E-ISSN
e-ISSN 2667-8721
Volume: 5 Issue: 2 August 2023

www.ejcritical.com

EURASIAN JOURNAL of CRITICAL CARE

EPAT
1999
Emergency Physicians Association of Turkey

Printing and Graphics Department

PUNTO
AJANS

Ofis Adres
Seyrantepe Mah. İbrahim Karaoğlanoğlu Cd. İspar İş Merkezi,
D: No: 105 D:124, 34418 Kâğıthane/İstanbul
Tel: 0553 199 95 59
www.puntoajans.com

Contents

Original Article
Eurasian Journal of Critical Care

Investigation of Eosinophil, Lymphocyte and Monocyte Values According to Age and Gender in Insect Bites in The Emergency Department

Mustafa Safa PEPELE[1], Zekiye KANAT[2]
[1] Malatya Turgut Ozal University, Faculty of Medicine, Department of Emergency Medicine, Malatya, Turkiye
[2] Malatya Turgut Ozal University, Faculty of Medicine, Department Of Dermatology, Malatya, Turkiye

Abstract

Background: The purpose of this study was to look at the seasonal distribution, age and gender distribution, and eosinophil, lymphocyte, and monocyte values according to age and gender in cases of insect bites that were brought to the emergency room over the course of a year.

Materials and methods: Retrospective analysis was performed on patients who were brought to the emergency room between 1.12.2021 and 1.12.2022 and had the ICD code W57 (Diagnosis Code - Bitten or stung by Nonvenomous Insects and Other Nonvenomous Arthropods). The following values were noted: age, gender, presenting season, CRP, Leukocyte, Platelet, Lymphocyte, Monocyte, Eosinophil, INR, PTZ, and Aptt levels.

Result: The study comprised a total of 694 patients—308 females and 386 males. The patients were 39.81 16.42 years old on average. Spring saw 9.4% of the patients, summer saw 67%, and fall saw 23.6%. According to the patients' gender, there were significant differences in the eosinophil (t:-3.535; p:0.0010.01) and monocyte (t:-4.909; p:0.0010.01) values. Regarding the season in which the patients were admitted, significant differences in lymphocyte (F:7.045; p:0.0010.01) and monocyte (F:3.208; p:0.0410.05) values were discovered. When the disparities in eosinophil, lymphocyte, and monocyte values were evaluated in relation to the patients' ages, significant differences in monocyte values were discovered (F:2.552; p:0.0270.05).

Conclusion: We commonly see insect bites in emergency rooms, which we can usually cure with straightforward remedies or occasionally without treatment, but in some unfortunate circumstances, we may have to deal with major issues and allergic responses (4). Almost little studies have been done on the seasonal distribution and evaluation of blood tests according to age and gender, despite the fact that there are many studies on this topic in the literature. We think that more study on this topic is necessary.

Keywords: Insect Bites, Emergency Department, Eosinophil, Lymphocyte and Monocyte

Introduction

'Insect bites' are a significant number of patients presenting to the emergency department. Due to the fact that not every patient is admitted to the hospital, the real incidence in the community is unknown. Patients are more likely to see a doctor if they are experiencing symptoms, are uncertain about what bit them, and are in fear. At the stung site, redness, edema, and even discomfort appear in minor cases. But they can also occasionally manifest as urticaria, shortness of breath, and anaphylactic shock. Of fact, treatment may not always be required in certain situations. However, therapy should be provided and hospitalization should be required in extreme cases and in vulnerable individuals (1,2).

Allergy symptoms and alterations in the blood picture can be brought on by insects. Eosinophilia in particular is a shift that is anticipated, but it has the potential to increase neutrophils, induce leukocytosis, and cause local skin infections. Other blood series may also undergo changes as a result (3). Numerous studies on insect bites have been published in the literature. The majority of research, however, focuses on certain insects like scorpions, ticks, and bees. Studies on other insect bites are relatively rare, particularly those whose type or nature the patient is unaware of.

In this study, we looked at the seasonal distribution, age and gender distribution, and values for eosinophils, lymphocytes, and monocytes according to age and gender in cases of insect bites that were brought to the emergency room within a year.

Material And Method

The study was approved by the Non-Interventional Research Ethics Committee of Malatya Turgut Özal University with the decision numbered B.67 on 15.11.2022. This study was

Corresponding Author: Mustafa Safa PEPELE **e-mail:** safa.pepele@ozal.edu.tr
Received: 29.05.2023 • **Revision:** 10.07.2023 • **Accepted:** 12.07.2023
DOI: 10.55994/ejcc.1305438

Cite this article as: Pepele MS, Kanat Z. Investigation of Eosinophil, Lymphocyte and Monocyte Values According to Age and Gender in Insect Bites in The Emergency Department. Eurasian Journal of Critical Care. 2023;5(2):37-41

conducted following the Principles of the Declaration of Helsinki.

Between 1.12.2021 and 1.12.2022, patients admitted to the emergency department with International Classification of Diseases (ICD) W57 (ICD 10 Diagnosis Code - Bitten or stung by a nonvenomous insect and other nonvenomous arthropods) were retrospectively analyzed.

Data of the patients were obtained from computer records and outpatient clinic physician records. Age, gender, season of presentation, Crp (normal values: 0-0.5 mg\dl), Leukocyte (normal values: 4.6-10.2 10^3\uL), Platelet (normal values: 142-424 10^3\uL), Lymphocyte % (normal values: 10-50), Monocyte % (normal values: 0-12), Eosinophil % (normal values: 0. 5-5), Inr (international standardized ratio, international normalized ratio) (normal values: 0.8-1.2), Ptz (normal values: 10-14 seconds) and Aptt (normal values: 56.76-147.45 seconds). Patients with incomplete data and patients under 18 years of age were excluded from the study. Demographic characteristics and laboratory findings of the patients were analyzed. The differences in eosinophil, lymphocyte, and monocyte values according to the gender of the patients and the season of presentation, and the differences in eosinophil, lymphocyte, and monocyte values according to the age of the patients were statistically evaluated.

Statistical Evaluation

Statistical Package for Social Science for Windows (SPSS) 24.0 package program was used to evaluate the data in the study. Frequency and percentage distribution analysis, mean, and standard deviation values were analyzed to determine the descriptive characteristics of the patients evaluated in the study.

Independent Samples t-test was used to determine the significant differences in eosinophil, lymphocyte, and monocyte values in terms of the gender of the patients, and One-Way ANOVA was used to examine the significant differences in terms of the age of the patients and the seasons in which they were admitted.

The results were considered significant at 99% ($p<0.01$) and 95% ($p<0.05$) confidence levels.

Result

A total of 694 patients whose data were accessed in a retrospective computer search were included in the study. Within the scope of the study, 308 (44.4%) of the patients were female and 386 (55.6%) were male. 9.4% of the patients applied in spring, 67% in summer, and 23.6% in fall. The mean age of the patients was 39.81±16.42 years. Table 1 shows the demographic characteristics of the patients. Table 2 shows the mean laboratory data of the patients. When the differences in eosinophil, lymphocyte, and monocyte values were analyzed according to the gender of the patients and the season of presentation; significant differences were found in the eosinophil (t:-3.535 ; p:0.001<0.01) and monocyte (t:-4.909 ; p:0.001<0.01) values in terms of the gender of the patients. Accordingly, eosinophil and monocyte values of male patients were found to be higher than female patients. No significant difference was found in lymphocyte values in terms of the gender of the patients.

Table 1: Demographic Characteristics of the Patients

Characteristics		
Gender	**N**	%
Female	308	44.4
Male	386	55.6
Season		
Spring	65	9.4
Summer	465	67.0
Fall	164	23.6
Age	**Average**	**s.s.**
	39.81	16.42

Significant differences were found in the lymphocyte (F:7.045; p:0.001<0.01) and monocyte (F:3.208; p:0.041<0.05) values in terms of the season in which the patients were admitted. The differences found were significant between the lymphocyte and monocyte values of the patients admitted in the fall and the values of the patients admitted in the spring and summer seasons. Accordingly, the lymphocyte and monocyte values of the patients admitted in the fall were lower than the lymphocyte and monocyte values of the patients admitted in the spring and summer seasons.

When the differences in eosinophil, lymphocyte, and monocyte values were analyzed according to the ages of the patients, significant differences were found in the monocyte (F:2.552; p:0.027<0.05) values of the patients in terms of the ages of the patients. The differences found were significant

Table 2: Laboratory Results of the Patients

Parameters	**Average**	**s.s. ±**
Crp (0-0.5 mg\dl)	0.33	0. 87
Leukocyte (4.6-10.2 10^3\uL)	9.32	2.64
Platelet (142-424 10^3\uL)	256.84	66.18
Lymphocyte % (10-50)	30.16	9.89
Monocyte % (0-12)	7.64	2.23
Eosinophil % (0.5-5)	2.35	1.94
Inr (0.8-1.2)	1.00	0.14
Ptz (10-14 minutes)	11.98	1.92
Aptt (56.76-147.45 minutes)	106.34	15.96

between the monocyte values of patients aged 20 years and younger and patients in other age groups. Accordingly, the monocyte values of patients aged 20 years and younger were higher than the monocyte values of patients in other age groups.

No significant differences were found in the eosinophil and lymphocyte values of the patients in terms of age.

