	15(93.7)
Boy, n (%)	41(56.2)	Yes	17(41.5)	7(41.2)	10(58.8)
		No	24(58.5)	2(8.3)	22(91.7)
Mean age (months)	34.7	Yes		36.1	33.8
		No		33.3	34.9
History	2(2.7)	Yes	2(100)	1(50)	1(50)
Mental motor retardation, n (%)		No	00(0)	00(0)	00(0)
Febrile convulsion, n (%)	6(8.2)	Yes	5(83.3)	2(40)	3(60)
		No	1(16.7)	00(0)	1(100)
Family History	7(9.6)	Yes	4(57.1)	2(50)	2(50)
Consanguineous marriages, n (%)		No	3(42.9)	0(0)	3(100)
Febrile convulsion, n (%)	10(13.7)	Yes	8(80)	4(50)	4(50)
		No	2(20)	0(0)	2(100)
Epilepsy, n (%)	11(15.1)	Yes	6(54.5)	4(66.7)	2(33.3)
		No	5(45.5)	0(0)	5(100)

Table 3. Decision to start antiepileptic therapy at discharge from hospital and seizure recurrence in patients with neurologic deficit

Antiepileptic therapy	Patients with neurologic deficit	Seizure recurrence	
		Yes	No
Started, n (%)	13(68.4)	5(28.5)	8(61.5)
Not started, n (%)	6(31.6)	0(0)	6(100)

Table 4. Results of EEG taken both during hospitalization (Early EEG) and after discharge (Late EEG), CR MRI taken after discharge, decision to start antiepileptic therapy at discharge from hospital and seizure recurrence

Investigation	Results	Patients	Anti-epileptic treatment	Patients	Seizure recurrence	
					Yes	**No**
Early EEG	Normal, n (%)	29(59.2)	Yes	8(27.6)	4(50)	4(50)
			No	21 (72.4)	1(4.8)	20(95.2)
	Pathologic, n (%)	20(40.8)	Yes	12(60)	4(33.3)	8(66.7)
			No	8(40)	1(12.5)	7(87.5)
Late EEG	Normal, n (%)	38(59.4)	Yes	16(42.1)	5(31.2)	11(68.8)
			No	22(57.9)	1(4.5)	21(95.5)
	Pathologic, n (%)	26(40.6)	Yes	15(57.7)	7(46.7)	8(53.3)
			No	11(42.3)	0(0)	11(100)
CR MRI	Normal, n (%)	46(80.7)	Yes	28(60.9)	10(35.7)	18(64.3)
			No	18(39.1)	2(11.1)	16(88.9)
	Pathologic, n (%)	11(19.3)	Yes	5(45.5)	3(60)	2(40)
			No	6(54.5)	1(16.7)	5(83.3)

CR: Cranial, EEG: Electroencephalogram, MRI: Magnetic resonance imaging

Discussion

Treatment

Our study is one of the few studies in the pediatric setting that conducted with the first unprovoked seizure and aimed to provide data on the risk of recurrence under the determinant of antiepileptic treatment use status.

Seizure recurrence rates in 2 years were 36% in prospective, 47% in retrospective research of a meta-analytic review which examined 16 articles (12). In a study that observed 208 children, seizure recurrence rates were found to be 14% in 1 year, 29% in 3 years, and 34% in 5 years (13).

In 397 patients with first unprovoked seizure aged 2 to 70 years, recurrence rate in 24 months follow-up was 25% in patients that randomized to immediate treatment group who started treatment within 7days and 51% in patients that randomized to delayed treatment group who treated after recurrence (14). This trial confirmed that immediate treatment of to the first unprovoked seizure decreases recurrence (14).

In another trial that assess the treatment that initiated for the first seizure, the recurrence rate was 24% in immediate treatment group and 42% in delayed treatment group (15). One year seizure free interval was estimated 87% versus 83%, and 2 years seizure free interval was estimated 68% versus 60%, in treated and untreated patients respectively (15). In untreated group, 50% of the patients, the seizure never recurred (15). This study concluded that antiepileptic treatment reduces recurrence risk after first unprovoked seizure, however was not effective at long-term follow-up (15).

In a randomized controlled trial, recurrence rate was 32%, 42% and 46% in immediate treatment group and 39%, 51%, and 52% in deferred treatment group, in 2, 5 and 8 years follow-up respectively (11). Two years remissions were 69%, 92%, 95% in immediately treated patients and 61%, 92%, 96% in patients whose

treatment were delayed, at 2, 5, 8 years follow-up, respectively (11). Within 2 years, immediate treatment group achieved 2-years remission at a higher rate than the delayed group, so immediate treatment extended seizure-free period in short-term, but by 5 and 8 years follow-up, treatment did not affect 2 years remission (11).

In updated Cochrane review which included 6 studies, immediate treatment group is compared with control group that included deferred treatment, placebo and no treatment (16). Immediate treatment lowers recurrence rate in following 12 months but this decline decreases at 2 and 5 years (16). At long term follow-up, treatment had no effect on time to 2 or 5 years remission (16). As a result, considering the short and long-term prognosis, the treatment decision should be individualized by taking into account the clinical characteristics of the patient (7,10,16).

In our study, treatment was statistically significant factor for seizure recurrence that in treated children recurrence rate was 39.4% while non-recurrence rate was 60.6% and in untreated children recurrence rate was 7.5% though non-recurrence rate was 92.5% (p=0,001) (Table 1). Under AET, recurrence risk was lower than non-recurrence risk (39.4% vs. 60.6%) which concludes that treatment could lower recurrence risk but could not completely eliminate the recurrence risk entirely (4,10).

Seizure recurrence rate was 45% in 815 children followed for 3 years without AET (17). Seizure recurrence rates in 283 children, 84% of whom did not receive AET, were 26%, 36%, 40% and 42% in 12, 24, 36 and 48 months, respectively (18). The study concluded that AET initiation did not alter recurrence risk and ultimately, noted that seizure could not recur even in follow-up without AET (18). In our study no recurrence was observed in the majority (92.5%) of children who were followed up without treatment for 1 year. Seizure may not recur in follow up without AET, so the decision of AET initiation for the first unprovoked seizure should definitely be questioned (7,15,18). The decision to initiate AET should be individualized (4,7,10,16). If the risk of recurrence is expected to be high after the first seizure, epilepsy is considered in the diagnosis and treatment is started without wasting time to protect the central nervous system from the damage of subsequent seizures (4,5,10,19).

EEG

Guidelines suggest that EEG is crucial in the assessment of first epileptic seizure for determining the risk of recurrence, to identify underlying epilepsy syndrome and to subclassify seizure type (3,5,7-10,20-24). The examination time of EEG is another curious question because, the timing of EEG may affect the accuracy of EEG in demonstrating epileptic activity (5,7,8,22,24). If the EEG is taken in the early period, the chance of catching sight of pathologic waves increases (5,10,19,22). But, it should be kept in mind that EEG demonstrates exaggerated discharges in the very early time period and after this higher excitability interval, excessive signaling activities will ease (5). Therefore, care should be taken in early EEG evaluation that early abnormal activities can be temporary (5).

In 169 children, epileptiform discharge was confirmed in 65.2% of EEGs performed within 12 hours and in 28.1% of the EEGs taken afterwards (p< 0.001) (22). In 300 patients 59 (20%) of whom children, epileptiform changes were higher in EEGs taken within 24 hours compared to the next timeframe (51% vs. 34%) (19). In another study, no statistical difference was found in terms of pathologic epileptic activities between EEGs performed urgently in 48 hours (37%) and EEGs delayed after 48 hours (40%) (8). In a study with 108 children, EEG was taken in the first 96 hours and 63% of them were abnormal (24). EEG abnormality was noted as a risk factor in terms of recurrence (24). Examination time of EEG was classified in 7 groups and each period was analyzed for EEG abnormalities, though no correlation was present (24).

In a study, according to EEG findings taken in the emergency room, 27.8% of 90 children who had new-onset seizures were diagnosed with epilepsy (21). A review evaluated the impact of EEG test on confirming the diagnosis of epilepsy and children analysis indicated 57.8% sensitivity, 69.6% specificity (23). The seizure recurrence rate and so epilepsy probability in children with abnormal EEG was 66%, while in children with normal EEG was 38%. (23). But, antiepileptic treatment factor that would affect the result of EEG test was not evaluated (23).

Our pathological EEG rates were 40.8% in early and 40.6% in late EEG. In pathological EEGs, antiepileptic treatment was started in 60% of the early recordings and 57.7% of the late recordings. Of pathological EEG, seizure recurrence rates were 33.3% and 46.7% under treatment, while they were 12.5% and 0% in follow-up without treatment (in early and late results, respectively) (Table 4).

Neuroimaging

Guidelines highlight neuroimaging monitoring after the first unprovoked seizure if essential, and MRI is the recommended procedure since lesions may be overlooked on CT and also MRI produces clearer, more detailed images compared to CT scan (4,7,9,10,25,26). MRI is the most accepted assessment that help to determine the risk of recurrence of the first epileptic seizure and classify epilepsy subtypes and discern patients in need of AET (9,20,25,26).

In a retrospective study with 96 children who had their first afebrile seizure, 92 CT and 4 MRI neuroimaging were performed within 48 hours after the seizure and 33% (32 out of 96) of them were pathological (27). Seizures recurrence was observed in 19% (6 out of 32) of pathological results (27).

A prospective study with 411 children of whom 218 (53%) had taken neuroimaging, seizure recurrence rate was 78% (35 out of 45) in patients with pathological results and 56% (97 out of 173) with normal results (26).

In the neuroimaging guide which includes 18 prospective and retrospective studies, it is stated that approximately 50% of neuroimaging findings were abnormal in the localized new-onset seizure, 15-20% were effective in etiological differentiation, and 2-4% has shown need of urgent medical intervention (25).

We had taken 57 CR MRIs and 19.3% of them were pathological. Antiepileptic was initiated in 45.5% of pathological scans. In patients with pathological scans, seizure recurrence rate was 60% under treatment and 16.7% without treatment (Table 4).

Study limitations

The biggest limitation of current study was our limited number of patients. Our insufficient sample size prevented the data distributions from reaching statistical significance. Second limitation of our study was its retrospective nature and could not extract more descriptive data. Third, this research was carried out in a single hospital located in the western region of Turkiye which may limit its national generalizability, and it is clear that large multicenter series are needed for useful results that broadly reflect national data. Finally, considering that our study is a 1-year observation, obviously long term observational studies are requisite to interpret seizure recurrence and treatment decision.

Conclusions

In our study, children who had their first unprovoked seizure were evaluated for seizure recurrence according to whether they received antiepileptic treatment or not. It is generally accepted that treatment should be initiated in patients with a high risk of recurrence, because it was thought to be the first seizure of epilepsy. Careful consideration should be given when immediately starting antiepileptic treatment after the first afebrile seizure in children. It should be kept in mind that seizure recurrence may not occur during follow-up without treatment after the first unprovoked seizure, because we found that in most of our untreated children seizure did not recur in 1 year follow-up.

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Analysis of Patients Hospitalised in the Comprehensive Palliative Care Service- 1-Year Experience

Kapsamlı Palyatif Bakım Servisinde Yatan Hastaların Analizi-1 Yıllık Deneyim

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Abstract

Background: It was aimed to evaluate the patients who were admitted to Samsun Training Research Hospital (STRH), palliative care service (PCS) since it was started to be admitted by family-medicine clinic.

Materials and Methods: Cross-sectional, retrospective study consisted of all PC-patients admitted to STRH-PCS between 01/12/2019-01/12/2020. Gender, age, occupation, blood type, diagnosis, where we were consulted from, how many days of received, how many hospitalizations were made, number of deaths, reason for hospitalization, requests for imaging, specific interventional procedures etc. was collected with the help of automation-system and analyzed in SPSS.

Results: The mean age of the participants in the study was 76.3±12.9 years, and the female ratio was 51.3%. The majority of the people's blood groups were found to be A Rh+ with 36.9%. The average hospitalization period of the individuals was 12.0±10.4 days, and it was determined that the most hospitalizations were made in winter with 46.7%. While 62.8% of the individuals were discharged from the hospital, it was determined that 21.7% of them died. It was determined that nearly half of the patients were hospitalized due to nutritional deficiencies. The primary diagnosis distributions of the individuals Lung-cancer (15.8%), Cerebrovasculer disease (CVD) (14.8%) and Alzheimer's disease (14.1%),

Conclusion: More consultation was requested from the emergency department and intensive care departments, and patients who were asked to have direct radiography as an imaging need died more.

