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REVIEW

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SARS-CoV-2 Variants of Concern and Their Properties

SARS-CoV-2 Endişe Verici Varyantları ve Özellikleri

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ABSTRACT

Since its first detection in December 2019, SARS-CoV-2 has resulted in the morbibidity of 174 million and mortality of 3.74 million people. As a typical Ribonucleic acid virus, SARS-CoV-2 undergoes genomic changes during its replication to maintain its evolutionary adaptation. Continous mutation has led into the emergence of numerous variants. Currently, the variants distinguished as the 'Variants of Concern' are the B.1.1.7 lineage (The United Kingdom variant) , B.1.351 (The South African variant), B.1.1.248/B1.1.28/P1(Brazilian Variant) , B.1.427/B.1.429 lineage (The Californian variant) and B.1.617.2 lineage (Indian variant). These variants impose a huge concern due to their properties of higher transmission and evasion of the immune system. The continuous emergence of such variants can be contained by vaccinating the population to reduce the circulation of the virus and by maintaining the major protective measures against the disease.

ÖZET

Aralık 2019'da tespit edilmesinden bu yana, SARS-CoV-2, 174 milyon insanın morbiditesine ve 3.74 milyon insanın mortalitesine neden olmuştur. Tipik bir Ribonükleik asit virüsü olarak, SARS-CoV-2, evrimsel adaptasyonunu korumak için replikasyonu sırasında genomik değişikliklere uğrar. Zaman içindeki sürekli mutasyonlar, çok sayıda varyantın ortaya çıkmasına neden olmuştur. Şu anda, 'Endişe Verici Varyantları' olarak ayırt edilen varyantlar B. 1.1.7 soyu (Birleşik Krallık varyantı), B. 1.351 (Güney Afrika varyantı), B. 1.1.248/B1.1.28/P1 (Brezilya varyantı), B. 1.427/B.1.429 soyu (Kaliforniya varyantı) ve B. 1.617.2 soyu (Hint varyantı) içermektedir. Bu Varyantlar, yüksek bulaşma özellikleri ve bağışıklık sisteminden kaçma yetenekleri nedeniyle büyük bir endişe yaratmaktadır. Bu tür varyantların sürekli ortaya çıkışı, virüsün dolaşımını azaltmak için popülasyonun aşılanması ve hastalığa karşı ana koruyucu önlemlerin sürdürülmesi ile kontrol edilebilir.

Keywords:
SARS-CoV-2
Variants of concern
Mutation
Immune system.

Anahtar Kelimeler:
SARS-CoV-2
Endişe verici varyantlar
Mutasyon
Bağışıklık sistem.

1. INTRODUCTION:

In December of the year, 2019 cases of viral pneumonia with the unknown etiologic agent were seen in the Chinese city of Wuhan. Patients were presented to the hospitals with symptoms like fever, malaise, dry cough, and dyspnea (1). On March 11 2020 the WHO declared that COVID-19 can be characterized as a pandemic due to the fast level of spread and mortality (2). Since the detection of the first case, the virus has been spreading at a very fast speed. By June 7, 2021, 174 million people worldwide had been infected with the virus. The death rate due to the virus also reached 7.34 million (3).

COVID-19 is a 70-90 nm in diameter, spherical enveloped virus-containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid composed of matrix protein (4). The coronaviruses RNA genome which codes for 4 major structural proteins: the nucleocapsid (N) protein, the transmembrane (M) protein, the envelope (E) protein, and the spike (S) protein (5).

As a typical RNA virus, SARS-CoV-2 maintain the average the evolutionary rate of roughly 10^{-4} nucleotide substitutions per site per year with mutations arising during every replication cycle. Thus, this mutation rate has led to the birth of SARS-CoV-2 strains containing key mutations that affect the severity of the disease, immune evasion, and treatment tolerance by the virus.

2. MAJOR SARS-COV-2 STRAINS

In the earlier stages of the pandemic, the virus was divided into two types; the L and S strains of SARS-CoV-2. These two major types were identified based on the presence of two single nucleotide polymorphisms (SNPs) at the 28,144 nucleotide in the genome. These are the "L" haplotype (Where C is substituted by T and Leucine is coded) and "S" haplotype (Where C is present and Serine is coded) (6). With the increase of variations in the genome of the virus, it has become essential to develop a nomenclature system which can include all the clades. So far Rambaut et al., Nextrain and Global Initiative on Sharing All Influenza Data (GISAID) have developed several nomenclatures for SARS-CoV-2 and all these nomenclature techniques can be used for the categorization of the virus subtypes and identification of the most globally circulating strains (7). One of the main classification criteria of SARS-CoV-2 by this method is the presence of a specific group of

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mutations.

In addition to this, certain organizations like the Centers For Disease Control and Prevention (CDC) have lately been using the terms 'Variants of Interest' and 'Variants of Concern' to address the newly discovered strains of the virus (8). Variants of interest refer to variants with mutations that are predicted to affect receptor binding, interaction with antibodies and the efficacy of treatments. The European Center for Disease prevention and control (ECDC) has categorized the variants B.1.525, P.3, B.1.616, B.1.617.1, B.1.617.3, B.1.620, B.1.621 as Variants of Interest (9). The Variant of Concern strains includes new variants with a characteristic of higher transmission ability. These variants may have developed the strength to neutralize antibodies generated from previous infections. Evidence of failures in treatments and diagnostic tests are also some of the defining characteristics of them. The main objective of this review is to describe the Variants of Concern. Moreover, it aims to discuss the characteristic mutations of the variants and their effects on the transmissibility of the disease and immune responses.

3. VARIANTS OF CONCERN

Up to this date, several variants of SARS-CoV-2 which have been considered as variants of concern due to their impact on public health have been identified. These are:

A. The B.1.1.7 lineage or Variant of Concern 2020/12 (The UK variant).
B. B.1.351 lineage or 501Y.V2 (The South African variant)
C. B.1.1.248/B1.1.28/P1 or 501Y.V3 (The Brazilian Variant)
D. B.1.427/B.1.429 lineage (The Californian variant)
E. B.1.617.2 Lineage (Indian variant) (10).

One of the depicting features of all of these variants is the presence of a common mutation D614G (11). The D614G mutation in was first identified in Germany in a sample collected in January and by March the mutation has spread throughout Europe. By April this mutation was dominantly seen in samples collected from Europe and North America (12). In the Global Initiative on Sharing All Influenza Data (GISAID) system of SARS-CoV-2 variant classification, strains containing the D614G the mutation is categorized in the G clade (13). Some studies found that the mutation 614G in the S protein along with variant 4715L in the ORF1ab are significantly correlated with fatality rates in 28 countries and 17 states in the United States of America (14).

A. The B.1.1.7 lineage or The UK Variant

The B.1.1.7 variant is one of the newest strains of the the virus which emerged in the UK in the mid of September 2020. This strain has been named SARS-CoV-2 VUI 202012/01 (Variant Under Investigation, the year 2020, month 12, variant 01) (15). Initial analysis indicates that the variant may spread more readily between people and several investigations are still ongoing to determine if this variant is associated with any changes in the severity of symptoms, antibody response or vaccine efficacy. This variant is characterized by the presence of a range of 14 mutations resulting in amino acid changes and three deletions. From these mutations, five amino acid replacements (D614G, A222V, N439K, Y453F and N501Y), one deletion is thought to be significant as they are located in the spike protein, especially the Receptor Binding Domain (RBD) (16). The N501 is located in the RBD peripheral region where the initial contact between the human Angiotensin Converting Enzyme-2 (ACE-2) and the RBD occurs. Studies performed in mouse indicated that mutation in the N501 i.e N501Y can increase the binding affinity between RBD and ACE2 (17). Another significant mutation in this variant is the P681H which is found directly near the furin cleavage site. This mutation is predicted to increase infection by promoting increased membrane fusion and is associated with higher viral load in Reverse Transcriptase- quantitative PCR (RT-qPCR) tests (18). The 69-70 and 144 deletions found in the solvent accessible β-hairpin loops in the N-terminal Domain (NTD) was first detected during the SARS-CoV-2 transmission in the mink population in Denmark. In normal, conditions monoclonal antibodies from convalescent COVID-19 patients interact with NTD of S protein. Thus it is predicted that the presence of these deletions can confer the virus an antibody resistance (19). Similarly, the presence of N439K and Y453F results in the increased affinity of the virus with the ACE2 thus leading to an increased viral transmission.

Currently, the B.1.1.7 variant is the most commonly observed variant of SARS-CoV-2 globally and a total of 824,608 whole-genome sequences of this variant have been uploaded to the GISAID (20). Since its first detection in the UK, a total of 249,637 cases has been reported in the country (21). Similarly, this variant has been the most prevalent one among the Türkish population. According to reports from the Ministry of Health, 85% of the Covid-19 cases in April 2021 were the B.1.1.7 variant (22).

B. B.1.351 lineage or the South African Variant

Another lately discovered variant is the B.1.351 or the N501Y.V2. This variant was first detected in South Africa on 2 January 2021. Its defining amino acid mutations are K1655N in the ORF1a, N501Y, E484K, D215G, D80A, K417N in the S protein, P71L in the E protein and T205I in the N protein (23). Some studies have reported that this variant have reported that this variant shows more resistance towards neutralization by convalescent plasma and vaccinee sera athan other variants (24). The E484K interacts with the K31 residue in the human ACE to moderately increase the affinity of the RBD protein with the ACE. Three of these mutations are in the RBD (K417N, E484K and N501Y) and are associated with high numbers of infections and increased transmissibility. E484K in combination with K417N, and N501Y induces conformational changes in spike protein and this can result in the evasion of antibodies against the virus (18). Since the main targets of type 1 and type 2 anti SARS-C0V-2 antibodies lie in the RBD sites which are specific for binding with the ACE, the presence of K417N, E484K and N501Y have shown to increase the resistance towards these antibodies (25). For instance A study by Houriiyah Tegally et.al. have indicated that the mutations N501Y and K417N may play a role in the resistance against type

1 antibody, while E484K may provide immune evasion against antibody type -2 (23). It has also been reported that IgG antibody from convalescent sera and vaccinated individuals exhibited decreased reactivity against this variant while no reduction was seen with the UK variant. These findings were further confirmed using the Viral Neutralization test and ACE inhibition test (26). So far a total of 21,018 whole-genome isolates which belonged to the South African variant have been uploaded into the GISAID database out of which 544 were originated from Turkey (20).

C. B.1.1.28 variant or the 501Y.V3 or P.1 (Brazilian Variant)

The third variant of concern, the B.1.1.28 variant or the 501Y.V3 or P.1 lineage, was identified in samples collected after November 2020 in Manaus, Brazil. This variant is characterized by the presence of 12 mutations (i.e. L18F, T20N, D614G, P26S, D138Y, R190S, H655Y, T1027I, V1176, K417T, E484K, and N501Y) in the spike protein out of which three mutations are located in the RBD (L18F, K417N, E484K) (27). One of the mutations in the S protein namely, N501Y is shared with the UK and the South African variants while L18F, K417T and E484K are also found in the South African isolates respectively. The presence of these mutations in this variant contributes to the transmissibility and evasion of antibody-mediated immunity. Specifically speaking, the presence of L18F, K417N, E484K in the RBD may enhance the interaction of hACE2 with the virus resulting in increased transmission. In agreement with this speculation, a study from the city of Manaus has recorded an increased transmission rate of 1.4 up to 2.2. then the other variants which were previously present in the city (28). Up to date, there is no available data about the efficacy of vaccines towards this variant but since it shares many mutations with the South African variant similar patterns antibody neutralization with the South African variant may be observed (10). So far a total of 26,053 whole-genome isolates which belonged to the South African variant have been uploaded into the GISAID database out of which 21 were originated from Turkey (20).

D. B.1.427/B.1.429 lineage (Californian Variant)

B.1.427 and B.1.429 lineage or the Californian variants of concern was first detected in May 2020. These variants contain amino acid mutations S13I, W152C in the NTD and the L452R in the RBD regions of the S protein (29). This variant was reported in about 50% of the total Covid cases in California with an increased transmission rate increase (18.6-24%) than the wild-type strain (30). The main culprit for this could be the L452R mutation which increases the interaction between the RBD and the ACE receptor by promoting structural changes to the protein (31). These variants have been detected in the 42 states of the US and 29 countries. These variants have shown moderate resistance to neutralization by different types of antibodies excerpted from vaccinated and previously infected patients (30). For instance, A study by McCallum et.al confirmed that the mutation L452R was able to reduce or even eliminate the neutralizing ability of 14 monoclonal antibodies specific to the RBD (31). In the GISAID, 44,398 isolates confirmed to be B.1.427 / B.1.429 lineage have been uploaded since its first detection, and only 2 of these isolates were originated from Turkey (20).

E. B.1.617.2 (The Indian variant)

B.1.617.2 or the Indian variant characterized by the presence of mutations T19R, Δ157-158, L452R, T478K, D614G, D950N and P681R was first reported in India in December 2020. This variant become the most dominant strain in India by mid of April 2020 and started spreading to 44 other countries (32). This strain is categorized as a variant of concern by the CDC and European Center for Disease Control and Prevention (ECDC) because of its high transmission rate (8-9). The variant was initially named as 'The double mutant' variant because of the presence of two important mutations that were previously the hallmarks of the South African variant and the Californian variant (L452R and E484Q). Even though there is no recorded invitro neutralization test data so far, the L452R is thought to contribute to the immune evasion by reducing neutralization of antibodies and increased transmission of the variant. Similarly the P681R may play a role in increasing replication which can result in leading to high viral loads thus higher pathogenic potential (33). Even though further detailed study about the effect of this variant toward vaccines is required, the earlier study indicated that the antibodies produced after taking the Pfizer vaccine was approximately 80% less effective against some of the mutations in the variant (34). In the GISAID, 31,353 isolates confirmed to be of the Indian lineage have been uploaded since its first detection, and only 3 of these isolates were originated from Turkey (20).

Conclusion and Future Perspective

The rise of new variants of SARS-CoV-2 have created a huge concern in the fight against the pandemic mainly due to fear of increased transmission, severity as well as immune escape. The variants classified as the 'Variants of Concern' have already exhibited some of these properties to an alarming extent. However to have a solid stand on the transmissibility, severity and the immune escape capabilities of the variants, collection of good quality genomic sequencing along with detailed clinical outcomes and long-term follow-ups are required. Another challenge faced due to the existence of these variants is the partial ineffective of the currently used diagnostic tests for the virus. Due to the presence of mutations and long deletions in the locations of the genome normally detected by the currently used RTqPCR protocols, false-negative results can be reported. Therefore, diagnostic tests for the virus should be designed to be inclusive of the most significant changes observed in the new variants.

As an RNA virus, SARS-CoV-2 undergoes continuous changes in its geneom as a result of adaptive evolution. This continuous change will obviously result in the birth of other variants that may have a more severe effect. Vaccination is considered to be the most effective way to combat newly appearing variants. Even though the efficacy of some of the authorized vaccines may decrease due to the presence of certain mutations, it is still recommended that vaccination should continue. Vaccination can provide immunity towards the majority of the variants and the

more people get vaccinated the less virus circulation will appear, this in turn can result in the decreased emergence of newer strains. In conclusion, consistent genomic sequencing of samples collected should always be adhered to for close surveillance of new variants with potential threatening effects.

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ORIGINAL ARTICLE

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The Effect of Lactate and Lactate Clearance on Mortality in Sepsis Patients Admitted to the Emergency Department

Acil Servise Başvuran Sepsis Hastalarında Laktat ve Laktat Klirensinin Mortaliteye Etkisi

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ABSTRACT

Objective: *Early prognosis of sepsis, which affects millions of people all over the world every year and, can have a mortality of more than 25%, is very important especially for emergency rooms where patients spend their most critical golden hours. Lactate and lactate clearance are also potential marker candidates that can be used to predict mortality, which has now started to take place in sepsis guidelines. The aim of this study is to investigate the power of lactate and lactate clearance to predict mortality in sepsis.*

Material and Method: *All patients over the age of 18 with a diagnosis of severe sepsis and septic shock who presented to the emergency department during a one-year period were included in this prospective observational cohort study. The lactate clearance was calculated by taking the blood gase samples of the patients at the time of admission and six hours later, and evaluated in terms of predicting mortality along with other parameters.*

Results: *The decrease in lactate values at the sixth hour of 90 patients included in the study was found to be statistically significant (p=0.001). A positive and significant correlation was found between the lactate values of the patients at admission and mortality (p=0.046). A negative significant correlation was found between lactate clearance of the patients and mortality (p=0.001).*

Conclusion: *In patients with sepsis, lactate level is important in determining prognosis. Regardless of arrival lactate level, the rise of lactate reduction rate at the sixth hour indicates a good prognosis. In addition, it was determined that the sixth hour lactate level also had an effect on predicting mortality. When all these results are taken into consideration, it can be said that the lactate level and lactate clearance are useful predictors of prognosis in sepsis patients admitted to the emergency department. However, they are not sufficient on their own to determine the prognosis and should be used together with other markers and clinical evaluation.*

ÖZET

Amaç: *Her yıl tüm dünyada milyonlarca insanı etkileyen ve mortalitesi %25'ten fazla olabilen sepsisin erken dönemde prognoz tayini özellikle hastaların en kritik altın saatlerini geçirdikleri acil servisler için çok önemlidir. Laktat ve laktat klirensi de artık sepsis kılavuzlarında yerini almaya başlamış mortalite öngörmede kullanılabilecek potansiyel belirteç adaylarındandırlar. Bu çalışmanın amacı laktat ve laktat klirensinin sepsiste mortaliteyi öngörme gücünün araştırılmasıdır.*

Gereç ve Yöntem: *Bu prospektif gözlemsel kohort çalışmasına bir yıllık dönemde acil servise başvuran 18 yaş üzeri tüm ağır sepsis ve septik şok tanılı hastalar dâhil edilmiştir. Hastaların başvuru sırasında ve altı saat sonra kan gazı alınarak laktat klirensi hesaplanmış ve diğer parametreler ile birlikte mortaliteyi öngörme açısından değerlendirilmiştir.*

Bulgular: *Çalışmaya alınan 90 hastanın altıncı saatteki laktat değerlerindeki düşme istatistiksel olarak anlamlı bulunmuştur (p=0.001). Hastaların başvurudaki laktat değerleri ile mortalite arasında pozitif yönde anlamlı ilişki saptanmıştır (p=0.046). Hastaların laktat klirensleri ile mortalite arasında negatif yönde anlamlı ilişki saptanmıştır (p=0.001).*

Sonuç: *Sepsis hastalarında geliş laktat değerinin mortalite ve prognozu belirlemede önemi vardır. Geliş laktat değerinden bağımsız olarak altıncı saatte laktatın düşme oranının yüksekliği iyi prognozu gösterir. Ayrıca altıncı saat laktat değerinin de mortaliteyi öngörmede etkisi olduğu belirlenmiştir. Tüm bu sonuçlar göze alındığında geliş laktat değerinin ve laktat klirensinin acil servise gelen sepsis hastalarında prognozu göstermede yararlı belirteçler olduğu söylenebilir. Ancak prognozu belirlemede tek başlarına yeterli değildirler, diğer belirteçler ve klinik değerlendirme ile beraber kullanılmalıdırlar.*

Keywords:
Emergency room
Lactate
Lactate clearance
Sepsis

Anahtar Kelimeler:
Acil servis
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Laktat klirensi
Sepsis

INTRODUCTION

Sepsis is a syndrome characterized by the development of life-threatening organ failure as a result of an uncontrolled inflammatory response to infection (1). More than 1/4 of millions of patients diagnosed with sepsis in the world die every year, and initiation of appropriate treatment in sepsis management is very effective in preventing mortality, so it is of great importance that emergency physicians recognize sepsis accurately and in a timely manner (2). Scoring systems are used to predict mortality in emergency and intensive care units. "Mortality in Emergency Department Sepsis" (MEDS), "Sequential Organ Failure

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Assessment" (SOFA) score is most commonly used scores in the emergency department, and the "Predisposition, Infection, Response and Organ Dysfunction" (PIRO) score has been developed for the intensive care unit (ICU). However, discussions about the usefulness of these scores continue and conflicting results have been reported in different studies (3-10). For years, data and results of patients with sepsis have been collected from many countries to create guidelines within the scope of the "Surviving Sepsis Campaign" (SSC). "Sepsis Severity Score" (SSS) was defined by Osborn et al. in 2014 to predict the prognosis of sepsis, by using the data of this

Table 1: Characteristics and Mortality

		n	%	Mortality		p
				No n=54 (60%)	Yes n=36 (40%)	
Age (years)	Min-Max (Median)	19-97 (62.5)		19-90 (61.5)	26-97 (68)	[a]0.113
	Mean±Sd	61.33±16.55		59.07±16.39	64.2±16.44	
	< 65 years	47	52.2%	31 (66.0%)	16 (34.0%)	
	≥ 65 years	43	47.8%	23 (53.5%)	20 (%46.5%)	
Blood Pressure	Hypotensive	28	31.1%	17 (60.7%)	11 (39.3%)	[b]0.844
	Normotensive	55	61.1%	32 (58.2%)	23 (41.8%)	
	Hypertensive	7	7.8%	5 (71.4%)	2 (28.6%)	
Systolic Blood Pressure	Min-Max (Median)	55-200 (102.5)		40-100 (70)	40-100 (70)	[a]0.767
	Mean±Sd	110.41±28.72		68.52±17.53	67.78±17.87	
Diastolic Blood Pressure	Min-Max (Median)	40-100 (70)		60-180 (102.5)	55-200 (102.5)	[a]0.846
	Mean±Sd	68.22±17.57		111.15±27.13	109.31±31.31	
Body Temperature	Min-Max (Median)	34-40 (37)		35.6-40 (37.7)	34-39 (36)	[a]0.001*
	Mean±Sd	36.93±1.36		37.54±1.09	36.02±1.21	
	Hypothermia	15	16.7%	0 (0%)	15 (100%)	
	Normothermia	36	40.0%	19 (52.8%)	17 (47.2%)	
	Hyperthermia	39	43.3%	35 (89.7%)	4 (10.3%)	
Respiratory Rate	Min-Max (Median)	16-40 (25)		16-40 (24)	16-40 (27)	[a]0.951
	Mean±Sd	26.20±6.24		26.17±6.08	26.25±6.56	
	Normal	21	23.3%	11 (52.4%)	10 (47.6%)	
	High	69	76.7%	43 (62.3%)	26 (37.7%)	
Glascow Coma Scale	Min-Max (Median)	3-15 (15)		8-15 (15)	3-15 (13)	[c]0.002*
	Mean±Sd	13.02±2.99		13.83±2.18	11,81±3.62	
Comorbidity	No	4	4.4%	2 (50.0%)	2 (50.0%)	[b]1.000
	Yes	86	95,6%	52 (60.5%)	34 (39.5%)	
	0	4	4.4%			
	1	42	46.7%			
	≥ 2	44	48.9%			
Need for Ventilation	No	46	51.1%	46 (100%)	0 (0%)	[d]0.001*
	Yes	44	48.9%	8 (18.2%)	36 (81.8%)	
Treatment area	Emergency Room	26	28.9%	26 (100)	0 (0)	[d]0.001*
	Other Clinics	21	23.3%	21 (100)	0 (0)	
	Intensive Care Unit	43	47.8%	7 (16,3)	36 (83,7)	

*[a]Student t Test [b]Fisher'sExact Test [c]Mann Whitney U Test [d]Pearson Chi-square Test *p<0.01*

Table 2: Sepsis Sources

		Total (%)	Mortality	
			No (%)	Yes (%)
Diagnosis	Pneumosepsis	41 (45.6%)	23 (42.6%)	18 (50%)
	Urosepsis	17 (18.9%)	14 (25.9%)	3 (8.3%)
	Gastrointestinal infection	7 (7.8%)	4 (7.4%)	3 (8.3%)
	Decubitus ulcer infection	7 (7.8%)	3 (5.6%)	4 (11.1%)
	Diabetic foot infection	5 (5.6%)	1 (1.9%)	4 (11.1%)
	Catheter infection	5 (5.6%)	4 (7.4%)	1 (2.8%)
	Soft tissue infection	4 (4.4%)	3 (5.6%)	1 (2.8%)
	Central nervous system infection	3 (3.3%)	2 (3.7%)	1 (2.8%)

very large patient population (11). In the same study, both the definition and validation of this scoring were carried out. This scoring, which is found to be very successful in estimating mortality in patients with sepsis, has some limitations (3).