Discussion

In emergency rooms, we commonly see patients who have been bitten by insects. Fortunately, most of the time, these patients can recover without therapy or with just minor complications from their bites (4). Almost little studies have been done on the seasonal distribution and evaluation of blood tests according to age and gender, despite the fact that there are many studies on this topic in the literature. Particularly, case reports predominate in studies pertaining to blood values. As a result, the majority of the conversation will be focused on our research.

It is possible that there are numerous undiscovered bug species in the planet, hence many different types of insects may be responsible for insect bites. The kind of bug that bit the person, especially the fluid inside the insect that is thought to be harmful to humans, has a direct impact on whether the patient experiences an allergic reaction and, if so, what kind and how severe the symptoms are. Everybody can get bitten by an insect, but whether or not a reaction happens, and if it does, how severe it is—how much the bite swells, itches, and is red—varies considerably from person to person and is more noticeable in vulnerable youngsters. In our study, patients under the age of 20 had monocyte levels that were greater than those of patients in other age groups. Due to hypersensitivity, lymphocytosis is expected in cases of bug bites, although monocytosis is less common (5).

Hypersensitivity to insect bites is the most common allergic dermatitis. At the cellular level, skin lesions are characterized by massive eosinophil infiltration caused by an underlying allergic response (6,7). In another study, in a patient who developed cellulitis as a result of an insect bite, no significant abnormality was found except mild eosinophilia in the complete blood count (8). In our study, eosinophil and monocyte values of male patients were found to be higher than those of female patients. No significant differences were found in eosinophil and lymphocyte values in terms of the age of the patients.

After an insect bite, symptoms such as localized itching, redness, and swelling usually occur on the skin. As expected, it is observed much more frequently in hot weather, especially in spring and summer (9). The reasons for this include a significant increase in the number of insects in hot weather and a preference for outdoor activities more frequently. In this study, 67% of the patients presented in the summer months. In winter months, the number of applications is almost negligible. In Bischof's study, the 2 months with the highest incidence of insect bites were August and September. Since the seasons were not divided into months in our study, we cannot say anything clear about this. However, in our findings, it was detected more in the fall than in the spring (10).

Again, a substantial difference between the lymphocyte and monocyte values of patients treated in the fall and those of patients admitted in the spring and summer was discovered when blood tests were evaluated according to the seasons. Therefore, compared to patients admitted in the spring and summer, the lymphocyte and monocyte levels of patients admitted in the fall were lower. This is not quite clear as to why. Perhaps as winter draws near, insects' capacity to elicit a response declines.

Sometimes, when an insect bite occurs in the early hours during the acute phase, there may be no reaction. Serious reactions, nevertheless, can happen later, sometimes even days after the bite. Therefore, the patient should be informed that more serious reactions could manifest if they receive insect bites at the emergency room or an outpatient clinic. If clinical progression occurs despite proper treatment, patients should be admitted to the hospital. The first few seconds after a bite typically involve unpleasant pain. Following that, the body reacts by manifesting an allergic reaction on the skin. At the bite site, there is an increase in warmth, itchiness, redness, and similar allergic symptoms. The compounds that the insect injects into our skin, either by its saliva or through its sting, cause the allergic reaction. These reactions are often modest in nature and go away quickly after an insect bite (4,11). However, symptoms may gradually worsen and cause serious health issues in people who are allergic to insect secretions.

Conclusion

We commonly see insect bites in emergency rooms, which we can usually cure with straightforward remedies or occasionally without treatment, but in some unfortunate circumstances, we may have to deal with major issues and allergic responses (4). Almost little studies have been done on the seasonal distribution and evaluation of blood tests according to age and gender, despite the fact that there are many studies on this topic in the literature. We think that more study on this topic is necessary.

Table 3: Differences in Eosinophil, Lymphocyte, and Monocyte Values According to the Gender of the Patients and the Seasons of Admission

		Average .±s.s.	t - F	p
Eosinophil % (0.5-5)	Female	2.06±1.79	t:-3.535	**.001[a]****
	Male	2.58±2.04		
Lymphocyte % (10-50)	Female	30.78±10.06	t:1.476	.140[a]
	Male	29.67±9.73		
Monocyte % (0-12)	Female	7.18±2.08	t:-4.909	**.001[a]****
	Male	8.01±2.28		
Eosinophil % (0.5-5)	Spring	2.19±1.73	F:.308	.735[b]
	Summer	2.38±1.91		
	Fall	2.33±2.12		
Lymphocyte % (10-50)	Spring	30.39±10.28	F:7.045	**.001[b]** (3-1. 3-2)**
	Summer	31.01±9.67		
	Fall	27.67±9.99		
Monocyte % (0-12)	Spring	8.03±2.19	F:3.208	**.041[b]* (3-1. 3-2)**
	Summer	7.71±2.25		
	Fall	7.29±2.17		

Table 4: Differences in Eosinophil, Lymphocyte, and Monocyte Values According to the Age of Patients

		Average .±s.s.	F	p
Eosinophil % (0,5-5)	20 ≥	2.19±1.68	F:1.513	**.183**
	21-30	2.63±2.36		
	31-40	2.26±1.84		
	41-50	2.31±1.46		
	51-60	2.46±2.27		
	61 ≤	2.03±1.51		
Lymphocyte % (10-50)	20 ≥	30.55±9.00	F:1.369	.234
	21-30	29.87±9.34		
	31-40	29.92±9.33		
	41-50	31.75±9.93		
	51-60	30.77±10.94		
	61 ≤	28.38±11.05		
	20 ≥	8.21±1.83		
Monocyte % (0-12)	21-30	7.92±2.64	F:2.552	**.027* (1-3. 1-4 1-5. 1-6)**
	31-40	7.72±2.04		
	41-50	7.52±2.38		
	51-60	7.53±2.13		
	61 ≤	7.08±2.20		
	Fall	7.29±2.17		

One-Way ANOVA , *p<0.05 , **p<0.01

References

1. Juckett G. Arthropod bites. Am Fam Physician. 2013 Dec 15;88(12):841-7. PMID: 24364549.
2. Turan E, Yeşilova Y, Uçmak D, Yurt N, Karakoca YB. Pederus Dermatiti: Batman Bölgesinden Sporadik Bir Olgu. Turk J Dermatol 2013; 7: 164-5 DOI: 10.4274/tdd.1326
3. Celiloğlu C, Tolunay O, Özdemir U, Sucu A, Çelik Ü. Örümcek Isırığı İle Gelişen Şiddetli Sistemik Toksisite ve Dermonekroz. Türkiye Çocuk Hast Derg/Turkish J Pediatr Dis / 2019; 5: 395-398
4. Singh S, Mann BK. Insect bite reactions. Indian J Dermatol Venereol Leprol. 2013 Mar-Apr;79(2):151-64. doi: 10.4103/0378-6323.107629. PMID: 23442453
5. Hatipoğlu H. , Erkal S. , Türkmen S, Engerek N, Kurt K , Şiraneci R. Enfeksiyon Hastalıklarının Tanısında Laboratuvar Bulguları Jopp Derg 3(1):5-11, 2011
6. (Dodiuk-Gad RP, Dann EJ, Bergman R. Insect bite-like reaction associated with mantle cell lymphoma: a report of two cases and review of the literature. Int J Dermatol. 2004 Oct;43(10):754-8. doi: 10.1111/j.1365-4632.2004.02145.x. PMID: 15485536.
7. Horiuchi Y. Insect bite as possible cause of eosinophilic pustular dermatosis. J Dermatol. 1999 Mar;26(3):196-7. doi: 10.1111/j.1346-8138.1999.tb03454.x. PMID: 10209929.
8. Özuğuz P, Kaçar SD, Karaca S, Aktepe F. Selülitle Karışan Artropod Isırığı: Olgu Sunumu Düzce Tıp Fakültesi Dergisi 2014; 16(3): 35-36.
9. Kar S, Dongre A, Krishnan A, Godse S, Singh N. Epidemiological study of insect bite reactions from central India. Indian J Dermatol. 2013 Sep;58(5):337-41. doi: 10.4103/0019-5154.117292. PMID: 24082174; PMCID: PMC3778769.
10. Bischof RO. Seasonal incidence of insect stings: autumn 'yellow jacket delirium'. J Fam Pract. 1996 Sep;43(3):271-3. PMID: 8797755.

Original Article
Eurasian Journal of Critical Care

Evaluation and Diagnostic Effectiveness of Hemogram, Biochemistry and Inflammatory Markers (Immature Granulocyte, Procalcitonin, CRP, NLR, PLR) in Patients with Sepsis

Muhammed Semih GEDIK[1], Muhammed CIFTCIOGLU[2]
[1] Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Emergency Medicine, Kahramanmaras, Turkiye
[2] Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Internal Medicine, Kahramanmaras, Turkiye

Abstract

Background: It was aimed to show the contributions of hemogram values and inflammatory markers involved in the pathology and progression of sepsis, and other biochemical markers like C-reactive protein, procalcitonin, delta neutrophil index (immature granulocyte), calcium and zinc levels to the diagnosis of sepsis, and the relationship of the relevant markers with each other.

Materials and methods: This is a descriptive epidemiological study. Patients aged 18 years and over who received the diagnosis of sepsis in the Emergency Department and Internal Diseases Service of Kahramanmaraş Sütçü Imam University Medical Faculty Hospital between 11.10.2022 - 11.06.2023 were prospectively involved in this study.