Keywords: Palliative care, Family practice, Holistic health

ÖZ

Amaç: Bu çalışmada, aile hekimliği kliniğince yürütülmeye başlandığı zamandan itibaren Samsun Eğitim ve Araştırma Hastanesi (SEAH) Palyatif Bakım Servisi'ne (PBS) yatan hastaları değerlendirmek amaçlanmıştır

Gereç ve Yöntem: Kesitsel, retrospektif dizayndaki çalışmanın evrenini SEAH PBS'ne 01 Aralık 2019- 01 Aralık 2020 tarihlerinde yatışı yapılan tüm PB hastaları oluşturmuştur. Cinsiyet, yaş, meslek, kan grubu, tanı, nereden konsülte edildiği, kaç gün kabul edildiği, kaç yatış yapıldığı, ölüm sayısı, yatış nedeni, görüntüleme istekleri, spesifik girişimsel işlemler vb. otomasyon sistemi yardımıyla toplandı ve SPSS'de analiz edildi.

Bulgular: Çalışmaya katılanların yaş ortalaması 76,3±12,9 yıl ve kadın oranı %51,3 idi. Kişilerin kan gruplarının %36,9 ile çoğunluğunun A Rh+ olduğu tespit edildi. Bireylerin ortalama yatış süresi 12,0±10,4 gün olup, en fazla yatışın %46,7 ile kış aylarında yapıldığı belirlendi. Bireylerin %62,8'i hastaneden taburcu edilirken, %21,7'sinin hayatını kaybettiği belirlendi. Hastaların yarıya yakınının beslenme yetersizliği nedeniyle hastaneye yatırıldığı tespit edildi. Kişilerin ilk 3 sıradaki primer tanı dağılımları sırayla Akciğer kanseri (%15,8), Serebrovasküler olay (SVO) (%14,8) ve Alzheimer hastalığı (%14,1) olduğu saptandı..

Sonuç: Acil departmanı ve yoğun bakım departmanlarından daha fazla konsültasyon istendiği, görüntüleme ihtiyacı olarak direkt grafi istenen hastaların daha fazla vefat ettiği saptanmıştır.

Anahtar Kelimeler: Palyatif bakım, Aile hekimliği, Bütüncül sağlık

- Integrating family medicine and palliative care a service experience shared.
- Consultations and hospital units were analyzed.
- Reasons for hospitalization and associated factors of diseases analyzed.

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Introduction

According to the World Health Organization (WHO) definition, palliative care is an approach to improve the quality of life of patients and their relatives who face a life-threatening disease and is a care that aims at early detection and treatment of physical, psychosocial and spiritual problems, especially pain (1, 2).

The most common end-of-life complaints and findings in palliative cancer patients are pain, malnutrition, nausea, weakness, shortness of breath, internal distress, confusion and pressure sores. In order to achieve quality and continuous care in case management, many professionals such as family physicians, specific branch specialists, nurses, dieticians, psychologists, spiritual support specialists, physiotherapists and sociologists should work together and clinical guidelines and care protocols should be used (3,4,5).

The goal should always be maximum benefit with minimum investigation and treatment. Palliative care does not aim to accelerate or postpone death and has many benefits in cancer patients. Integrating the psychosocial aspects of patient care into physical care, supporting patients to lead an active life as much as possible until the last moment, providing support to patients' relatives to cope with their own grief processes during and after the disease process, using a team approach to meet the needs of patients and their relatives, including grief counseling when necessary, improving quality of life, and positively affecting the disease process are just a few of these (6). There are a wide variety of palliative care practices in the world. Worldwide Hospice Palliative Care Alliance (WHPCA) stated that palliative care services are provided in 3 of 5 continents (7). There are various palliative care practices around the world. Palliative care services have entered a rapid development process in developed countries such as the Scandinavian countries, the UK and Canada since the early 1990s (8). Palliative care is not intended to hasten or postpone death but has many benefits for cancer patients. Integrating psychosocial aspects of patient care into physical care, supporting patients to lead an active life as much as possible until the end, providing support to patients' relatives to cope with their own grief processes during and after the disease process, using a team approach to meet the needs of patients and their relatives, including grief counseling when necessary, improving quality of life, and positively affecting the disease process are just a few of these. In this study, we aimed to evaluate the patients hospitalized in the comprehensive palliative care service of Samsun Training and Research Hospital (STRH) since the beginning of its implementation by the family medicine clinic.

Materials and Methods

This study was cross-sectional, retrospective and analytical in design. The beds allocated for palliative care in the Comprehensive Palliative Care Service of Samsun Training and Research Hospital. The sample of the study consists of 304 patients admitted to the palliative care service for palliative care between December 1, 2019 and December 1, 2020. All palliative care patients who were hospitalized will be included. Without sharing the private information of the patients, gender, age, blood group, diagnosis, from where they were consulted, how many times consultation requests were made by us, how many days of service they received, how many times they were hospitalized, in which seasons they were hospitalized, the number of deaths, the number of discharges, the number of transfers, where the transfers were to, the specific interventional procedures performed, from which province and district they were hospitalized, information was collected with the help of the automation system

Statistical Analysis

Descriptive measures: mean and standard deviation, minimum-maximum values were presented. Chi-square test was used to compare the analytically expressed data, statistical analyses were evaluated using SPSS version 19 package program. (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY: IBM Corp.) The conformity of the data to normal distribution was checked by Kolmogorov-Smirnov test. Chi-square or Fisher's exact test was used to compare the distributions between age groups The significance level was taken as $p<0.05$. Volunteers were included in the study as male and female and over 18 years of age. Ethical approval: written permission was obtained from the following institution for the study Health Sciences University Samsun Training and Research Hospital Non-Interventional Clinical Research Ethics Committee GOKA/2021/3/2 decision by 13.02.2021 date. Since this study was retrospective, informed patient consent statement was not collected.

Results

A total of 304 patients were included in the study. The mean age of those included in the study was 76.3±12.9 years and the female sex ratio was 51.3% (n:156). The majority of the blood groups were A Rh+ (36.9%) and 0 Rh+ (31.2%). The mean duration of hospitalization was 12.0±10.4 (median: 9) days and it was found that most

hospitalizations were made in winter months. While 62.8% of the patients were discharged from the hospital, 21.7% of the patients died. Direct radiography was performed in 49.3% (n: 150) of the patients and the average number of radiographs was 2.5. It was found that the majority of the patients resided in Samsun province (93.1%) (n:283) and 72.4% (n:207) of the patients residing in Samsun province lived in the central districts. While the reason for hospitalization of almost half of the people was nutritional deficiency, respiratory palliation and wound site care were found to be the other high frequency reasons. The distribution of the primary diagnoses in the provinces in the order of the 3 primary diagnoses were Lung cancer (15.8%, n: 48), CVD (14.8%, n: 45) and Alzheimer's disease (14.1%, n: 43). Specialized interventional procedures were performed in 24.3% (n: 74) of the patients and the most common interventional procedure was PEG opening. The vast majority of the patients were hospitalized by the outpatient or outpatient clinic. Among those who were hospitalized, the mean hospitalization was 1.2±0.5. The majority of the patients were hospitalized from the emergency medicine outpatient clinic. The mean number of consultations made to us was 0.8±0.7 and the mean number of consultations made by us was 9.3±8.2 (median:7) **(Table 1).**

Table 1. Descriptive characteristics of the participants

				City, n (%)	
Age, Mean± SD	76.3±12.9*	**Hospitalization Season,** n (%)		Samsun	283 (93.1)
Sex, n (%)		Autumn	66 (21.7)	Other	21 (6.9)
Male	148 (48.7)	Winter	142(46.7)	**District,** n (%)	
Female	156 (51.3)	Spring	20 (6.6)	Center	207 (72.4)
Age Group, n (%)		Summer	76 (25)	Periphery	79 (27.6)
18-64	52 (17.1)	**Discharge Form,** n (%)		**Reason for Hospitalization** n (%)	
65-74	73 (24)	Transfer to Another Service	7 (2.3)	Pain palliation	25 (8.2)
75-84	86 (28.3)	Discharged from Hospital	191 (62.8)	Lack of Nutrition	154 (50.7)
Over 85	93 (30.6)	External Referral	1 (0.3)	Respiratory Deficiency	40 (13.2)
Hospitalization Day, Mean± SD	12± 10.4	Transfer to Intensive Care	7 (2.3)	Wound Site Care	40 (13.2)
Blood Type, n (%)		Death	66 (21.7)	Other	45 (14.8)
A Rh+	97 (36.9)	**Radiology,** n (%)		**Primary Diagnosis** n (%)	
A Rh -	18 (6.8)	Direct radiography	150 (49.3)	Gastrointestinal Cancer	53 (17.4)
B Rh+	23 (8.7)	Tomography	48 (15.8)	Respiratory Tract Cancers	53 (17.4)
B Rh-	4 (1.5)	MR	19 (6.3)	Other Cancers	39 (12.8)
AB Rh+	21 (8)	USG/ECO	96 (31.6)	Alzheimer-Parkinson-Dementia	62 (20.4)
AB Rh-	6 (2.3)			Cerebrovascular Diseases	45 (14.8)
		Frequency of radiological examinations requested, Mean± SD			
0 Rh+	82 (31.2)	Direct radiography	2.5 ± 2.4	Other Diagnoses	52 (17.1)
0 Rh-	12 (4.6)	Tomography	2.0± 1.6		
		MRI	1.2 ± 0.5		
		USG/ECO	1.9 ± 1.4		

Table 1. Descriptive characteristics of the participants (continued)

Admitted to services, n(%)	
Outpatient	8 (2.6)
Handover	119 (39.1)
Home health services	53 (17.4)

Polyclinic	124 (40.8)
How many hospitalizations Mean±SD	1.2 ± 0.4
Where the patient was admitted, n(%)	
Emergency Medicine Department	120 (39.5)
Intensive Care	94 (30.9)
Internal Clinics	31 (10.2)
Surgical Clinics	6 (2)
Home Health Services	53 (17.4)
How many times have we been consulted, Mean±SD (Median)	0.8 ± 0.7 (1)
How many times have we consulted? Mean±SD, (Median)	9.3 ± 8.2 (7)

PCS is a multidisciplinary clinic that works with a wide range of procedures and serves all types of patient groups and diseases. Our main findings also show results in this direction.