In addition, at the "The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis 3)" meeting held in 2016, "respiratory rate, systolic blood pressure and mental status change" was introduced in order to evaluate patients outside the intensive care unit and to identify patients at risk of death in terms of sepsis early. A new scoring system consisting of three parameters has been defined. This score is a modified version of the currently used SOFA and is named as quick SOFA (qSOFA) (1,12,13). However, this scoring system has also been discussed since its definition, and it is suggested that it may be insufficient in estimating mortality and its effectiveness should be supported by prospective studies.

The study of Rivers et al. revealed that one of the targets of hemodynamic therapy in early stage is to reduce lactate level, and that there is a strong relation between decreased lactate level reduced mortality in the early period (14). In general, lactate increases when tissue perfusion is impaired in all types of shock, and the degree of elevation is associated with mortality (15).

In this study, the power of predicting mortality of lactate level at the time of admission and the role of lactate clearance in predicting mortality after appropriate targeted therapy were investigated in patients diagnosed with sepsis admitted to the emergency department.

MATERIAL AND METHOD

All patients with a diagnosis of severe sepsis and septic shock, aged >18 years, who applied to a university hospital emergency medicine outpatient clinic between 2016 and 2017, were included in this prospective observational cohort study after obtaining their or their first-degree relatives' consent. The study was carried out in accordance with the ethics committee approval of the faculty, dated 13/03/2017 and numbered 31887016-604.01.02-98644.

For the diagnosis of sepsis, standard sepsis criteria determined in the Sepsis Survival Campaign 2016 guideline were used. Sepsis treatment was carried out in line with the same guideline, taking into account the clinical picture of the patient.

Data Collection

Demographic characteristics, hospitalization diagnoses, comorbidities, systolic and diastolic blood pressure values, respiratory rate, fever, laboratory values, glaskow coma scores were recorded under the heading of vital signs within the first 24 hours of the diagnosis of sepsis and septic shock. The lactate values in arterial blood gas taken at the first admission to the emergency department (H0) and the lactate values taken at the sixth hour (H6) after appropriate treatment were recorded. Lactate clearance was calculated and recorded according to the appropriate formula.

Lactate Clearance = [(Initiative lactate – Follow-up lactate)/ l Initiative lactate] x 100%]

The focus of infection was recorded as lung, urinary system, catheter, soft tissue, diabetic foot, decubitus ulcer, central nervous system and gastrointestinal system.

The antibiotic treatments received by the patients, the need for ventilation, the service they were followed, their discharge status and thirty-day mortality status were determined and recorded.

RESULTS

Most of the 90 sepsis patients included in the study were over 65 years of age. While 60.0% (n=54) of the cases could be treated, 40.0% (n=36) died. When the relationship between mortality and descriptive data was investigated, a statistically significant negative correlation was found between Glascow Coma Score (GCS) and mortality ($p=0.002$; $p<0.01$). A statistically significant negative correlation was also found between the degree of

Table 3: Antibiotic Therapy

Antibiotic	n	%
Piperacillin-Tazobactam	24	26.7%
Meropenem + Vancomycin	16	17.8%
Piperacillin-Tazobactam +Clarithromycin	13	14.4%
Seftriakson	13	14.4%
Meropenem + Teicoplanin	6	6.7%
Piperacillin-Tazobactam + Teicoplanin	4	4.4%
Ertapenem	4	4.4%
Meropenem	3	3.3%
Teicoplanin	2	2.2%
Meropenem + Vancomisin + Acyclovir	2	2.2%
Meropenem + Vancomisin + Antituberculosis	2	2.2%
Ampicillin-Sulbactam	1	1.1%

Table 4: Laboratory Results and Mortality

				Mortality		p
		n	%	No (n=54) n (%)	Yes (n=36) n (%)	
Hemoglobin	Min-Max (Median)	5.6-15.8(9.5)		6-15.8(9.6)	5.6-13.9(9.5)	[a]0.890
	Mean±Sd	9.87±2.06		9.84±2.09	9.90±2.05	
	Normal	54	60.0%	32 (59.3)	22(40.7)	
	Low	36	40.0%	22 (61.1)	14(38.9)	
WBC	Min-Max (Median)	400-84.000(13950)		600-84.000(13750)	400-73900(15150)	[b]0.234
	Mean±Sd	15.888±14.157		15029.63±14685.77	17177.78±13426.27	
	Low	13	14.4%	10(76.9)	3(23.1)	
	Normal	19	21.1%	10(52.6)	9(47.4)	
	High	58	64.4%	34(58.6)	24(41.4)	
Platelet	Min-Max (Median)	14-562(211)		49-562(212)	14-507(210)	[b]0.526
	Mean±Sd	235.72±135.45		243.25±134.22	224.42±138.40	
	Low	26	28.9%	15(57.7)	11(42.3)	
	Normal	47	52.2%	29(61.7)	18(38.3)	
	High	17	18.9%	10(58.8)	7 (41.2)	
Neutrophil count	Min-Max (Median)	0.10-66(8.8)x10 9/L		0.1-66(6.6)	0.1-61.6(11.3)	[b]0.002**
	Mean±Sd	10.39±10.38 x10 9/L		8.38±9.45	13.40±11.10	
Neutrophil (%)	Min-Max (Median)	21-98.2(80)		23-95(73.5)	21-98.2(87)	[b]0.005**
	Mean±Sd	74.83±19.37		70.60±19.66	81.19±17.32	
Neutrophil count	Low	11	12.2%	9 (81.8)	2(18.2)	[b]0.002**
	Normal	20	22.2%	16 (80.0)	4(20.0)	
	High	59	65.6%	29(49.2)	30(50.8)	
CRP	Min-Max (Median)	1-500(164)		10-500(137)	1-471(175)	[b]0.556
	Mean±Sd	181.48±123.19		175.54±123.17	190.39±124.42	
	Normal	1	1.1%	0(0)	1(100)	
	High	89	98.9%	54(60.7)	35(39.3)	
AST	Min-Max (Median)	5-898(28)		5-898(21.5)	11-633(35)	[b]0.001**
	Mean±Sd	63.65±127.52		48.32±128.92	86.64±123.61	
	Normal	64	71.1%	45(70.3)	19(29.7)	
	High	26	28.9%	9(34.6)	17(65.4)	
ALT	Min-Max (Median)	2.2-443(19)		2.2-443(18.5)	6.5-410(19.5)	[b]0.052
	Mean±Sd	40.64±71.81		35.38±71.45	48.53±72.63	
	Normal	68	75.6%	43(63.2)	25(36.8)	
	High	22	24.4%	11(50.0)	11(50.0)	
Total bilirubin	Min-Max (Median)	0.14-49(0.7)		0.14-12(0.5)	0.2-49(0.9)	[b]0.003**
	Mean±Sd	2.34±6.34		0.91±1.64	4.48±9.51	
	Normal	68	75.6%	45(66.2)	23(33.8)	
	High	22	24.4%	9(40.9)	13(59.1)	
Urea	Min-Max (Median)	11-455(71)		11-230(61)	15-455(98.5)	[b]0.015*
	Mean±Sd	91.33±81.77		69.19±47.11	124.56±108.41	
	Normal	34	37.8%	22(64.7)	12(35.3)	
	High	56	62.2%	32(57.1)	24(42.9)	
Creatinine	Min-Max (Median)	0.23-9.9 (1.2)		0.23-9.9(1)	0.4-9.1(1.5)	[b]0.063
	Mean±Sd	1.79±1.84		1.59±1.69	2.10±2.02	
	Normal	50	55.6%	34(68.0)	16(32.0)	
	High	40	44.4%	20(50.0)	20(50.0)	

*[a]Student t Test [b]Mann Whitney U Test *p<0.05 **p<0.01*

temperature and mortality (p=0.001; p<0.01). However, a statistically significant positive correlation was found between the need for ventilation, intensive care unit tranfers and mortality (p=0.001; p<0.01). Descriptive Characteristics and mortality analyses are in Table 1.

The most common infection source of the patients is the

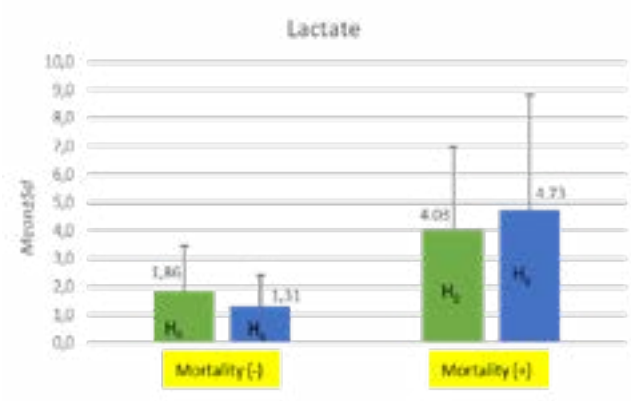

Figure 1: Lactate Levels According to the Presence of Mortality

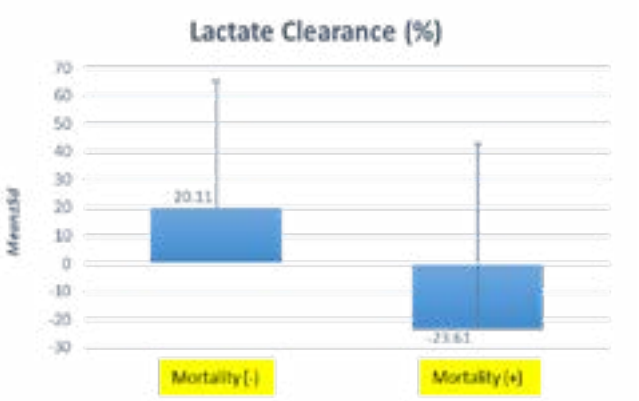

Figure 2: Lactate Clearance (%) Levels According to the Presence of Mortality

lungs followed by the urinary system. Less frequently, gastrointestinal tract, catheter, diabetic foot ulcers and decubitus ulcers are also seen to be the source (Table 2).

The most commonly used antibiotic in the treatment of sepsis is piperacillin-tazobactam combination. Detailed antibiotic therapy is available in Table 3.

The majority of patients have elevated CRP, leukocytosis and neutrophilia. When the relationship between laboratory findings and mortality is examined, neutrophil count ($p=0.002$; $p<0.01$), neutrophil percentage ($p=0.005$; $p<0.01$), AST ($p=0.001$; $p<0.01$), ALT ($p=0.052$; $p>0.05$) total bilirubin ($p=0.003$; $p<0.01$) 0.01), urea ($p=0.015$; $p<0.05$), and creatinine ($p=0.063$; $p>0.05$) levels were positively correlated with mortality. Other laboratory values and mortality rates are available in Table 2.

Lactate and Lactate Clearance

H0 lactate levels of all cases ranged from 0.4 to 13, with a mean of 2.73±2.46; The lactate level of 43.3% (n=39) was normal and of 56.7% (n=51) was high. H6 lactate measurements of the cases ranged from 0.4 to 18.7, with an average of 2.67±3.20.

The decrease in the H6 lactate levels of the cases compared to the H0 hour was statistically significant ($p=0.001$; $p<0.01$). Accordingly, lactate level of 2.2% (n=2) of the cases remained normal, while 63.3% (n=57) decreased and 34.4% (n=31) increased.

According to the presence of mortality, a statistically significant positive correlation was found between the H0 lactate levels of the cases ($p=0.046$; $p<0.05$); H0 lactate levels of the cases with mortality were significantly higher than those without mortality. A statistically significant positive correlation was found between the H6 lactate levels of the cases according to the presence of mortality ($p=0.001$; $p<0.01$); H6 hour lactate levels of cases with mortality were significantly higher than those without mortality (Table 5).

The decrease in the H6 lactate levels of the cases without mortality was statistically significant ($p=0.001$; $p<0.01$). The change in the H6 lactate levels of the cases with mortality was not statistically significant ($p=0.289$; $p>0.05$).

The change in the H6 lactate levels of the cases showed a statistically significant difference according to the presence of mortality ($p=0.001$; $p<0.01$). While a decrease was observed in lactate levels in patients without mortality, an increase was observed in patients with mortality (Table 5, Figure 1).

The lactate clearance (%) of the cases ranged from -200 to 80, with a mean of 2.62±58.39 and a median of 15. Accordingly, 40.0% (n=36) of the cases' lactate were low and 60.0% (n=54) were high.

A statistically significant negative correlation was found between the lactate clearance (%) of the cases according to the presence of mortality ($p=0.001$; $p<0.01$); lactate clearance (%) of cases with mortality were significantly lower than those without mortality (Table 5, Figure 2).

DISCUSSION

Among the parameters that are thought to affect mortality in sepsis patients, lactate level is preferred because it is fast, practical, inexpensive, does not require invasive intervention, and is available in all emergency services (14). In recent years, lactate and lactate clearance have gained importance in the follow-up of sepsis patients and in determining the weight, since it has been reported to have prognostic value in studies conducted abroad (15). In the light of these studies, lowering the lactate value is among the treatment goals in the latest guideline (1,12,13). In a study conducted by Marty et al. in 2013, 91 intensive care patients were examined and lactate clearance was calculated by taking H0 H6 H12 H24 lactate values by being followed for 24 hours (16). Based on 28-day mortality, it has been shown that treatment with a 20% clearance target has a strong effect on reducing mortality. In our study, lactate clearance was calculated using H0 and H6 lactate values, and it was found that patients with a clearance above 10% had a lower 30-day mortality compared to other patients.

Again, in a study conducted between 2006 and 2008 in which 348 intensive care patients with a lactate level >3 mEg/L were included, the effect of normalizing the lactate level on tissue oxygenation was investigated. The patients were divided into two groups as the lactate group (171 patients) and the control group (177 patients), and the treatment protocol determined for that group was applied to both patient groups for 8 hours. While it was aimed to reduce the lactate level by 20% within 2 hours in the lactate group, the central venous oxygen saturation (ScvO2) target value of 70% was used in the control group. When the 28-day mortality rates of both patient groups were compared, it was found that the mortality rate was lower

Table 5: Lactate, Lactate Clearence (%) and Mortality

		Total (n=90)	Mortality		p
			No (n=54)	Yes (n=36)	
H0 Lactate	Min-Max (Median)	0.4-13 (1.9)	0.4-10.6 (1.4)	0.8-13 (2.9)	0.001**
	Mean±Sd	2.73±2.46	1.86±1.58	4.03±2.96	
	Normal	39 (43.3%)	32 (82.1%)	7 (17.9%)	
	High	51 (56.7%)	22 (43.1%)	29 (56.9%)	
H6 Lactate	Min-Max (Median)	0.4-18.7 (1.4)	0.4-5.8 (0.9)	0.7-18.7 (3.6)	0.001**
	Mean±Sd	2.67±3.20	1.31±1.11	4.73±4.11	
H0 - H6 change	Min-Max (Median)	-4.8-12.7 (-0.3)	-4.8-3.1 (-0.4)	-4.8-12.7 (0.3)	0.006**
	Mean±Sd	-0.06±2.26	-0.56±1.2	0.7±3.14	
	Normal	2 (2.2%)	2 (100%)	0 (0%)	
	Decreased	57 (63.3%)	43 (75.4%)	14 (24.6%)	
	Increased	31 (34.4%)	9 (29.0%)	22 (71.0%)	
Lactate clearance (%)	Min-Max (Median)	-200 – +80 (15)	-123 – +75 (33)	-200 – +80 (-17)	[a]0.001**
	Mean±Sd	2.62±58.39	20.11±45.07	-23.61±66.43	
	Low	36 (40.0)	12 (33.3)	24 (66.7)	
	High	54 (60.0)	42 (77.8)	12 (22.2)	

[a]Mann Whitney U Test *$p<0.05$ **$p<0.01$

in the lactate-reducing targetted group (17). In the light of all these studies, the recommendation to normalize the lactate level has taken its place in the 2012 guideline. In our study, the upper limit of lactate was accepted as 1.2, and patients with an admission lactate below this value were also included in the study. In our study, the effect of lowering the lactate level with treatment on mortality was investigated, and in accordance with this study, patients with lactate clearance below 10% had a higher mortality.

In the study conducted by Levraut et al. in 2003, the pronogstic value of lactate clearance was investigated in 56 intensive care unit patients with a lactate level <3mmol (18). Control arterial blood gas was taken 45 minutes after sepsis patients whose admission lactate was not high, and lactate clearance was calculated, and it was found that patients with low admission lactate were associated with poor outcome, independent of their admission lactate values. In our study, H0 lactate value was found to be effective on mortality. This may be because patients with normal and high lactate levels were included in the study. Again, H6 lactate value was found to be associated with mortality in our study. The absolute value of the control lactate value is effective on mortality, and at this point, our study is compatible with this study. The H0 value was found to be ineffective in this study, and at this point, our study is inconsistent with this study.

In a study conducted by Mikkelsen et al. in the emergency department in May 2009, the effect of elevated serum lactate on mortality independent of organ failure and shock was investigated in 830 severe sepsis patients (19). The patients were divided into low <2mmol, moderate (2-3.9) and high >4 lactate groups, and the presence of shock, hypotension, severity of the disease, age, gender, and organ failure were recorded. Mortality was found to be high in patients with moderate and high lactate, independent of other factors. In our study, it was determined that the presence of comorbidity had no effect on mortality. However, it was observed that the presence of kidney and liver dysfunction increased mortality. In addition, lactate values were not grouped, and values of 1.2 and above were considered high. Therefore, it can be said that our results are partially compatible with this study. However, the fact that we did not evaluate lactate elevation independently of other factors may be a shortcoming of our study.

In the study conducted by Nguyen et al. in August 2004, it was seen that patients with high lactate clearance compared to H0 and H6 values in 111 patients with sepsis who were taken from the emergency room before the intensive care unit and taken to the intensive care unit during follow-up showed less mortality compared to those with low lactate clearance (20). These results are consistent with our study. However, in our study, patients whose H6 lactate control was performed outside the emergency department were excluded from the study. As a result of insufficient number of intensive care beds in the hospital, patients in need of intensive care are mostly referred to intensive care units in an external center. As a result, patients who were referred before 6 hours were not included in the study, as there would be problems in the H6 follow-up of the patients.

In our study, the mean age was 61.33, 52% of patients were under 65 years old, 47.8% of them were over 65 years of age. In the study of Nguyen et al., the average age is higher, and this may be due to the fact that our hospital is a university hospital where young immunological hematological patients with a large number of sub-branch departments are followed.

In the study conducted by Philippe Marty et al. in sepsis patients in 2013, mortality was found to be 45%, in the study of Levraut et al. 38%, and similarly 40% in our study (16,18).

In the study of Mikkelsen et al. on sepsis, the mean lactate value was found to be 2.9, and it was similarly found to be

2.7 in our study (19).

When we look at the relationship between thrombocytopenia and sepsis, it was reported in a short review published in 2016 that thrombocytopenia is a common source of morbidity and increases mortality in sepsis patients (21). In our study, platelet count was found to be ineffective on mortality. This result may be due to the smaller number of patients with thrombocytopenia in our study and the fact that the majority of thrombocytopenia was not caused by sepsis.

Rhiong zahi et al. investigated the effect of total bilirubin elevation on mortality and the risk of 60-day ARDS and mortality in 1006 sepsis patients in the USA (22). Bilirubin was found to be higher in the patient group with mortality, and it was determined that each 1mg/dl increase in total bilirubin increased the mortality rate by 7%. In our study, according to the presence of mortality, the total bilirubin measurements of the cases were higher than those without mortality ($p=0.003, p<0.01$).

In a retrospective, multicenter study conducted in Germany in 2007 and including 3877 sepsis patients in the intensive care unit, the rate of acute renal failure was found to be 41.4% in sepsis patients (23). In our study, this rate was found to be 62%. This may be because patients with chronic renal failure were not excluded from our study. Again in this study, patients with high urea and creatinine levels were found to have higher mortality than those without. The results of our study are compatible with this study.

In our study, it was determined that there were significant differences in terms of glaskow coma scale, respiratory rate, fever, neutrophil count, urea, creatinine, ventilation need, follow-up of the patient in the intensive care unit, AST, total bilirubin, and mortality in sepsis patients. However, it was observed that blood pressure, age, comorbidities, hemoglobin, platelet count, CRP, ALT values had no effect on mortality.

In a prospective multicenter randomized controlled study conducted by Clemmer et al. in 1992, a 9% hypothermia rate was observed (24). In our study, this rate was 16.7% (n=15). While mortality in hypothermic patients was 70% in this study, it was 100% in our study. In our study, a significant relationship was found between body temperature and mortality in sespsis. Mortality was higher in hypothermic patients compared to normothermic and hyperthermic patients. This may be due to the fact that the low immune system response of these patients affected the fever response and the host response to sepsis was weak for the same reason. Our study is compatible with these studies in terms of hypothermia-mortality relationship.