Result: In the present study, it was found that leukocyte, neutrophil, platelet lymphocyte ratio, neutrophil lymphocyte ratio, immature granulocyte, copper, phosphorus, blood glucose, C-reactive protein, and procalcitonin values were high in patients with sepsis. Albumin, calcium, zinc and lymphocyte levels were found to be low.

Conclusion: The use of biomarkers in sepsis has increasingly become important in diagnosing, following treatment, determining prognosis and predicting mortality. The biomarkers examined in this study are believed to be a reference for future studies on their use in diagnosing and treating sepsis, and following its prognosis.

Keywords: Sepsis, Hemogram, Biochemistry, Immature granulocyte, Copper, Zinc.

Introduction

Sepsis is a clinical syndrome that most frequently causes mortality and morbidity around the world. Sepsis is a severe organ dysfunction that is induced by an uncontrolled host response to infection (1). Sepsis, which is also referred as systemic inflammatory response syndrome (SIRS), is identified as a severe multi-organ dysfunction. It is crucial to detect significant bacterial infections like sepsis in the early period so that infectious diseases can be treated and controlled. Organ dysfunction in sepsis refers to an acute increase of at least two points in the SOFA (Sequential Organ Failure Assessment) score due to infection. Septic shock is a subcomponent of sepsis and refers to the requirement for vasopressor therapy to increase the serum lactate level above 2 mmol/L and to keep the mean arterial pressure above 65 mmHg. In sepsis, clinical characteristics may vary depending on the conditions such as the infection site, causative microorganism, manifestation of organ dysfunction, and the underlying health status of the host (1, 2). In addition to clinical findings, there are also some laboratory tests such as leukocyte count and C-reactive protein (CRP) in the diagnosis of sepsis, however, sepsis is diagnosed based on clinical and inflammatory markers and blood culture results since these tests are not specific to sepsis. The major issue in the detection of bacterial infections is that the clinical presentation of signs and symptoms usually overlaps with other inflammatory disorders. Despite the widespread use of microbiological, biochemical and molecular methods for diagnosing the infections, they involve some restrictions with regard to sensitivity and specificity. Thus, there is still no gold standard marker. It is necessary to determine the proposed biomarkers by fast, cost-effective, reliable, simple, specific, and sensitive methods (2).

For the assessment of inflammatory processes that included in the progression and pathology of sepsis, CRP, procalcitonin (PCT), and complete blood count tests are employed. White blood cell count (WBC), neutrophil, lymphocyte, platelet

Corresponding Author: Muhammed Semih GEDİK **e-mail:** semihgedik86@hotmail.com
Received: 11.07.2023 • **Revision:** 25.07.2023 • **Accepted:** 26.07.2023
DOI: 10.55994/ejcc.1330716

Cite this article as: Gedik MS, Ciftcioglu M. Evaluation and Diagnostic Effectiveness of Hemogram, Biochemistry and Inflammatory Markers (Immature Granulocyte, Procalcitonin, CRP, NLR, PLR) in Patients with Sepsis. Eurasian Journal of Critical Care. 2023;5(2): 42-48

(PLT) and mean platelet volume (MPV) values, that are among the complete blood count parameters, and the ratios of these values to each other are employed as inflammatory markers (3). A few of the most important of these markers are neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR). Furthermore, delta neutrophil index is a recent inflammatory marker which is calculated in routine hemogram examination without causing additional cost. Upon reviewing the literature, delta neutrophil index was not evaluated much in patients with sepsis.

Immature granulocytes in the peripheral circulation is indicated by delta neutrophil index (DNI). Studies revealing that DNI generally increases in cases of inflammation are available (4). Immature/total granulocyte ratio or neutrophil band count is increased by stress, infection, and systemic inflammation, so it is possible to employ DNI as a measure of the existence of immature granulocytes and also as an indicator of a granulocyte shift to the left (5).

It was reported that hypocalcemia was observed in sepsis patients with critical condition. Nevertheless, the significance of hypocalcemia in sepsis has not been studied thoroughly. Hypocalcemia is frequently seen in patients with sepsis and is considered to be significantly related to organ dysfunction and sepsis-related mortality (6).

It was aimed to show the contributions of inflammatory markers involved in the pathology and progression of sepsis, and other biochemical markers such as CRP, PCT, complete blood count parameters, delta neutrophil index, calcium, zinc levels to the diagnosis of sepsis and the relationship of relevant markers with each other.

Material and Method

This is a descriptive epidemiological study. Patients aged 18 years and over who received the diagnosis of sepsis in the Emergency Department and Internal Diseases Service of Kahramanmaraş Sütçü Imam University Medical Faculty Hospital between 11.10.2022 - 11.06.2023 were prospectively involved in this study. No sample was selected.

Sepsis patients' sociodemographic data like age and gender and laboratory tests in blood such as hemogram, biochemistry, inflammatory markers and electrolyte levels were analyzed. Hemogram, biochemistry, routine inflammatory markers, complete blood count parameters, CRP, PCT, WBC, neutrophil, lymphocyte, NLR, PLT, PLR, immature granulocyte level, and zinc, copper, magnesium, sodium, potassium, calcium, chloride, phosphate, pH, and glucose levels were taken within the scope of laboratory tests. The patients' data were received from the hospital automation system and patient files and saved in an excel file. Then, the statistical evaluation was performed.

SPSS v.23.0 package program (SPSS Inc, Chicago, Illinois, USA) was employed to statistically evaluate the data obtained in the study. During the evaluation of the data, descriptive statistics were given as frequency and percentages for qualitative data, and as frequency, mean, and standard deviation for numerical data. The suitability of the parameters to the normal distribution was assessed using analytical methods (Kolmogorov-Smirnov and Shapiro-Wilks tests). Since parametric assumptions could not be met in the comparison of quantitative data, the Mann-Whitney U test, which is a non-parametric method, was employed to compare means between two independent groups. A p-value of <0.05 was considered as the level of statistical significance. The values were expressed as mean and standard deviation.

Ethical committee approval was obtained for the study from Kahramanmaraş Sütçü İmam University Faculty of Medicine Clinical Research Ethics Committee with session no: 2022/28, decision no: 03, dated 11.10.2022. The study is consistent with the Declaration of Helsinki.

Results

Table 1: Sociodemographic characteristics of the patients diagnosed with sepsis in the study

	Number	%
Gender		
Female	23	63,9
Male	13	36,1
Total	36	100
Age		
18 – 64	3	8,3
65 – 79	18	50,0
80 and above	15	41,7
Total	36	100

A total of 36 participants, consisting of males by 36.1% (n=13) and females by 63.9%, were included in the study. While 8.3% (n=3) of the participants were aged between 18-64 years, 50% (n=18) and 41.7% (n=15) of them were aged between 65-79 years and 80 years and above, respectively (Table 1).

The mean leukocyte count and the mean neutrophil count of the patients diagnosed with sepsis in the study were found to be 16.45 (SD:7.7) and 14.79 (SD:7.4), respectively. Leukocyte and neutrophil levels of sepsis patients were found to be higher than normal (Table 2).

It was found that patients' mean platelet lymphocyte ratio and mean neutrophil lymphocyte ratio were 479.382 (SD: 792.268) and 28,629 (SD:39.768), respectively. These values were found to be higher than normal limits (Table 2).

The mean immature granulocyte level and the percentage of immature granulocyte of the patients with sepsis were

found to be 329.17 (SD:399.49) and 1.739 (SD: 1.918), respectively. The relevant value was found to be higher than normal limits (Table 2).

It was found that the mean RDW value of the patients with sepsis was high by 55.66 (SD: 12.50) (Table 2).

The mean C reactive protein value of the patients was found to be 163.84 (SD:93.3). It was found that patients diagnosed with sepsis had high levels of C-reactive protein (Table 2).

The mean procalcitonin levels of the patients with sepsis were found to be 33.23 (SD:59.84). It was found that the procalcitonin levels were high in patients with sepsis (Table 2).

The mean albumin value of the sepsis patients included in our study was found to be low by 26.30 (SD: 5.90) (Table 2).

In patients with sepsis, the mean calcium value and the mean zinc value were found to be low by 7.90 (SD:0.66) and 48.93 (SD:18.53), respectively (Table 2).

It was found that the mean glucose level of the patients with sepsis was 154.94 (SD:73.29) (Table 2).