The statistical analysis revealed no significant relationship between season distribution and hospitalization location **(Table 3)**. According to chi-square analysis, a statistically significant difference in mortality rates was found between individuals who required direct radiography and those who did not ($p<0.001$) **(Table 4)**. The statistical analysis showed that there was no significant difference in the distribution of blood groups between males and females. The prognosis of patients did not show any statistically significant relationship with their blood groups, as found by the statistical analysis. The statistical analysis found that patients who died most frequently had a primary diagnosis of respiratory cancers and there was a significant difference between this group and others. Besides, the emergency medicine department or intensive care unit was statistically significantly more likely to request consultation than other units **(Table 6**). As a result of the statistical analysis, no statistically significant difference was detected between age groups in terms of life prognosis **(Table 2)**. It was determined that the people who died were most frequently diagnosed with respiratory cancers and there was a statistically significant difference between the groups **(Table 5).**

Table 2. Comparison of prognosis distributions between age groups and comparison of hospitalization durations between age groups analysis

Age, n (%)	**Discharge or Referral**	**Exitus**	**Total**	**P**
18-64	39 (16.4)	13 (19.7)	52 (17.1)	0.246
65-74	53 (22.3)	20 (30.3)	73 (24.0)	
75-84	67 (28.2)	19 (28.8)	86 (28.3)	
Over 85	79 (33.2)	14 (21.2)	93 (30.6)	

**Chi-square*

Table 3. Examination of the relationship between the season of hospitalization and the distribution of reasons for hospitalization

	Season				**P**
Reasons for hospitalization, n (%)	**Autumn**	**Winter**	**Spring**	**Summer**	
Pain palliation	6 (24)	7 (28)	3 (12)	9 (36)	0.242
Lack of nutrition	31 (20.1)	71 (46.1)	17 (11)	35 (22.7)	
Lack of respiration	9 (22.5)	23(57.5)	2 (5)	6 (15)	
Wound site care	5 (12.5)	14 (35)	4 (10)	17 (42.5)	
Other	8(17.8)	21(46.7)	3(6.7)	13(28.9)	

**Chi-square*

Table 4. Examination of the relationship between prognosis in patients with and without the need for direct radiography

Prognosis, n (%)	Direct radiography		*P*
	No	**Yes**	
Discharge or Referral	134 (87)	104 (69.3)	0.001
Death	20 (13)	46 (30.7)	

**Chi-square*

Table 5. Examination of the relationship between primary diagnosis and mortality status

Diagnosis, n (%)	Exitus		*P*
	No	Yes	
Gastrointestinal cancer	38 (16)	15 (22.7)	0.041
Respiratory cancers	37 (15.5)	16 (24.2)	
Other cancers	28 (11.8)	11 (16.7)	
Alzheimer-Parkinson-Dementia	49 (20.6)	13 (19.7)	
Cerebrovascular diseases	38 (16)	7 (10.6)	
Other diagnoses	48 (20.2)	4 (6.1)	

**Chi-square*

Table 6. Examination of the relationship between consultation request and place of hospitalization

Departments, n (%)	Consultation Request		*P*
	No	**Yes**	
Emergency medicine department	40 (35.1)	80 (42.1)	0.001
Intensive care	15 (13.2)	79 (41.6)	
Internal clinics	13 (11.4)	18 (9.5)	
Surgical clinics	0 (0)	6 (3.2)	
Home health services	46 (40.4)	7 (3.7)	

**Chi-square*

Discussion

We shared the first regular PCS data since the day it was managed by the family medicine clinic in Samsun.

In the study conducted by Benli et al. on the coordinated work of home health services and palliative service, the mean age of the patients was 74.93±14.61 years, 42.95% were male and 57.04% were female, while in this study woman avarege more than Benli's et al. work (9). As expected, PCS data, which is expected to serve the older age group, served more patients of the female gender due to the higher life expectancy of women in Turkey (10). Data from both studies confirm this information. In a study conducted by Pektaş et al. the mean duration of hospitalization in the palliative care unit was 11.2±13.3 (Lowest: 1, Highest: 94) days (11). The results again overlap with the literature and are in accordance with the rapid circulation required for ideal care.

Pektaş et al. 55% of the patients were referred to another department or hospital, 33% were discharged and 11% died, whereas in this study 62.8% of the patients were discharged from the hospital and 21.7% died (11). The reason for this difference may be that it is a socio-culturally different city, and patients may want to spend their last period in the hospital rather than at home. In a study by Al-Jamal et al. the ex-rate was 52.9% and the

discharge rate was 40%. The fact that the study hospital is a foundation hospital, or a private institution changes the statistics. In this study, it was aimed to discharge patients with adequate care in an effective time by targeting 20 days of care as Al-Jamal et al. did. The fact that the patient population did not consist only of cancer patients may have caused the death rate to be lower than the death rate of Al-Jamal et al. (12).

The reason for hospitalization of nearly half of the individuals was nutritional deficiency, while respiratory palliation and wound site care were found to be the other most frequent reasons. In a study by Yürüyen et al. the most common reason for hospitalization was oral intake disorder with 35% (13). In the study by Benli et al. the most common reason for hospitalization was determined as malnutrition. In the study by Al-jamal et al. oral intake disorder was the most common symptom expressed by patients during hospitalization with 35%. Studies conducted in different centers show that nutritional deficiency is a major problem in patients hospitalized with PCS and the physician and his/her team should be knowledgeable about this issue and provide effective care to the patient and his/her relatives. While many diseases and their symptoms are intertwined and specialized and expensive interventions can be performed in the branch branch for the management of each of them, a holistic perspective has built a clinical functioning that saves unnecessary costs with patient and effective expenditure. A systematic review by Mathew et al. emphasized the cost benefit of palliative care. The top 3 primary diagnoses were lung cancer (15.8%), CVD (14.8%) and Alzheimer's disease (14.1%). Regarding both genders, lung cancer is the most common cancer in the world. CVD is a common disease with many risk factors such as heart diseases, diabetes mellitus, hyperlipidemia, smoking and alcohol (14). Management of each disease group by family physicians can reduce the risk and reduce the occupancy of PCS beds due to preventable risk factors.

Gastrointestinal system tumors, cases with brain metastases, Alzheimer's, dementia, Parkinson's, etc. are destructive processes that contribute to the patient's need for PEG opening (15). In the study of Ozturk and his colleagues, the most common tumor in the palliative service is gastrointestinal system tumors. (16) In this study, it was found that 24.3% of the individuals underwent a specific interventional procedure and the most common interventional procedure was PEG opening. In a review by Çakır et al., it is pointed out that the risk of pressure ulcers in patients hospitalized in palliative care is higher than in the normal population and increases with age. (17). In this process, the facilities of the tertiary care were mobilized for the patients by offering VAC treatment, which is one of the special treatments of pressure ulcers. 8 patients (2.5%) underwent VAC treatment. In PCS, from wound biopsy to foot amputation, a wide range of problems were dealt with. While a wound biopsy was performed for a case of suspected malignancy with incomplete diagnostic workup and dermatology was involved, another case of foot amputation demonstrates how close the surgical approach is.

It was determined that the majority of people were hospitalized from the emergency medicine outpatient clinic. In the consultation analysis sent to the PCS, it is seen that applications from the emergency medicine outpatient clinic are more common. The high number of patients admitted and admitted to the emergency medicine outpatient clinic and the fact that the hospitalization criteria for palliative care are not fully known may have led to this situation (18). As a result of the statistical analysis, it was found that the unit requesting consultation was statistically significantly more likely to be the emergency medicine department or intensive care unit than the other units. This may be due to the health policies of the Republic of Turkey. Patients may not have been able to participate in the system in a certain order due to the lack of a specific referral chain, the accessibility of the application to emergency services, and the lack of deterrence of social security institution responsibilities for patients and their relatives. With the widespread use of home health services and the development of palliative care, patients can be supported in a timely manner to receive early services instead of emergency services. With the development of the hospice concept and improvements in the application system, the burden on the emergency medicine outpatient clinic can be removed. As a result of the statistical analysis, it was found that the most common people who died were those with a primary diagnosis of respiratory tract cancers and there was a statistically significant difference between the groups. When evaluated in terms of respiratory tract cancers, the importance of effective fight against preventable risk factors becomes clear once again. In particular, smoking is the primary cause of respiratory tract cancers, but smoking-induced diseases such as COPD may not play a role in both the course of the disease and the development of cancer in the future. The fact that most of the inpatients are in the city center and that there is a significant statistic in terms of mortality may be an idea for future studies in terms of air pollution.

Study Limitations

This study is based on hospital archives due to its single-center, retrospective design. Due to the coronavirus

pandemic that started in December 2019, PCS could not provide service between April 2020 and June 2020. Due to the pandemic, it may have been difficult to reach the patient group due to patients and their relatives who wanted to stay at home. The reduction in the number of beds during the pandemic led to a quantitative decrease in the services provided. During the period when it was a pandemic hospital due to the pandemic, patient selection was based on stricter clinical observations and services may have been provided in response to needs and delayed needs instead of early services. These are the limitations of our study.

Conclusion

In conclusion, in this study, hospitalizations in the first 3 diseases in patients followed up in the palliative service run by the family medicine clinic were made in a way to serve the purpose of palliative care. The bulk of patients were discovered to have come from the emergency medicine outpatient clinic. It was discovered that people who needed direct radiography died at a higher rate than those who did not need direct radiography and this difference was statistically significant. There appeared to be a statistically significant difference between the groups, with respiratory tract malignancies being the most typical initial diagnosis among the deceased. Emergency medicine or intensive care units were shown to have a statistically significantly higher likelihood of asking consultation than the other units. Due to the growing demand over the past century, palliative care services have begun to naturally evolve and integrate into the system.

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Prognostic Value of the Status Epilepticus Severity Score in Clinical Outcomes

Status Epileptikus Şiddet Skorunun Klinik Sonuçlardaki Prognostik Değeri

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Abstract

Background: Status epilepticus (SE) is a neurological emergency associated with high morbidity and mortality. The Status Epilepticus Severity Score (STESS) has been proposed as a prognostic tool to predict outcomes in SE patients. This study aims to evaluate the effectiveness of STESS in predicting clinical outcomes and in-hospital mortality rates among SE patients.

Materials and Methods: We conducted a retrospective analysis of patient data collected between January 2020 and February 2024 at Harran University Faculty of Medicine Hospital. The study included 29 patients diagnosed with SE, who were categorized based on etiological factors and treatment modalities. STESS was calculated for each patient, and its correlation with clinical outcomes and mortality rates was analyzed using statistical methods.

Results: The mean age of the study group was 37.55±18.81 years, and the mortality rate was 13.8% (n=4). Acute symptomatic etiology played a 31% role in the overall etiology. The most common etiology was central nervous system (CNS) infections (17.2%) and the most common comorbidity was DM (17.2%). 13.8% of the patients died during follow-up. There was no significant difference between the survivors and the deceased patients in terms of mean age, duration of hospitalization and duration of status (p>0.005). The mean STESS score of the patients was 1.48±1.05. Age was significantly higher in patients with STESS scores 3-6 (p=0.004). Mortality was significantly higher in patients with higher STESS scores (p=0.005). The sensitivity of STESS in predicting mortality was 95.7%, specificity was 50% and PPV 75%, NPV 12%.

Conclusion: The study demonstrates the prognostic value of STESS in predicting clinical outcomes in SE patients. Utilizing STESS in clinical practice can help identify high-risk patients and guide therapeutic strategies to improve patient outcomes. Further research is warranted to validate these findings in larger, multi-center studies.

Keywords: Status Epilepticus, STESS, Prognosis, Mortality, Clinical Outcomes

ÖZ

Amaç: Status epileptikus (SE), yüksek morbidite ve mortalite ile ilişkili bir nörolojik acil durumdur. Status Epileptikus Şiddet Skoru (STESS), SE hastalarında sonuçları öngörmek için önerilen bir prognostik araçtır. Bu çalışmanın amacı, STESS'in SE hastalarında klinik sonuçları ve hastane içi mortalite oranlarını öngörmedeki etkinliğini değerlendirmektir.

Gereç ve Yöntem: Ocak 2020 ile Şubat 2024 tarihleri arasında Harran Üniversitesi Tıp Fakültesi Hastanesi'nde toplanan hasta verilerinin retrospektif bir analizini yaptık. Çalışmaya, etiyolojik faktörlere ve tedavi yöntemlerine göre kategorize edilen SE tanısı konmuş 29 hasta dahil edilmiştir. Her hasta için STESS hesaplandı ve klinik sonuçlar ve mortalite oranları ile korelasyonu istatistiksel yöntemler kullanılarak analiz edildi..

Bulgular: Çalışma grubunun yaş ortalaması 37,55 ± 18,81olup mortalitenin %13,8 (n=4) olduğu, etiyolojide akut semptomatik etiyolojinin %31 rol oynadığı belirlendi. Saptanabilen etyolojide en sık merkezi sinir sistemi (MSS) infeksiyonlarına rastlandı (% 17.2). En sık komorbidite olarak ise DM'e rastalandı (% 17.2). Hastaların %13,8'i takipte öldü. Hayatta kalanlarla ölenler arasında ortalama yaş, hastanede yatış süresi ve status süreleri açısından anlamlı farklılık yoktu (p>0,005) Hastaların STESS skoru ortalamaları 1,48 ± 1,05 idi. STESS 3-6 puan alanlarda yaş anlamlı olarak daha yüksekti (p=0,004). STESS skoru yüksek olan hastalarda mortalite anlamlı olarak daha yüksek olduğu gözlendi (p=0.005). STESS'nun mortaliteyi ön görmedeki duyarlılığı %95,7, özgüllüğü %50 ve PPV %75 NPV %12 olduğu bulundu.