The retrospective study of Haas at al. showed that decreased lactate clearence and high lactate levels (>10 mmol/L) have strong relation with high mortality rates in critically ill patient (25). A retrospective study wich compares lactate level and lactate clearance with 1060 septic shock patients demonstrate that both are convenient goals for treatment howewer 6th hour lactate level is better for predicting prognosis and mortality (26). So using lactate clearence as a objective for guiding early sepsis therapy could improve mortality rates in adult (27). According to a recent meta-analyse to use lactat clearence based therapy in early sepsis (6th hour) is more beneficial in terms of reducing mortality, ventilation need, in hospital time and APACHE-II scores in ICU than ScvO2 based therapy (28). Despite all this, the lactate mechanism is actually very complex, its clearence may not jus due to an over production or poor metabolisation so simply reducing the lactate level may not be a logical goal (29).

As a result of this study, it was found that the lactate value at admission and the decrease in lactate level after six hours were effective on mortality, and the absolute lactate value at the sixth hour was effective on determining mortality. Therefore, taking into account the lactate value in arterial blood sample taken at the time of admission to the emergency department, it may be appropriate to apply lactate-reducing treatment in the follow-up. However, the rate of clearance, not the absolute value of the control lactate value, is more effective on mortality. At the other hand, it may be more appropriate to use all markers together instead of a single marker in determining the prognosis in sepsis patients. Lactate clearance can be an important prognostic marker when combined with other factors.

As a conclusion, the high rate of lactate level decrease at the sixth hour indicates a good prognosis in sepsis patients, regardless of the lactate value. When all these results are taken into consideration, it can be said that the lactate value and lactate clearance are useful markers in predicting prognosis in sepsis patients admitted to the emergency department. However, they are not sufficient on their own to determine the prognosis and should be used together with other markers and clinical evaluation.

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Conflict of interests: The authors declare that there are no conflicts of interest.

Ethic: Clinical Research Ethics Committee of Cerrahpaşa Medıcal Faculty, Date: 04,04,2017 an Number: 31887016-604,01,02-98644

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ORIGINAL ARTICLE

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Serum Lactate may be a Marker for Determining 30-Day Mortality in Patients with Acute Upper Gastrointestinal System Bleeding

Serum Laktat Akut Üst Gastrointestinal Sistem Kanamalı Hastalarda 30 Günlük Mortaliteyi Belirlemede Belirteç Olabilir

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ABSTRACT

Ojective: *We aimed to examine the role of serum lactate level in predicting 30-day mortality in patients with upper gastrointestinal bleeding (GIB).*

Matarial and Method: *377 upper GIB cases included in the study. Age, gender, symptoms and signs, comorbidity and drugs, hemoglobin, amount of red blood cells administered, lactate level, mortality rates were recorded. The patients were divided into 2 groups as those who died and those who survived after GI bleeding. The clinical and laboratory variables of the groups were compared. Chi-square test and Mann-Witney U test were used to compare the groups. The ROC curve was plotted to determine the sensitivity and specificity of serum lactate level in determining 30-day mortality. A p value of <0.05 was considered statistically significant.*

Results: *The median lactate level of 42 (11.1%) deceased patients was 3 mmol/L (QR: 3.3 mmol/L), and the median lactate level of the surviving patients was 1.7 mmol/L (QR: 1.3 mmol/L). The lactate level of the patients who died was found to be significantly higher (p<0.001). The ROC curve was plotted to determine the sensitivity and specificity of serum lactate in determining 30-day Mortality. for 3 mmol/L; sensitivity was 79.5% and specificity was 53.8%.*

Conclusion: *It was determined that patients with high serum lactate levels were more mortal.*

ÖZET

Amaç: *Üst gastrointestinal sistem kanamalı (GİSK) hastalarda serum laktat düzeyinin 30 günlük mortaliteyi öngörmedeki yerini incelemeyi amaçladık.*

Gereç ve Yöntem: *Çalışmaya 377 üst GİSK'lı hasta dahil edildi. Hastaların yaş, cinsiyet, semptom ve bulgular, komorbidite ve ilaçlar, hemoglobin, verilen eritrosit miktarı, laktat düzeyi, mortalite oranları kaydedildi. Hastalar GIS kanama sonrası ölen ve yaşayanlar olarak 2 gruba ayrıldı. Grupların klinik ve laboratuar değişkenleri karşılaştırıldı. Grupların karşılaştırılmasında Ki-kare testi ve Mann-Witney U testi kullanıldı. 30 günlük mortaliteyi belirlemede serum laktat düzeyinin sensitivite ve spesifitesini belirlemek için ROC eğrisi çizdirildi. P<0,05 değeri istatistiksel olarak anlamlı kabul edildi.*

Bulgular: *Eksitus olan 42 hastanın (%11.1) laktat düzeyi ortancası 3 mmol/L (QR:3.3 mmol/L), yaşayan hastaların laktat düzeyi ortancası 1.7 mmol/L (QR:1.3 mmol/L) olduğu saptandı. Eksitus olan hastaların laktat düzeyi anlamlı olarak yüksek saptandı (p<0.001). 30 günlük Mortaliteyi belirlemede serum laktatın sensitivite ve spesifitesini belirlemek için ROC eğrisi çizdirildi. 3 mmol/L için; sensitivite %79.5 ve spesifite 53.8 olarak saptandı*

Sonuç: *Serum Laktat düzeyi yüksek olan hastaların daha mortal seyrettiğini tespit edildi.*

Keywords:
Upper gastrointestinal bleeding
Lactate
Mortality

Anahtar Kelimeler:
Üst gastrointestinal kanama
Laktat
Mortalite

GİRİŞ

Gastrointestinal sistem kanamaları (GİSK), sindirim sisteminin herhangi bir bölümünden olan kanamalardır. Kendi içerisinde üst ve alt GİSK'si olarak sınıflandırılırlar. Üst GİSK bölgesi duedenumda Treitz ligamentinin üstündeki alanda olan kanamlar olup, sıklığı alt GİSK'ten 4 kat fazladır (1).

Üst GİSK'ları acil servise sık başvuran ve mortal seyredebilen patolojilerdir. Yıllık insidansı 10000 vakada 5-10 olup, mortalite oranı %5-6 düzeyindedir (1-3). Üst GİSK kanamaların %80-85'i destekleyici tedavi ile kendiliğinden dursa bile, kalan kısım için girişimsel müdahale gerekmektedir (1-6).

Serum kan laktat ölçümü, acil serviste; bazı patolojilerde tanı, prognoz ve tedavininin şekillendirilmesinde yardımcı olarak kullanılmaktadır. Laktat düzeyinin sepsis, akciğer embolisi, GİSK, akut batın ve senkop gibi diğer birçok hastalığın tanı ve prognozunda faydalı olabileceği gösterilmiştir (5). Laktik asidoz hipovolemi (kanama veya dehidrasyon), şiddetli anemi, septik şok ve ciddi hipoksemi durumlarında ciddi oranda artar (2). Laktatın hastalık ciddiyetini göstermede etkin olarak kullanılabileceği ifade edilmiştir 4, 7).

Çalışmamızda üst gastrointestinal sistem kanamalı (GİSK)

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hastalarda serum laktat düzeyinin 30 günlük mortaliteyi belirlemedeki yerini incelemeyi amaçladık

MATERYAL VE METOD

Çalışmamız, etik kurul onayı alınarak (2019/148), Bolu Abant İzzet Baysal Üniversitesi Tıp Fakültesi acil servisine 01.01.2014-31.12.2018 tarihleri arasında retrospektif olarak yapıldı. Çalışmaya 380 hasta dahil edildi.

Hastaların demografik özellikleri, komorbditeleri ve ilaçları, vital parametreleri, endoskopi sonuçları, kan gazında laktat düzeyi, hemoglobin sonuçları, eritrosit süspansiyonu (ES) ihtiyacı, hastanede kalış süresi ve mortalite durumları incelendi.

18 yaş altı hastalar, yapılan endoskopi sonucu GİS kanama dışlanan hastalar, hasta kartları/otomasyon sisteminden verilerine ulaşılamayan, kardiyopulmoner resüsitasyon yapılmış, sebebi net olarak belirlenemeyen arrest olguları ve laktik asidoza yol açan diğer metabolik hastalıklara sahip patolojileri olan hastalar dışlandı.

Veriler SPSS for Windows® 22.0 paket programı ile değerlendirildi. Verilerin normal dağılıma uygunlukları Kolmogorov-Smirnov testi ile belirlendi. Sürekli değişkenlerin gösteriminde ortanca, interquantile range (IQR); kategorik verilerin gösteriminde hasta sayısı (n) ve percentil (%) kullanıldı. Hastalar GIS kanama sonrası 30 gün içinde ölen hastalar (Grup 1) ve yaşayan hastalar (Grup 2) olarak 2 gruba ayrıldı. Gruplar arasında karşılaştırmalar yapıldı. Sürekli verilerin, karşılaştırılmasında Mann Whitney-U, kategorik verilerin karşılaştırılmasında ki-kare testi kullanıldı. 30 günlük mortaliteyi belirlemede serum Laktat düzeyinin sensitivite ve spesifitesinin belirlenmesi için ROC eğrisi çizdirildi. $p<0.05$ değeri istatistiksel anlamlı olarak kabul edildi.

BULGULAR

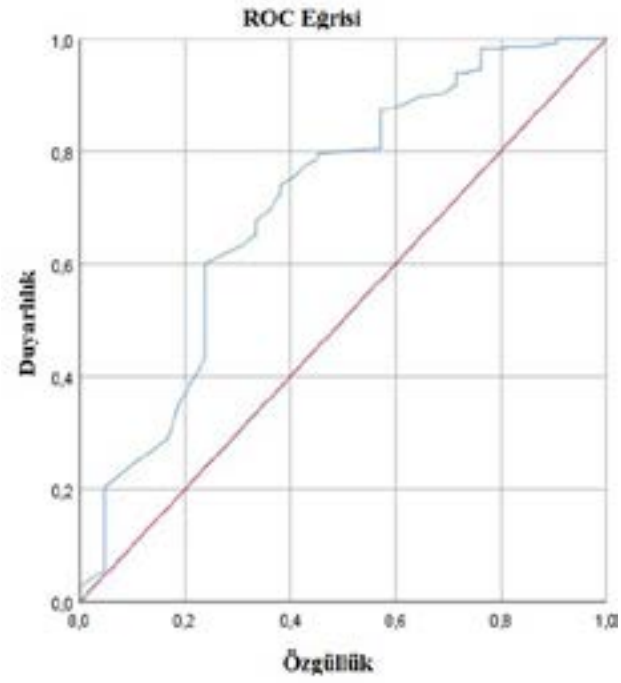
Çalışmamıza 380 GİS kanamalı olgu dahil edildi. Hastaların yaş ortancası 66 (IQR: 30) yıldı, hastaların 240'i (%63,5) erkekti. Hastaların klinik ve demografik verileri Tablo 1 de özetlendi. Çalışmamızda eksitus olan hastaların yaş ortancası anlamlı yüksekti ($p<0,05$). Eksitus olan hastaların hematemez sıklığı yüksek; melena ve baş dönmesi sıklığı anlamlı olarak düşüktü ($p<0,05$). Eksitus olan hastaların HT, DM, malignite öyküsü, karaciğer hastalığı ve böbrek yetmezliği sıklığı anlamlı olarak yüksekti ($p<0,05$). Endoskopide gastrit çıkan hastaların mortalite sıklığı anlamlı olarak düşük, kitle saptananların anlamlı olarak yüksekti ($p<0,05$). Diğer parametreler ile mortalite arasında ilişki saptanmadı (Tablo 1).

Tablo 1: Gruplara göre demografik ve klinik özellikler

		Grup 1 (n:42)	Grup 2 (n:338)	p
Yaş		72.5 (23)	65 (31)	0.030*
Cinsiyet	Erkek	32 (76,2)	208 (61,5)	0,063
	Kadın	10 (32)	130 (38,5)	
Semptomlar	Melena	17 (40,5)	205 (61,2)	0,010*
	Hematemez	31 (73,8)	168 (50,1)	0,004*
	Senkop	4 (9,5)	40 (11,9)	0,802
	Baş dönmesi	2 (4,8)	40 (11,9)	0,04*
	Hematokezya	5 (11,9)	16 (4,8)	0,058
	Çarpıntı	3 (7,1)	9 (2,7)	0,139
	Nefes darlığı	0	3 (0,9)	>0,999
Komorbidite	Hipertansiyon	20 (47,6)	106 (31,6)	0,039
	Kalp hastalığı	12 (28,6)	102 (30,4)	0,803
	GİS kanama öyküsü	11 (26,2)	90 (26,9)	0,926
	Diabetes mellitus	20 (47,6)	76 (22,7)	<0,001*
	KOAH	10 (23,8)	82 (24,5)	0,924
	Malignite öyküsü	20 (47,6)	38 (11,3)	<0,001*
	Karaciğer hastalığı	15 (35,7)	41 (12,2)	<0,001*
	Böbrek yetmezliği	15 (35,7)	33 (9,9)	<0,001*
	Diğer	19 (45,2)	116 (34,6)	0.176
İlaç kullanım öyküsü	Antiagregan	8 (19)	89 (26,6)	0,293
	NSAİİ kullanımı	10 (23,8)	86 (25,7)	0,794
	Antikoagülan kullanımı	7 (16,7)	45 (13,4)	0,567
Endoskopi	Gastrit	12 (28.6)	205 (61,7)	<0,001*
	Ülser	20 (47,6)	193 (58,1)	0,195
	Erozyon	4 (9,5)	58 (17,5)	0,192
	Varis	10 (23,8)	45 (13,6)	0,077
	Özefajit	7 (16,7)	45 (13,6)	0,583
	Kitle	9 (21,4)	36 (10,8)	0,047*
	Mallory-Weis	0	9 (2,7)	0,606

**Mann Whitney U testi, GİS: Gastrointestinal sistem, KOAH:kronik obstruktif akciğer hastalığı, NSAİİ: Nonsteroid antiinflamatuar ilaç*

Eksitus olan 42 hastanın (%11,1) laktat düzeyi ortancası 3 mmol/L (QR:3,3 mmol/L), yaşayan hastaların laktat düzeyi ortancası 1,7 mmol/L (QR:1,3 mmol/L) olduğu saptandı. Eksitus olan hastaların laktat düzeyi anlamlı olarak yüksek saptandı (p<0,001). 30 günlük Mortaliteyi belirlemede serum laktatın sensitivite ve spesifitesini belirlemek için ROC eğrisi çizdirildi. 3 mmol/L için; sensitivite %79,5 ve spesifite 53,8 olarak saptandı (AUC=0,708, (%95Cl 0,618-0,799)) (Şekil 1).



Şekil 1: Mortalite ve serum laktat için ROC analizi

TARTIŞMA

Laktat düzeyi bozulan hipoperfüzyona sekonder gelişen mikro dolaşım anormallikleri sonucu meydana gelen anaerobik glikoliz, artan strese bağlı adrenerjik kaynaklı aerobik glikoliz, hepatik yetmezliğe bağlı laktatın temizlenememesi ve mitokondriyal disfonksiyon sonucu artar (8, 9).

Çalışmamız sonucunda 30 günlük Mortaliteyi belirlemede serum laktatının 3 mmol/L değeri için sensitivite %79,5 ve spesifite 53,8 olarak saptandı. Konyar ve ark. GİS kanamalı hastalarda mortalite laktat arasında ilişki saptanmamış, sensitivitesinin %37,5, spesifitesinin %80,7 olarak bildirmiştir (2). Shah ve ark. GİS kanamalı hastalarda laktat seviyesinin 4 mmol/L'den fazla olması durumunda mortalitenin 6,4 kat artırdığını belirtmiştir (10). Aynı çalışmada mortalite için laktat için cut-off değerinin 4.0 mmol/L olması durumunda spesifitenin %94, sensitivitenin %33 olduğu belirlenmiştir. Shapiro ve ark. cut-off değerinin 4,0 mmol/L olması durumunda laktat için spesifitenin %92, sensitiviteyi %36 olarak bildirmiştir (11). Diğer çalışmalarda cut-off değerinin bizim çalışmamızdakine kıyasla daha üst seviyelerde alınması sensitiviyeyi düşürmüş, spesifiteyi arttırmış olabilir. Serum laktat düzeyi 3 mmol/L 'nin üstünde olan hastaların yakın monitorizasyonu gerektiğini düşünmekteyiz

Çalışmamızda mortalite oranı %11,1 olup, mortal seyreden hastalarda laktat düzeyi anlamlı olarak yüksek saptandı. Yapılan çalışmalarda üst GİSK'ine bağlı mortalite oranının % 4,5-31 arasında olduğu bildirilmiştir (1,2,12-17). Hemodinaminin aşırı bozulması ve araya giren ek problemler sebebiyle laktat düzeyinin üst düzeylerde çıktığı ve dolaşımın irreversibl olarak bozulması sonucu ölüm oranlarının arttığı kanısındayız.

Yapılan çalışmalarda GİSK'nın yaşlı ve erkek popülasyonda daha sık görüldüğü belirtilmiştir (1,4,5,15-18). Çalışmamızda literatür ile uyumlu olarak GİS kanamanın erkeklerde ve ileri yaşlarda sık olduğu saptandı. Çalışmamızda yaşlı hastaların daha mortal seyrettiği saptandı. Bu durumun ileri yaşlarda gelişen katabolik sürece bağlı olarak mide mukozası ve damarsal yapıların bozulması, komorbid hastalıkların artması ve erkeklerin daha düzensiz beslenmeleri ile ilişkili olabileceği kanısındayız.

Daha önce yapılan çalışmalarda GİSK'li hastalarda en sık septomum hematemez, en nadir semptomun ise baş dönmesi olduğunu ifade etmiştir (1,2,15-17). Shrestha ve ark. GİSK'li hastalarda yaptıkları çalışmada hematemez ve bilinç bozukluğu olan hastaların daha yüksek oranda laktat pozitifliği olduğunu; karın ağrısı ve hematokezya olan hastalarda daha az oranda laktat pozitifliği olduğunu ifade etmiştir (4). Çalışmamızda literatür ile uyumlu olarak, en sık rastlanan semptomlar melena ve hematemez olduğu saptandı. Hastalar kusmuklarında veya dışkılarında kan gördükleri zaman endişeye kapılmakta ve hemen doktora başvuruyor görünmektedir.

Yapılan çalışmalarda komorbid hastalıklar ve kullanılan bazı ilaçların GİSK sıklığını artırdığı belirtilmiş; en sık komorbid hastalığın hipertansiyon ve en sık kullanılan ilaçların NSAİ olduğu ifade edilmiştir (19-22). Shrestha ve ark. yaptıkları çalışmada geçmiş dönem GİSK öyküsü, komorbidite indeksi ve kullanılan ilaçlar (antikoagülan, antiagregen ve NSAİ) laktat pozitifliği sıklığı ilişkisiz olduğunu ifade etmiştir (4). Çalışmamızda literatür ile uyumlu olarak en sık komorbidite hipertansiyon ve en sık kullanılan ilacın NSAİ olduğu saptandı. Hasta popülasyonumuzun yaşlı olması sebebiyle toplumda HT'nin sık görülmesi ve yine bu hastalarda sık görülen kas ve eklem ağrılarının giderilmesi amacıyla NSAİ yaygın kullanıldığı kanısındayız. Eksitus olan hastaların HT, DM, malignite öyküsü, karaciğer hastalığı ve böbrek yetmezliği sıklığı anlamlı olarak yüksekti. Sirozda gelişen kanama bozuklukları, DM gibi patolojilerde gelişen damar bozuklukları ve lösemi/lenfoma gibi malignitelerdeki kan hücrelerinin azalması veya fonksiyon bozukluğu kanama miktarının artışına ve mortalite artışına yol açmış olabilir. Literatürde. en sık GİSK nedeninin mide ülseri olduğunu ifade etmiştir (1,5,15). Çalışmamızda literatür ile benzer olarak en sık rastlanan patolojilerin gastrit ve ülser olduğu saptandı. Endoskopide gastrit çıkan hastaların mortalite sıklığı anlamlı olarak düşük, kitle saptananların anlamlı olarak yüksekti.

SONUÇ

Çalışmamız sonucunda Laktat düzeyi yüksek olan hastaların daha mortal seyredebileceği görüldüğünden klinisyenin bu hastaların takip ve tedavisinde daha dikkatli olması gerekmektedir.