Table 2: Laboratory Results of the Patients

	n	Mean ± SD	Normal Values*
WBC (10^9/L)	36	16,45 ± 7,7	3,39 – 8,86
Neutrophil (10^9/L)	36	14,79 ± 7,4	1,5 – 5
Neutrophil percentage (%)	36	87,91 ± 9,61	40,1 – 71,4
Platelet (10^9/L)	36	239,56 ± 141,09	150 – 400
Lymphocyte (10^9/L)	36	0,911 ± 0,551	1,05 – 3,17
Lymphocyte percentage (%)	36	7,24 ± 7,37	21,6 – 49
NLR (%)	36	28,629±39,768	0,91 – 5,6
PLR (%)	36	479,382±792,268	40 - 140
RDW (fL)	36	55,66 ± 12,50	38,9 – 50
MCV (fL)	36	90,36 ± 6,83	87 – 102,2
MPV (fL)	36	10,74 ± 0,97	9,2 – 12,2
IG count	36	329,17 ± 399,49	10 – 40
IG percentage (%)	36	1,739 ± 1,918	0,16 – 0,62
Na (mmol/L)	36	138,67 ± 7,56	132 – 146
K (mmol/L)	36	4,31 ± 0,78	3,5 – 5,5
Ca (mg/dL)	36	7,90 ± 0,66	8,6 – 10
P (mg/dL)	36	4,42 ± 2,44	2,5 – 4,5
Cl (mmol/L)	36	106,17 ± 5,69	96 – 106
pH	36	7,34 ± 0,11	7,35 – 7,45
CO2 (mmHg)	36	34,89 ± 13,47	35 – 45
PCT (µg/l)	36	33,23±59,84	<0.1
CRP (mg/L)	36	163,84 ± 93,3	<5
Albumin (g/L)	36	26,30 ± 5,90	39,7 – 49,4
Zn (µg/dL)	36	48,93 ± 18,53	50 – 150
Mg (mg/dL)	36	1,77 ± 0,39	1,6 – 2,6
Cu (µg/dL)	36	96,17 ± 35,40	70 – 140
Glucose (mg/dL)	36	154,94±73,29	74 – 100

Ca: calcium, Cl: chlorine, CO2: carbon dioxide, CRP: c-reactive protein, Cu: copper, IG: immature granulocyte, K: potassium, MCV: mean corpuscular volume, Mg: magnesium, MPV: mean platelet volume, n: number of patients, Na: sodium, NLR: neutrophil-lymphocyte ratio, P: phosphorus, PCT: procalcitonin, PLR: platelet-lymphocyte ratio, RDW: red blood cell distribution width, SD: standard deviation, WBC: white blood cell count, Zn: zinc

* The relevant variables were compared with the normal values in the literature. During comparison with the normal values, the parameters that increased with sepsis were compared with upper limit of normal while the parameters that decreased with sepsis were compared with lower limit of normal. No correlation was investigated for the parameters within normal limits.

Table 3: Hemogram, biochemistry, inflammatory markers and electrolyte levels of the patients diagnosed with sepsis in the study by gender

	Gender						
	Male				Male		P
	n	Mean	SD	n	Mean	SD	P
WBC (10^9/L)	13	14,48	1,24	23	17,56	1,88	0,193
Neutrophil (10^9/L)	13	12,80	1,13	23	15,91	1,81	0,193
Neutrophil percentage (%)	13	88,10	1,68	23	87,80	2,35	0,348
Platelet (10^9/L)	13	230,46	31,97	23	244,70	32,53	0,908
Lymphocyte (10^9/L)	13	0,945	0,174	23	0,892	0,107	0,856
Lymphocyte percentage (%)	13	7,05	1,34	23	7,35	1,79	0,553
Neutrophil/Lymphocyte Ratio	13	38,28	17,48	23	23,17	3,39	0,705
Platelet/Lymphocyte Ratio	13	715,47	350,2	23	345,9	58,0	0,633
RDW (fL)	13	51,31	3,17	23	58,12	2,64	0,063
MCV (fL)	13	89,41	1,47	23	90,90	1,59	0,633
MPV (fL)	13	10,59	0,23	23	10,83	0,22	0,542
IG count	13	186,15	55,27	23	410,00	39,31	0,106
IG percentage (%)	13	1,21	0,28	23	2,04	0,47	0,198
Na (mmol/L)	13	141,46	2,16	23	137,09	1,49	0,109
K (mmol/L)	13	4,34	0,24	23	4,29	0,16	0,895
Ca (mg/dL)	13	8,00	0,19	23	7,84	0,14	0,498
P (mg/dL)	13	3,68	0,63	23	4,85	0,52	0,182
Cl (mmol/L)	13	106,69	1,78	23	105,87	1,12	0,596
pH	13	7,36	0,31	23	7,33	0,22	0,339
CO2 (mmHg)	13	33,82	2,52	23	35,49	3,25	0,974
Procalcitonin	13	39,56	20,71	23	29,66	10,67	0,729
CRP (mg/L)	13	189,16	31,22	23	149,53	16,61	0,270
Albumin (g/L)	13	27,01	1,65	23	25,90	1,25	0,610
Zn (µg/dL)	13	49,25	4,85	23	48,75	4,06	0,792
Mg (mg/dL)	13	1,84	0,12	23	1,73	0,08	0,517
Cu (µg/dL)	13	105,94	7,77	23	90,65	8,01	0,229
Glucose	13	150,08	18,69	23	157,70	16,21	0,780

Ca: calcium, Cl: chlorine, CO2: carbon dioxide, CRP: c-reactive protein, Cu: copper, IG: immature granulocyte, K: potassium, MCV: mean corpuscular volume, Mg: magnesium, MPV: mean platelet volume, Na: sodium, NLR: neutrophil-lymphocyte ratio, P: phosphorus, PCT: procalcitonin, PLR: platelet-lymphocyte ratio, RDW: red blood cell distribution width, SD: standard deviation, WBC: white blood cell count, Zn: zinc
The P value was found using Mann–Whitney U test and/or Student's t test.

In sepsis patients, it was determined that leukocyte count, neutrophil count, platelet count, lymphocyte percentage, RDW, immature granulocyte count/percentage, phosphorus and glucose levels were higher in female patients compared to male patients, however, it was found that calcium, zinc and albumin values were lower in female patients compared to male patients. No statistically significant difference was observed between genders in terms of other parameters (Table 3).

Table 4: Hemogram, biochemistry, inflammatory markers and electrolyte levels of the patients diagnosed with sepsis in the study by age

	Age						
	Below 80 years				80 years and above		P
	n	Mean	SD	n	Mean	SD	P
WBC (10^9/L)	21	14,76	1,32	15	18,80	2,42	0,205
Neutrophil (10^9/L)	21	12,95	1,23	15	17,36	2,32	0,163
Neutrophil percentage (%)	21	85,62	2,36	15	91,10	1,74	**0,009**
Platelet (10^9/L)	21	232,86	28,11	15	248,93	41,55	0,835
Lymphocyte (10^9/L)	21	0,982	0,107	15	0,811	0,163	0,194
Lymphocyte percentage (%)	21	8,37	1,81	15	5,67	1,50	**0,050**
NLO	21	16,73	2,63	15	45,28	14,69	**0,033**
PLO	21	300,58	59,42	15	729,70	299,8	0,163
RDW (fL)	21	56,58	3,00	15	54,37	2,81	0,665
MCV (fL)	21	88,78	1,40	15	92,58	1,80	0,116
MPV (fL)	21	10,75	0,22	15	10,73	0,24	0,797
IG count (109/L)	21	273,33	65,14	15	407,33	131,7	0,470
IG percentage (%)	21	1,87	0,46	15	1,55	0,43	0,847
Na (mmol/L)	21	138,62	1,78	15	138,73	1,79	0,797
K (mmol/L)	21	4,50	0,17	15	4,03	0,18	0,131
Ca (mg/dL)	21	8,11	0,14	15	7,60	0,16	0,021
P (mg/dL)	21	4,05	0,46	15	4,95	0,73	0,404
Cl (mmol/L)	21	106,33	1,40	15	105,93	1,21	0,628
pH	21	7,35	0,21	15	7,33	0,33	0,552
CO2 (mmHg)	21	34,73	1,72	15	35,10	4,93	0,360
Procalcitonin	21	24,32	10,41	15	45,71	19,01	0,574
CRP (mg/L)	21	187,75	20,94	15	130,38	20,91	0,075
Albumin (g/L)	21	26,54	1,28	15	25,97	1,59	0,898
Zn (µg/dL)	21	52,30	4,55	15	44,21	3,62	0,260
Mg (mg/dL)	21	1,74	0,09	15	1,81	0,09	0,356
Cu (µg/dL)	21	105,29	7,59	15	83,41	8,58	0,080
Glucose	21	140,10	13,77	15	175,73	21,52	0,158

Ca: calcium, Cl: chlorine, CO2: carbon dioxide, CRP: c-reactive protein, Cu: copper, IG: immature granulocyte, K: potassium, MCV: mean corpuscular volume, Mg: magnesium, MPV: mean platelet volume, Na: sodium, NLR: neutrophil-lymphocyte ratio, P: phosphorus, PCT: procalcitonin, PLR: platelet-lymphocyte ratio, RDW: red blood cell distribution width, SD: standard deviation, WBC: white blood cell count, Zn: zinc

In sepsis patients, it was determined that leukocyte count, neutrophil count, neutrophil percentage, platelet count, PLR, NLR, immature granulocyte count, procalcitonin, phosphorus and glucose values were higher in patients aged above 80 years compared to patients aged below 80 years, however, it was found that calcium, zinc and albumin values were lower in patients aged above 80 years compared to patients aged below 80 years. No statistically significant difference was observed between the ages in terms of other parameters (Table 4).

Discussion

Despite the availability of many screening tests used in the early diagnosis of sepsis, the sensitivity of these tests varies between 30% and 90% (7). This study attempted to evaluate

the hemogram, biochemical and inflammatory markers involved in the diagnosis, pathology and progression of sepsis and to determine the relationship between these markers.

In their study, Yalınbaş et al. determined that leukocyte levels, neutrophil levels, PLR and NLR values were higher in sepsis patients compared to the healthy control group (7).