Sonuç: Çalışma, STESS'in SE hastalarında klinik sonuçları öngörmedeki prognostik değerini göstermektedir. Klinik uygulamada STESS'in kullanılması, yüksek riskli hastaların belirlenmesine ve tedavi stratejilerinin yönlendirilmesine yardımcı olabilir. Bu bulguları daha geniş, çok merkezli çalışmalarda doğrulamak için daha fazla araştırmaya ihtiyaç vardır.

Anahtar Kelimeler: Status Epileptikus, STESS, Prognosis, Mortalite, Klinik Sonuçlar

Highlights

- Higher Status Epilepticus Severity Score (STESS) is associated with increased mortality, indicating its prognostic value in clinical outcomes.
- Acute symptomatic etiology was found to be the most common cause of SE, with central nervous system infections.
- STESS showed a high sensitivity in predicting mortality, making it a valuable tool for identifying high-risk SE patients and guiding treatment strategies.

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Introduction

Status epilepticus (SE) is a neurological emergency. SE's mortality rate ranges between 8.6% to 46.5% (1-4). It is difficult to treat as it is necessary to stabilize effectiveness and quickly stop seizures and toxicity to reduce complications. This difficulty is further increased by the heterogeneity of SE etiology, semiology and severity, and usually requires individualized treatment (5). In this context, evaluating the individual patient's prognosis as early as possible in the management of SE is very important to avoid overtreatment and its potentially harmful consequences or inadequate treatment (6). Prognostic scores furnish clinicians and families with predictive information regarding clinical outcomes. They provide a practical way to classify the severity of SE and guide individualized treatment (3). The Status Epilepticus Severity Score (STESS) has been proposed as a valuable and quick-to-use clinical prognostic scale that supports neurologic assessment for outcome prediction and developed by Rossetti et al.(7). The STESS is the first score used for SE prognosis classification based on four outcomes: level of consciousness, seizure type, age and seizure history. Rossetti et al. found an optimal cut-off value at ≥3 with a sensitivity of 0.94 and specificity of 0.60 in STESS with a maximum score of 6. The negative predictive value (NPV) was 0.97 and the positive predictive value (PPV) was 0.39 (7). The prognostic performance of STESS has been investigated in various studies and recently outlined in a meta-analysis, showing that it has a high NPV for short-term mortality but a very low PPV (5). In other terms, it is more influential in accurately forecasting patients who will survive but not as effective in forecasting death (8). A retrospective study by Ciurans et al. found that STESS was associated with inpatient mortality in 49 patients with refractory status epilepticus (RSE) in the intensive care unit (9). A report studying prognostic scores among 55 SE patients admitted to the neurology intensive care unit reported the STESS was sensitive but did not assess its prognostic value in terms of mortality (10).

The objective of this study was to assess the clinical findings, etiology and prognosis in SE and to determine the role of STESS in predicting prognosis and mortality.

Materials and Methods

During the period from January 2020 to February 2024, a total of 29 adult patients diagnosed with SE as a result of changes in mental status or seizures by a neurologist while hospitalized at Harran University Faculty of Medicine Hospital's neurology department or other clinics were part of the research study. Patients with anoxic-ischemic SE were excluded. The demographic and clinical features of the patients, as well as their prognosis and prognosis predictors, were recorded. SE is defined as a patient's neurologic status lasting longer than five minutes or having two or more sequential seizures without returning to baseline between seizures. RSE was described as SE that continued even after benzodiazepine and a minimum of two doses of parenteral antiepileptic therapy at proper doses. Super-refractory status epilepticus (SRSE) was described as SE lasting over 24 h despite treatment with antiepileptic drugs and anesthetics. Mortality was defined as in-hospital mortality, recorded from the time of admission to the hospital until death within the hospital. The diagnosis of non-convulsive status epilepticus (NCSE) was made in accordance with the Salzburg Consensus Criteria (11). Patients were also etiologically classified according to the International League Against Epilepsy (ILAE) SE classifications (12). To facilitate statistical analysis, factors likely to be associated with mortality were categorized and STESS was then calculated (7). A STESS score of 0 - 2 was considered indicative of a good prognosis, while a STESS score of 3 - 6 was associated with an poor prognosis. Two groups of outcomes were defined as 'return to baseline' and 'death'. The study was granted permission from the Ethics Committee of Harran University Faculty of Medicine (HRU/24.05.36), Date: 29.04.2024.

Statistical Analysis

Statistical analysis was performed using IBM SPSS for Windows version 20.0 package program. While evaluating the study data, frequencies (number, percentage) were given for categorical variables and descriptive statistics (mean, standard deviation) were given for numerical variables. The normality assumptions of the numerical variables were examined by Shapiro Wilk normality test. Mann Whitney U and Chi-square tests were used to compare categorical variables. In the comparison of numerical changes between independent groups, the Independent sample T Test was used for normally distributed variables. Statistical significance was interpreted at the ≤0.05 level. Sensitivity, specificity, PPV, NPV of STESS in predicting mortality were given.

Results

Our study included 29 SE patients, 12 (41.1%) females and 17 (58.6%) males. The mean age was 37.55±18.81 years (19-87). NCSE was diagnosed in 1 (3.4%), RSE in 25 (86.2%) and SRSE in 3 (10.3%) patients. 24 patients (82.7%) had a known history of epilepsy. While no etiology was identified in 44% (n=11) of the patients, acute symptomatic etiology was observed in 31% (n=9), progressive symptomatic etiology in 6.8% (n=2) and distant

symptomatic etiology in 24.1% (n=7). The most common etiologic cause was CNS infections (n=5, 17.2%) and the most common comorbid disease was DM (n=5, 17.2%). Mortality was 13.8% (n=4), and there was no additional mortality during follow-up. Of these patients, 2 (50%) were known to have had epilepsy previously. There was no significant difference between the survivors and the deceased patients in terms of mean age, duration of hospitalization and duration of status (p>0.005) **(Table 1).**

Table 1. Clinical characteristics of the survivors and non-survivors

Variables	Survivors	Non-survivors	*p*
Patients, n (%)	25 (86.2)	4 (13.8)	
Gender, n (%)			0.659
Male	15 (88.2)	2 (11.8)	
Female	10 (83.3)	2 (16.7)	
Age, year, mean ± SD	36.12 ± 18.92	46.50 ± 17.71	0.339
<65 years, n (%)	23 (92)	4 (100)	
>65 years, n (%)	2 (8)	0(0)	
Length of hospital stay (day)	6.68 ± 3.94	5.75 ± 2.50	0.553
Status duration (min)	109.40 ± 84.96	97.50 ± 66.52	0.764
History of epilepsy, n (%)			0.066
History of epilepsy (+)	22 (88)	2 (50)	
History of epilepsy (-)	3 (12)	2 (50)	
Comorbidities, n (%)			0.075
Comorbidity (+)	13 (52)	4 (100)	
Comorbidity (-)	12 (48)	0(0)	
Etiology, n (%)			0.075
Etiology determined	13 (52)	4 (100)	
Etiology not determined	12 (48)	0(0)	
Type of etiology, n (%)			
Cryptogenic	11 (44)	0 (0)	
Acute Symptomatic	6 (24)	3 (75)	
Progressive Symptomatic	2 (8)	0 (0)	
Distant Symptomatic	6 (24)	1 (25)	

The mean STESS score of the patients was 1.48±1.05. The mean age of patients with STESS scores 0-2 was significantly lower than the group with STESS scores 3-6 (p = 0.004). No significant difference was found in these groups in terms of length of hospitalization, duration of SE and comorbid diseases. Fifty percent (n=3) of patients with a STESS score of 3-6 and only 4.3% (n=1) of patients with a STESS score of 0-2 died. Mortality was significantly higher in patients with higher STESS scores (p = 0.005) **(Table 2).** The sensitivity of STESS in the context of mortality prediction was 95.7%, specificity was 50% and PPV 75%, NPV 12%. In the treatment of SE, 72.4% (n=21) of the patients received diazepam and 17.2% (n=5) received midazolam. The most commonly used second-line antiepileptic drug was IV levetiracetam (69%, n=20), the second most common drug was IV phenytoin (37.8% n=11), and the third most common drug was IV valproic acid (34.5% n=10). Of the 3 patients

evaluated as SRSE, 2 (6.9%) received thiopental and one received ketamine.

Table 2. Clinical characteristics according to STESS

Variables	Group 1 (STESS=0-2)	Group 2 (STESS=3-6)	*p*
Patients, n (%)	23 (79.3)	6 (20.7)	
Gender, n (%)			0.711
Male	10 (43.5)	2 (33.3)	
Female	13 (56.5)	4 (66.7)	
Age, year, mean (SD)	30.48±11.20	64.67±17.78	**0.004**
<65 years, n (%)	23 (100)	4 (66.7)	
>65 years, n (%)	0	2 (33.3)	
Length of hospital stay (day)	6.26±2.84	7.67±6.43	0.622
Status duration (min)	107.61±88.45	108.33±54.55	0.980
History of epilepsy, n (%)			0.827
History of epilepsy (+)	22 (95.7)	2 (33.3)	
History of epilepsy (-)	1 (4.3)	4 (66.7)	
Comorbidities, n (%)			**0.032**
Comorbidity (+)	12 (52.2)	5 (83.3)	
Comorbidity (-)	11 (47.8)	1 (16.7)	
Death, n (%)			**0.005**
Survivors	22 (95.7)	3 (50)	
Non-survivors	1 (4.3)	3 (50)	
Etiology, n (%)			**0.000**
Etiology determined	14 (60.9)	3 (50)	
Etiology not determined	9 (39.1)	3 (50)	
Type of etiology			
Cryptogenic	9 (39.1)	2 (33.3)	
Acute Symptomatic	5 (21.7)	4 (66.7)	
Progressive Symptomatic	2 (8.7)	0	
Distant Symptomatic	7 (30.4)	0	

Discussion

In this study, the significance of the STESS in prognostic assessment of SE patients was demonstrated. Our findings indicate that patients with higher STESS scores have significantly increased mortality. This study aligns with previous research showing variable SE outcomes and highlights the importance of using prognostic scores in guiding treatment strategies.

Several factors associated with poor outcome of SE include age ≥60 years (13), longer duration of SE (14), no past history of seizures (15), low Glasgow coma scale score at presentation (13, 15), type of SE (7), acute symptomatic etiology (16), and the presence of periodic lateralized epileptiform discharges on EEG (13). Prognostic scores are

valuable instruments for guiding the medical strategy and management of patients with SE (3). This study was conducted in a tertiary care hospital and it was observed that SE was more common in men and under 65 years of age, and CNS infection was the most common etiology in cases. The mortality rate was found to be high in cases with high STESS score.

Age is a predictor of mortality in SE patients (17). Although it is an unchangeable prognostic factor, age, which is a variable also included in STESS, should be taken into account in the overall evaluation. In our study, the mean age was lower compared to similar literature data and higher compared to male prevalence (18). In the present study, age was significantly higher in the group with STESS 3-6 ($p=0.004$). Advanced age (>65 years) has been shown as a poor prognostic factor in similar studies (19). In a study using STESS to predict clinical outcomes of SE, age and gender did not differ significantly between survivors and non-survivors (20). Reports on the sex of patients with SE are conflicting; some studies have shown a higher prevalence in males, whereas others have indicated a higher prevalence in females (21-23). In the current research, there was a higher prevalence of males.

The role of the underlying etiology is crucial in influencing short-term mortality, especially if it is acute and fatal (24). Like in previous studies, the current research also identified acute symptomatic etiology as the most common cause of SE. While CNS infection was the top reason for SE in Western China, strokes were more prevalent in the United States and certain developed European nations based on Zhou et al.'s study (25-27). This is linked to the elevated occurrence of CNS infections, particularly encephalitis and tuberculous meningitis in developing countries (25). Similarly, the presence (type and number) of comorbidities may influence short-term mortality and may indicate higher baseline frailty in patients who are less likely to survive. Identification and, if possible, treatment of comorbidities may improve prognosis and reduce mortality (28). In a case report, muscle damage in a patient with SE was noted and patients at risk of acute kidney injury were recommended to be closely monitored for creatinine kinase and urine output (29). A retrospective observational study in patients with RSE examined the impact of comorbidities on functional outcome and mortality and showed that STESS and chronic kidney disease were associated with mortality (9).