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ORIGINAL ARTICLE

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The Relationship of Attachment with Functionality, Insight and Adaptation to the Treatment in Patients with Schizophrenia

Şizofreni Hastalarında Bağlanmanın İşlevsellik, İçgörü ve Tedaviye Uyum ile İlişkisi

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ABSTRACT

Objective: *This study was conducted with patients diagnosed with schizophrenia registered in Rize State Hospital Community Mental Health Center. Again, adherence to treatment, insight and functionality are important concepts in terms of the prognosis of chronic mental disorders. The aim of this study is to examine the relationship between attachment styles, functionality, adherence to treatment, and insight in patients with schizophrenia.*

Material and Method: *100 schizophrenic patients registered at Rize State Hospital Community Mental Health Center for at least 3 years were included in the study. Patients were selected according to exclusion criteria. Clinical interviews were made with the patients, and informed consent was obtained from the patients who could be included in the study and their legal guardians. Socio-demographic data form prepared by us, Evaluation scale of the three components of Insight, Brief functionality scale, Medical treatment compliance rate scale, Adult attachment style scale were used in the study. The data of the study were evaluated by number, percentage, frequency, Kolmogorov-Smirnov Test/Shapiro-Wilk Test, pearson correlation tests in SPSS 22nd Edition.*

Results: *The mean age of the patients participating in the study was 34, the number of female patients was 32, and the number of male patients was 68. In the evaluation of scale scores, no significant relationship was found between the Functioning scale and avoidant attachment, secure attachment, and anxious attachment. A significant negative correlation was found between insight scale scores and avoidant attachment. No significant correlation was found between insight scale scores and secure attachment. A positive and significant relationship was found between the insight scale scores and the anxious attachment scale scores. There was no significant relationship between adherence to treatment scale scores and avoidant attachment, secure attachment and anxious attachment.*

Conclusion: *Attachment occupies an important place in the course of many psychiatric diseases, including schizophrenia. In our study, a relationship was found between insight and anxious and avoidant attachment. It is thought that childhood attachment processes may be related to the course and prognosis of the disease. New studies are needed in this area.*

Keywords:
Attachment
Schizophrenia
Insight

ÖZET

Amaç: *Bu çalışma Rize Devlet Hastanesi Toplum Ruh Sağlığı Merkezine kayıtlı şizofreni tanılı hastalarla yapılmıştır. Çalışmanın amacı şizofreni hastalarının bağlanma stillerinin, işlevsellik, tedaviye uyum ve içgörü ile ilişkisini incelemektir. Kronik seyirli bir hastalık olan şizofrenide hastalığın iyi prognozu açısından tedaviye uyum, iç görü ve işlevsellik önemli kavramlardır.*

Gereç ve Yöntem: *Çalışmaya Rize Devlet Hastanesi Toplum Ruh Sağlığı Merkezine en az 3 yıldır kayıtlı 100 şizofreni hastası dâhil edilmiştir. Hastalar dışlama kriterlerine göre seçilmişlerdir. Hastalarla klinik görüşmeler yapılmış, çalışmaya dâhil olabilecek hastalardan ve yasal vasilerinden onam alınmıştır. Çalışmada tarafımızca hazırlanmış Sosyodemografik Veri Formu, İçgörünün Üç Bileşenini Değerlendirme Ölçeği, Kısa İşlevsellik Ölçeği, Tıbbi Tedaviye Uyum Oranı Ölçeği, Erişkin Bağlanma Biçimi Ölçeği Ölçeği kullanılmıştır. Çalışmanın verileri SPSS 22. Sürümünde sayı, yüzde, frekans, Kolmogorov-Smirnov Testi/Shapiro-Wilk Testi, pearson korelasyon testleri ile değerlendirilmiştir.*

Bulgular: *Çalışmaya katılan hastaların yaş ortalaması 34±10.137, kadın hasta sayısı 32, erkek hasta sayısı 68 idi. Ölçek puanları değerlendirmesinde İşlevsellik ölçeği ile kaçıngan bağlanma, kaygılı bağlanma arasında anlamlı ilişki saptanmamıştır. İçgörü ölçek puanlamaları ile kaçıngan bağlanma arasında negatif yönde anlamlı bir ilişki saptanmıştır. İçgörü ölçek puanlamaları ile güvenli bağlanma arasında anlamlı ilişki saptanmamıştır. İçgörü ölçek puanlamaları ile kaygılı bağlanma ölçek puanları arasında pozitif yönde anlamlı bir ilişki saptanmıştır. Tedaviye uyum ölçek puanları ile kaçıngan bağlanma, güvenli bağlanma ve kaygılı bağlanma arasında anlamlı ilişki saptanmamıştır.*

Sonuç: *Bağlanma şizofrenide dâhil birçok psikiyatrik hastalığın seyrinde önemli bir yer kaplamaktadır. Çalışmamızda iç görü ile kaygılı ve kaçıngan bağlanma arasında ilişki saptanmıştır. Çocukluk dönemi bağlanma süreçlerinin hastalığın seyri ve prognozu ile ilişkili olabileceği düşünülmektedir. Bu alanda yeni çalışmalara ihtiyaç duyulmaktadır.*

Anahtar Kelimeler:
Bağlanma
Şizofreni
İçgörü

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GİRİŞ

Şizofreni toplumda %1 oranında görülen tedavi maliyeti yüksek, belirgin yeti yitimi ile seyreden psikiyatrik bir bozukluktur. Hastalığın etiyolojisi net açıklanamamıştır. Genellikle genç yaşlarda başlangıç göstermekte ve kronik bir seyir izlemektedir (1). Hastalığın uzun sureli seyir göstermesi, kronik seyretmesi nedeni ile yıkım gözlenmektedir. Hastaların toplumsal yaşama uyumlarının artması ve hayat kalitelerinin iyileşmesi için tedaviye uyum, iç görü gibi kavramlar önemlidir. Tüm bu etkileşimlerle birlikte hastaların bir kısmı normal hayatlarını sürdürebilmekte, toplumsal düzene ayak uydurabilmektedirler (2).

Bağlanma bireyin erken çocukluk döneminde bakım verici ile kurduğu ilişkidir. En basit haliyle güvenli bağlanma ya da güvensiz bağlanma şeklinde kurulur ve ilerleyen hayat evrelerinde bu süreç devam eder (3). Bakım verenle amaçlı kurulan bu yakınlık bireyin gelişim dönemlerinde ve yetişkinlik dönemlerinde çeşitli psikopatolojilerin gelişiminde rol oynayabilir. Yetişkinlik evresinde sorunlarla başa çıkma becerileri çocukluk döneminde güvenli bağlanma ile ilişkilidir (4). Bağlanma kuramı ilk olarak Bowlby nin teorileri ile geliştirilmiştir (5). Bu kurama göre bebekler doğumdan sonra bakım veren ile sürekli bir iletişim içerisine girer. Bebek ancak daimi bir bakım verenin varlığında hayatını sağlıklı sürdürebilir (6). Bakım verenden uzaklaşıldığında bebekte fizyolojik belirtiler gözlenir. Ayrıca bu fizyolojik belirtilere nörolojik sistemlerdeki gelişim bozuklukları da eşlik edebilir (7).

Bağlanmanın ileriki dönemde gelişecek psikopatoloji ile ilişkisi gösterilmiştir. Ayrıca her zaman için bağlanma ve psikopatoloji arasındaki ilişki dikkat çekici olmuştur. Güvensiz bağlanma kişilik bozuklukları, depresyon ve anksiyete gelişimi gösterildiği gibi ayrıca psikotik bozukluklarda yapılan çalışmalarda bağlanma bozuklukları daha sık oranlarda gözlenmektedir (8). Bağlanmaya ilişkin patolojilerin erişkinlik döneminde psikopatoloji ile ilişkisi olduğu gibi kişilerin sorun çözme becerileri stresi tolere etmeleri yaşam becerileri tedavi süreçlerine uyumları ve dolaylı olarak işlevsellikleri ile de ilgisi düşünülmektedir (9).

Şizofreni toplumda sık görülen düşünce bozukluğu, algı bozukluğu, toplumsal içe çekilme, işlevsellikte bozulma gibi belirtilerle ortaya çıkmaktadır (10). Şizofrenide hastalıkla ilgili eğitimler verilmesi, ailenin bilgilendirilmesi, tedaviye uyumun dikkatle takip edilmesi hastanın iyileşmesi ve işlevselliği açısından önemlidir. Ayrıca hastanın içgörüsü tedaviye uyumunu da etkilemektedir. Hastaların tedaviye uyumları ile birlikte nükslerde azalma ve yaşam kalitelerinde artış söz konusudur (11).

Şizofreni hem kronik seyri hem yeti yitimi ile birlikte ilerlemesi nedeni ile önemli bir hastalıktır. Hastalıkta içgörü, tedaviye uyum ve işlevsellik hastalığın seyri açısından önemli kavramlardır. Çalışmamızın bu anlamda literatüre katkı sağlayacağı düşünülmektedir.

GEREÇ VE YÖNTEM

Çalışmamız 01.07.2017-01.02.2018 tarihleri arasında yapılmıştır. Çalışmamıza Rize Devlet Hastanesi Toplum Ruh Sağlığı birimine en az 3 yıldır kayıtlı şizofreni tanılı hastalar alınmıştır. Hasta sayısı 100 hasta olarak belirlenmiştir. Hastaların merkeze kayıtları yapılırken klinik görüşmeler ile tanıları konulmakta ve merkezde takipleri yapılmaktadır. Çalışmaya katılacak hastalarda gönüllülük esas alınmış olup kendilerinden ve yasal vasilerinden gönüllü olur formu alınmıştır. Hastalara klinik görüşmede tarafımızdan hazırlanmış olan sosyodemografik veri formu, içgörünün üç bileşeni ölçeği, kısa işlevsellik ölçeği, tıbbi tedaviye uyum ölçeği, erişkin bağlanma biçimi ölçeği uygulanmıştır. Çalışmaya okuma yazması olan, aktif psikotik bulgusu olmayan, ölçeklere uyum sağlayabilecek, ek kronik hastalığı ve komorbid psikiyatrik tanısı olmayan, 18-65 yaş aralığında 100 hasta dâhil edilmiştir. Hastalarla klinik görüşmeler yapılıp DSM 5 tanı kriterlerine göre şizofreni tanısı konmuş ve diğer tanılar dışlanmıştır. Aktif psikotik atak döneminde olan hastalar çalışmadan dışlanmıştır. Hastaların psikotik semptomları pozitif ve negatif sendrom ölçeği ile değerlendirilmiştir. Çalışmanın etik Kurul onayı Recep Tayyip Erdoğan Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulundan alınmıştır (Etik Kurul Kararı Onay Tarihi: 21.06.2017 Karar No: 2017/125).

Araçlar

Sosyodemografik Veri Formu: Sosyodemografik form tarafımızca hazırlanmıştır. Kişilerin demografik bilgilerini, yaşadıkları ortamı, gelirlerini, iş durumu, aile durumlarını, eğitim seviyelerini sorgulayan, çoktan seçmeli şekilde hazırlanmış bir formdur.

İçgörünün Üç Bileşeni Ölçeği: sekiz sorudan oluşan ve içgörünün niceliksel olarak değerlendirmesini yapan bir ölçektir. Ölçek puanı arttıkça hastanın içgörüsünün arttığı görülmektedir. Klinisyen tarafından uygulanmaktadır. Türkçe geçerlilik ve güvenilirliği Arslan ve ark. Tarafından yapılmıştır (12). Kısa işlevsellik ölçeği: Likert tipi ölçektir. Görüşmeci tarafından yapılır. Artan puanlar işlevsellikte azalmayı gösterir. İşlevselliğin mesleki, toplumsal, kişisel ilişkiler açısından işlevselliği değerlendirmektedir. Türkçe geçerlilik ve güvenilirliği yapılmıştır (13).

Tıbbi Tedaviye Uyum Ölçeği: 10 sorudan oluşan bir ölçektir. Hastanın son dönemdeki ilaç uyumunu değerlendirmektedir. Yükselen ölçek puanı tedaviye uyumun artışı ile ilişkilidir. Türkçe geçerlilik ve güvenirliği Koç tarafından yapılmıştır (14).

Erişkin Bağlanma Biçimi Ölçeği: Ölçek iki bölümden oluşmaktadır. İlk bölüm 3 sorudan oluşmaktadır. Daha çok tanımlayıcı sorular içermektedir ve puanlamaya çoğunlukla katılmamaktadır. İkinci bölümünde bağlanma stilleri 5 farklı madde ile belirtilmiştir. En az 1 puan en çok 7 puan olacak şekilde değerlendirilmektedir. 3 farklı kaçıngan, güvenli ve kaygılı bağlanma tipini incelemektedir (15).

Pozitif ve negatif belirtiler ölçeği: 30 maddeden oluşan hastaların negatif ve pozitif semptomlarını ölçen bir ölçektir. Ölçekteki puanlamaların yedisi pozitif yedisi negatif ve diğer on altı ölçek diğer psikiyatrik semptomları taramaktadır. Likert tipi 1 ile 7 puan arasında puanlama sisteminden oluşmaktadır (16).

İstatistik

Araştırma verisi “SPSS (Statistical Packagefor Social Sciences) for Windows 22.0 (SPSS Inc, Chicago, IL)” aracılığıyla bilgisayar ortamına yüklendi ve değerlendirildi. Tanımlayıcı istatistikler ortalama±standart sapma,

frekans dağılımı ve yüzde olarak sunuldu. Değişkenlerin normal dağılıma uygunluğu görsel (histogram ve olasılık grafikleri) ve analitik yöntemler (Kolmogorov-Smirnov Testi/Shapiro-Wilk Testi) kullanılarak incelendi. Normal dağılıma uyduğu saptanan değişkenler arasındaki ilişki için pearson korelasyon uygulandı. İstatistiksel anlamlılık düzeyi $p<0.05$ olarak kabul edildi.

BULGULAR

Çalışmamıza toplam 100 şizofreni hastası dâhil edilmiştir. Hastaların sosyodemografik bilgileri tablo.1 de verilmiştir. Çalışmaya katılan hastaların cinsiyetleri kadın n=32 (%32), erkek n=68 (%68) ti. Yaş ortalaması 34±10.137 olarak bulundu. Katılımcıların n=64 (%64) ü evli, n= 33 (%33) ü bekâr, n=3 (%3) ü duldu (eşi vefat etmiş ya da ayrılmış). Katılımcıların n=10 (%10) u ilkokul, n=53 (%53) ü ortaokul, n=8 (%8) i lise, n=20 (%20) si üniversite mezunuydu.

Araştırmaya katılan hastaların ölçeklerden aldığı toplam ve alt ölçek ortalama puanları tablo. 2 de verilmiştir.

Katılımcıların tedaviye uyum ölçek puanları, iç görü ölçek puanları ve işlevsellik ölçek puanlarının bağlanma stilleri ölçek puanları ile karşılaştırılması tablo. 3 de verilmiştir. Katılımcıların ölçek puanları pearson korelasyon analizi ile karşılaştırıldı. İşlevsellik ölçeği ile kaçıngan bağlanma (r= -0,038; p=0,710), güvenli bağlanma (r=0,016; p=0,872), kaygılı bağlanma (r= -0,035; p=0,732) arasında anlamlı ilişki saptanmamıştır. İçgörü ölçek puanlamaları ile kaçıngan bağlanma (r= -0,2; p=0,043) arasında negatif yönde anlamlı bir ilişki saptanmıştır. İçgörü ölçek puanlamaları ile güvenli bağlanma (r= -0,137; p=0,174) arasında anlamlı ilişki saptanmamıştır. İçgörü ölçek puanlamaları ile kaygılı bağlanma ölçek puanları arasında (r=0,417; p=0,00) pozitif yönde anlamlı bir ilişki saptanmıştır. Tedaviye uyum ölçek puanları ile kaçıngan bağlanma (r=0,006; p=0,952), güvenli bağlanma (r=0,108; p=0,284) ve kaygılı bağlanma (r= -0,099; p=0,329) arasında anlamlı ilişki saptanmamıştır.

Tablo 1: Hastaların Sosyodemografik ve klinik özellikleri

	Min-Max	Ort±S.S
Yaş	18-64	34±10.137
		n (%)
Cinsiyet		
Kadın		32 (32)
Erkek		68 (68)
Medeni Durum		
Evli		64 (64)
Bekar		33 (33)
Dul		3 (3)
Eğitim Seviyesi		
İlkokul		10 (10)
Ortaokul		53 (53)
Lise		8 (8)
Üniversite		20 (20)

Ort±SS: Ortalama±Standart sapma

TARTIŞMA

Çalışmanın sonuçlarına göre hastaların işlevsellikleri, tedaviye uyumları ile bağlanma stilleri arasında ilişki saptanmazken, iç görü ile bağlanma arasında ilişki saptanmıştır. Yapılan çalışmalarda hastaların bağlanma stilleri ile özellikle kişiler arası ilişkilerinin ilişkili olduğu, sosyal ilişkilerde bağlanma stillerine bağlı değişiklik gözlendiği bildirilmiştir (17). Hastalarda kaliteli bağlanma özellikleri ile tedaviye uyumun arttığı, aile desteğinin varlığı tedavi sürecine olumlu katkı sağladığına dair veriler mevcuttur (18). İç görü hastanın hastalığının farkındalığı şeklinde tanımlanabilir. França ve arkadaşlarının yaptığı bir çalışmada şizofreni hastalarının içgörüleri ile bağlanma stilleri arasında ilişki saptanmıştır. Literatürde bu bilgiye ait fazla veri olmasa da içgörünün bağlanma stilleri ile ilişkili olabileceği düşünülmektedir (19). Çalışmamızda iç görü ile kaçıngan bağlanma arasında negatif yönde ilişki, kaygılı bağlanma ile pozitif yönde ilişki saptanmışken güvenli bağlanma arasında ilişki saptanmamıştır. İç görü ile bağlanma stilleri arasındaki ilişkiye ait veriler kısıtlıdır. Kaçıngan bağlanma örüntüsü olan bireylerde çekingenlik, reddedilme duygusu, sürekli eleştirel ebeveyn tutumlarının olması görülmektedir (20). Hastalarda içe kapanma, dış dünyadan uzaklaşma, gerçeklik algısından kopuş için tetikleyici bir sebep olabilir. Hastanın emosyonel farkındalığının azalması, gerçekliği tam olarak fark edememesi iç görüde azalmaya yol açabilmektedir (21). Bu varsayımlar ışığında hastalarda kaçıngan bağlanma düzeyi arttıkça içgörüde azalma beklenmektedir. Bu bilgiler çalışmamızdaki verilerle uyumludur. Çalışmamızın sonuçlarına göre kaygılı bağlanma düzeyleri arttıkça içgörü düzeyleri de artmaktadır. Kaygılı bağlanma biçimi ile anksiyete bozukluklarının gelişimi ile ilişkisine dair bilgiler mevcuttur. Güvenli bağlanmanın olmayışı, aile desteğinin azlığı hastalarda duygu durum bozukluğu, psikotik semptomlarda artış tedaviye uyumsuzluk gibi semptomlara yol açabilmektedir. Ancak çalışmamızda bu bilgileri destekler sonuçlara ulaşılamamıştır (22). Bağlanma ilk olarak Bowlby nin çocuklar üzerindeki gözlemlerine dayanarak ortaya attığı bir kavramdır. İnsanın doğuştan başlattığı bu ilişki ömür boyu sürmekte ve

Tablo 2: Ölçek puanlarının toplam alt, üst ölçek puanları ve ortalama değerleri

	n	Minimum	Maximum	Mean	Std. Deviation
İçgörü ölçeği	100	0	18	8,39	3,921
Klinik işlevsellik ölçeği	100	4	91	41,84	16,477
Tıbbi tedaviye uyum ölçeği	100	1	10	5,54	2,451
Kaçıngan bağlanma	100	8	34	18,95	6,923
Güvenli bağlanma	100	5	34	21,31	6,872
Kaygılı bağlanma	100	5	39	22,63	8,574

Tablo 3: Verilerin Korelasyon Analiz Sonuçları

	Kaçıngan Bağlanma		Güvenli Bağlanma		Kaygılı Bağlanma	
	r	p	r	p	r	p
İşlevsellik	-0,038	0,710	0,016	0,872	-0,035	0,732
İç Görü	-0,2	0,043	-0,137	0,174	0,417	0,00
Tedaviye Uyum	0,006	0,952	0,108	0,284	-0,099	0,329

psikopatolojilerin gelişimine zemin hazırlayabilmektedir. Bebeğin ilk doğumundan itibaren bakım vereni ile kurduğu romantik ilişki aslında bağlanmanın temelini oluşturmaktadır. Bakım verenin sürekliliği, oluşturulan ilişkinin kalitesi, bebeğin gerekli güven ortamına sahip olması erişkin kişilik örüntüsünün gelişimine katkı sağlamaktadır (23). Güvenli bağlanma bebeğin özgüven gelişimi açısından bakım vereniyle yeterli ve kaliteli ilişki kurması üzerine kuruludur. Sağlıklı bir kişilik gelişimi için gereklidir. Kaçıngan bağlanma ve kaygılı bağlanma bebeğin bakım verenden ayrıldığında tepki gösterdiği bakım verenle ilişkide sürekliliği sağlayamadığı ilişki stillerinde gözlenir (24). Bağlanma kuramının üzerine birçok araştırmalar yapılmış, kuram genişletilmiştir.

Çalışmamızda bağlanma stillerinin şizofreni hastalarında içgörüyü, hastaların tedaviye uyumunu ve işlevselliği ne yönde etkilediğine dair bir hipotez geliştirilmiş ve araştırılmıştır. Bağlanmanın psikopatoloji ile ilişkisini araştıran çalışmalar mevcuttur. Ancak bu bilgiye ait veriler kısıtlıdır. Bu anlamda daha fazla ileri çalışmalara ihtiyaç duyulmaktadır. Bağlanma teorisi özellikle son yıllarda dikkat çeken bir konu olmuştur. Hastaların çocukluk çağında kurdukları ebeveynleri ile olan ilişkileri erişkinlik dönemine yansımaları psikiyatrik hastalıklarda yer edinmektedir. Güvenli bağlanmanın varlığı psikostresörler varlığında koruyucu bir rol oynamaktadır. Özellikle nevrotik bozukluklarda rolü daha fazla anlaşılmış olmakla birlikte psikotik bozukluklarda da bu konuda çalışmalara ihtiyaç duyulmaktadır.

Çalışmanın Kısıtlılıkları

Çalışmamızda hastaların antipsikotik kullanımları, hastalık süreleri başlangıç yaşı gibi etkileyici faktörler ayrı ayrı değerlendirilmemiştir. Ayrıca çalışma örneklemimiz belli bir kültürel topluluktan oluşmakta ve yöresel yetiştirilme tutumları ile yetişmiş bireylerden oluşmaktadır. Daha fazla sayıda hasta ile çok merkezli olarak bu çalışmalar artırılabilir.

SONUÇ

Bağlanma her dönemde psikiyatrinin önemli konularından biri olmuştur. Çalışmamızda içgörü ile bağlanma stilleri arasında ilişki saptanmıştır. Güvenli bağlanan bireylerin daha sağlıklı ve olumlu kişilik gelişimi gösterdikleri görülmektedir. Ülkemizde ki aile yapısı göz önünde bulundurulduğunda daha duygu odaklı geleneksel aile tutumları gözlenmekle birlikte değişen dünyada bu durumda değişmektedir. Psikiyatrik hastalıkların değerlendirilmesinde, tedavi sürecinde bağlanmanın yeri önemlidir. Literatürde bağlanmaya yönelik çalışmalar kısıtlıdır ve daha çok belirli topluluklar üzerinde yoğunlaşmaktadır. Bu konuda daha fazla çalışmaya ihtiyaç duyulmaktadır.

Çıkar çatışması: Yazarlar arasında çıkar çatışması olmadığını beyan etti.
Etik: Recep Tayyip Erdoğan Üniversitesi Girişimsel Olmayan Araştırmalar Etik Kurulundan alınmıştır (Etik Kurul Kararı Onay Tarihi: 21.06.2017 Karar No: 2017/125).