In their study, Alkan et al. found that immature granulocyte, leukocyte and neutrophil values were higher in patients with sepsis (8)

In another study conducted by Arcagok et al., it was found that PLR values were higher in patients with sepsis (9)

In the study of Can et al., it was observed that PLR and NLR values were higher in sepsis patients (10).

In our study examining patients with sepsis, it was determined that leukocyte, neutrophil, PLR, and NLR values were high in patients with sepsis, in consistent with the literature. Lymphocyte levels were observed to be low in sepsis patients.

In studies carried out by Jong Wan et al. and Ha et al, delta neutrophil index, which reflects immature granulocyte levels and immature granulocyte, was indicated as a biomarker that could be used in the diagnosis of sepsis patients, in the evaluation of prognosis, in the prediction of mortality and in the evaluation of the severity of sepsis (11, 12).

Similar to the literature, it was found that immature granulocyte levels were high in sepsis patients in our study. Immature granulocyte level stands out as a new biomarker that can be tested in routine hemogram examination without additional cost and examination. We believe that immature granulocyte levels, which have been increasingly used recently and increase in sepsis patients and inflammatory conditions, will provide convenience in the diagnosis of sepsis.

Leukocyte, neutrophil, NLR, PLR and immature granulocyte values, which are considered as the markers of systemic inflammation, are simple and easy parameters that can be calculated in complete blood count, one of the routine laboratory data, without the need for an additional technique and no additional cost to the health system (13). Therefore, hemogram parameters with easy access can also be considered as suitable parameters that can be used for diagnosing sepsis.

In their study, Liu et al. reported that acidosis, hypoalbuminemia, hypocalcemia and hyperphosphatemia were observed in sepsis patients (6).

In their study, Fatih et al. found that the magnesium level was low, but the platelet and lymphocyte counts were low in patients with sepsis. It was found that leukocyte, procalcitonin and C-reactive protein levels were high (14).

In their study, İdris et al. determined that copper levels were high and zinc levels were low in patients with sepsis (15).

In this study in which we examined the hemogram and biochemical values of sepsis patients, it was found that copper values and phosphorus values were high, while calcium and zinc values were low in sepsis patients. No difference was found in other elements. Acidosis was found in the blood pH levels. It is believed that serum copper, phosphorus, calcium and zinc values as well as hemogram parameters can be used in the diagnosis of patients with sepsis.

In their study, it was reported by Ece et al. that serum CRP and procalcitonin levels increased in patients with sepsis and that they were a reliable prognostic factor in sepsis (2).

In consistent with the literature, it was determined that procalcitonin levels were high in sepsis patients in this study. It was found that CRP levels, which are positive acute phase reactants, were high, but albumin values, which are negative acute phase reactants, were low.

In their study, Levent D. indicated that stress hyperglycemia and insulin resistance were common in sepsis and were associated with mortality (16)

In the present study, blood glucose levels of sepsis patients were also found to be high. It is possible to achieve improvements in the prognosis of sepsis patients by controlling the blood glucose level.

In this study, it was determined that leukocyte values, neutrophil values, platelet values, immature granulocyte count and percentage, phosphorus and glucose levels were higher in female patients compared to male patients. Lymphocyte, NLR, PLR, procalcitonin, CRP, albumin, zinc and copper values were found to be lower in female patients.

In this study, it was determined that leukocyte values, neutrophil values, neutrophil percentage, platelet values, immature granulocyte count, NLR, PLR, phosphorus, procalcitonin and glucose levels were higher in patients aged above 80 years compared to patients aged below 80 years. It was determined that lymphocyte, calcium, CRP, albumin, zinc and copper values were lower in patients aged above 80 years.

Conclusion

The use of biomarkers in sepsis has increasingly become important in diagnosing, following treatment, determining prognosis and predicting mortality. In our study, leukocyte, neutrophil, NLR, PLR, immature granulocyte, copper, phosphorus, blood glucose, CRP and procalcitonin values were found to be high in patients with sepsis. Albumin, calcium, zinc and lymphocyte levels were found to be low. The biomarkers examined in this study are believed to be a reference for future studies on their use in diagnosing and treating sepsis, and following its prognosis.

Conflict of Interest: *No conflict of interest was declared by the authors.*

Funding: *The author(s) received no financial support for the research, authorship, and/or publication of this paper.*

Informed consent: *Consent was obtained from the patients and/or their relatives using an informed consent form.*

Author contributions: *All authors contributed at every stage of the article writing process.*

References

1. Meltem Malkoç, Birgül Vanizor Kural. Presepsin: Sepsis Tespiti İçin Umut Verici Yeni Bir Biyobelirteç. CBU-SBED, 2021, 8(3): 553-557. DOI: 10.34087/cbusbed.887818
2. Cem Ece, İlkin Çankayali, Canan Bor, Kubilay Demirağ, Mehmet Uyar, Ali Reşat Moral. Yoğun bakım hastalarında serum CRP düzeylerinin sepsis değerlendirmesindeki yeri. Ege Tıp Dergisi / Ege Journal of Medicine 2020; 59 (3): 174-180. https://doi.org/10.19161/etd.790461
3. Sönmezer MÇ, Tülek N. Bakteriyel İnfeksiyonlarda ve Sepsiste Biyobelirteçler. Klimik Dergisi 2015; 28(3): 96-102. DOI: 10.5152/kd.2015.20
4. Seok Y, Choi JR, Kim J, Kim YK, Lee J, Song J, et al. Delta neutrophil index: a promising diagnostic and prognostic marker forsepsis. Shock. 2012 Mar;37(3):242-6. doi: 10.1097/SHK.0b013e3182454acf
5. Nilgün Eroğlu, Gülseren Şahin, Ferda Özbay Hoşnut, Gürses Şahin. Çölyak Hastalığı Diyet Uyumunda Yeni Bir Belirteç: Delta Nötrofil İndeks? Kocatepe Medical Journal 22:294-299/Temmuz 2021. https://doi.org/10.18229/kocatepetip.864099
6. Yalan Liu, Yannan Chai, Zhihui Rong, Yan Chen. Prognostic Value of Ionized Calcium Levels in Neonatal Sepsis. Ann Nutr Metab. 2020;76(3):193-200. doi: 10.1159/000508685
7. Emine Esin Yalınbaş, Hüseyin Bilgin. Geç Neonatal Sepsis Tanısında Trombosit Parametreleri Ve Nötrofil Lenfosit Oranlarının Değerlendirilmesi. Kocatepe Tıp Dergisi. 21:104-109/2020 Özel Sayısı (1). https://doi.org/10.18229/kocatepetip.557896
8. Alkan Baylan F., Orak F., Doğaner A., Güler S., İnal Ş., Sağer H. İmmatür Granülositler; Gerçek Bakteriyemiyi Kontaminasyondan Ayırabilir Mi? JHS. 2022; 31(2): 164-168. https://doi.org/10.34108/eujhs.860436
9. Arcagok BC, Karabulut B. Platelet to Lymphocyte Ratio in Neonates: A Predictor of Early onset Neonatal Sepsis. Mediterr J Hematol Infect Dis. 2019 Sep 1;11(1):e2019055. doi: 10.4084/MJHID.2019.055
10. Can E, Hamilcikan Ş, Can C. The Value of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio for Detecting Early-onset Neonatal Sepsis. J Pediatr Hematol Oncol. 2018 May;40(4):e229-e232. doi: 10.1097/MPH.0000000000001059
11. Kim JW, Park JH, Kim DJ, Choi WH, Cheong JC, Kim JY. The delta neutrophil index is a prognostic factor for postoperative mortality in patients with sepsis caused by peritonitis. PLoS One. 2017 Aug 1;12(8):e0182325. doi: 10.1371/journal.pone.0182325
12. Ha SO, Park SH, Park SH, Park JS, Huh JW, Lim CM, et al. Fraction of immature granulocytes reflects severity but not mortality in sepsis. Scand J Clin Lab Invest. 2015 Jan;75(1):36-43. doi: 10.3109/00365513.2014.965736
13. Omran A, Maaroof A, Saleh MH, Abdelwahab A. Salivary C-reactive protein, mean platelet volüme and neutrophil lymphocyte ratio as diagnostic markers for neonatal sepsis. J Pediatr (RioJ).2018;94(1):82-87. DOI: 10.1016/j.jped.2017.03.006
14. Fatih Aygün. Çocuk yoğun bakımda magnezyum düzeyi prognoz ve enfeksiyon ile ilişkili midir? Online Türk Sağlık Bilimleri Dergisi 2019, Cilt 4, Sayı 1, 37-46. https://doi.org/10.26453/otjhs.442454
15. İdris Akkaş. Sepsis hastalarında eser elementlerin araştırılması/Investigation of trace elements in sepsis patients. (Tıpta Uzmanlık Tezi). Düzce Üniversitesi / Tıp Fakültesi / Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Ana Bilim Dalı, 2018, 99s.
16. Levent Döşemeci. Sepsis Ve Kan Şekeri Kontrolü. ANKEM Derg. 2006;20(Ek2):67-69.

Original Article
Eurasian Journal of Critical Care

Tracheostomy Complications in Children: Single Center Experience

Selçuk UZUNER[1]
[1] Department of Pediatrics, Faculty of Medicine, Bezmialem Vakif University, İstanbul, Turkey.