A retrospective study of prognostic assessment in SE patients in the ICU found that diabetes was strongly associated with mortality (30). A study on 173 patients with SE discovered that having diabetes increased the likelihood of in-hospital mortality (31). In a separate SE study (32), hyperglycemia was reported to be a predictor of poor outcome and has been suggested in connection with exacerbation of seizures and SE-induced hippocampal damage (33). In the present study, DM was the most common comorbid disease. The STESS score of those with comorbid diseases was significantly lower and all of those who died had at least one comorbid disease. While causality is uncertain, patients in the ICU with SE and diabetes may face complications such as extended intubation and sepsis as a result of high blood sugar levels. Managing high blood sugar levels in these patients continues to be crucial due to its adverse effects on critically ill patients (34).

Reliable prognostic indicators are needed to support the clinical approach and prevent both under- and over-treatment (35). With its convenience and ease of use, STESS has been commanly used to estimate SE outcomes and stratify patients (36). Former reports have shown that STESS is an important prognostic predictor (7). Different mortality rates have been reported in studies conducted with epilepsy patients (37, 38). In the current study, the acute symptomatic group had the highest mortality rate. Mortality rate was similarly in both sexes in the group with and without a history of epilepsy. In Göl et al.'s research, 48.5% of individuals with a STESS score of 3-6 died, compared to zero deaths in the group with a STESS score of 0-2 (39). Goyal et al. found a strong correlation between elevated STSS scores and negative neurological outcomes upon discharge, the requirement for inducing coma, and a lack of response to treatment within one hour. A STESS score of less than 3 had a high negative predictive value of 96.9% for mortality, 96.7% for poor neurological outcome at discharge, and 96.7% for requiring coma induction. On the other hand, a STESS score of less than 2 had a perfect negative predictive value of 100% for mortality, coma induction, and poor neurological outcome at discharge. (40). In the present study, 50% of patients with STESS scores of 4-6 and only 4.3% of patients with STESS scores of 0-3 died. Mortality was significantly higher in patients with higher STESS scores. The sensitivity of STESS in predicting mortality was 95.7%, specificity was 50% and PPV 75%, NPV 12%.

Study Limitations

As a limitation, in addition to its retrospective nature and limited number of patients, this study only assessed in-hospital mortality, did not include variables related to physical disability or long-term mortality and life quality after discharge. Furthermore, STESS scoring is based on physicians' judgment and may therefore introduce bias. There is a need for improved scales or indicators for the determination of the whole prognosis of patients with SE. Given the low primary outcome rates, the power analysis of the study is limited. Increasing the sample size in

future studies would enhance the generalizability of the findings and provide more robust conclusions.

Conclusion

Finally, in our research, it was noted that SE was more common in males and under 65 years of age, and CNS infection was the most frequent etiology in cases. The mortality rate was found to be high in cases with high STESS score. Underlying etiology, age and comorbidities are important determinants of prognosis. In the light of our data and the literature, low (<3) STESS has a good NPV for unfavorable results. In SE with low STESS, intensive treatment protocols can be avoided at least in the initial phase and treatment-related complications can be prevented. The STESS score is an easily applicable scoring tool that helps predict mortality.

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Original Article

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The Effect of Albumin Level and Neutrophil Lymphocyte Ratio on Mortality and Recovery in Fournier's Gangrene

Fournier Gangreninde Albumin Düzeyi ve Nötrofil Lenfosit Oranının Mortalite ve İyileşme Üzerine Etkisi

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Abstract

Background: Fournier's gangrene (FG) is a polymicrobial bacterial infection with a high mortality and morbidity rate, and early diagnosis and treatment in FG is crucial. The mainstay of treatment for FG comprises antibiotics and surgical debridement. Our study aimed to predict mortality more accurately in patients with Fournier's gangrene.

Materials and Methods: The medical records of 60 patients who underwent surgical intervention for FG at our clinic between 2016 and 2021 were retrospectively reviewed.

Results: Of the patients, 15% were urogenital, 61.7% colorectal and 23.3% idiopathic origins. Albumin level was lower for people who died (27.35±4.66) compared to those who recovered (34.53±7.75) (p=0.001). Both the number of surgical debridement and duration of hospitalization were observed to be lower in patients who survived (p<0.05). Being above the age of 59.50 and albumin levels below 31.25 were found to be risk factors for FG mortality. Neutrophil- lymphocyte ratio had no significant effect on mortality (p=0.733 **Conclusion:** Serum albumin level was found to be a predictive value for mortality and recovery in patients with Fournier's gangrene. No significant effect of neutrophil-lymphocyte ratio on mortality and recovery in patient with Fournier's gangrene was found.

Keywords: Fournier's gangrene, albumin level, neutrophil-lymphocyte ratio.

ÖZ

Amaç: Fournier gangreni, mortalite ve morbidite oranı yüksek olan polimikrobiyal bakteriyel enfeksiyondur ve erken tanı ve tedavi önemlidir. Tedavisinin temeli antibiyotikler ve cerrahi debridmandır. Çalışmamızda Fournier gangreninde mortaliteyi daha doğru tahmin etmeyi amaçladık..

Gereç ve Yöntem: 2016 ile 2021 arasında kliniğimizde Fournier gangreni nedeniyle opere edilen 60 hastanın tıbbi kayıtları geriye dönük olarak incelendi.

Bulgular: Hastaların %15'i ürogenital, % 61.7'si kolorektal ve %23.3'ü idiopatik kaynaklıydı. Albümin değeri excitus bireylerde (27.35±4.66), iyileşenlerdeki albümin değerine kıyasla (34.53±7.75) daha düşüktü (p=0,001). Debridman sayısı ve hastanede yatış süresi yaşayan hastalarda düşük gözlendi (p<0,05). Yaşın 59,50 düzeyinin üzerinde olması mortalite de risk teşkil ettiği görüldü. Albumin değerinin 31,25 değerinin altında olmasının mortaliteye risk teşkil ettiği tespit edildi. Nötrofil lenfosit oranının mortalite üzerinde anlamlı etkisinin olmadığı görüldü (p=0.733).

Sonuç: Serum albumin düzeyinin Fournier gangreni hastalarında mortalite ve iyileşme üzerinde prediktif bir değer olduğu tespit edildi. Nötrofil lenfosit oranının Fournier gangreninde mortalite ve iyileşme üzerinde anlamlı etkisi tespit edilmemiştir.

Anahtar Kelimeler: fournier gangreni, albümin düzeyi, nötrofil lenfosit oranı

Highlights

- Fournier's gangrene (FG) is a polymicrobial bacterial infection with a high mortality and morbidity rate.
- Albumin is an important factor both in recovery and wound healing in patients who underwent surgery.
- NLR (neutrophil-lymphocyte ratio) is an indicator of inflammatory processes and immune response.
- Serum albumin level was found to be a predictive value for mortality and recovery in patients with FG.

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Introduction

Fournier's gangrene (FG) is a suppurative polymicrobial bacterial infection with high mortality and morbidity rate. It affects anorectal and perineal regions, as well as the genitourinary tract, and is linked to certain systemic disorders. In other words, FG is acute and potentially fatal infection that causes thrombosis of subcutaneous vessels and progresses with necrotizing fasciitis and gangrene of the skin. The etiologic factors of FG include anorectal infections, abscesses and their surgical interventions, colorectal infections and colorectal surgical interventions, urogenital infections and urogenital surgical interventions, and trauma. The most cases of FG originate in the colorectal region (30-50%), followed by urologic system (20-40%) and skin (20%) (1).

Fournier's gangrene, which first described by Jean Alfred Fournier, a French venerologist-dermatologist, in 1883, is a necrotizing fasciitis involving the scrotum and penis in men and vulva and perineum in women, and may progress to the abdominal wall in advanced stages. It can be fatal if left untreated. FG occurs ten times more frequently among males than females (2,3). Some systemic diseases may be predisposing factors for Fournier's Gangrene by weakening the immune system.

Predisposing factors for this condition include diabetes mellitus, alcoholism, immunosuppression, hepatic and renal failure, obesity, heart failure, hypertension, SLE, leukemia, steroid therapy, local trauma, extravasation of urine into the periurethral area, perirectal or perianal infection, and certain surgical procedures (circumcision, herniorrhaphy, hemorrhoidectomy) (3,4). Today, FG may occur in all age groups but more common among patients older than 50 years (5,6).

Due to the potentially fatal nature of FG, early diagnosis and prompt initiation of treatment are crucial. Consideration should be given to concurrent examination findings in genitourinary tract infections and interventions, perianal infections and interventions, and perineal and scrotal region. Even nonspecific conditions should not be overlooked. Erythema, crepitation and bullae may develop before necrosis, and thus require special medical attention. (3,4,7,8). Treatment should be initiated with emergency surgery. Necrotized and devitalized areas should be extensively and completely debrided until viable tissue is reached. Namely, the mainstay of treatment are broad-spectrum antibiotics and aggressive surgical debridement (4,9). Additionally, intravenous fluid support is required. Routine blood tests are important in follow-up. Concomitant diabetes and renal failure or conditions that may weaken the immune system, if any, should be followed up with the necessary blood tests. There are many factors affecting mortality and morbidity in patients with Fournier gangrene. The common denominator of all comorbid risk factors is impaired immune resistance due to decreased cellular immunity in the organism (2).

In the literature review, Engin et al. investigated the factors affecting mortality in patients with Fournier's gangrene including age, prevalence of infection, presence of comorbidities and duration of intensive care unit (ICU) stay (10). In our study, we aimed to understand the effect of albumin level and neutrophil- lymphocyte ratio on mortality and recovery.

Material and Methods

The medical records of patients who underwent surgical intervention for Fournier's gangrene in our clinic between 2016 and 2021 were retrospectively reviewed. Patients were physically examined at the time of admittance and FG was diagnosed with genital and perineal skin necrosis, cyanosis, gangrene; and subcutaneous crepitation findings. The infected and necrotic tissues were debrided with broad-spectrum antibiotic therapy. The tissues were cleaned with hydrogen peroxide and povidone iodine during and after debridement. In complicated cases with extensive and deep necrosis, VAC was performed with second debridement. In recovered patients, the defect was closed by primary suture or graft. Patients with perianal abscess or simple skin infection without Fournier gangrene were not included in the study.

Statistical Analysis

The fitness of the data to normal distribution was tested using Shapiro Wilk test, Student t test was used to compare the normally distributed characteristics in 2 independent groups, and Mann Whitney u test was used to compare the non-normally distributed characteristics in 2 independent groups. The analysis of the relationship between categorical variables observed in two independent groups was analyzed by Pearson Chi-square test. ROC curve was plotted based on the cutoff values for predicting mortality rate using the variables age, albumin level, the number of debridement and duration of the hospitalization. As descriptive statistics, mean ± standard deviation values were given for numerical variables and number and % values were given for categorical variables. SPSS Windows version 23.0 package program was used for statistical analysis and $P<0.05$ was

considered statistically significant.

Results

Of the 60 patients studied, 16 (24.4%) were female and 44 (75.6%) were male. The mean age of the entire group was 56±14.08 (years). The mean duration of hospitalization was 16.93±19.57 days. The mean number of debridement performed was 2.08±2.19. 15 (25%) patients were over 65 years of age and 35 (58.3%) patients had DM. 10 (16.7%) of our patients died due to FG. The mean time of admission to hospital was 9.23±6.94 days **(Table 1)**. An assessment of underlying etiologic factors in patients revealed that urogenital and colorectal causes were the etiologic factors in 9 (15%) and 37 (61.7%) patients, respectively. The etiologic factor of 14 (23.3%) patients could not be determined **(Figure 1).**

Considering the duration of hospitalization, it was observed that patients with colorectal causes and patients with high albumin values had a shorter hospital stay **(Table 3)**.

Considering the factors affecting mortality, female gender, advanced age and patients with FG due to causes other than colorectal and urogenital causes were found to have a higher mortality rate **(Table 4)**.