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ORIGINAL ARTICLE

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Examination of Geriatric Trauma Patients Presenting to the Emergency Department

Acil Servise Başvuran Geriatrik Travma Hastalarının İncelenmesi

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ABSTRACT

Objective: *We aimed to determine the demographic characteristics, trauma severity scores, place of occurrence of the trauma, consultations requested and the way it ended in geriatric trauma patients. At the same time, we aimed to reveal the relationship between the occurrence of the event and admission to the emergency department and the relationship between trauma scores and mortality.*

Material and Method: *This study was conducted retrospectively with 250 patients aged 65 and over who applied to the Emergency Department of Erciyes University Faculty of Medicine between 01.01.2011 and 31.12.2011. Gender, age, time elapsed after trauma, trauma mechanism, diagnoses, requested consultations, injury site, GCS, ISS and outcome patterns were investigated.*

Results: *51.6% of these patients were female and 48.4% were male. The mean age of the patients is 73.3. While 32.4% of the patients were in the first 1-hour period, 11.2% of them applied to the emergency department after the first 24-hour period. While soft tissue trauma (36.4%) was the most common in the patients, when the trauma areas were examined, it was determined that the extremities were the most common with 51.6%. While 86 of the patients did not want consultation from any branch; Orthopedics consultation was requested for 79 patients and neurosurgery consultation was requested for 44 patients. 54.8% of the patients in the study were discharged from the emergency room after treatment, 28.4% were hospitalized, 12% were followed up under intensive care conditions, and 4.8%, 12 patients, died. The duration of admission to the emergency department, GCS and ISS scores of the patients and their outcomes in the emergency department were compared and a statistically significant relationship was found.*

Conclusion: *Geriatric trauma patients are mortal and morbid patients. Depending on the old age, there are usually additional medical problems. Treatment processes are more laborious and demanding. Therefore, patients should be evaluated more carefully and multisystemically.*

ÖZET

Amaç: *Geriatrik travma hastalarındaki demografik özellikleri, travma şiddet skorları, travmanın oluş mekanlarını, hastalara istenen konsültasyonları ve sonlanış şekillerini tespit etmeyi hedefledik. Aynı zamanda olayın oluşu ile acil servise başvuru arasında geçen sürenin ve travma skorlarının mortalite ile ilişkisini ortaya çıkarmayı amaçladık.*

Gereç ve Yöntem: *Bu çalışma retrospektif olarak 01.01.2011-31.12.2011 tarihleri arasında Erciyes Üniversitesi Tıp Fakültesi Acil servisine 65 yaş ve üzeri başvuran 250 hasta ile yapılmıştır. Cinsiyet, yaş, travmadan sonra geçen süre, travma mekanizması, tanılar, istenilen konsültasyonlar, yaralanma bölgesi, GKS, ISS ve sonlanış şekilleri araştırılmıştır.*

Bulgular: *Bu hastaların %51,6'sı kadın, %48,4'ü erkektir. Hastaların yaş ortalaması 73,3'tür. Hastaların %32,4'ü ilk 1 saatlik zaman diliminde iken %11,2'si ilk 24 saatlik zaman dilimi sonrası acil servise müracaat etmiştir. Hastalarda sırasıyla en çok yumuşak doku travması (%36,4) saptanmışken travma bölgelerine de bakıldığında en sık %51,6 oranla ekstremite olduğu da tespit edilmiştir. Hastaların 86'sına herhangi bir branştan konsultasyon istenmezken; 79 hastaya ortopedi, 44 hastaya beyin cerrahi konsültasyonu istenmiştir. Çalışmadaki hastaların %54,8'i acil servisten tedavi sonrası taburcu olmuş, %28,4'ü servise yatmış, %12'si yoğun bakım şartlarında takibe alınmış ve %4,8'i yani 12 hasta exitus olmuştur. Hastaların acil servise başvuru süreleri, GKS ve ISS puanları ile acil serviste sonlanışları kıyaslanmış ve istatistiksel olarak anlamlı ilişki tespit edilmiştir.*

Sonuç: *Geriatrik travma hastaları daha mortal ve morbid seyretmektedir. Yaşlılığa bağlı olarak genellikle medikal ek problemleri de mevcuttur. Tedavi süreçleri daha zahmetli ve emek istemektedir. Bu nedenle hastalar daha dikkatli ve multisistemik olarak değerlendirilmelidir.*

Keywords:
Geriatric trauma
Glasgow coma score
Injury severity score

Anahtar Kelimeler:
Geriatrik travma
Glaskow koma skoru
Yaralanma şiddet skoru

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GİRİŞ

Travma genç erişkinler başta olmak üzere genel popülasyonda önde gelen morbidite ve mortalite sebeplerindendir. Geriatrik hastaların travmaya maruz kalma oranı gençlere kıyasla daha azdır. Ancak yaşlı hastalarda travma sonucu mortalite, morbidite, hastanede kalış süresi rehabilitasyon süresi fazlalığı nedeniyle önemli bir sağlık sorunu oluşturmaktadır (1).

Geriatrik travma hastalarının genellikle komorbid hastalıkları mevcut olduğundan dolayı travma hastası olarak değerlendirilirken hem de medikal bir hasta olarak dikkatlice değerlendirilmelidir. Bu hastalardaki mevcut hemodinamiyi ve şuur durumunu altta yatan hastalığa bağlamak eksik tanı ve yaklaşıma sebep olabilir. Aynı zamanda bütün bulguların travma nedeniyle oluştuğunu düşünmek de gereksiz yere maliyeti artırmaya ve zaman kaybına sebep olabilir. Bu nedenle ayrıntılı anamnez almak, doğru ve etkili tanı açısından çok önemlidir.

Bu çalışmada Erciyes Üniversitesi Tıp Fakültesi Acil Servisine 2011 yılında 12 aylık dönemde başvuran geriatrik travma hastalarındaki demografik özellikleri, travma şiddet skorları, travmanın oluş mekanlarını, hastalara istenen konsültasyonları ve sonlanış şekillerini tespit etmeyi hedefledik. Aynı zamanda olayın oluşu ile acil servise başvuru arasında geçen sürenin ve travma skorlarının mortalite ile ilişkisini ortaya çıkarmayı amaçladık.

GEREÇ VE YÖNTEMLER

Bu çalışma retrospektif olarak 01.01.2011-31.12.2011 tarihleri arasında bir yıllık süreçte Erciyes Üniversitesi Tıp Fakültesi Acil Servisine 65 yaş ve üzeri başvuran 250 hasta ile yapılmıştır. Travma nedeniyle acil servisimize başvuran 65 yaş ve üzeri hastalar için, önceden oluşturulmuş geriatrik travma hastalarını değerlendirme formu kullanılmıştır. Çalışmaya dahil edilen hastaların başvuru tarihi, cinsiyeti, yaşı, travma oluşundan sonra acil servise başvurana kadar geçen süre, travma mekanizması, tanıları, hastalar için istenen konsültasyonlar, glaskow koma skoru (GKS), yaralanma bölgeleri, travma şiddet skorları (ISS), acilde kalış süreleri ve acil serviste sonlanım şekilleri kayıt altına alınmıştır.

Hastanın acilde sonlanım şekline göre hastalar gruplanmış ve acil servise başvuru sürelerine, ISS, GKS puanlarına kıyaslaması yapılmıştır.

Verilerin normal dağılıma uygunluğu histogram, Q-Q grafikleri ve Shapiro-wilk testi ile değerlendirildi. Kategorik verilerin karşılaştırmalarında Pearson $\chi 2$ analizi kullanıldı. Gruplar arası karşılaştırmalarda nicel değişkenler için Mann-Whitney U testi uygulandı. İkiden fazla gruplar arası karşılaştırmalarda Kruskal Wallis testi kullanıldı. Çoklu karşılaştırmalar için Dunn-Bonferroni testi uygulandı. Verilerin analizi R 4.0.3 (www.r-project.org) yazılımında gerçekleştirildi. Anlamlılık düzeyi $p<0.05$ olarak kabul edildi.

Çalışma için Erciyes Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan 03.02.2017 tarih ve 2017/58 karar numaralı etik izin alınmıştır.

BULGULAR

Çalışmamıza kayıtlarına eksiksiz ulaşılabilen toplam 250 hasta dahil edilmiştir. Bu hastaların 129 (%51,6)' u kadın, 121 (%48,4)' i erkektir. Hastaların yaş ortalaması 73,3' tür. Acil servise geliş şekillerine göre bakıldığında 192 (%76,8)' sinin ayaktan başvuru olduğu tespit edilmiş ve 146 (%58,4)'sı kendi aracı ile müracaat ettiği görülmüştür. Hastaların 81 (%32,4)'i ilk 1 saatlik zaman diliminde acil servise müracaat etmiş iken 28 (%11,2)'i ilk 24 saatlik zaman dilimi sonrası müracaat etmiştir. 176 (%70,4) hastada ev içi faaliyetlerde travma meydana gelmiştir ve 85 (%34)'inde yüksekten düşme sonrası travma meydana gelmiştir (Tablo 1).

Hastaların primer tanılarına bakıldığında sırasıyla en çok yumuşak doku travması (%36,4) saptanmıştır. Ayrıca tüm tanılar incelendiğinde yaşlıların en sık ortopedik travmalar sonucu acil servise başvurduğu görülmüştür. Travma bölgelerine de bakıldığında en sık %51,6 oranla ekstremite olduğu da tespit edilmiştir (Tablo 2).

Hastaların değerlendirilme sürecinde istenen konsültasyonlar incelendiğinde 86'sına herhangi bir branştan konsultasyon istenmezken; 79 hastaya ortopedi, 44 hastaya beyin cerrahi konsültasyonu istendiği tespit edimiştir. Diğer cerrahi bölümlerden daha az sayıda konsültasyona ihtiyaç duyulmuştur (Tablo 3).

Hastaların acil servisten sonlanım şekillerinin değerlendirilmesinde %54,8'i acil servisten tedavisi sonrası taburcu olmuş, %28,4'ü servise yatmış, %12'si yoğun bakım şartlarında takibe alınmış ve %4,8'i exitus

Tablo1: Hastaların özellikleri

	Sayı	**Yüzde**
Cinsiyet		
Kadın	129	51,6
Erkek	121	48,4
Geliş şekli		
Ambulansla	97	38,8
Kendi aracı	146	58,4
Bilinmiyor	7	2,8
Sevk Durumu		
Sevkli	58	23,2
Ayaktan başvuru	192	76,8
Travmadan sonra geçen süre		
0-1 saat	81	32,4
1-3 saat	66	26,4
3-6 saat	46	18,4
6-12 saat	19	7,6
12-24 saat	10	4
> 24 saat	28	11,2
Olay yeri		
Ev içi	176	70,4
Ev dışı	74	29,6
Travma mekanizması	Sayı	Yüzde
Yürürken düşme	66	26,4
Yüksekten düşme	85	34
AİTK	32	12,8
ADTK	7	2,8
Diğer	60	24

Tablo 2: Acil servisteki tanılar

Tanılar	Sayı	Yüzde
Yumuşak doku travması	91	36,4
Minor kafa travması	20	8
Modarete kafa travması	10	4
Major kafa travması	18	7,2
Kot fraktürü	12	4,8
Pnömotoraks	4	1,6
Hemotoraks	1	0,4
Batın içi kanama	1	0,4
Omurga fraktürü	15	6
Pelvis fraktürü	4	1,6
Ekstremite fraktürü	74	29,6
Travma Bölgeleri		
Baş-Boyun	92	36,8
Toraks	49	19,6
Batın	19	7,6
Ekstremite	129	51,6
Omurga	21	8,4

Tablo 3: Hastalara istenen acil konsültasyonlar

İstenen konsültasyonlar	Sayı	Yüzde
Konsultasyon yok	86	34,4
Beyin cerrahisi	44	17,6
Ortopedi	79	31,6
Genel cerrahi	1	0,4
Kulak burun boğaz	4	1,6
Göz hastalıkları	14	5,6
Plastik ve rekonstruktif cerrahi	7	2,8
Göğüs cerrahisi	11	4,4
Kalp ve damar cerrahisi	1	0,4
Diğer	3	1,2

Tablo 4: Hastaların acil serviste sonlanım durumları

Acil Serviste Sonlanış	Sayı	Yüzde
Taburcu	137	54,8
Eksitus	12	4,8
Servise yatış	71	28,4
YBU yatış	30	12
Yattığı branş		
AS den taburcu	137	54,8
Beyin cerrahisi	12	4,8
Ortopedi	42	16,8
Göz hastalıkları	6	2,4
Göğüs cerrahisi	8	3,2
YBU	30	12
Diğer	3	1,2

olmuştur (Tablo 4).

Hastalar acil servisten sonlanım şekillerine göre acil servisten taburcu edilenler, acil serviste eksitus olanlar, acil servisten servise yatışı yapılanlar ve acil servisten yoğun bakım ünitesine yatışı yapılanlar olarak gruplandırılmış ve bu gruplar olay olduktan sonra acil servise başvurana kadarki geçen süre ile kıyaslanmış ve acil servise erken başvuranların servis ve yoğun bakım ünitesine yatışlarında istatistiksel olarak anlamlı fark tespit edilmiştir ($p<0,001$). Yine aynı şekilde acil servisten sonlanış grupları ile hem ISS ve hem de GKS puanları kıyaslanmış olup istatistiksel olarak anlamlı sonuç elde edilmiştir ($p<0,001$) (Tablo 5).

TARTIŞMA

Ülkemizde ve dünyada; ortalama yaşam sürelerindeki uzama, yaşam kalitesinin tıbbi gelişmeler sayesindeki iyileşmesi, nüfus artış hızındaki azalmaya paralel olarak yaşlı nüfus giderek artış göstermektedir (2). Yaşlı nüfusun ve yaşlı insanların aktif yaşam oranındaki artışlardan dolayı geriatrik travma başvuruları her geçen gün artmaktadır. Travma; tüm yaş gruplarına bakıldığında kalp hastalığı, kanser ve inmeden sonra görülen 4. en sık ölüm nedenidir. Ayrıca travma nedeniyle ölenlerin %28'i geriatrik yaş grubu olgularıdır (3).

Abdulhayoğlu E. nin Hacettepe Üniversitesinde yapmış olduğu çalışmaya göre geriatrik travma hastalarının ortalama yaşı 76,6 olarak saptanmıştır (4). Güneytepe ve arkadaşlarının çalışmasında da geriatrik travma hastalarının yaş ortalaması 72 olarak bulunmuştur (5). Bizim çalışmamızda da geriatrik travma hastalarının yaş ortalaması 73,3 olarak bulunmuş olup literatürdeki veriler ile uyumludur.

Çalışmaya alınan hastaların cinsiyetleri incelendiğinde, geriatrik travma hastalarımızda kadın cinsiyetin fazla görüldüğü (%51,6) tespit edildi. ABD'de 2006 yılında yapılan bir çalışma sonucu, düşme sebebi ile başvuran kadın oranı %70,2, erkekler ise %29,8 olarak bulunmuştur (6). Çalışmamızdaki erkek/kadın oranı 0,94 olarak bulunmuştur. Literatüre bakıldığında geriatrik travma hastalarında erkek/kadın oranı 0,5 ile 1,4 arasında değişen değerlerde bulunmuştur (7,8,9). Çalışmamızdaki veriler literatür verilerine benzer bulunmuştur.

Hastaların acil servise ulaşma şekilleri incelendiğinde %38,8'lik kısmının ambulans ile geldiği tespit edilmiştir. Geriatrik hastaların diğer yaş gruplarına oranla daha fazla ambulans kullandığı bilinmektedir. Foo ve ark.'nın yaptığı çalışmada acil servise ambulans ile başvuran geriatrik hastaların oranı %39,9 bulunmuştur (10). Tokuda ve ark.'nın Tokyo'da yaptıkları çalışmaya göre ambulans ile acil servise başvuruların %34'ünü 65 yaş ve üzeri hastalar oluşturmaktadır (11). Ambulans aracılığı ile başvuran hastaların oranının yüksek olması özellikle geriatrik yaş grubunda düşük enerjili travmalar sonucunda daha ciddi yaralanmalar gerçekleşmesi ve hastanemizin bölge travma hastanesi olmasına bağlı olduğu öngörülmüştür.

Hastalarımızın travma mekanizmaları sorgulandığında, büyük çoğunluğu (%60,4) düşmeye, %12,8'i motorlu taşıt kazasına, %2,8'i yaya motorlu araç çarpışmasına bağlı travma sebebiyle acil servisimize başvurduğu saptanmıştır. Ev içi travma sonrası meydana gelen yaralanmalarda 65 yaşın üzerindeki hastalarda genç popülasyona göre daha çok tedavi ihtiyacı doğmakta ve

Tablo 5: Hastaların acil serviste sonlanım durularına göre kıyaslanması

	Sonlanım Şekli				p
	Taburcu	Eksitus	Servis yatış	YBU yatış	
Acil serise başvuru süresi (/h)					
0-1	58 (42,3)a	5 (41,7)a,b	9 (12,7)b	9 (30,0)a,b	<0,001
1-3	36 (26,3) a	1 (8,3) a	19 (26,8) a	10 (33,3) a	
3-6	21 (15,3) a	3 (25) a	17 (23,9) a	5 (16,7) a	
6-12	5 (3,6) a	2 (16,7) a	8 (11,3) a	4 (13,3) a	
12-24	3 (2,2) a	0(0) a	5 (7,0) a	2 (6,7) a	
>24	14 (10,2) a	1 (8,3) a	13 (18,3) a	0 (0) a	
ISS	2.0(1.0-5.0)a	29.0(25.0-45.0)b	9.0(9.0-9.0)a	23.0(17.0-29.0)c	<0.001
GKS	15.0(15.0-15.0) a	3.0(3.0-3.0) b	15.0(15.0-15.0) a	14.5(11.8-15.0) c	<0.001

Veriler ortanca (1.çeyrek-3.çeyrek) ve n (%) olarak ifade edilmiştir.

80 yaş üzerinde bu oran %50'ye kadar çıkmaktadır (12). Tanrıkulu ve arkadaşlarının Erzurum'da 1540 hasta ile yaptıkları çalışmada, travma sebepleri arasında en sık düşmelere (%82), ikinci sıklıkta motorlu taşıt kazalarına (%11) rastlanmıştır (13). Ayrıca Schwab ve ark.'nın çalışması ile Osler ve ark.'nın yapmış olduğu çalışmada da en sık travma nedeni olarak düşmeler tespit edilmiştir (14,15). Bizim çalışmamızdaki veriler bu çalışmalar ile örtüşmektedir.

Hastalarımızda sırasıyla en çok yumuşak doku zedelenmesi (%36,4), ekstremite fraktürü (%29,6), minor kafa travması (%8) ve kot fraktürü (%4,8) saptanmıştır. Owens ve ark.'nın yapmış olduğu çalışmada, düşmelere bağlı %41 oranında kırıklar, %22,6 oranında yüzeyel yaralanmalar, %21,4 oranında da açık yaralar meydana geldiği tespit edilmiştir (16). Ayrıca tüm tanılar incelendiğinde yaşlıların en sık ortopedik travmalar (%51,6) sonucu acil servise başvurduğu görülmüştür. Bunun sebebi, literatürde de belirtildiği gibi geriatrik travma hastalarının çoğunluğunu düşme sebebiyle oluşan izole ortopedik travmalar olması nedeniyledir (1). Daha önce yapılan birçok çalışmada yaşlılarda travma sonucu en fazla görülen yaralanmaların yumuşak doku zedelenmesi ve cilt laserasyonlarını içeren yüzeyel yaralanmalar olduğu, tespit edilen kırıkların çoğunun kalça (proksimal femur) fraktürü olduğu, bunun yanında kot fraktürüne de sık rastlandığı tespit edilmiştir. Yine benzer çalışmalarda en fazla görülen yaralanma tipinin ortopedik yaralanmalar olduğundan bahsedilmiştir (5, 8, 17).

Hastalarımızda acil servisten taburcu olan, servise yatan, yoğun bakıma yatan ve exitus olanlar travma skorları açısından karşılaştırılmış olup hem GKS hem ISS değerleri istatistiksel olarak anlamlı bulunmuştur. Çalışmamızda geriatrik travma hastalarının %87,6'sı normal bilinç düzeyine sahip bulunmuştur. Bunun yanında 12 hastanın GKS' si 3, 19 hastanın da 3 ile 14 arasında olarak saptandı. Abdulhayoğlu ve arkadaşlarının yapmış olduğu çalışmada GKS' si mortalite ve morbidite açısından değerli olduğu bulunmuştur (4). Güneytepe ve arkadaşlarının yaptığı çalışmada da geriatrik travma hastalarının GKS, ISS değerleri açısından ölen ve yaşayan olgular arasında anlamlı fark saptanmıştır (5). Çevik ve arkadaşlarının 2013 yılında yaptığı çalışmada da travma skorları araştırılmıştır. Bu travma skorları arasında, en kuvvetli mortalite gösterici skor olarak ISS skoru bulunmuştur (18).

Yaşlı travma hastaları acil servise başvuru esnasında mevcut akut patolojilerinin yanı sıra mevcut sahip oldukları kronik patolojileri de göz önünde bulundurularak değerlendirilmelidirler.

Çıkar çatışması: Yazarlar arasında çıkar çatışması olmadığını beyan etti.

Etik: Çalışma için Erciyes Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan 03.02.2017 tarih ve 2017/58 karar numaralı etik izin alınmıştır.

Bu çalışma 13. Ulusal Acil Tıp Kongresi, 4th intercontinental Emergency Medicine Congress, 4th international Critical Care and Emergency Medicine Congress' te 18-21 Mayıs 2017 tarihinde Antalya'da poster bildiri olarak sunulmuştur.

KAYNAKLAR

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ORIGINAL ARTICLE

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Evaluation of DNA Versus Collagen Perception in Scientific Articles Examining Cancer and Chemotherapy: Implication for Collagen Based Approaches

Kanser Kemoterapisini İnceleyen Bilimsel Makalelerde DNA'ya Karşı Kolajen Algısının Değerlendirilmesi: Kollajen Temelli Yaklaşımlar için Çıkarım

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ABSTRACT

Objective: *Although cancer chemotherapy has been used for more than seventy years, its definitive mechanism of action is not known. Many studies indicate that beyond DNA the collagen connective tissue matrix is also affected. This database analysis aims to determine the extent of DNA versus collagen perception in scientific papers indexed under PubMed.*

Material and Method: *The PubMed database scanned on September, 15, 2021 using following keywords and combinations; "cancer", "cancer chemotherapy", "cancer chemotherapy AND damage", "chemotherapy AND mechanism AND damage", "chemotherapy AND clinical" as nominator. The number of items found for each search was proportioned in terms "DNA versus collagen" and the ratio was accepted as the perception shift coefficient.*

Results: *Tested with the p1-p2 analysis to calculate the difference between the two proportions in both search items. Based on the main rule under the assumption that "all cells have DNA and all cells live in the collagen matrix". In the p1-p2 analysis of the data, a significant ($p < 0.001$) difference was obtained for all dichotomy scans.*

Conclusion: *This data analysis supports the argument that both cancer and chemotherapy perception is DNA-based rather than collagen, since the synthesis and degradation process of very slow; it is not possible to observe it in short term studies. Chemotherapy should be further analyzed by this manner in purpose of collagen matrix.*

ÖZET

Amaç: *Kemoterapi yetmiş yıldan fazla bir süredir kullanılmasına rağmen, kesin etki mekanizması bilinmemektedir. Birçok çalışma, DNA'nın ötesinde kolajen bağ dokusu matrisinin de etkilendiğini göstermektedir. Bu veri tabanı analizi, PubMed altında indekslenen bilimsel makalelerde DNA'ya karşı kolajen algısının kapsamını belirlemeyi amaçlar.*

Gereç ve Yöntem: *Aşağıdaki anahtar kelimeler ve kombinasyonlar kullanılarak 15 Eylül 2021'de taranan PubMed veri tabanı; Aday olarak "kanser", "kanser kemoterapisi", "kanser kemoterapisi VE hasarı", "kemoterapi VE mekanizması VE hasarı", "kemoterapi VE klinik". Her arama için bulunan öğe sayısı "DNA'ya karşı kolajen" ve oran algı kayması katsayısı olarak kabul edildi.*

Bulgular: *Her iki arama öğesindeki iki oran arasındaki farkı hesaplamak için p1-p2 analiziyle test edildi. "Bütün hücrelerin DNA'sı vardır ve tüm hücreler kolajen matriks içinde yaşar" varsayımı altındaki ana kurala dayanmaktadır. Verilerin p1-p2 analizinde tüm dikotomi taramaları için anlamlı ($p < 0,001$) fark elde edildi.*

Sonuç: *Bu veri analizi, hem kanser hem de kemoterapi algısının, sentez ve degradasyon süreci çok yavaş olduğu için kolajenden ziyade DNA bazlı olduğu argümanını desteklemektedir; kısa süreli çalışmalarda bunu gözlemlemek mümkün değildir. Kemoterapi, kolajen matriks amacıyla bu şekilde daha fazla analiz edilmelidir.*

Keywords:
Chemotherapy
DNA
Collagen
Dichotomy

Anahtar Kelimeler:
Kemoterapi
DNA
Kolajen
Dikotomi

INTRODUCTION

Cancer is a global health problem increasing with industrialization and the second cause of death in developed countries (1-3). Although archaeological studies indicate that cancer can be observed also in ancient times, it is generally accepted that the incidence of the disease is increasing rapidly today (4, 5).