Abstract

Background: To evaluate the frequency and the type of complications in children with tracheostomy in our center

Materials and methods: Single-center retrospective study of pediatric patients undergoing tracheostomy between 2017 and 2022. Age, sex, indication of tracheostomy, tracheostomy time, the features of complications and presence of mortality were evaluated.

Result: Fifty children (22 girls, 28 boys) were included the study. The mean age of patients 93.5 months. The tracheostomy time was before one year of age for 27 patients. The most common indication for tracheostomy was long-term ventilation. There were 30 complications for 23 patients.(46%) We did not report any early complication. The most common late complication was the development of granulation tissue. The second most common complication was cannula obstruction. Only one patient died due to massive bleeding associated with tracheostomy. We decannulated 7 patients (14%).

Conclusion: The rates of complication may vary in the literature. The reason for this differentiation may be related to the different study design and population features.Also socio-economic level of the family and the responsibility awareness of the parents may contribute to these factors. Education of parents and caregivers about the appropriate postoperative management is very important for preventing complications rates.

Keywords: Tracheostomy, Children, Complication

Introduction

Tracheostomy is a common procedure in critically ill patients such as for management of upper-airway obstruction or prolonged ventilation. Over the last decade, tracheostomy has been increasingly performed in children with complex and chronic conditions because of the increasing survival rate. In children population, this procedure is technically more difficult and complication rates are higher than adults. Indications, timing and complications of tracheostomy in adults have been well described in the literature but these are still controversial in the pediatric population. Tracheostomy-related complications may occur sometimes during the procedure and sometimes afterwards. Type and rates of complications vary depending on different parameters such as the study design, different patients number, and patient follow-up. These complications can be categorized as early or late. This definitaion is made according to passed time between procedure and complication. The complications of tracheostomy can be called as early complications such as hemorrhage, accidental tube decannulation and infection. Late complications include hemorrhage, tracheal stenosis, accidental tube decannulation, and fistula formation (1-8).

There are some studies reported in literature that evaluated the indication and complication of pediatric tracheostomy. The aim of this study is to evaluate the frequency and the type of complications in children with tracheostomy in our institution.

Material and Methods

This study's design was a single-center and retrospective. We evaluated the records of children with tracheostomy who were followed in our palliative care clinic between 2017 and 2022. Age, sex, tracheostomy time, indication of tracheostomy, the type of complication, and presence of mortality were evaluated. Tracheostomized pediatric patients (0-18 years old) were included in the stduy. Patients with missing records were excluded. Early complications were defined as those within the first week of procedure and late complications were defined as those after one week (8).

Corresponding Author: Selçuk UZUNER **e-mail:** esuzuner@yahoo.com
Received: 09.07.2023 • **Accepted:** 22.09.2023
DOI: 10.55994/ejcc.1324926

Cite this article as: Uzuner S. Tracheostomy Complications in Children: Single Center Experience. Eurasian Journal of Critical Care. 2023;5(2): 49-51

Statistical Analyses

Descriptive statistical analysis was performed with Microsoft Excel, and the data obtained were calculated as mean and percentage.

Results

Fifty children were available for analysis. 22 (44%) were girls and 28 (56%) were boys. The mean age of patients was 93.5 months (15-214 mo).Long term ventilation was the most common indication (41, 82%) Primary causes of this indication were cardiopulmonary disease and neuromuscular disease. The indications are shown in Table 1.

Table 1: Indication of tracheostomies

Prolonged ventilation	n=41
Neuromusculer disease	22
Lung disease	11
Metabolic disease	6
Congenital heart disease	2
Airway obstruction	n=9
Subglottic stenosis	4
Craniofacial anomaly	3
Laringomalasia	2

In our study, there were not intraoperative or postoperative early complications. We detected total 30 late complications for 23 patients (46%). 17 patients had only one, 5 patients had two and only one patient had 3 complications. The most common late complication was the development of granulation tissue. The second most common complication was cannula obstruction. All complications are shown in Table 2. Only one patient was death due to massive bleeding associated with tracheostomy. The cause of other deaths were complications from their primary disease..

Table 2: Complications of tracheostomies

	n=30
Granulation tissue	9
Canal obstruction	4
Accidental decanulation	2
Skin lesion (dermatitis)	1
Tracheocutaneous fistula	2
False passage	2
Infection	5
Suprastomal granulation tissue	1
Bleeding	2
Tracheal stoma enlarging	1
Tracheal stoma stenosis	1

We decannulated 7 patients (14%). The tracheostomy time was before 1 year of age for 27 patients (54%). The others were after 1 year of age.

Discussion

Tracheostomy is a relatively common procedure performed on children in tertiary care centers. The prevalence and type of complications is variable in the literature. Complications ranges from 11% to 51%. Published data on both indications and complications of tracheostomy in pediatric population is limited. Indications for pediatric tracheostomy have changed over years. In the past years, before the vaccines development,the most common cause was infections. According to latest data the main indications in children are upper airway obstruction and prolonged ventilator dependence secondary to chronic lung disease or neuromuscular disorders. (1,4,9,10) We found that long term ventilation was the most common indication for tracheostomy. Robert et al., Duymaz et al., as well as other authors reported similar results (4,5). Akdağ et al. reported 56 patients and Itamoto et al. reported 58 patients that upper airway obstruction was the most common indication. (6,7) Recently, due to advancement in diagnosis, treatment and critical care life expectancy in chronic disease such as neuromusculer and chronic lung disease has increased . Thus, it is not suprising that prolonged ventilation is the most common cause.

Our study showed that the majority of patients had their tracheostomy performed under 1 year of age. In the literature studies reported that almost two thirds of tracheostomies are performed on children under 1 year of age similar to our result. The number of male patients were more than female patients. In the literature, this situation is explained as males being are more susceptible to both congenital and acquired defects.(2,3,9)

Tracheostomized pediatric patients need a carefully long-term care for reducing the early and late complications risks. In the literature, there are a lot of studies about complications associated with adult tracheostomy. But, in pediatric population there is not enough research about tracheostomy. The complications of tracheostomy can be called as early complications if they occur within the first week following placement. Early complications include hemorrhage, tube decannulation, extratracheal air subcutaneous emphysema, pneumothorax, pneumomediastinum and infection. The critically ill patients who have with multiple comorbidities may have late complications due to presence prolonged tracheostomy tube placement. Late complications include hemorrhage, tracheal stenosis, tube decannulation, and fistula formation. We reported only 30 late complications (17 patients, 34%). Robert et al. evaluated 153 children and identified 16 early postoperative complications occurring in 15 children (9.8%) and 72 late complications occurring in 61 children (40%). Their most common early complication

was tube displacement and the most common late complication was granulation tissue similar to other series (3,4,8). In our country, Akdağ et al. have found that complication rates were 14.2% for early and 11.2% for late complitacions in their study. Accidental decannulation was the most common postoperative complication in their study (6). Duymaz et al. reported one early and seven late complications who had only granulation tissue.(5) In contrast to other and our reports they had lower rates of complications. In our study, the granulation tissue was the most common complicatiaon like Robert et al. (4). We did not see any early complications in our study group. This result may be explained because of the tracheostomy procedure was planned in advance and not an emergency procedure..

Obstruction of the lumen of a tracheostomy tube can result from such as factors dried secretions, mucous plugs, clotted blood, and partial tube displacement. It can be seen at any time.(11) We reported 4 patients who had cannula obstruction because of mucous plugs

The incidence of tracheocutaneous fistula in the series is between 3.1% and 57.3%.(9) In our study, two patients (4%) had this complication. In children, the mortality associated with tracheostomy in the literature varied between 0.7% and 6% depending on patient characteristics and follow-up duration (4). Mortality was due to tracheostomy-related accidents, that included accidental decannulation, hemorrhage from tracheostomy, and mucus plugging. We reported only one patient (2%) who died due to hemorrhage from tracheostomy.

The decannulation rate is reported that ranged between 17% and 78%. It is depending on the variety of tracheostomy indications and associated comorbid diseases. Decannulation chance decreases in patients with multiple comorbidity. Our study group consisted of most patients who had chronic neuromusculer disease.

Study Limitations

The limitations of this study the number of included the patients was low due to missing records. Also, most of the patiens had multiple comorbidites. This condition may contribute to the a lack of data.

Conclusion

Regardless of the reason and technique used, several complications have been described. Its prevalence rates may vary in the literature. The reason for this differentiation may be related to the socio-economic level of the family and the responsibility awareness of the parents. The risk of complications decreases in tracheostomies performed under appropriate care and conditions by healtcare team and patients family. Education of parents and caregivers as to the appropriate postoperative management is very important for preventing complications rates.