Albumin level was statistically significantly lower for the mortality group (27.35±4.66) compared to that of recovered group (34.53±7.75) (p=0.001). According to the ROC curve analysis on age, albumin, number of debridement and duration of hospitalization, which showed statistically significant differences on mortality; it was shown that age over 59.50 was effective in mortality (sensitivity 90%, specificity 72%), similarly, albumin level below 31.25 (sensitivity 66%, specificity 90%) similarly increased mortality.

Table 1. Patient Characteristics

Parameters	N	%	Mean ± SD
Patients (total number)	60		
Female/Male ratio	16/44	26.7/73.3	
Mean age (years)			56.00 ± 14.08
Geriatric patients (over 65 years of age)	15	25	
Patients with a known source	46	76.7	
Patients with a history of diabetes mellitus	35	58.3	
Mean duration of hospitalization (days)			16.93 ± 19.57
Mean number of debridements			2.08 ± 2.19
Mortality rate	10	16.7	
Time for admission to hospital			9.23 ± 6.94

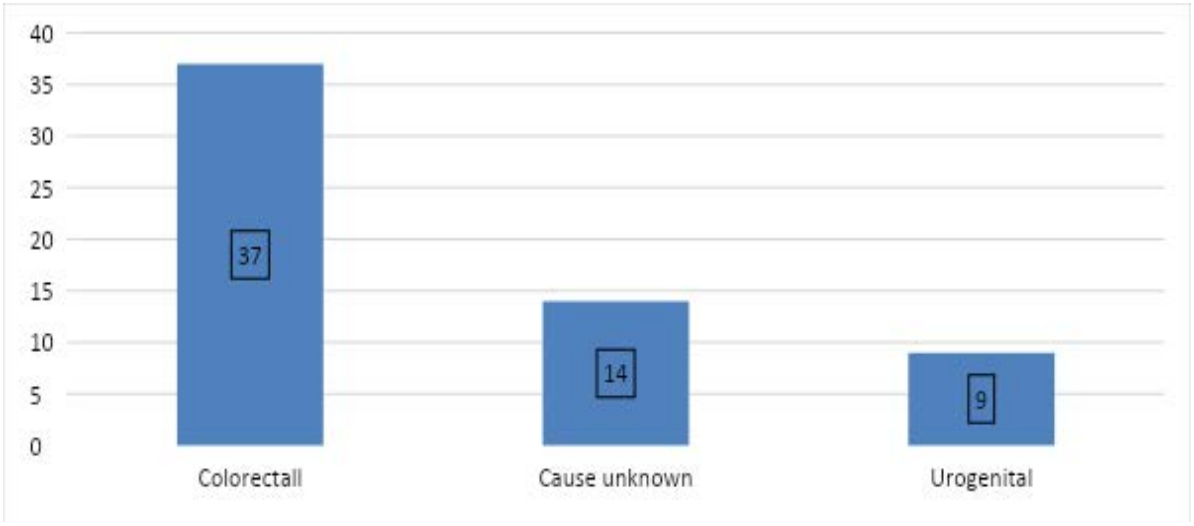

Figure 1. Origin of infection in cases of Fournier's gangrene

Table 3. Factors affecting the duration of hospitalization

Parameters	≤14 gün	>14 gün	p
Number of patients n (%)	41 (63.8)	19 (31.7)	
Female/male ratio n (%)	10(24.4)/31(75.6)	6(31.6)/13(68.4)	0.558
Age (years) (mean±SD)	53.90 ± 14.75	60.53 ± 11.62	0.090
Urogenital n (%)	4 (9.8)	5 (26.3)	0.095
Cause unknown n (%)	8 (19.5)	6 (31.6)	0.304
Colorectal n (%)	29 (70.7)	8 (42.1)	**0.034**
Patients with a history of diabetes mellitus n (%)	22 (53.7)	13 (68.4)	0.281
Time (days) of admission to hospital (mean±SD)	7.73 ± 5.43	12.47 ± 8.73	0.063
Neutrophil-to-lymphocyte ratio (mean±SD)	11.80 ± 12.65	27.48 ± 75.37	0.733
Platelet-to-lymphocyte ratio (mean±SD)	250.33 ± 325.04	237.28 ± 135.52	0.201
Albumin level (mean±SD)	35.31 ± 7.87	29.08 ± 5.72	**0.004**

Table 4. Factors affecting mortality

Parameters	Death	Recovery	p
Number of patients n(%)	10 (16.7)	50 (83.3)	
Female/male ratio n(%)	6(60)/4(40)	10(20)/40(80)	**0.009**
Age (years) (mean±SD)	69.0 ± 15.10	53.40 ± 12.47	**0.001**
Urogenital n(%)	1 (10.0)	8 (16.0)	0.628
Cause unknown n(%)	5 (50.0)	9 (18.0)	**0.029**
Colorectal n(%)	4 (40.0)	33 (66.0)	0.123
Patients with a history of diabetes mellitus n(%)	8 (80.0)	27 (54.0)	0.128
Time (days) of admission to hospital (mean±SD))	16.90 ± 8.48	7.70 ± 5.51	0.063
Neutrophil-lymphocyte ratio (mean±SD)	21.72 ± 17.71	15.77 ± 47.10	0.733
Platelet-lymphocyte ratio (mean±SD)	456.97 ± 577.14	204.04 ± 144.84	0.201
Albumin level (mean±SD)	27.35 ± 4.66	34.53 ± 7.75	**0.001**
Number of debridement (mean±SD)	2.60 ± 2.37	1.98 ± 2.16	**<0.001**
Duration of Hospitalization (days) (mean±SD)	20.70 ± 18.51	16.18 ± 19.87	**<0.001**

Table 5. Roc analysis for mortality

Parameters	Cut-off	AUC	p	Sensitivity	Specificity
Age	>59,50	0,822	0,001	0,90	0,72
Albumin level (first hospitalization)	<31,25	0,771	0,007	0,66	0,90
Number of debridements under anesthesia	>1,5	0,626	0,211	0,70	0,52
Total duration of hospitalization	>6,5	0,654	0,127	0,99	0,44

Abbreviations: AUC: Area Under Curve

Discussion

FG is a rapidly progressive clinical condition characterized by severe necrosis that may affect the fascia and subcutaneous tissues in the perianal, perineal and genitourinary regions. The disease can affect both sexes at any age but predominantly affects adult males. The disease is a polymicrobial infection, both aerobic and anaerobic. The disease is characterized by polymicrobial and synergistic infection. The pathophysiology is probably triggered by endarteritis obliterans and microthrombosis of the small vessels in subcutaneous tissues (11,12). As is known, its pathophysiology is characterized by the heparinase and collagenase produced by the anaerobes and platelet aggregation and complement fixation induced by the aerobes and lead to microvascular thrombosis and dermal necrosis. Due to its rapid and aggressive progression, it remains a highly lethal in course. Depending on the degree of progression, the skin may appear normal, red or shiny or may show signs of ecchymosis and crepitation (13). An urgent and multidisciplinary approach is required in treatment.

In our study, the mean duration of admission of patients who died was 16.9+-8.48 days and the mean duration of admission of patients who recovered was 7.7+-5.51 days, which was not statistically significant (p=0.063).

A study found that patients who had died were admitted to the hospital at least 5 days after the onset of the symptoms (14). Our study found that the duration of admission was not significant factor for the death of patients, but a study showed that laboratory findings deteriorated rapidly if there was a delay in Necrotizing Fasciitis (14).

FG generally requires surgery and broad-spectrum antibiotic therapy, maintenance fluid therapy and additional surgical treatments such as cystostomy and colostomy if necessary. Testicular involvement is rare in FG because of the separate blood supply to the testes. The testes are usually spared as their blood supply originates intra-abdominally through spermatic cord. The involvement of the testis suggests retroperitoneal origin or spread of infection (7,8). However, orchiectomy and penectomy may occur rarely. In our study, additional surgeries such as cystostomy, colostomy and orchiectomy were not required.

Surgical debridement should be performed carefully until viable tissue is reached. It should be supported with broad-spectrum antibiotics and maintenance fluid therapy. It may be required to perform repeated debridement as necrotic tissues manifest. The number of debridement was significantly lower for patients who survived in our series. This could be due to the fact that the necrosis was not severe, rendering debridement unnecessary.

The mortality rate for FG remains high (43-53%) notwithstanding the progress made in intensive care and medical treatment, owing to its fulminating nature (15,16). Our study observed a significantly lower mortality rate (16.7%) in comparison to the literature.

According to the origin of onset, FG has been classified into four categories in studies: colorectal, genitourinary, dermatologic, and idiopathic (4,6,17). In these series, it was reported that 56% of cases were genitourinary, 22% were colorectal, 17% were dermatologic, and 5% were idiopathic origins. In our series, 15% of cases were urogenital, 61.7% were colorectal, and 23.3% were idiopathic origins.

There are several risk factors for FG. These include poor nutritional status, diabetes mellitus, immunosuppressive therapy, malignancy, alcoholism, and certain systemic diseases that have detrimental effects on blood circulation. Hyperglycemia has been found to affect the adhesion, chemotaxis, and bactericidal activity of phagocytes. It has also been demonstrated to have detrimental effects on cellular immunity (12,18). Hyperglycemia has been shown to be a risk factor for FG and to negatively affect the recovery process. In our series, DM was detected among 58.3% of the patients and was found to be a risk factor. However, no negative effect on hospitalization duration and mortality was observed.

Studies have shown the predictive value of BUN/albumin ratio in sepsis and hospital-acquired pneumonia (19,20). Another research found that BUN/albumin ratio was associated with a severe course in acute pancreatitis (21). The risk of mortality, the need for intensive care unit admission and the duration of hospitalization are expected to increase as BUN/albumin ratio raises. Ferzad Allameh et al. studied the BUN/albumin ratio in terms of FG mortality and prognosis and showed that the BUN/albumin ratio significantly affected mortality (22).

A study made to determine hospital mortality in critically ill intensive care patients found that the BUN level and BUN/albumin ratio of non-survivors were higher, and the albumin level of non-survivors was lower. Albumin <3.2 g/dL, BUN ≥32 mg/dL, and BUN/albumin ratio ≥10 found to be statistically significant on mortality. This study also showed that hypoalbuminemia alone is a more powerful predictor of in-hospital mortality than BUN or BUN/albumin ratio in those patients (23). In another study albumin is also found to be a valuable parameter predicting no-reflow rates in patients with ST elevated myocardial infarction (24)

In our study, the albumin level was significantly lower for patients who died (27.35±4.66) compared to the albumin level observed in recovered patients (34.53±7.75) (p=0.001). The number of debridement and duration of hospitalization were also significantly lower for patients who survived (p<0.05).

Our study also showed that albumin level was effective in prognosis, duration of hospitalization and intensive care unit admission. ROC analysis revealed that age over 59.50 was associated with a higher a risk for mortality (sensitivity 90%, Specificity 72%) and similarly, as did albumin level less than 31.25 (sensitivity 66%, Specificity 90%). Similarly, a study of 34 patients revealed a mean age of 58.4 years (14).

A research discovered that high NLR (neutrophil-lymphocyte ratio) and PLR (platelet-lymphocyte ratio) levels were associated with statistically significant increases in the number of surgical debridement, duration of hospitalization, cost and mortality rate.(25) Although NLR and PLR have been used in the literature to predict the prognosis of patients with different inflammatory and ischemic events, Şahin Kahramanca et al. found strong correlations between these parameters and the prognosis of the disease in their study and high NLR and PLR levels were associated with statistically significant increases in the number of surgical debridement, duration of hospitalization, cost and mortality rate (26,27). However, in our study found that NLR had no significant effect on mortality rate (p=0.733).

To date, the following indices have been used in predicting the prognosis of Fournier's gangrene prognosis: Fournier Gangrene Severity Index (FGSI), Uludag Fournier Gangrene Severity Index (UFGSI), Age-Adjusted Charlson Comorbidity Index (ACCI), Laboratory Risk Indicator for Necrotizing Fasciitis (LINEC) score, Combined Urology and Plastic Index (CUPI), as well as neutrophil-to-lymphocyte ratio (NLR) and surgical APGAR (sAPGAR) parameters were included (22).

Study Limitations

In this study, although the limited number of patients and the retrospective design are limitations, the evaluation of neutrophil and lymphocyte levels along with albumin levels in relation to patient recovery makes our research stand out.