Despite the disease burden and economic cost caused by cancer, studies conducted to understand the etiopathogenesis of the disease is behind the expected success, indicating the possibility of a biased error rather than a random one. For instance, etiopathological explanations of diseases in medicine generally accepted a cell-centered approach. According to this idea, cancer is considered as uncontrolled cell proliferation, focusing on the cell itself (6). In the middle of the last century, after the approvement that genetic information is encoded in DNA, this idea also led to the acceptance that cell division is controlled by DNA (7,8) This perspective evoked an influence that the biological effects of both radiotherapy and chemotherapy are directly related to the damage or changes in DNA.

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An important invention in a field could diffuse to the other areas and influence in a similar manner, which is called as Zeitgeist effect (9). The interpretation of cancer through DNA affected the proposed mechanism of action of chemotherapeutic drugs in the same manner. The development of chemotherapeutic drugs emerged in the second half of the twentieth century in demand for relevant treatment strategies elevated, as the incidence of leukemia and lymphomas rise. This period starts with the use of alkylating agents, followed by many candidate chemicals which have been rapidly tested in cell culture (10, 11). In this period, DNA attracted all the scientific attention as a miracle molecule, which leads to the interpretation of the effects of chemotherapeutic agents through interference with DNA synthesis (12). In addition, DNA has a relatively simple molecular structure which facilitates studies utilizing DNA-based research.

However, unlike the cell culture in the tissue cells are located in the connective tissues composed of collagen. Indeed, collagen is the main component of connective tissue and establishes a class of more than 30 divers molecules, the largest part of body structural proteins. Apart from being difficult to investigate since collagen shows a very slow production-destruction cycle in the organism, its effect on the emergence of the disease has not been adequately studied (13-15).

The DNA-based approach argues that genetic information as the cause of cancer for all that genetic cancers or mutations leading to malignancies are very limited, accounts for only a very small proportion of the cases (16,17). The genetic perspective focuses on the "clonogenic cell" idea and categorizes the disease as a genetic coding error. On the other hand, cancer disease is still under interpretation, even today, due to both its etiopathogenesis and therapeutic modalities. The changes that lead to malignancy could also be explained as a connective tissue disorder. However, it is not easy to determine how large an alternative explication is covered by the mainstream explanation. For this purpose, one can analyze the entire database by using keywords. The basic logic of this method is that the concepts studied are in the same system, but not directly related to each other. The observed and the detected values in any data analysis are the sums of the actual, coincidental and false results (bias). Although everything can affect the other one in living systems, choosing the right keywords will narrow the possibility of error. This study is a database analysis performed to determine the bias of "DNA versus collagen" perception on the basis of cancer and chemotherapy.

MATERIAL AND METHOD

The database of The United States National Library of Medicine encodes scientific publications under keywords (Medical Subject Headings, MeSH) defined as medical titles (18). This database structure gives a numerical value for any MeSH if used as a nominator. When a second MeSH keyword for the dichotomy is added to the search (fuzzification), the numerical values obtained indicate the association of the nominator with the second concept. The ratio of the numerical result given by the same nominator with the two sub-concepts obtained by dichotomy will determine the severity of the research direction (19).

In order to evaluate the perception of cancer and chemotherapy retrospectively, the PubMed database was searching on September, 15, 2021 using the medical keywords "cancer", "cancer chemotherapy", "cancer chemotherapy AND damage", "chemotherapy AND mechanism AND damage", "chemotherapy AND clinical" as nominator. In the second phase, the association of these key terms were searched by creating a dichotomy by adding "DNA" or "collagen" MeSH for each item. A separate search was carried out by changing the order of the words used in order to test whether the "AND" logic shows a sort of relationship with the words on the search results. It was observed that the obtained article order and numerical values completely overlapped, thus it was confirmed that the PubMed database was not affected by the keyword ranking.

The sizes of the numerical numbers obtained with keywords were accepted as the "correlation value". No exclusion criteria were used in screening. Since the database contains a large number of articles, it was not possible to evaluate all the results, and samples were selected by considering the random numbers table. The accessed results with each MeSH or combination were randomly reviewed for 50 articles and the search was expanded by increasing the number of words that occur together the possibility of biases was refused. The numbers obtained by each nominator either with DNA or collagen subtitles were divided to the each other; obtained results were called the perception shift ratio.

Statistics

When interpreting a confidence interval that compares two population proportions, one should always be sure to use the words of the problem and to phrase the interpretation in terms of how much larger (or smaller) the first proportion is compared to the second one. This procedure is valid because both samples were taken randomly and independently. In this way it is common to compare two independent groups with respect to the presence or absence of a dichotomous characteristic or attribute, when the outcome is dichotomous, the analysis involves comparing the proportions of successes between the two groups.

There are several ways of comparing proportions in two independent groups. One can compute a proportion difference, which is computed by taking the difference in proportions between comparison groups and is similar to the estimate of the difference in means for a continuous outcome. Generally, the reference group (e.g. chemotherapy) is considered in the denominator of the ratio. The dichotomy ratio is a good measure of the strength of an effect (ie. DNA versus collagen) and therefore provides an indication for a reason attributed. When the outcome of interest is relatively uncommon (e.g., <10%), a dichotomy ratio has a good predictive value, confidence interval estimates for the dichotomous difference.

In this study, the results obtained were tested with the p1-p2 analysis to calculate the difference between the two proportions in both search items. Based on the main rule under the assumption that "all cells have DNA and all cells live in the collagen matrix" H0 hypothesis has

been created for significance; H0: p1-p2 = 0 and H1: p1-p2 ≠ 0 as exclusion criteria. The numerical results were statistically analyzed for the fact of H0> H1 condition, p <0.01 was considered significant.

RESULTS

Results are shown in the table and figures. In the articles containing "cancer", "cancer chemotherapy", "chemotherapy AND damage," chemotherapy AND mechanism AND damage, "chemotherapy AND clinical", the association with DNA was found to be higher than with collagen. While 396,459 of the 4,430,969 articles with the word cancer in them was DNA passed, collagen was passed together in 29,217. When the screening was done with the keywords "cancer chemotherapy" as nominator, 315,921 results were obtained, whereas 68,174 articles were obtained when "DNA" was used for dichotomy, 4,968 for "collagen" were obtained respectively. DNA dichotomy rate was found 3.88 to 62.51 times higher in all search MeSHs compared to collagen in the database (20, 21).

In the p1-p2 analysis of the data, a significant (p <0.001) difference was obtained for all dichotomy scans. Thus, the H0 hypothesis was excluded and the H1 hypothesis was confirmed, it has been shown in the PubMed database for search items "cancer", "cancer chemotherapy", "chemotherapy AND damage," chemotherapy AND mechanism AND damage, " chemotherapy AND clinical", have a statistically significant association with DNA than collagen.

DISCUSSION

Search and analysis of classified and stored data is called data mining (22, 23). In practical view, (i) the data must be stored in an integral accessible electronic concept. (ii) The searched elements should be coded with a characteristic term (Medical Subject Headings, MeSH) that will not cause confusion (iii) The database should be open to the "AND/OR" proposition. United States National Library of Medicine consist a data base in which the scientific publications are encoded with keywords since its establishment (24, 25).

The development of computers and the communication technology enable to search and handle big databases. Since the PubMed database is big enough, it can be explored how much a concept had been associated with other related one (dichotomy) if valid keywords are used (eg.DNA vs. collagen). This database does not contain duplications and therefore allow objective data analysis. In this way scientific articles could be searched with two or more MeSH keywords. Searching this specific

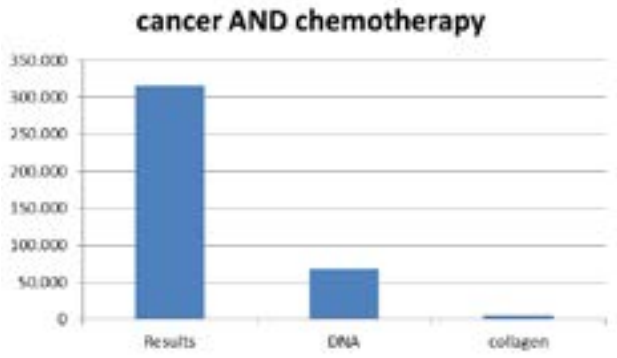

Figure 1: Results for "cancer AND chemotherapy '' MeSH, following bars demonstrate DNA versus collagen dichotomy.

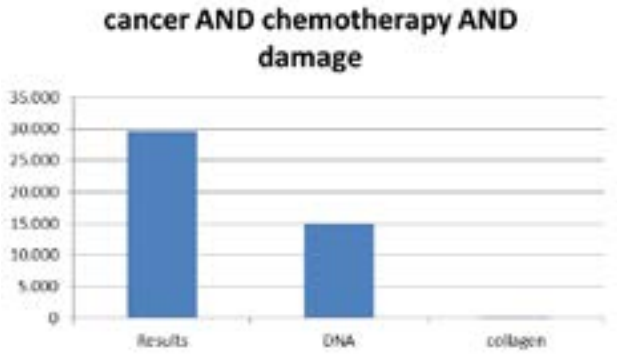

Figure 2: Results for "cancer AND chemotherapy AND damage '' MeSH, following bars demonstrate DNA versus collagen dichotomy.

Figure 3: Results for "chemotherapy AND mechanism AND damage '' MeSH, following bars demonstrate DNA versus collagen dichotomy.

Table : Results and statistical analysis obtained by each PubMed database search according to nominator and dichotomous MeSH words.

KEYWORDS	Results	DNA	Collagen	DNA/Collagen	Z value	P value
cancer	4430969	396459	29217	13.57	25415.454.	< .00001
cancer AND chemotherapy	315921	68174	4968	13.73	2949.4758.	< .00001
cancer AND chemotherapy AND damage	29673	14940	239	62.51	419.5045.	< .00001
chemotherapy AND mechanism AND damage	23744	6881	536	12.84	617.8065.	< .00001
chemotherapy	3580290	127482	32821	3.88	62451.289.	< .00001
chemotherapy AND clinical	1326524	45989	10798	4.26	38463.3885.	< .00001

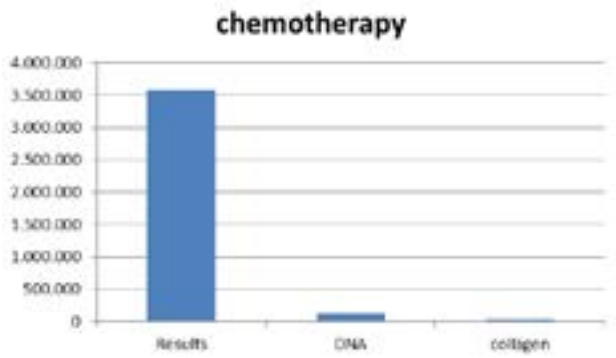

Figure 4: Results for ‘‘chemotherapy ‘’ MeSH, following bars demonstrate DNA versus collagen dichotomy.

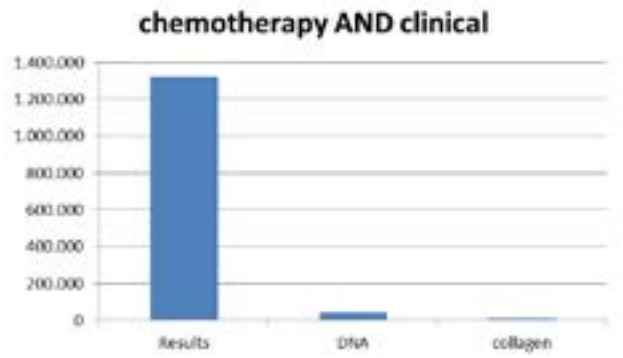

Figure 5: Results for ‘‘chemotherapy AND clinical ‘’ MeSH, following bars demonstrate DNA versus collagen dichotomy.

nominator reference group along with other MeSH item will provide dichotomy, which is indicative for assuming relationships; i.e. the keywords “cancer and DNA” or “cancer and collagen”.

The dichotomy subjects in this study are DNA and collagen, the reference groups used before dichotomy is completely different, and so it is not possible to interpret the results with bias. On the other hand, the vastness of the database creates homogenization within itself, even if there is a random bias, its effect could be excluded due to homogenization. It can be also argued that the journals published in different fields may lead to biases but selecting the keywords from the MeSH scope limits this possibility.

The results of this database analysis support that even cancer or chemotherapy perception is DNA-referred. However, most tumors occur with tissue changes over several years (26). In addition, it should be noted that since genes that are thought to be associated with cancer are actually found in all cells, which also operate completely different functions.

Chemotherapy is one of the main therapeutic approaches in cancer treatment, which was developed in the second half of the last century. The mechanisms of action of chemical substances used for chemotherapy have been attributed to DNA but have not been studied in detail. Indeed, most of them are not selective and interacts with mechanisms other than DNA, which make sense when the side effect profiles take into consideration. Most antibiotics can disrupt the extracellular matrix (27), i.e., drugs like docetaxel that affect the formation of mitotic spindles, can interact directly or indirectly with the inner and outer cytoskeleton (28).

On the other hand, studies to explore the effects of chemotherapy on connective tissue have limitations. Since the synthesis and degradation process of collagen is very slow, it is not possible to observe it in short-term studies. In addition, there is no known exact biochemical methodology to evaluate the degradation end-products of most collagen types, even in experimental systems (29,30). However, some studies in this area indicate that chemotherapeutics could interact with collagen (31). Cisplatin, which is used in many gastrointestinal cancer protocols, interferes with the synthesis process of collagen (32). Adriamycin, which is frequently used in breast cancer and soft tissue sarcomas, causes modifications in collagen structure (33, 34). Bleomycin, an antibiotic chemotherapeutic agent commonly used in the treatment of testicular cancers, causes the alterations of the extracellular matrix (35). These data also indicate that the occurrence of cardiomyopathy, which is long-term and dose-limiting adverse effect of Adriamycin, can be explained by its interaction with the fibrous skeleton of the heart. Similarly, bleomycin-induced lung fibrosis could be explicated through its relation with specific lung collagen structure (36).

CONCLUSION

In conclusion, this data analysis supports the argument that both cancer and chemotherapy perception is DNA-based, but it could be also attributed to collagen, the main component of connective tissue. Although the data in the literature are very limited, it is clear that collagen and extracellular matrix constitutes a new and productive field for investigating the effects of chemotherapy. Future studies could be very beneficial if objected to connective tissue instead of a DNA-based perception.

Conflict of interest: No conflict of interest was declared by the authors

Ethics: The study does not require ethics committee approval. This study is an evaluation of statistical results in accordance with our own ideas. It is not in the category required for the ethics committee approval application. There is no such thing as any blood, saliva, violation of the rights of the patient, etc.

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Clinical Comparison of MASCC and CISNE Scores in Neutropenic Febrile Patients in the Emergency Department

Acil Serviste Nötropenik Ateşli Hastalarda MASCC ve CISNE Skorlarının Klinik Karşılaştırılması

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ABSTRACT

Objective: *Febrile neutropenia is an important condition that needs to be well managed in the emergency department. Home treatment and hospitalization requirements of the patients are made according to some risk classifications. The most commonly used MASCC score may involve risks in terms of early discharge. Our aim in this study is to show that these risks can be reduced if the MASCC score is supported by the CISNE score. In addition, it is to determine the contribution of procalcitonin values to these classifications.*

Material and Method: *Neutropenic febrile patients over the age of 18 who came to the emergency department between 2019 and 2020 were included in the study. MASCC and CISNE scores of the patients were calculated. The relationship between scores and mortality was examined. Mortality estimation was made by using MASCC and CISNE scores together. In addition, patients were divided into 4 groups according to their proclacytonin values. The relationship between MASCC, CISNE and mortality between the groups was examined.*

Results: *Of the 103 patients included in the study, 70.9% were male. The most common reason for admission was found to be acute gastroenteritis with 22.3%. 40.8% of the patients died. According to the MASCC score, 35.9% of the patients were found to be at high risk. Despite this, 85.4% of them were hospitalized and treated. There was an inverse, moderate statistically significant correlation with MASCC (r=-0.542, p=0.000), and a weak statistically significant correlation with CISNE (r=0.385, p=0.000). There was a moderately significant correlation between procalcitonin, one of the acute phase indicators, and mortality (r=-0.555, p=0.000).*

Conclusion: *Evaluating neutropenic febrile patients with MASCC score for high-risk patients and CISNE score for low-risk patients in the emergency department gives more accurate results in determining poor prognosis. If these two scores are evaluated together with procalcitonin, the out-of-hospital mortality rate can be further reduced. For this, prospective studies in which risk scores are modified with a marker such as procalcitonin are needed.*

ÖZET

Amaç: *Febril nötropeni acil serviste iyi yönetilmesi gereken önemli bir durumdur. Hastaların ev tedavisi ve hastane yatış gerekliliği bazı risk sınıflamalarına göre yapılmaktadır. En sık kullanılan MASCC skoru erken taburculuk yönünden riskler içerebilmektedir. Bu çalışmadaki amacımız MASCC skorunun CISNE skoru ile desteklenmesi durumunda bu risklerin azaltılabileceğini göstermektir. Ayrıca prokalsitonin değerlerinin bu sınıflamalara katkısını belirlemektir.*

Gereç ve Yöntem: *2019-2020 yılları arasında acil servise gelen 18 yaş üstü nötropenik ateşli hastalar çalışmaya dahil edildi. Hastaların MASCC ve CISNE skorları hesaplandı. Skorlar ile mortalite ilişkisi incelendi. MASCC ve CISNE skorunun birlikte kullanılarak mortalite tahmini yapıldı. Ayrıca proklasitonin değerlerine göre hastalar 4 gruba ayrıldı. Gruplar arası MASCC, CISNE ve mortalite ilişkisi incelendi.*

Bulgular: *Çalışmaya dahil edilen 103 hastanın %70,9'u erkekti. En sık başvuru nedeni %22,3 ile akut gastroenterit olarak bulundu. Hastaların %40,8'i öldü. MASCC skoruna göre %35,9 oranında hasta yüksek riskli bulundu. Buna rağmen %85,4'ü hastaneye yatırılarak tedavi altına alındı. MASCC ile ters yönlü, orta dereceli istatistiksel olarak önemli korelasyon vardı (r=-0.542, p=0.000), CISNE ile zayıf istatistiksel olarak önemli korelasyon vardı (r=0.385, p=0.000). Akut faz göstergelerinden prokalsitonin ile mortalite arasında orta derece anlamlı bir korelasyon vardı (r=-0.555, p=0.000).*

Sonuç: *Nötropenik ateşli hastaları acil serviste yüksek riskli olanları MASCC skoru ile düşük riskli hastaları ise CISNE skoru ile değerlendirmek kötü prognozu belirlemede daha doğru sonuçlar veriyor. Bu iki skor eğer prokalsitonin ile birlikte değerlendirilirse hastane dışı mortalite oranı daha da azaltılabilir. Bunun için risk skorlarının prokalsitonin gibi bir belirteçle modifiye edildiği prospektif çalışmalara ihtiyaç var.*

Keywords:
CISNE score
Febrile neutropenia
MASCC score
Mortality
Procalcitonin

Anahtar Kelimeler:
CISNE skoru
Febril nötropeni
MASCC skoru
Mortalite
Prokalsitonin

INTRODUCTION

Chemotherapy not only affects rapidly proliferating mucosal cells, but also leads to a decrease in the number of neutrophils. The patient who has both lost the mucosal barrier and has neutropenia becomes open to infections (1). Infections are an important cause of mortality in cancer patients (2). While the risk of developing respiratory, heart and kidney failure is 25-30%, death can reach up to

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11%. If the condition progresses to sepsis, especially in-hospital mortality approaches 50%. For this reason, early initiation of antibiotic therapy and/or antifungal therapy is recommended for these patients, and hospitalization is recommended according to the risk classification (3). Orally home treatment amoxicillin clavunate or quinolone is recommended. In the hospital, intravenous (iv) antibiotics such as broad-spectrum piperacillin-tazobactam are recommended (4). The Multinational Association of Support Care in Cancer (MASCC) score is commonly used to determine risk. A score above 21 is defined as low risk. Significant complications were observed in 11% of patients with low risk. For this, it is recommended to use the Clinical Index of Stable Febrile Neutropenia (CISNE) scoring. In addition to these scores, the socioeconomic opportunities of the patient are effective in the decision of hospitalization (3). An important reason for some problems in determining the risk is that solid masses show an occlusive feature in the area where they are located. Therefore, the risk of aspiration pneumonia, cholangitis or serious urinary infections may make it difficult to determine the risk (5). There are studies in which the mortality rate is 80% in hematological cancer patients admitted to the intensive care unit. This suggests that a MASCC score below 21 is not an indicator of high risk alone. Additional diseases of the patient, the presence of a catheter, leukemia or myeloproliferative dysplasia are among the other high-risk causes that are not included in the MASCC score (6).

Emergency departments are a difficult part of hospitals where intensive, rapid and critical decisions are made. Febrile neutropenia (FN) is a condition that requires quick decisions about where and how to treat. The number of studies comparing MASCC and CISNE scores is scarce in the literature. Our aim in this study is to see the effect of the two scores on the clinical decision making process in the emergency department. We aimed to show the contribution of acute phase indicators, especially procalcitonin value, to risk scores and mortality by examining the relationship. Thus, it is to determine the most appropriate approach in terms of use in the emergency department.