References

1. Jain MK, Patnaik S, Sahoo B, Mishra R, Behera JR. Tracheostomy in Pediatric Intensive Care Unit: Experience from Eastern India Indian J Pediatr. 2021 May;88(5):445-449.
2. Dal'Astra AP, Quirino AV, Caixêta JA, Avelino MA. .Tracheostomy in childhood: review of the literature on complications and mortality over the last three decades.Braz J Otorhinolaryngol. 2017 Mar-Apr;83(2):207-214
3. Watters KF. Tracheostomy in Infants and Children.Respir Care. 2017 Jun;62(6):799-825.
4. Roberts J, Powell J, Begbie J, Siou G, McLarnon C, Welch A, McKean M, Thomas M, Ebdon AM, Moss S, Agbeko RS, Smith JH, Brodlie M, O'Brien C, Powell S. Pediatric tracheostomy: A large single-center experience.Laryngoscope. 2020 May;130(5):E375-E380
5. Duymaz YK, Sahin Yılmaz A, Onder S, Tarlanova A, Gergin Tinay O. Pediatric Tracheotomy: 5-years of Experiences at a Tertiary Care Center. The Turkish Journal of Ear Nose and Throat 2021;31(3):66-69
6. Akdag M, Baysal Z, Pirinccioglu Gozu A, Gul A, Ozkurt FE, Topcu I. Retrospective Analysis of Pediatric Tracheostomy. Advances in Otolaryngology Volume 2014. Article ID 848262
7. tamoto CH, Lima BT, Sato J, Fujita RR. Indications and Complications of Tracheostomy in Children. Braz J Otorhinolaryngol. 2010 May-Jun;76(3):326-31
8. Fernandez-Bussy S, Mahajan B, Folch E, Caviedes I, Guerrero J, Majid A. Tracheostomy Tube Placement Early and Late Complications.J Bronchology Interv Pulmonol. 2015 Oct;22(4):357-64.
9. Lubianca Neto JF, Castagno OC, Schuster AK. Complications of tracheostomy in children: a systematic review Braz J Otorhinolaryngol. 2022 Nov-Dec;88(6):882-890
10. Ayvaz OD, Celayir A, Çakmak MH.Tracheostomy Experiences in 37 Children during 12 Years: A Retrospective Study. South. Clin. Ist. Euras. 2023;34(1):91-96
11. Bontempo LJ, Manning SL. Tracheostomy Emergencies. Emerg Med Clin North Am. 2019 Feb;37(1):109-119.

Original Article
Eurasian Journal of Critical Care

Evaluation of Etiology in Patients who Admitted to Dermatology Outpatient Clinic with Acute Urticaria

Ulas GUVENC[1], Nazan TASLIDERE[2], Didem DIZMAN[3]
[1] VM Mersin Medikalpark Hospital, Depertment of Dermatology, Istanbul, Türkiye
[2] Istinye University, Faculty of Medicine, Medical Park Gaziosmanpaşa Hospital, Dermatology and Venereology Department, Istanbul, Türkiye
[3] Bezmialem Vakif University, Faculty of Medicine, Dermatology and Venereology Department, Istanbul, Türkiye

Abstract

Background: The purpose of this review is to describe the causes of patients with acute urticaria who admitted dermatology outpatient clinic.

Materials and methods: Adult patients (age > 18 years) who were diagnosed with acute urticaria were included in our study. Our sample consisted of 159 patients with acute urticaria who applied to three different dermatology outpatient clinics between 2021-2022 years. Age, gender, duration of disease, history of angioedema, presence of triggering factor, history of chronic urticaria, and admission to the emergency department were collected retrospectively from records.

Result: A total of 159 patients 102 (%64.1)were female and 57 (%35.8) were male. 82 (51.6%) patients had a triggering factor and no factor was detected in the remaining 77 (48.4%) patients. The total number of patients who admitted to the emergency department was 42 (26.4%). The most common triggering factor was drugs (n=31, 37.8%) followed by infections. The most commonly used drug type was Non-steroidal anti-inflammatory drugs and the most common infection was upper tract ınfections.

Conclusion: Our study revealed that drugs and infections are common causative factors for acute urticaria consistent with the literature. When we examined patients with acute urticaria, especially in the emergency department or dermatology outpatient clinic, we need to keep in mind that detecting possible triggering factors can prevent the disease from recurring or the development of life-threatening symptoms.

Keywords: Emergency Dermatology, Acute urticaria, Triggering.

Introduction

Urticaria is erythematous, edematous, pruritic papules and /or plaques that involve the skin and mucous membranes. These urticarial papules/plaques usually appear suddenly and disappear spontaneously within less than 24 hours. Acute urticaria (AU) is defined by a repeated appearance of wheals with or without angioedema over a period of up to 6 weeks. Acute urticaria is common and the lifetime prevalence is approximately 20%. It can be seen in all age groups. It is one of the most common dermatologic conditions presented to many emergency departments. Because most of the patients who have the first attack of acute urticaria usually visit the emergency department. Acute urticaria is caused by various etiologies such as infections (viruses, bacteria, fungi, and parasites), allergic reactions to foods and drugs, insect bites, or physical stimuli. Sometimes no known cause may be also seen. In the literature, the frequency and variety of infections can be different because of the patient population and geographic region. It is often difficult to determine the exact etiological factor. Identifying the underlying etiology is important for the effectiveness of treatment. Elimination of detectable etiologic causes and avoiding triggers constitute the first step of treatment. (1-6). The purpose of this review is to describe the causes of patients with acute urticaria who are admitted dermatology outpatient clinic.

Materials and Method

Adult patients (age > 18 years) who were diagnosed with acute urticaria were included in our study. The exclusion criteria were as follows: The patients who were under 18 years of age, with a history of urticaria for more than 6 weeks and missing data in files. Our study was retrospective design. The total number of patients who were diagnosed with acute urticaria during this period was set at 520. But our sample consisted of 159 patients with AU who applied to three different dermatology outpatient clinics between 2021-2022

Corresponding Author: Didem DİZMAN **e-mail:** didemdizman1@gmail.com
Received: 06.05.2023 • **Accepted:** 16.05.2023
DOI: 10.55994/ejcc.1293105

Cite this article as: Guvenc U, Taslidere N, Dizman D. Evaluation of Etiology in Patients who Admitted to Dermatology Outpatient Clinic with Acute Urticaria. Eurasian Journal of Critical Care. 2023;5(2): 52-55

years in our country. Age, gender, duration of disease, history of angioedema, presence of triggering factor, history of chronic urticaria, and admission to the emergency department were collected retrospectively from records.

Statistical Analyses: *Descriptive statistical analysis was performed with Microsoft Excel, and the data obtained were calculated as mean and percentage.*

Results

In total, we analyzed 520 patients diagnosed with AU in all three dermatology outpatient clinics. This study included only 159 of these patients because of inclusion criteria. Of a total of 159 patients, 102 (%64.1)were female and 57 (%35.8) were male included in this study. The mean age of the patients was 37.44 ± 13.89 years and the mean duration of urticaria complaints was 13,23 ± 11.70 (range, 1-40 days). Angioedema was present in 10.0% (n = 16) of the patients with urticaria. The total number of patients who were admitted to the emergency department was 42 (26.4%). The presence of a history of chronic urticaria in the past was detected in only 11(6.9%) patients. In evaluated according to the presence of triggering factor, 82 (51.6%) patients had

Drugs (31,%37.8)	NSAII (12, %38.7) Antibiotics (10, %32.2) Beta lactam (9, %90) Doksisiklin (1, %10) Paracetamol (3, %9.6) Others (6,%19.3) Antifungal (1,%5.1) İron(1,%5.1) Contrast agent(1,%5.1) Collajen(1,%5.1) Hormone(1,%5.1) Herbal(1,%5.1)
Infections (27,%32.9)	Upper respiratory tract infection (10,%37.0) Dental infections (5,%18.5) Covid 19 infection(5,%18.5) Urinary infection (3,%11.1) Gastroenteritis (3,%11.1) Cutaneous infections (1,%3.7)
Infections and drugs	9 (%10,9)
Chemical	5(%6.0)
Stress	3(%3.6)
Phyisical	3(%3.6)
Insect bite	2(%'.43)

Table 1: Triggering factors of acute urticaria

Drugs 31(37.8)	NSAID 12 (38.7)	
	Antibotics 10 (32.2)	Beta lactam 9 (90)
		Doksisiklin 1 (10)
	Paracetamol 3 (9.6)	
	Others	Antifungal 1 (5.1)
		Iron 1 (5.1)
		Contrast agent 1 (5.1)
		Collegen 1 (5.1)
		Hormone 1 (5.1)
		Herbal 1 (5.1)
Infections	Upper respiratory tract infection 10 (37)	
	Dental infection 5 (18.5)	
	COVİD-19 5 (18.5)	
	Urinary infection 3 (11.1)	
	Gastroenteritis 3 (11.1)	
	Cutaneous infection 1 (3.7)	
Infection and drugs 9 (10.9)		
Chemical 5 (6)		
Stress 3 (3.6)		
Phyisical 3 (3.6)		
Insect bite 2 (1.43)		

n (%): n= Number, %= percent

triggering factor and no factor was detected in the remaining 77 (48.4%) patients. Of 82 patients, 73(45.9%) patients had at least one triggering factor and 9 (5.6%) patients had more than one. The most common triggering factor was drugs (n=31, 37.8%). Infections were the second most triggering factor, followed by both drug and infection coexistence. All identified triggering factors are listed in Table 1. The most commonly used drug type was Non-steroidal anti-inflammatory drugs (NSAIDs) (%38.7, n = 12), followed by antibiotics (%32.2, n = 10). When infections are classified in order of frequency, the most common infections were upper tract ınfections (%37.0,n=10), followed by dental infections and covid 19 infections.