Conclusion

FG is still an illness with a high mortality rate. Early and effective treatment is as critical as early diagnosis. Decreased albumin and increased NLR levels can predict poor prognosis. If albumin is determined to be high and NLR is determined to be low, it may be of particular importance for FG patients to receive more aggressive treatments and close follow-up. More studies with large sample sizes are needed to better determine whether these parameters are effective or not.

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Effect of Inflammation on Amino Acid Profile in Heart Failure Patients

Kalp Yetersizliği Hastalarında İnflamasyonun Amino Asit Profili Üzerine Etkisi

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Abstract

Background: Heart failure (HF) is a complex disease and inflammation play a crucial role in its pathophysiology. The metabolism of energy substrate alters in HF and these changes may lead to the impairment in amino acid (AA) metabolism by increasing the heart's dependence on AAs. Limited studies evaluated the relationship between inflammation and AA profile in patients with HF. In this study, we aimed to evaluate the AA profile in patients with HF and to reveal its relationship with inflammation.

Materials and Methods: Seventy-two patients with HF and 64 healthy controls were included in this study. C-reactive protein/albumin ratio (CAR) was used to assess inflammatory status of the patients. High performance liquid chromatography technique was used to evaluate the AA profile.

Results: We detected that AAs profile was significantly changed in HF patients compared to controls. HF patients had also significantly higher CAR ($p<0.001$) level. The best cut-off value of CAR for predicting HF was 0.91, and patients were divided into 2 groups according to this cut-off value: CAR≥0.91 (high inflammation group) and CAR<0.91 (low inflammation group). When compared to low inflammation, patients with high inflammation had significantly different AAs profile. Correlation analysis showed that CAR was positively correlated with phenylalanine, tyrosine and asparagine whereas negatively correlated with valine, leucine and methionine levels.

Conclusion: We found that AA profile was significantly changed in patients with HF. Also, the impairment in AA metabolism was more pronounced in patients with higher inflammation compared to patients with lower inflammation. We suggest that main mechanism underlying the impaired AA profile in HF may be increased inflammation.

Keywords: Heart failure, inflammation, CRP to albumin ratio, amino acid profile

ÖZ

Amaç: Kalp yetmezliği (KY) kompleks bir hastalıktır ve inflamasyon patofizyolojisinde önemli bir rol oynar. KY'de enerji substratının metabolizması değişir ve bu değişiklikler kalbin amino asitlere (AA) bağımlılığını artırarak AA metabolizmasında bozulmaya yol açabilir. KY hastalarında inflamasyon ve AA profili arasındaki ilişkiyi değerlendiren çalışmalar sınırlıdır. Bu çalışmada, KY hastalarında AA profilini değerlendirmeyi ve inflamasyon ile ilişkisini ortaya koymayı amaçladık.

Gereç ve Yöntem: Yetmiş iki KY hastası ve 64 sağlıklı kontrol çalışmaya dâhil edildi. Hastaların inflamatuvar durumunu değerlendirmek için C-reaktif protein/albümin oranı (CAR) kullanıldı. AA profilini değerlendirmek için yüksek performanslı sıvı kromatografi tekniği kullanıldı.

Bulgular: AA profilinin, KY hastalarında kontrollere kıyasla anlamlı derecede değiştiğini saptadık. KY hastaları ayrıca, anlamlı olarak daha yüksek CAR seviyesine sahipti ($p<0.001$). CAR'ın KY'yi öngörmede en iyi kesim değeri 0.91 idi ve hastalar bu kesim değerine göre 2 gruba ayrıldı: CAR≥0.91 (yüksek inflamasyon grubu) ve CAR<0.91 (düşük inflamasyon grubu). Düşük inflamasyonla karşılaştırıldığında, yüksek inflamasyonlu hastaların AA profili anlamlı derecede farklıydı. Korelasyon analizi CAR'ın fenilalanin, tirozin ve asparajin ile pozitif korelasyon gösterdiğini; aksine valin, lösin ve metiyonin seviyeleri ile negatif korelasyon gösterdiğini ortaya koydu.

Sonuç: KY hastalarında AA profilinin önemli ölçüde değiştiğini bulduk. Ayrıca, AA metabolizmasındaki bozulma, inflamasyonu daha yüksek olan hastalarda, inflamasyonu daha düşük olan hastalara kıyasla daha belirgindi. KY'de bozulmuş AA profilinin altında yatan ana mekanizmanın artmış inflamasyon olabileceğini düşünüyoruz.

Anahtar Kelimeler: Kalp yetmezliği, inflamasyon, CRP/ albümin oranı, amino asit profili

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Highlights

- Altered amino acid (AA) metabolism has been reported in patients with heart failure (HF).
- We also found that AA profile significantly was changed in patients with HF.
- This change in AA metabolism was more pronounced in patients with higher inflammation state.

Introduction

Heart failure (HF) is a clinical syndrome caused by a structural and/or functional cardiac abnormality resulting in reduced cardiac output. It is a serious public health problem worldwide and has an enormous burden on healthcare systems (1). Its incidence has gradually increased with increasing life expectancy, and this number is expected to more increase in future (2). In these patients, multiple system disorders may occur due to decreased cardiac output. Therefore, HF is known to affect not only the cardiovascular system but also the immune, neuroendocrine, renal and musculoskeletal systems. Despite improved modern treatment approaches, the prognosis of HF patients is still poor (3).

Heart failure has a complex pathophysiology. Inflammation, immune system and neurohormonal activation play critical roles both in the development and progression of HF (2,4,5). To date, many conventional biochemical markers have been studied to evaluate inflammatory status and identify their association with HF (3). Recently, a novel inflammatory marker, C-reactive protein (CRP) to albumin ratio (CAR), has emerged and this ratio reflects the balance of the CRP and albumin (6). Studies reported that CAR may be more sensitive than either CRP or albumin separately for assessing the inflammatory process, and its clinical importance has been well documented in patients with coronary artery disease (6-8). However, limited studies evaluated CAR in patients with HF and showed its association with the prognosis of HF (9,10).

The heart may utilize many substrates to meet its high energy demand, including fatty acids, glucose, ketone bodies and amino acids (AAs). Although AAs are essential nutrient metabolites for normal cellular development in the human body, the heart uses very small amounts of AA for direct energy production. It frequently uses AAs to regulate energy metabolism and myocardial protein turnover (11). However, if HF develops, the metabolism of substrates used by the heart for energy needs is significantly altered. For example, the primary substrate utilized for the energy demand changes from fatty acids to glucose in HF (12). In addition, the heart's dependence on AAs increases during HF because of increased myocardial anabolic activity (13). Therefore, the metabolism of AAs in HF patients is altered compared to healthy individuals.

Studies have demonstrated that the plasma AA profile is altered in HF patients and the evaluation of AA profile may have an important impact on risk stratification and prognosis in these patients (12). However, the mechanism underlying impaired AA metabolism in HF patients has not been fully elucidated yet. Limited studies evaluated the relationship between inflammation, which is a main pathophysiological process in HF, and AA profile in patients with HF. In the present study, it was aimed to evaluate the AA profile in patients with HF and to reveal its relationship with inflammation.

Material and Methods

A total of 72 consecutive patients with compensated HF who were admitted to our cardiology clinic between 01 July 2021 and 01 October 2021 were included in the study as the patient group. Also, age- and gender-matched subjects who applied to our cardiology outpatient clinic with any symptom and were not detected heart failure after the detailed examinations were consecutively included as the control group, between the same dates. The diagnosis of HF was made according to the European Society of Cardiology Heart Failure guidelines (1). Patients with compensated HF, left ventricular ejection fraction (LVEF) <40%, and those patients whose archive data were available were included in the study. Patients with decompensated HF, preserved and mildly reduced EF, active infection, thyroid diseases, inflammatory or hematological diseases, intestinal malabsorption diseases, history of malignancy, steroid use and chronic renal failure were excluded from the study. Approval for the study was obtained from the ethics committee of Harran University Faculty of Medicine (number: HRU/21.11.19, date: 07.06.2021). It was implemented in accordance with the rules of the Declaration of Helsinki and informed consent was obtained from all patients included in the study. Baseline characteristics, clinical features and comorbid

conditions of all participants were recorded.

Blood samples were collected from the participants under appropriate conditions. Baseline hemogram and biochemical parameters were analyzed from the blood samples. An automatic device (Coulter LH 780 Hematology Analyzer, Beckman Coulter Corp, Hileh, Florida) was used for complete blood count. Biochemical parameters were measured by standard techniques. CRP to albumin ratio was calculated by dividing CRP to albumin. In addition, 1 tube of blood was sent to the biochemistry laboratory for examination of the amino acid profile. Plasma and serum obtained by centrifugation at 5000 rpm for 5 minutes were separated into ependorfs and stored at -80^{o}C. High performance liquid chromatography technique was used for AA profile (14).

Echocardiographic evaluation was performed with Vivid S5 (General Electrics, Vivid S5 echocardiography, Milwaukee, WI, USA). Detailed echocardiographic evaluation was performed to all patients and LVEF was calculated with Simpson methods.

Statistical Analysis

Statistical analysis was performed with SPSS 22 (SPSS, Chicago, IL, USA) software program. Kolmogorov-Smirnov test was used to determine the normality of continuous variables. Normally distributed variables were presented as mean ± SD and compared with Student-t test. Non-normally distributed variables were presented as median (25-75th interquartile range) and were compared with Mann-Whitney U test. Categorical variables presented as number and percentage and compared with chi-square test. Receiver optic characteristics (ROC) curve analysis was performed to determine optimal cut off value of CAR for predicting the presence of HF. Pearson and/or Spearman correlation coefficients were used for correlation analysis. A p value of <0.05 was considered as statistically significant.

Results

Seventy-two patients with HF and 64 healthy subjects were included in this study. Baseline clinical and laboratory variables of the patients and control group are listed in Table 1. Age (p=0.260) and gender (p=0.510) were similar between two groups. However, the frequency of hypertension (p=0.037) was significantly higher and LVEF (p<0.001) was lower in HF patients than in the healthy subjects. Regarding laboratory parameters, it was found that CRP (p<0.001), CAR (p<0.001) and leukocyte (p=0.039) values were significantly higher whereas hemoglobin (p=0.035) was significantly lower in HF patients **(Table 1)**.

Table 1. Comparison of baseline demographic and laboratory characteristics of the heart failure patients and healthy control

Variables	Heart failure group (n = 72)	Control group (n = 64)	P
Age, years	60.03 ± 8.83	58.30 ± 8.99	0.260
Gender, male (%)	41 (56.9)	40 (62.5)	0.510
Hypertension (%)	25 (34.7)	12 (18.8)	0.037
Diabetes mellitus (%)	20 (27.8)	14 (21.9)	0.427
Smoking (%)	13 (18.1)	11 (17.2)	0.895
LVEF (%)	32.24 ± 7.89	56.33 ± 3.80	<0.001
Creatinine, mg/dl	0.96 ± 0.22	0.87 ± 0.22	0.009
Glucose, mg/dl	98.71 ± 21.10	100.67 ± 18.70	0.569
Total cholesterol, mg/dl	161.49 ± 39.64	172.42 ± 41.34	0.118
LDL- cholesterol, mg/dl	108.58 ± 25.89	106.54 ± 19.18	0.605
HDL- cholesterol, mg/dl	40.01 ± 12.18	40.91 ± 9.17	0.631
Triglyceride, mg/dl	134.82 ± 49.73	143.33 ± 56.12	0.350
CRP, mg/dl	6.80 (2.83-10.0)	2.10 (0.62-5.89)	<0.001
Albumin, g/dl	4.08 ± 3.49	4.18 ± 0.59	0.813
CAR	1.87 (0.70-2.80)	0.51 (0.15-1.32)	<0.001
Hemoglobin, g/dl	12.80 ± 1.89	13.44 ± 1.58	0.035
Leukocytes, x10^3/mL	11.55 ± 2.47	10.75 ± 1.86	0.039
Platelets, x10^3/mL	260.92 ± 79.16	273.24 ± 53.02	0.294

Abbreviations: LVEF: left ventricular ejection fraction, LDL: low density lipoprotein, HDL: high density lipoprotein, CRP: C-reactive protein, CAR: CRP to albumin ratio

Comparison of amino acid profile of the HF patients and healthy control are presented in **Table 2**. When compared to the control group, patients with HF had significantly lower valine (p=0.040), leucine (p<0.001) and methionine levels (p=0.001) whereas significantly higher phenylalanine (p<0.001), tyrosine (p=0.027), asparagine (p<0.001), arginine (p<0.001), glycine (p=0.006) and ornithine (p=0.035). Alanine, cytosine and glutamine levels were similar between two groups.