MATERIAL AND METHOD

Study design

This study was planned as a single-center and retrospective study in the emergency department of a training and research hospital. Patients admitted to the emergency department due to FN between 01/January/2019-31/December/2020 were determined. The information was obtained from the hospital data processing system. The study was carried out according to the Declaration of Helsinki. After obtaining the approval of the ethics committee, the data were performed as an archive scan over the computer system.

Study protocol and selection of patients

Data of 230 patients with febrile neutropenia were scanned. 30 patients were neutropenic without FN and due to missing data, 97 patients were excluded due to different reasons such as bleeding from the gingiva, epistaxis and gastrointestinal tract, trauma, cerebrovascular disease, myocardial infarction and acute abdomen. 103 patients were included in the study. Patients over the age of 18 who met the FN criteria were included in the study. Neutropenic patients under the age of 18, with missing data and who did not meet the FN criteria were excluded

Table 1: MASCC and CISNE scores

MASCC Variables	Point		CISNE Variables	Point	
Disease symptom	Asymptomatic/mild	+5	ECOG** Performance Status	<2	0
	Moderate	+3		≥2	+2
	Severe	0			
Hypotension	No	+5	Baseline blood glucose ≥121 mg/dL or ≥250 mg/dL in diabetics or taking steroids	No	0
	Yes	0		Yes	+2
COPD*	No	+4	COPD*	No	0
	Yes	0		Yes	+1
Type of cancer	Solid	+4	Cardiovascular disease	No	0
	Hematogenous + no fungal infection	+4		Yes	+1
	Hematogenous + There is fungal infection	0			
Dehydration	No	+3	Monocyte	≥200/µL	0
	Yes	0		<200/µL	+1
Age	<60	+2	Mucositis grade ≥2 Painful erythema, edema or ulcer, but eating/swallowing possible	No	0
	≥ 60	0		Yes	+1
Fever	Outpatient	+3	0 points low risk, 1-2 points medium risk, ≥3 points high risk		
	Inpatient	0			
Total point ≥ 21 low risk, <21 high risk			0,1,2 outpatient, ≥3 inpatient		

**COPD: Chronic obstructive pulmonary disease, **ECOG: Eastern Cooperative Oncology Group*

from the study. A form was prepared for the study. Age, gender, comorbidities, neutrophil counts, leukocyte counts (WBC), C-reactive protein (CRP), procalcitonin (PCT), MASCC/CISNE scores, foci of infection, culture results, patient's treatment impression (home therapy/ hospitalization) and mortality were recorded. Neutrophil, leukocyte, CRP and PCT values were correlated with mortality. The superiority of MASCC and CISNE scores (low risk/high risk) over mortality was examined. The relationship between using the scores separately and using them together was determined. In addition, patients were divided into 4 different subgroups according to their PCT values. PCT value below 0.5 ng/mL was determined as group 1, 0.5-2 ng/mL group 2, over 2 ng/mL group 3, and over 10 ng/mL group 4. The relationship of these four groups with MASCC, CISNE and mortality was examined.

Defination

The criterion for the diagnosis of FN is fever equal to or higher than 38°C for at least 1 hour or 38.3°C once orally. The criterion for neutropenia is neutrophil count less than 500 µL or decrease from 1000 µL to less than 500 µL within 48 hours. MASCC and CISNE scores are summarized in table 1 (3).

PCT below 0.5 ng/mL is mild risk of progression to severe infection (sepsis-septic shock), intermediate risk between 0.5-2 ng/mL, high risk above 2ng/ml and high probability of sepsis above 10 ng/ml. It can be defined as septic shock (7).

Outcome

Our main outcome is that the mortality rate increases with decreasing MASCC score. Our other outcomes were an increase in the CISNE score, an increase in acute phase reactants, and an increase in the mortality rate.

Statistical analysis

Study data were analyzed with SPSS for Windows v.17 and MedCalc trial version 23. Data are presented as frequency (n), percentage (%), median, and interquartile range. The distribution of continuous data was evaluated using the Kolmogorov-Smirnov test. They were found to not normally disperse. Therefore, Mann-Whitney U test, which is one of the non-parametric tests, was used. $p<0.05$ was considered statistically significant.

RESULTS

Considering the gender distribution of the patients, 70.9% (n=73) were seen in men. The patients were found to be at high risk with the MASCC score of 35.9% and the CISNE score of 44.6%. The high risk was found to be 46.6% when the two scores were used together. The most common reason for admission was acute gastroenteritis with 22.3% (n=23). 85.4% (n=88) of our patients were hospitalized and treated for intravenous (iv.) antibiotic therapy. Our rate of patients with solid malignancy was 67%. Considering the culture results of our patients, there was a growth rate of 43.7%. The most frequent growth occurred in blood cultures with 32 patients. 40.8% of our patients died. These data of the patients are summarized in Table 2.

There was a weak, statistically significant inverse correlation between mortality and WBC (r=-0.322, p=0.001). There was a weak but statistically significant correlation between mortality and CRP (r=0.278, p=0.005). A moderate correlation between mortality and PCT and there was a statistically significant correlation (r=-0.555, p=0.000). The data are summarized in table 3.

There was a moderate statistically significant correlation between subgroups of PCT value and mortality (r=0.579, p=0.000). There was an inverse, moderate statistically significant correlation between MASCC score and mortality (r=-0.542, p=0.000). Weak statistical correlation between CISNE and mortality. There was a significant correlation (r=0.385, p=0.000). The data are summarized in table 4.

Table 2: The distribution of neutropenic fever patients by gender, score, focus of infection, culture results and mortality status

Variable		n	%
Gender	Male	73	70.9
	Female	30	29.1
Groups to the value of procalcitonin	Group 1	49	47.6
	Group 2	13	12.6
	Group 3	19	18.4
	Group 4	22	21.4
MASCC* score	< 21	37	35.9
	≥ 21	66	64.1
CISNE** score	High risk	46	44.6
	Low risk	57	55.4
MASCC+CISNE	İnpatient	48	46.6
	Outpatient	55	53.4
Source of infection	None	29	28.2
	Pneumonia	15	14,6
	Mucositis	11	10.7
	Urinary tract infection	16	15.5
	Acute gastroenteritis	23	22.3
	Esophagitis	1	1
	Bacteremia	6	5.8
	Dental abscess	1	1
	Perianal abscess	1	1
Type of malignancy	Solid	71	69
	Hematogenous	32	31
Antibiotic	Intravenous	88	85.4
	Oral	15	14.6
Hospitalization	Inpatient	88	85.4
	Outpatient	15	14.6
Mortality	Alive	61	59.2
	Death	42	40.8
Culture	Negative	40	38.9
	Positive	45	43.7
	None	18	17.5
Culture type	No reproduction	57	55.3
	Blood	32	31.1
	Urine	10	9.7
	Trachea	2	1.9
	Sputum	2	1.9

**MASCC: Multinational Association of Support Care in Cancer, **CISNE: Clinical Index of Stable Febrile Neutropenia*

Table 3: Distribution of patients' age and acute phase indicators according to mortality

Variable	Alive	Death	p
Age	65 (15)	66 (13)	0.06
WBC*	0.80 (0:70)	0.50 (0.44)	0.001
CRP** (mg/L)	88.40 (131.8)	140.50 (157)	0.005
PCT*** (ng/mL)	3.31 (1.62)	4.65 (21.85)	0.000

**WBC: White blood cell, **CRP: C-reactive protein,*
****PCT: Procalcitonin*

Table 4: Distribution of risk scores and procalcitonin values according to mortality of patients

Variable		**Alive**	**Death**	**p**
MASCC* score	< 21	11	26	0.000
	≥ 21	50	16	
CISNE** score	High risk	15	31	0.000
	Low risk	46	11	
MASCC+CISNE	İnpatient	18	31	0.000
	Outpatient	43	11	
Groups to the value of procalcitonin	Group 1	43	6	0.000
	Group 2	6	7	
	Group 3	8	11	
	Group 4	4	18	

**MASCC: Multinational Association of Support Care in Cancer,*
***CISNE: Clinical Index of Stable Febrile Neutropenia*

DISCUSSION

Evaluation of FN patients in the emergency department has a rapid and critical importance. Risk scoring has been developed to identify high-risk patients and initiate the hospitalization process. Although the MASCC score is often used, there are other scores such as CISNE. However, the use of scoring alone may include complications that may develop later. For this reason, studies are carried out to support the MASCC score in order to select patients who can be followed up well (3,8). In our study, MASCC included determining the poor outcome in patients who were determined to be low risk in the use of CISNE scores separately and together. In addition, we showed the contribution of acute phase indicators and especially procalcitonin value to these scores. Our study was a hospital in which oncological treatment methods were applied, in which tertiary health care was given retrospectively. For this reason, most of the oncological patients in our city are provided with emergency health services. An important point in our study is that we detected a source of infection in 81.8% of our patients. On the other hand, in 43.7% of these patients, there was growth in the cultures taken. In-hospital mortality rate of the patients in whom we detected FN was 40.8%. While gastroenteritis was the most common emergency department admission, culture growth was the most common in the blood, making us think that bacterial translocation is effective in this situation. Chemotherapy causes damage to the mucous membranes of the gastrointestinal tract and accelerates this transition. Ulcers may occur on the mucosal surfaces. It facilitates opportunistic pathogens in ulcerated tissue (9). One study found severe gram-positive bacteremia in patients with a low-risk MASCC score. Gram-negative bacteremia was more intense and fatal in those with high risk, especially in those below 15 points (10).

It was observed that the majority of the patients in our study were hospitalized and treated with iv antibiotics. This shows that patients identified as low risk are also hospitalized and monitored due to the concerns of physicians. This appeared to be a limiting factor for the study. This made it difficult for us to determine the effect of home follow-up of low-risk patients on poor outcome. Despite this, the high mortality rate of our patients in the low risk group according to the MASCC score justifies the physician's concerns. CISNE identified more high-risk patients based on the MASCC score. The combined use of the two scores suggested more hospitalization at the point of hospitalization. Coyne et al., on the other hand, found that the group with a CISNE score of 0 in low-risk patients could be safely taken to early oncology outpatient control (11). While Moon et al. recommended that the MASSC score be used in the initial evaluation in their study, they suggested that the CISNE score be evaluated secondarily in the low-risk patient group (12). Although the MASCC score was originally used to identify low-risk patients, it was found to be more successful in patients with poor outcomes. In addition, the CISNE score is more prominent in identifying low-risk patients (13-14).

When the relationship between WBC, CRP and PCT values of our patients and mortality was examined, there was a statistically significant correlation. In particular, PCT gained a little more importance. In the grouping made according to PCT values, mortality rates were higher in groups 2, 3 and 4, where the value was higher than in group 1. Mortality peaked when the value increased above 10 ng/mL. PCT had a higher mortality rate among those at high risk among PCT and risk scores. This made us think that MASCC and CISNE scores could reach more accurate results with PCT values. PCT is found at very low levels in healthy individuals. In case of serious bacterial infection, significant increases in PCT value are observed. It has been determined that the value of sepsis increases above 2 ng/mL (7,14). Keskin et al. showed that PCT increases in the early phase of sepsis and provides important information in prognosis (15). In our study, it was shown that the mortality risk of FN increased as the PCT value increased above 0.5 ng/mL.

CONCLUSION

Emergency physicians in FN may prefer MASCC or CISNE score first when identifying high-risk patients. However, in patients they consider low risk, we recommend that a secondary score or an increase in acute phase indicators, especially procalcitonin value, may contribute to the decision process. Our most important recommendation is to perform larger prospective studies with acute phase reactants modified for MASCC and CISNE scores.

Conflict of interest: The authors declare that there are no conflicts of interest.
Ethics: The study was carried out with the E1-22-2321 numbered decision of Ankara City Hospital Ethics Committee.

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CASE REPORT

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A Rare Case: Myocardial Infarction During Pregnancy

Nadir Bir Vaka: Gebelikte Miyokard Enfarktüsü

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ABSTRACT
Acute myocardial infarction (AMI) is rare during reproductive ages, but is three to four times more common in pregnant women than nonpregnant women. AMI during pregnancy is associated with high maternal and fetal mortality. We present a 22-year-old patient with 28 weeks pregnancy who was admitted to emergency department with chest pain and diagnosed with AMI in her follow-up.

ÖZET
Akut miyokard enfarktüsü (AMI) üreme çağında nadirdir, ancak hamile kadınlarda hamile olmayan kadınlara göre üç ila dört kat daha yaygındır. Hamilelik sırasında AMI, yüksek maternal ve fetal mortalite ile ilişkilidir. Acil servise göğüs ağrısı ile başvuran ve takibinde AMI tanısı alan 22 yaşındaki 28 haftalık gebeliği olan hastayı sunuyoruz.

Keywords:
Pregnancy
Acute myocardial infarction
Treatment

Anahtar Kelimeler:
Gebelik
Akut Miyokard Enfarktüsü
Tedavi

INTRODUCTION

Cardiac disease can be seen in pregnant women at a rate of 0.5 - 1% and is the biggest cause of death during pregnancy in developed countries (1). Acute myocardial infarction (AMI) is rare during reproductive ages, but is three to four times more common in pregnant women than non-pregnant women (1-6). AMI during pregnancy is reported to be 3 – 10 out of every 100.000 births (3,7,8), and it is associated with high maternal and fetal mortality (2-5,7,10-13). Pregnancy can lead to increased platelet adhesion and decreased fibrinolysis leading to hypercoagulopathy, and these changes in hemostasis may lead to an increase in thromboembolic events (7). We present a 22-year-old patient with 28 weeks pregnancy who was admitted to the emergency department with chest pain and diagnosed with AMI in her follow-up.

CASE

A 22-year-old primigravid patient with 28 weeks of gestation was admitted to the emergency department with sudden onset pressure-like chest pain radiating to left arm, and concurrent dyspnea. No additional diseases or conditions were mentioned in the medical history of the patient and family history was negative for any chronic illnesses or sudden deaths.

Her cardiac pace was rhythmic, there were no additional sound or murmur, peripheral pulses were clear, no pathological findings on other system examinations. Her vital signs were; arterial blood pressure: 110/70 mmHg on both upper extremities, pulse: 84 beats/min, oxygen saturation: 97%, body temperature: 36,9 ° C, respiratory rate: 22/min. The electrocardiogram (ECG) showed ST segment elevation that did not exceed 1 mm in the aVF and DIII leads and ST segment depression that did not exceed 1 mm in the aVL lead on admission. Cardiology consultant evaluated the patient with echocardiography (ECHO), there were no pathological findings on her ECHO. Cardiology consultant considered early repolarisation, and suggested monitorization of cardiac parameters (Figure 1).

A single live fetus compatible with 28 weeks was observed in the obstetric ultrasonography (USG) of the patient. No pathology was found in terms of obstetrics. The laboratory values on admission were measured as Creatine Kinase (CK): 57 U/L (0-170), Creatine Kinase-MB (CK-MB): 22.3 U/L (0-25), Troponin-I: 0.01 ng/It (0-0,04). There were no ECG changes during the patient's observation in the emergency room, but there were significant changes in terms of laboratory values taken at 8th hour as; CK: 365 U/L, CK-MB: 57.9 U/L, Troponin-I: 3.55 ng/mL. After cardiology consultation, inferior myocardial infarction was diagnosed and the patient was hospitalized for coronary angiography. The angiography was performed using lead shields to protect the fetus from radiation. The posterior descending limb of the right coronary artery was evaluated as 100% occluded. No pathological findings were found in other coronary arteries. On the third day of hospitalization, the patient had no symptoms and complaints, she was hemodynamically stable and cardiac parameters were regressing so she was discharged with Metoprolol and Acetylsalicylic acid prescription. The

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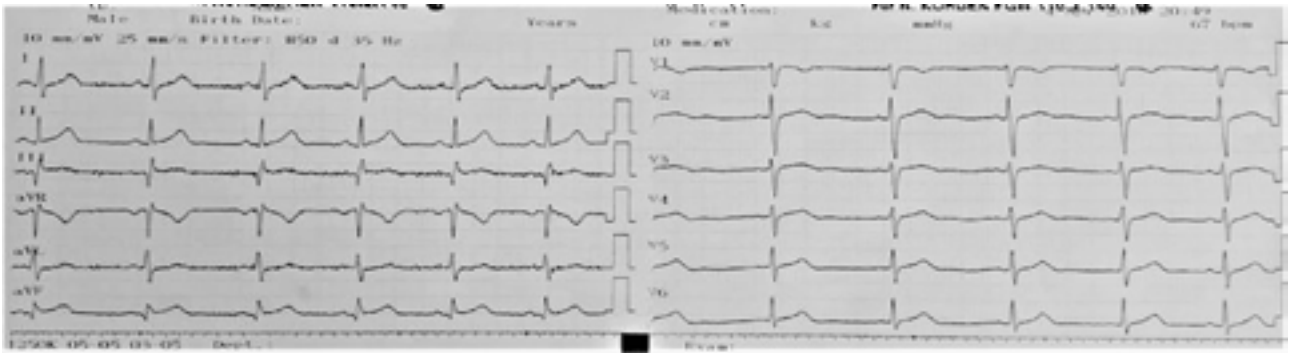

Figure 1: The electrocardiogram (ECG) shows ST segment elevation that did not exceed 1 mm in the aVF and DIII leads and ST segment depression that did not exceed 1 mm in the aVL lead on admission.

pregnancy of the patient continued in a healthy manner and gave birth to a healthy baby.

DISCUSSION

Our case differs from the literature in some aspects. Almost all of the pregnant AMI cases in the literature are in the third trimester and over 33 years of age multigravida women (2,3,6,8,12). In our case, the patient is 22 years old, which is quite young compared to other cases in the literature. There are cases under 30 years of age but have underlying organic heart diseases (13). In addition to being young, our patient had no underlying diseases in her medical history. Infarcts seen in this period most commonly affect the left ventricular anterior wall (3,8,10,12). In our case, unlike the literature, there was an inferior wall infarction. Half of pregnant AMI cases have no risk factors identified (2).

Physiological changes of the pregnancy can be a risk factor for AMI alone and these changes can mask pathologic findings and lead to delayed diagnosis (1,2). Regardless of patients' age, who come to the emergency department with chest pain during pregnancy, the lethal diagnoses that can be caused by the physiology of pregnancy should be kept in mind and the follow-up period in the emergency department should be extended (1,12). For this reason, patients with chest pain in emergency departments should be monitored by serial ECG and laboratory tests. Despite being very young, our case was considered as high risk because of the typical chest pain, so the follow-up period was extended. Although there were no ECG changes at the 8th hour of the observation in the emergency department, the increase in cardiac parameters supported our diagnosis. As in pregnancy, the diagnosis of AMI should be confirmed by angiography, and the fetus should be protected from radiation exposure during the procedure (2,4,7). In our case, coronary angiography was performed by cardiology after covering the abdominal region of the mother with lead covering; AMI was confirmed and treated with pharmacological agents.

Acetylsalicylic acid and heparin, among the medications used in the emergency treatment of AMI, are considered safe to be used in pregnancy (12). Morphine sulfate could be used for pain control and coronary vasodilatation in pregnancy. Morphine rapidly passes through the placenta, because of that, respiratory depression could occur in the newborn if given immediately before birth (5). For this reason, if a patient that was given morphine is in labor, the delivery room should be informed. Morphine was not given to our patient.

CONCLUSION

As a result, pregnant and early postpartum patients admitting to the emergency department with chest pain should be carefully examined considering the physiology of pregnancy, even if the causes of lethal chest pain are excluded, observation period should be prolonged in terms of cardiological pathologies. The prolongation of the follow-up period will ensure that the rare pregnant AMI cases are not missed and maternal and fetal mortality may be reduced.

Conflict of interest: Authors declare no conflict of interest.

Ethic: Our case report is suitable with the principles of World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (amended in October 2013).

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CASE REPORT

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Spontaneous Pneumothorax Developing in the Late Period in Association with COVID-19 Infection: A Case Report

COVID-19 Enfeksiyonuna Bağlı Geç Dönemde Gelişen Spontan Pnömotoraks; Vaka Sunumu

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ABSTRACT
Several studies have been published concerning radiological findings in COVID-19 pneumonia. Spontaneous pneumothorax is one very rarely reported such finding. Spontaneous pneumothorax can develop in association with fibrotic changes occurring in the lungs, or with long-term positive-pressure intubation. In report we describe a case of a 27-year-old man who presented to the emergency department due to fever, who had no thoracic computed tomography (CT) findings at his first presentation, but who re-presented with spontaneous pneumothorax as the infection progressed.

ÖZET
COVID-19 pnömonisinde radyolojik bulgular ile ilgili birçok çalışma yayınlanmıştır. Bu bulgular içinde spontan pnömotoraks çok nadir bildirilenlerdendir. Spontan pnömotoraks, akciğerlerde meydana gelen fibrotik değişikliklere veya uzun süreli pozitif basınçlı entübasyona bağlı gelişebilir. Biz bu vaka sunumunda 27 yaşında erkek hastanın acil servise ateş şikâyeti ile başvurup, ilk başvurusunda toraks bilgisayarlı tomografi (Toraks BT) bulgusu olmayan, sonrasında enfeksiyonu progresyon gösterdikçe spontan pnömotoraks gelişerek tekrar başvuran bir olguyu sunduk.

Keywords:
Spontaneous pneumothorax
COVID-19
Complication

Anahtar Kelimeler:
Spontan pnömotoraks
COVID-19
Komplikasyon

INTRODUCTION

The COVID-19 infection that emerged in the city of Wuhan in the Chinese province of Hubei in late 2019 has attracted worldwide attention due to the respiratory failure it causes (1). The essential feature of this infection is that it causes pneumonia. The formation of exudate with high protein density in the alveoli, infiltration of pneumocytes by multinuclear giant cells despite a high inflammatory response, and development of edema are events involved in the pathogenesis of COVID-19 pneumonia. Fibrosis subsequently develops secondary to this inflammatory response. Lung elasticity decreases in association with this process (2). Positive-pressure ventilation of these lungs exhibiting decreasing elasticity increases the risk of pneumothorax. Although COVID-19 infection appears with several radiological findings, spontaneous pneumothorax is one rarely seen complication of this infection. This case report discusses a case of spontaneous pneumothorax developing after approximately 20 days in association with the progression of COVID-19 pneumonia. Informed consent was obtained from the patient before the article.

CASE

A 27-year-old man initially presented to our emergency department with weakness and fever persisting for three days. He had no history of chronic disease, and was a non-smoker. The patient had no personal or family history of pneumothorax. No cough or respiratory distress was present at this presentation on 27.03.2020, and physical examination was normal. No pathology was detected at thoracic computed tomography (CT), and the viral nucleic acid real-time reverse transcriptase-polymerase chain reaction (RT-PCR) test performed for COVID-19 was negative. Since kidney and liver functions and electrolytes were normal at routine biochemistry tests, the patient was discharged and instructed to re-present if new symptoms occurred.

The patient re-presented on 04.04. 2020, when fever and shortness of breath were present. Minimal bilateral basal crepitant rales were present at physical examination. The patient's body mass index was 24,35. Oxygen saturation at room temperature was 95%, heartbeat 84/min, body temperature 37.90 C and arterial blood pressure 120/80. At thoracic CT, ground-glass opacity was present in the periphery of both lungs, and particularly in the lower lobes. This appearance was highly typical for COVID-19 infection (Figure 1).

A repeat RT-PCR test resulted positive. Blood test values were leukocytes 5.4 x103/uL (normal 3.8-10x103/uL), neutrophils 3.3x103/uL (normal 1.56-6.13x103/uL), lymphocytes 0.78 x103/uL (normal 1.18-3.74x103),

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platelet 300 x103 /uL (normal 150-400x103), and high sensitive C reactive protein 82 mg/L (N:0-3 mg/L). No pathological finding was present at blood gas analysis. Blood pH, and partial oxygen and partial carbon dioxide pressures were normal. The patient's general condition was good. Due to his high socio-cultural level and the fact he was capable of self-isolating at home, he was treated on an outpatient basis. Treatment included hydroxychloroquine, azithromycin, and paracetamol. The patient's contact details were noted, and he was discharged, with advice to return to the emergency department if shortness of breath occurred.

The patient re-presented with sudden onset shortness of breath and severe chest pain on 15.04.2020. He had no history of exposure to trauma capable of causing pneumothorax. No findings of paraseptal emphysema, cavitary lesion, or cystic bronchiectasis were also present at the previous thoracic CT examination. His body temperature was normal, but saturation was 88%. Arterial blood pressure was 100/70-mmHg and heart rate was 110/min. Auscultation at physical examination revealed decreased respiratory sounds on the left side, and crepitant rales in all zones on the right (Figure 2).

No pathology was present at other system examinations. Left-sided pneumothorax was detected at thoracic CT. Closed underwater drainage was applied, and the patient was transferred to the chest diseases hospital.

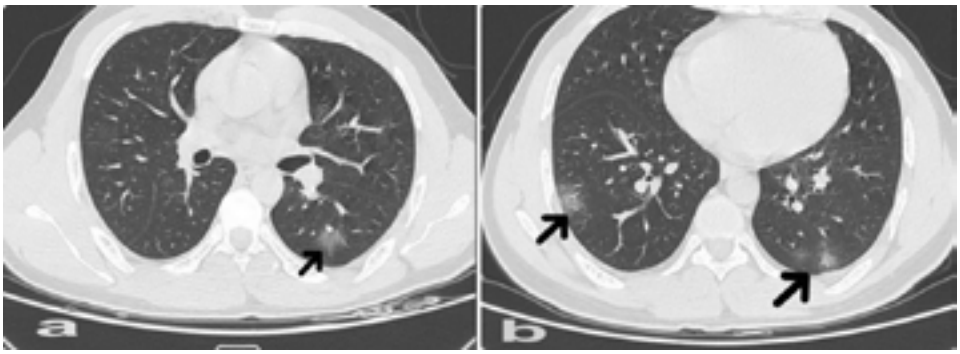

Figure 1: Chest computed tomography shows **a)** Infiltration in ground-glass opacity in the left lower lobe superior segment and **b)** Multifocal peripheral and subpleural ground-glass opacity in the bilateral lower lobe basal segments

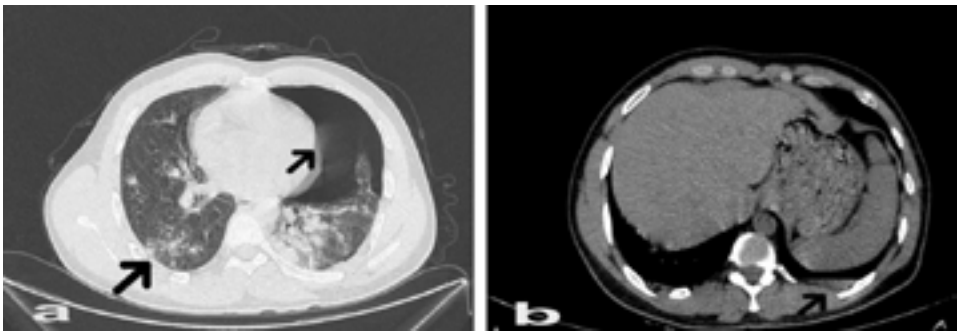

Figure 2: Chest computed tomography shows **a)** Pronounced air between the pleural leaves in the left lung (pneumothorax), compression collapse in the pulmonary parenchyma, and minimal pleural effusion in the basal region and **b)** Marked pleural effusion in the left lower lobe posterior basal segment

DISCUSSION

There may be several predisposing causes of spontaneous pneumothorax. Thin men, smokers, and individuals with chronic cough or chronic obstructive pulmonary disease have a greater disposition to pneumothorax development. Spontaneous pneumothorax essentially involves air leakage into the pleural space in association with development of alveolar rupture. Our patient had no underlying chronic disease or history of smoking for the development of spontaneous pneumothorax. One study involving tomographic findings of COVID-19 infection reported a 1% development rate for pneumothorax. In that study, Chen et al. attributed the development of pneumothorax to positive-pressure mechanical ventilation (3). Spontaneous pneumothorax development has been very rarely reported in COVID-19 infection (4-6). These cases have generally involved patients receiving positive-pressure respiratory support after intubation. The cause of the pneumothorax developed in the

patient may be microembolism in the pulmonary arterioles. Or, although there was no lung lesion in our patient's first application, it may have occurred due to the rupture of an existing fibrotic area. There are a number of very important points to be noted in the present case. The first is that our patient's symptoms at first presentation were mild, and progressed gradually. The negative PCR test at that time discouraged a diagnosis of COVID-19 infection. However, a PCR test performed consecutively over several days might have been diagnostic of COVID-19 infection, and treatment could thus have been started earlier. A second important point is our decision to treat on an outpatient basis despite the presence of tomographic findings at the second presentation. Our patient's generally good condition, his ability to self-isolate, and the likelihood that he would adhere to treatment led us to discharge him. Although such patients can be treated at home, they still require close follow-up. The third important point is our observation that COVID-19 pneumonia may lead to pneumothorax at subsequent periods. Although the cause of pneumothorax is not fully clear, it may have developed in association with an inflammatory process in the lung, or circulation disorder in the alveolar vessels. Severe cough can also cause pneumothorax in a lung with decreased elasticity.

CONCLUSION

In conclusion, pneumothorax may develop at later stages in COVID-19 pneumonia. Care must be taken in terms of pneumothorax development if the disease exhibits progression during the follow-up of these patients.

Conflict of Interest: Authors declare no conflict of interest.

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CASE REPORT

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Peripartum Cardiomyopathy in Emergency Department: A Case Report

Acil Serviste Peripartum Kardiyomiyopati: Bir Olgu Sunumu

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ABSTRACT

Peripartum cardiomyopathy (PPCM) is a form of dilated cardiomyopathy, which is one of the potential life-threatening complications of pregnancy. Peripartum cardiomyopathy is observed between the last 4 weeks of the pregnancy and the postpartum 5th month. It is related to high rate of maternal and infant mortality. Although the underlying factor has not been clearly understood yet, many factors such as infections, myocarditis, immunological factors or oxidative stress caused by prolactin have been attributed. We aimed to discuss the emergency management of postpartum PPCM in our case report.

ÖZET

Peripartum kardiyomiyopati (PPKM), gebeliğin potansiyel olarak hayati tehlike arz eden komplikasyonlarından olarak bir dilate kardiyomiyopati formudur. PPKM, gebeliğin son 4 haftası ve postpartum 5. aylar arasında görülmektedir. PPKM yüksek anne ve bebek mortalitesi ile ilişkilidir. Altta yatan kesin neden belli olmamakla birlikte enfeksiyonlar, myokardit, immünolojik faktörler, prolaktinin neden olduğu oksidatif stres gibi birçok neden suçlanmaktadır. Olgu sunumumuzda postpartum gelişen PPKM olgusunun acil yönetimini tartışmayı amaçladık.

Keywords:
Dyspnea
Pregnancy
Cardiomyopathy

Anahtar Kelimeler:
Dispne
Gebelik
Kardiyomiyopati

INTRODUCTION

Pregnancy leads to several anatomical and physiological changes. These changes affect the pulmonary and cardiovascular systems to an important extent (1). Dyspnea is a frequent complaint in the peripartum period, and venous thromboembolism, amniotic fluid embolism, pulmonary edema secondary to preeclampsia, aspiration pneumonia, tocolytic pulmonary edema, peripartum cardiomyopathy, pneumomediastinum, air embolism, asthma, pneumonia and cardiac pathologies should be considered in the differential diagnosis (1). Pregnancy may lead to an exacerbation in the predisposing disease, particularly in those with a cardiopulmonary disease prior to pregnancy, whereas several situations develop during pregnancy only or specific to pregnancy (1). In our case report, we aimed to discuss emergency management in a case with postpartum dyspnea.

CASE

A 29-year old female patient presented to our emergency department (ED) with complaints of respiratory distress, swelling in the legs and feet, and chest pain within the last 10 days. The patient gave a spontaneous vaginal birth 4 days prior to her admission to the ED. Her history included 3 years of marriage, gravida 2, and parity 2.

She had a moderately pale appearance on her physical examination. She had the complaint of dyspnea and orthopnea. Her blood pressure was 135/75 mmHg, heart rate 76 beats/min., oxygen saturation 94% and the respiratory rate 22 breaths/min. Respiratory sounds were reduced and rales were auscultated in the lower zones of both lung. The patient had bilateral 3+ pretibial edema with pitting.

ECG demonstrated normal sinus rhythm. There was an increment in cardiothoracic ratio and increased density at the inferior zones of both lungs in chest X-ray.

Laboratory findings included hemoglobin 10.7 g/dL (normal range (NR): 12-16 g/dL), D-dimer: 2946.2 ng/ml (NR: <500) and arterial blood gases with pH: 7.40, PCO2: 38.3mmHg, pO2: 85 mmHg, HCO3: 22 mmol/L.

The pre-diagnoses of pulmonary embolism and peripartum cardiomyopathy were considered for the differential diagnosis of dyspnea. Treatment with 2 L/min nasal oxygen, anticoagulation and diuretic was begun. No deep vein thrombosis was reported on the lower extremity venous doppler ultrasonography. Echocardiography revealed mild a hypokinetic left ventricle, an ejection fraction of %40 (NR:%55-70), pulmonary arterial pressure 25 mmHg (NR:<25mmHg) and normal right atrial and ventricular evaluation. In the light of these findings, the patient was hospitalized in the coronary care unit with the diagnosis of 'Peripartum Cardiomyopathy'.

DISCUSSION

The European Heart Society has been defined 'Peripartum Cardiomyopathy (PPCM)' as a form of dilated cardiomyopathy, which is one of the potential life-threatening complications of pregnancy. It is rare and leads to congestive heart failure in the last months of pregnancy or within the first 5 months following labor (2).

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Although the underlying factor has not yet been clearly understood, many factors such as infections, myocarditis, immunological factors or oxidative stress caused by prolactin has been blamed as the cause. The data confirm previous reports of high incidences of pre-eclampsia in patients with PPCM and further support the suggestion that this condition, which is often used as an exclusion criterion, is strongly associated with predisposition to PPCM, most likely as a result of shared pathophysiological mechanisms (3). It is related to a high rate of maternal and infant mortality (25-50%). Although the actual incidence of the disease is unknown, 1000 - 1300 women per year are affected within the United States of America. It has been observed that 25-75% of the patients are young and having their first babies (4). About 20% of the patients recorded in the PPCM registry to date have documented cardiomyopathy related to a previous pregnancy (3).

Despite marked differences in the sociodemographic parameters and ethnic backgrounds of patients from around the world, the baseline characteristics of subjects with PPCM are surprisingly similar (5). The most frequent complaints of the patients with PPCM are respiratory distress (90%), fatigue, tachycardia and edema (6). Demakis et al. have described the clinical diagnostic criteria in 1971 as follows: 1. Heart failure observed in the last month of pregnancy or within the first 5 months after labor; 2. The absence of another reason explaining heart failure; 3. The absence of a cardiac disease diagnosed prior to the latest month of pregnancy (7). Later, the presence of left ventricular dysfunction manifesting with reduced ejection fraction on echocardiography (left ventricular ejection fraction < 45% and left ventricular end-diastolic width > 2,7 cm/m²) was added to these criteria (2).

Treatment of PPCM can be carried out in the same way with conventional heart failure treatment including oxygen support, salt restriction, diuretics, digitalis and vasodilator agents. Angiotensin Converting Enzyme Inhibitors are contraindicated in the antenatal period. Data on beta-blocker drugs are limited. Other treatment recommendations include: calcium channel blockers, statins, monoclonal antibodies, interferon beta, immune-adsorption, therapeutic-apheresis and cardiomyoplasty (2,4). The use of bromocriptine and cessation of breastfeeding has been controversial. This is especially important because there is a potential risk associated with using bromocriptine in the peripartum period (8), and potential harm to mothers and newborn infants associated with the suppression of lactation, especially in the developing world (4). Breastfeeding, however, was not found to have a detrimental effect on recovery of left ventricular (LV) function in the IPAC study (9). Prolactin suppression and new high-dose immunoglobulin agents are under research for the treatment (4). Recent elegant research in animals has implicated an important role of unbalanced oxidative stress during pregnancy that causes proteolytic cleavage of the hormone prolactin (PRL) into a vasotoxic, proapoptotic and proinflammatory 16-kDa PRL fragment that leads to endothelial and myocardial dysfunction (2,4). The use of bromocriptine for inhibition of PRL in the same models was shown to prevent the formation of cardiomyopathy. A benefit of bromocriptine in women with PPCM has also been reported in a randomized study conducted in South Africa. PPCM may lead to congestive heart failure, atrioventricular arrhythmia, thromboembolism and sudden death (2). Data on the prevalence of ventricular arrhythmias and risk for sudden death in PPCM is limited. In a retrospective review carried out, 38% of reported mortality was ascribed to sudden death (5). This information further supports the use of wearable cardioverter-defibrillators in women with PPCM as a bridge to recovery or implantable cardioverter-defibrillators in women with persistent LV dysfunction (8). Women with PPCM who are young and otherwise healthy are usually not interested in continuing to take medications after recovery. Because of the lack of long-term data, the effects of discontinuing heart failure medications are unclear. Previous studies have reported a high incidence of LV thrombus in women with PPCM that is probably related to the hypercoagulable state of pregnancy and the postpartum period. For this reason, anticoagulation treatment has been recommended for women with PPCM (8).

CONCLUSION

Although PPCM is a rare disease among pregnant women, it progresses with high maternal and infant mortality. Diagnosis necessitates exclusion of other possible diagnoses in patients with dyspnea within the last month of pregnancy and the first 5 months after labor. Careful and thorough examination increases the possibility of a rapid and accurate diagnosis for the patient with dyspnea during pregnancy, which can improve the prognosis.

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IMAGE PRESENTATION

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Bennett's Fracture

Bennett Kırığı

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A 24-year-old female patient applied to our clinic with the complaint of falling from a ladder. She had no history of illness or drug use. In the anamnesis, it was learned that he fell after his foot slipped. Vital signs were stable. On physical examination, there was no feature other than tenderness in the proximal left 1st metacarpal bone. Fracture fragment was observed in the proximal of 1st metacarpal bone in conventional radiography imaging (figure 1). A plaster cast was applied after closed reduction. Conservative treatment was planned, and the patient was discharged.

Bennett's fracture is the retention of the bone to which the beak ligament is attached, and the dorsoradial and proximal subluxation of the base of the metacarpal detached from this part (1). Key features are intra-articular fracture, oblique fracture pattern, and volar-dorsal fragment. The medial small piece remains in place and maintains its relationship with the second finger via the volar oblique ligament (Beak ligament). However, the fractured metacarpal body is displaced proximally and laterally by the abductor pollicis longus and thenar intrinsic muscles. These types of fracture-dislocations are prone to slipping and are not stable; therefore, it should be treated more aggressively (2). Inadequate placement and replacement can lead to posttraumatic arthritis and disability. In Bennett fracture-subluxations, if the joint stepping is greater than 2 mm, percutaneous fixation with a K-wire is performed after closed correction and replacement (3).

Conflict of interest: Authors declare no conflict of interest.

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LETTER TO EDITOR

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Increasing Importance of Infectious Diseases Specialization in the Management of Healthcare-Related Infections in the Pandemic

Pandemide Sağlık Hizmetiyle İlişkili Enfeksiyonların Yönetiminde Enfeksiyon Hastalıkları Uzmanlık Dalının Artan Önemi

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2- Özel Lara Anadolu Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Antalya, Türkiye

Sayın Editör;

Ozdemir Sirekbasan ve Yıldız (1) tarafından Temmuz 2021'de derginizde yayınlanan 'COVID-19 Pandemisi Ne Zaman Bitecek? Hedefe Ne Kadar Yakınız?' isimli makaleyi ilgiyle okuduk. Bu makalede de belirtildiği üzere pandeminin henüz sonlanması mümkün gibi görünmemektedir. Biz de bu yazımızla pandemide bir başka tehlike olan sağlık hizmetiyle ilişkili enfeksiyonların (SHİE) önemini vurgulamayı ve farkındalığı arttırmayı amaçladık.

Antibiyotiklerin keşfi ile beraber enfeksiyon hastalıklarına bağlı ölümler de azalma olmuş, bu da insan ömrünün uzamasına neden olmuştur. Ancak uygunsuz antibiyotik kullanımının artması sonucu çoğul antibiyotik dirençli mikroorganizmalara bağlı enfeksiyonların sayısı artmıştır. Ülkemiz Avrupa ülkeleri arasında en fazla antibiyotik tüketimi ve en yüksek antibiyotik direnç oranlarına sahip ülkeler arasında ilk sıradadır (2,3).

Ülkemizde yapılan bir çok merkezli çalışmanın sonuçları endişe vericidir. Bu çalışmada, SHİE'ların epidemiyolojisindeki değişim ve antibiyotik dirençlerine göre 2015-2018 yılları kıyaslanmıştır. 2015 yılında 30 günlük ölüm oranı %22 iken, 2018 yılında bu oran %25'e yükselmiştir. Kan dolaşım enfeksiyonlarında Candida ve enterokokların, pnömonide ise Pseudomonas cinsinin saptanma sıklığının arttığı saptanmıştır. Ayrıca Pseudomonas cinsinde kolistin direncinin; Staphylococcus aureus cinsinde ise metisilin direncinin arttığı bildirilmiştir (4).

Pandemi öncesi dönemde yapılan 22 ülkeden 53 merkezi içeren bir çok uluslu çalışmada, acil servislere başvuran hastaların %17'sinin herhangi bir enfeksiyonu olduğu saptanmıştır. Hatta bu hastaların %21'i servislere, %5,1'i yoğun bakım ünitesine (YBÜ) yatırılmış olup, mortalite oranı %0,9 olarak bildirilmiştir. Bu çalışma verilerinin sonucu olarak da antibiyotik tedavisinin önemi bir kez daha vurgulanmıştır (5). Koronavirüs 2019 (COVID-19) enfeksiyonunun pandemi olarak ilan edildiği Mart 2020 tarihinden itibaren, Enfeksiyon Hastalıkları uzmanları diğer bir çok branşla beraber en ön safhada yer almıştır. Zaten pandemi öncesi dönemde de, gerek artan antibiyotik dirençleri, gerek toplumdan gelen enfeksiyonu olan hastaların yönetimi gibi bir çok iş yükü olan Enfeksiyon Hastalıkları branşının önemi giderek artmıştır (6,7).

Pandemi sırasında Enfeksiyon Hastalıkları uzmanları artmış iş yüklerinin yanısıra, artmış hastane/ yoğun bakım yatışları enfeksiyon kontrol ve antimikrobiyal yönetim politikalarının gevşemelere neden olmuştur. Bu değişikliklerin istenmeyen sonuçlarının antimikrobiyal direnç oranları üzerinde net olumlu veya olumsuz bir etkisi olup olmayacağı açık değildir (8). Almanya, İtalya ve Amerika Birleşik Devletleri'nden yapılan çeşitli araştırmalarda, COVID-19 salgını sırasında çoklu ilaca dirençli bakterilerin neden olduğu enfeksiyonlarda artış olduğunu bildirilmiştir (9). Global olarak odaklanılan pandeminin kontrolü olsa da, uzun vadeli antimikrobiyal dirençte artma ihtimali ürkütücüdür (9).

Önceki yıllarda; ülkemizden 41 merkezden toplam 214 YBÜ'nin dahil edildiği bir çalışmada, lavaboların %3-11'inde sabun, %10-18'inde kağıt havlu yokken, el dezenfektan ünitelerinin %1-4,7'sinde alkol bazlı el dezenfektanı olmadığı saptanmıştır. Sonbaharda hafta içi günlerde sabun ve kağıt havlu bulunan lavabo sayısı, hafta sonunda anlamlı olarak daha düşük olarak saptanmıştır (10). El hijyeni enfeksiyonların önlenmesinde en maliyet etkin enfeksiyon kontrol önlemlerinden birisidir (11). Ayrıca yine 2017 YBÜ'lerindeki hemşire ve personel sayısının değerlendirildiği ülkemizden 41 merkezin katıldığı çalışmada, Enfeksiyon kontrol hemşiresi sayısı 41 merkezden sadece 12'sinde yeterli olduğu, özellikle üçüncü basamak YBÜ'lerde sağlık personeli sayısının yetersiz ve yaklaşık hemşire ve personelin ¼'inin nispeten deneyimsiz olduğu saptanmıştır (12).

Sonuç olarak, pandemi nedeniyle hasta sirkülasyonun arttığı, izolasyon önlemlerine tam uyulamadığı göz önüne alınacak olursa, zaten ağır klinik tabloya neden olan COVID-19 hastalarında gelişebilecek SHİE'ların gerek mortalite, gerek hastane yatış süresinde artışa neden olabileceği düşünülebilir. Enfeksiyon kontrol önlemlerine uyum konusunda sağlık çalışanlarının bilgilendirilmelerinin arttırılması ve uygunsuz antimikrobiyal kullanımlarının önüne geçilmesi, enfeksiyon kontrol ve antimikrobiyal yönetim politikalarının pandemide dahi devam ettirilmesi gerekmektedir. Ayrıca personel ve hemşire sayısının yanı sıra hastanelerdeki el dezenfeksiyonu için gerekli malzemeler başta olmak üzere dezenfeksiyon/ sterilizasyon işlemleri için gerekli malzemelerin eksiksiz temini de elzemdir.

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