ROC curve analysis was performed to determine the optimal cut-off value of CAR for predicting the presence of HF **(Figure 1).** CAR ≥ 0.91 predicted the presence of HF with a sensitivity of %72.2 and specificity of %71.9 (p<0.001). Heart failure patients were divided into two groups according to this cut-off value: HF patients with CAR ≥ 0.91 (high inflammation status group, n=52) and CAR < 0.91 (low inflammation status group, n=20), and comparisons were made. It was detected that patients with high inflammation status had significantly higher phenylalanine (p<0.001), tyrosine (p<0.001), asparagine (p<0.001) and ornithine (p=0.006) levels whereas lower valine (p<0.001) and leucine levels (p<0.001) **(Table 3).**

Table 2. Comparison of amino acid profile of the heart failure patients and healthy controls

Variables	Heart failure group (n = 72)	Control group (n = 64)	P
Valine	124.63 (111.15-150.43)	137.00 (113.45-175.98)	0.040
Leucine	91.88 (79.35-113.26)	108.37 (95.55-128.99)	<0.001
Methionine	9.72 (8.07-12.82)	11.10 (10.23-14.47)	0.001
Phenylalanine	55.25 (45.79-77.71)	40.54 (36.46-42.30)	<0.001
Tyrosine	67.40 (52.31-76.82)	56.24 (50.34-70.14	0.027
Asparagine	97.05 (88.73-123.86)	62.03 (43.74-76.39)	<0.001
Alanine	164.53 (138.52-204.29)	170.58 (144.76-204.57)	0.585
Arginine	46.96 (39.39-72.33)	36.87 (28.47-43.22)	<0.001
Cytosine	38.63 (28.97-46.55)	37.24 (31.49-41.17)	0.096
Glycine	233.81 (191.14-275.62)	196.82 (172.57-247.30)	0.006
Ornithine	106.16 (90.17-129.62)	88.52 (62.75-133.57)	0.035
Glutamine	194.62 (159.61-222.64)	184.66 (174.33-223.44)	0.780

Table 3. Comparison of amino acid profile of the heart failure patients with high and low inflammation status

Variables	High inflammation group (CAR ≥ 0.91) (n = 52)	Low inflammation group (CAR < 0.91) (n = 20)	P
Valine	116.75 (104.88-131.00)	155.57 (139.22-175.87)	<0.001
Leucine	83.65 (74.90-104.12)	98.66 (95.45-115.31)	<0.001
Methionine	9.56 (8.09-13.18)	9.88 (8.06-11.97)	0.821
Phenylalanine	68.68 (48.88-86.22)	43.77 (40.52-47.76)	<0.001
Tyrosine	69.81 (57.00-81.18)	51.89 (48.78-56.30)	<0.001
Asparagine	105.0 (96.0-132.13)	90.83 (78.98-95.41)	<0.001
Alanine	165.41 (138.52-218.02)	156.01 (135.62-167.60)	0.197
Arginine	46.96 (38.86-81.05)	46.86 (41.64-63.73)	0.715
Cytosine	38.91 (28.48-47.80)	38.19 (29.81-43.38)	0.493
Glycine	238.22 (191.17-274.30)	225.25 (189.20-284.13)	0.841
Ornithine	115.31 (95.11-133.23)	88.40 (82.57-104.07)	0.006
Glutamine	194.30 (159.61-222.64)	206.82 (146.27-221.76)	0.815

Correlation analysis was performed to determine the correlation of amino acids with clinical parameters. We found that CAR was positively correlated with phenylalanine, tyrosine and asparagine levels whereas negatively correlated with valine, leucine and methionine levels. In addition, LVEF was positively correlated with valine, leucine and methionine levels whereas negatively correlated with phenylalanine, tyrosine and asparagine levels **(Table 4)**.

Table 4. Correlation analysis of amino acids with clinical parameters

	Valine	Leucine	Methionine	Phenylalanine	Tyrosine	Asparagine
CAR	r = −0.221 p = 0.010	r = −0.402 p < 0.001	r = −0.193 p = 0.025	r = 0.454 p < 0.001	r = 0.202 p = 0.018	r = 0.361 p < 0.001
LVEF	r = 0.110 p = 0.203	r = 0.342 p < 0.001	r = 0.264 p = 0.002	r = −0.543 p < 0.001	r = −0.135 p = 0.118	r = −0.469 p < 0.001

Abbreviations: CRP to albumin ratio, LVEF: left ventricular ejection fraction

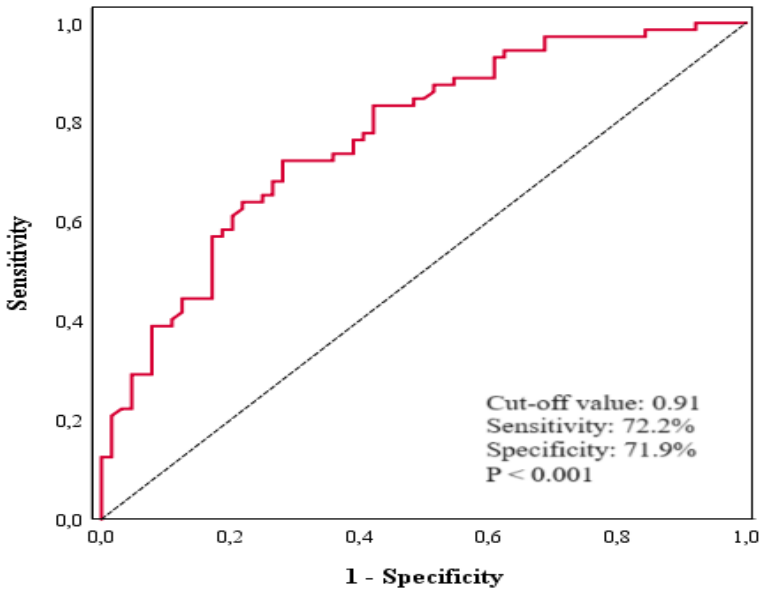

Figure 1. ROC curve analysis to determine the optimal cut-off value of CAR for predicting heart failure

Discussion

In current study, it was aimed to investigate the relationship between inflammation, which is a main pathophysiological process in HF, and AA profile. Main finding of the current study was that the AA profile was impaired in HF patients compared to healthy controls and this impairment was more pronounced in patients with higher inflammation status.

Heart failure is a major public health problem worldwide and its incidence is gradually increasing as life expectancy is prolonged (1,2). Because these patients have poor prognosis, better elucidation of the underlying mechanisms may allow to improve the prognosis in HF. Although there are many factors in the pathophysiology of HF, increased inflammatory response is considered as a major pathophysiological contributor in these patients and has a critical role in the development and progression of heart failure (3-5). CAR has emerged as a novel marker of inflammatory status and its use in daily practice is gradually increased. It reflects the balance between CRP and albumin levels and has found that the combination of these two parameters is more sensitive than CRP and albumin alone (6,7). In this study, we found that HF patients had significantly higher CAR value than healthy controls. This result support the hypothesis of an increased inflammatory response in patients with HF. In addition, recent studies performed in patients with HF have demonstrated that CAR is independently associated with advanced HF, higher hospitalization frequency, severe New York Heart Association (NYHA) classification and may be used to predict mortality in these patients (9,10,15). When all these findings evaluated together, it can be concluded that CAR is an important parameter that can be used in HF patients to predict high risk status.

The heart requires high energy as it pumps blood throughout the body. Fatty acids are the primarily energy sources; however, the metabolism of the substrates' changes dramatically in a failing heart. The primary energy source switches to glucose from fatty acids due to higher anabolic activity and cardiomyocyte energy shortage, and the hearts' dependence on AAs increases during HF (11-13, 16). Because of all these reasons, the metabolism of AAs in patients with HF may be altered. Previous studies showed that AAs profile was significantly changed in patients with HF compared to the controls (13,17,18). In addition, the AAs profile was found to be correlated

with LVEF, HF severity and NYHA classification and a good predictor of prognosis (19,20). Although we could not evaluate the NYHA classification and prognosis, we also found that AAs profile of HF patients was significantly different form the healthy controls and it was showed a significant correlation with LVEF in the current study. Accordingly, it can be concluded that AAs profile is altered in patients with HF and this altered plasma level of AAs are related to the severity of cardiac impairment.

When the change in AA types was analyzed, it was found that valine, leucine and methionine levels decreased, whereas phenylalanine, tyrosine, asparagine, arginine, glycine, ornithine levels increased in patients with HF compared to the healthy controls in our study. Similarly, Liu et al. (21) showed that valine level was lower whereas phenylalanine, tyrosine and ornithine levels were higher in patients with HF compared to the controls. Supporting to these results, it was demonstrated that lower valine, leucine and methionine levels and higher phenylalanine, tyrosine and ornithine levels were associated with poor prognosis in HF patients (22-26). On the other hands, the results obtained in studies evaluating AA levels in patients with HF may differ. Aquilani et al. (13) reported that HF subjects had lower levels of aspartic acid, glutamic acid, cysteine, methionine and taurine compared to healthy subjects whereas did not find significantly increased AAs in HF patients. Saleem et al. (17) found that HF group had significantly higher levels of valine, leucine, isoleucine, tyrosine, phenylalanine, glutamate and asparagine while lower levels of aspartate, methionine, alanine, arginine, lysine, serine, and threonine versus controls. Hakuna et al. (18) observed that HF group had lower amounts of histidine and tryptophan, whereas higher amounts of phenylalanine, tyrosine, asparagine, glycine, ornithine, serine, glutamate, citrulline, cystine and β-alanine compared to controls. The possible reason for these differences in AA levels in the studies may be due to diet and vitamin supplements, because it has been shown that plasma AA concentrations can be affected by these factors (12,27). In our study, we did not investigate these possible confounders. We think that further studies are needed that evaluating the AA profile in HF patients by taking into account diet and vitamin (AAs) supplementation.

Although the AA profile of HF patients has been analyzed in previous studies, the underlying mechanism of impaired AA metabolism has not been investigated in detail. In the present study, the effect of inflammatory response on the impaired AA profile was investigated. Because previous studies showed CAR had a higher accuracy than other conventional parameters (6,7), we used CAR as the inflammatory marker in current study. The optimal cut-off value of CAR for predicting HF was determined by ROC curve analysis, and the study population was divided into two groups according to this cut-off value. Accordingly, HF patients with CAR ≥0.91 was defined as the high inflammation group, while patients with CAR <0.91 was defined as low inflammation group. We observed that AAs profile was significantly altered in high inflammation group compared to low inflammation group, and CAR levels were significantly correlated with the level of these AAs. Supporting to our findings, Chen et al. found that higher phenylalanine levels were correlated with higher C-reactive protein levels and inflammatory cytokines in their recent study (26). According to these results, we speculate that the main mechanism underlying the impaired AA profile in HF may be the increased inflammatory response. Future prospective studies are required to better elucidate the relationship between inflammation and AAs profile in patients with HF.

Study Limitations

The main limitation of our study was the small number of patients. Second, other traditional inflammatory parameters were not analyzed. Third, patients were not followed up for long-term prognosis. Long-term follow-up of the patients and determination of prognosis according to the deterioration in AA profile could have made an additional contribution to our study. Fourth, since some medications, such as statins, are known to have anti-inflammatory properties, they could have had an impact on the study results. However, unfortunately we did not record the medical treatment of the patients. Last, determining the NYHA class and comparing the AAs profile according to this variable could have increased clinical importance of the study.

Conclusion

We found that AAs profile altered significantly in patients with HF compared to healthy controls. In addition, impaired AAs profile was more prominent in HF patients with higher inflammation compared with HF patients with lower inflammation. Therefore, it can be suggested that increased inflammation may be the main mechanism underlying the impaired AA profile in HF patients.

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