Discussion

Diagnosis of acute urticaria is made by clinical appearance and anamnesis. Detailed history taking is essential in all urticaria patients. Sometimes it can be confused with other dermatological diseases such as viral eruptions, drug eruptions, connective tissue diseases, and urticarial vasculitis. Therefore, detailed anamnesis is very important both in the emergency department and in the dermatology outpatient clinics. The time between the possible etiologic factor and the onset of the disease and the presence of accompanying systemic symptoms are helpful factors in the differential diagnosis. Acute urticaria usually does not require a diagnostic workup apart from anamnesis. (4-7)

Previous studies reported a high prevalence of females and young to middle-aged patients with acute urticaria similar to our study. Drugs and infections generally cause acute urticaria**.** Acute urticaria may be seen from 1-2 hours or 15 days after oral intake of the drug. If the drugs are given in intravenously, urticaria can occur immediately (8). In our study, the majority of patients had a history of drug use for triggering AU. Melikoğlu et al. evaluated 284 patients with AU between 2017 and 2021 years. They found that the most triggering factor was drug use in our study. And they said that NSAIDs were the most causative drug among other types of drugs like us(4). Losappio et al.investigated 351 adult patients with acute urticaria in the emergency department. In their series, the etiology of acute urticaria was not determined in most of the patients but among triggering factors the drugs were detected in most of the patients(7).In one study by Comert et al., they evaluated 281 patients and found that drugs especially NSAIDs were the most common causative factor(5). The patients use painkillers for many different reasons in daily life. Thus, it may explain why NSAIDs are more than antibiotics in results.

Antibiotics of the beta-lactam group are the most commonly used antibiotics in our country and worldwide. In our study, Thus we do not surprise by this result. Infections such as respiratory infections, dental infections, urinary tract infections, and gastrointestinal tract infections cause acute urticaria. In the literature, some studies have found infections as the most common causative factor for acute urticaria. But in our study, we detected ınfections were the second common causative factor like Melikoğlu et al.and Comert et al. We evaluated all of the patients according to anamnesis without laboratory parameters. This evaluation may have contributed to these results for infections the second most common factor. The frequency and variety of infections can vary based on patient population and geographic region. This should be taken into account when evaluating patients (4,5).

Some patients had drug use and the same time signs of infection. In these patients group, they had upper tract infections and used antibiotics and NSAIDs drugs like Melikoğlu et al.(5) Therefore, a possible factor could not be detected in these patients. In this patient group, determining the time between drug intake and infection may be helpful in diagnosis.

Food-related acute urticarial eruptions are more common in children. We detect foods in the etiology at very lower rates (only two patients) because our study included only the adult population. Santa et al. Said that food was detected as a triggering factor in only 6 children with acute urticaria. Melikoğlun et al. found 9 patiens had food alergy (4-6).

Stress is a potential triggering factor for AU in some studies but the relationship between them is not clear yet. Comert et al. reported that stress was the third common triggering factor for their patients series (5). We detected only 3 patients had a history of stress.

Physical factors can cause acute urticaria. It may develop due to external factors such as pressure, hot and cold. Acute urticaria may be due to insect bites, especially in the pediatric population (8). In our study population, only two patients had a history of insect bites.

In our study, the total number of patients who were admitted to the emergency department was 42. Losappio et al.studied patients who were admitted emergency room for AU. Their some results were like our results. Thus, patient's detailed history is very important for AU either the emergency department or dermatology outpatient clinic. When the cause of the disease is determined in the emergency department and the appropriate approach is taken, the occurrence of other attacks of the patients may be prevented (7).

Study Limitation: *The main limitation of the present study was the retrospective study design. We evaluated all of the patients according to anamnesis without laboratory parameters thus more objective methods are necessary to more clearly determine the etiology of AU.*

Conclusion

In conclusion, our study revealed that drugs and infections are common causative factors for AU consistent with the

literature. Acute urticaria is generally a spontaneously resolving disease but sometimes angioedema can occur. Thus, when we examined patients with acute urticaria, especially in the emergency department or dermatology outpatient clinic, we need to keep in mind that detecting possible triggering factors can prevent the disease from recurring or the development of life-threatening symptoms.

References

1. Sabroe RA. Acute Urticaria. Immunol Allergy Clin North Am. 2014;34(1):11-21 doi: 10.1016/j.iac.2013.07.010.
2. Techasatian L, Phungoen P, Chaiyarit J, Uppala R. Etiological and predictive factors of pediatric urticaria in an emergency context. BMC Pediatr. 2021 ;21(1):92. doi: 10.1186/s12887-021-02553-y.
3. Kolkhir P, Giménez-Arnau AM, Kulthanan K, Peter J, Metz M, Maurer M. Urticaria. Nat Rev Dis Primers. 2022 Sep 15;8(1):61. doi: 10.1038/s41572-022-00389-z.
4. Melikoglu M, Pala E, Bayraktar M. Etiological causes in patients with acute urticaria and angioedema: A cross-sectional study. Allergol Immunopathol (Madr). 2022 Dec 21;50(S Pt 2):15-23. doi: 10.15586/aei.v50iSP2.784.
5. Comert S, Celebioglu E, Karakaya G, Kalyoncu AF. The general characteristics of acute urticaria attacks and the factors predictive of progression to chronic urticaria. Allergol Immunopathol (Madr). 2013 Jul-Aug;41(4):239-45. doi: 10.1016/j.aller.2012.05.007.
6. Santa C, Valente CL, Mesquita M, Lopes J, Cardoso I, Rodrigues J, et al. Acute urticaria in children: from pediatric Emergency Department to allergology consultation at a Central Hospital. Eur Ann Allergy Clin Immunol. 2022 Jul;54(4):168-174. doi: 10.23822/EurAnnACI.1764-1489.204.
7. Losappio L, Heffler E, Bussolino C, Cannito CD, Carpentiere R, Raie A,et al. Acute urticaria presenting in the emergency room of a general hospital. Eur J Intern Med. 2014 Feb;25(2):147-50. doi: 10.1016/j.ejim.2013.11.003.
8. Kayiran MA, Akdeniz N. Diagnosis and treatment of urticaria in primary care. North Clin Istanb. 2019 Feb 14;6(1):93-99. DOI: 10.14744/nci.2018.75010

Original Article
Eurasian Journal of Critical Care

The Effect of White Blood Cell and Platelet Values on Mortality in Patients With Abdominal Aortic Aneurysm

Demirel ME[1], Korkmaz UTK[2], Cetin O[1], Guldal H[3], Bogan M[3]
[1] Bolu Abant İzzet Baysal University, Medicine Faculty, Department of Emergengy Medicine, Bolu, Turkiye
[2] Bolu Abant İzzet Baysal University, Medicine Faculty, Department of Cardiovascular Surgery, Bolu, Turkiye
[3] Düzce University, Medicine Faculty, Department of Emergengy Medicine, Duzce, Turkiye

Abstract

Background: In this study, we aimed to investigate the relationship between preoperative inflammatory markers, length of hospital stay, and mortality in patients with abdominal aortic aneurysm (AAA) who underwent surgical repair.

Materials and methods: A total of 83 patients diagnosed with AAA were included in the study. A complete blood count (CBC) was performed on the first visit (pre-op 0-1 hour) in all patients. Non-ruptured cases (AAA) and ruptured cases (AAA-R) were compared.

Result: 14.5% (n=12) of the patients died. Higher White blood cells and neutrophils were obtained in patients who died than in surviving patients (respectively, p=0.0002, p=0.001). Higher WBC and NALP in AAA-R patients were determined.

Conclusion: WBC and Neu's values were higher in AAA patients who died post-operatively and who were detected rupture pre-operatively but PLT and HB values were similar. Normal or near-normal HB and PLT values that will be seen in the first examination of AAA cases in the emergency department may mislead clinicians or cause them to display a more optimistic attitude.

Keywords: Abdominal aortic aneurysm, Mortality, White blood cell, Neutrophil

Introduction

An abdominal aortic aneurysm (AAA) is a disease that occurs where the aortic wall is weak and is characterized by enlargement of the vessel diameter (>1.5 times). Structural changes in the wall and arterial pressure lead to thinning of the wall and separation of the extracellular matrix [1]. Despite significant advances in diagnostic methods, surgical repair, and anesthesia techniques, aortic aneurysms remain serious and early diagnosis is important [2]. The frequency of diagnosis of aortic aneurysms is increasing day by day due to the increase in life expectancy and the developments in imaging techniques worldwide. AAA is a disease mostly seen in the elderly and men, the most important risk factor being smoking [4]. Other risk factors include atherosclerosis, hypertension, hyperlipidemia, and genetic factors (it has great importance) [4]. AAA is difficult to diagnose clinically and is usually detected during imaging for other purposes. Ultrasound and CT are commonly used diagnostic methods [5, 6]. While the risk of rupture is quite low in small AAAs, it is higher in large AAAs [7]. There are two main methods for the management of AAAs, open surgery and endovascular aneurysm repair (EVAR) [6, 8]. Despite new procedures, mortality in FMF remains high despite improved therapies [9].

Aneurysm formation results from a complex process characterized by infiltration of the aortic wall by inflammatory cells [10]. Neutrophilia has been implicated in several mechanisms potentially relevant for aneurysmal disease, including the secretion of proinflammatory mediators, induction of endothelial cell damage, and prothrombotic states [11, 12]. In addition, neutrophilia has been associated with a significantly increased risk of major adverse cardiovascular events [13].

Lymphopenia is mainly due to the margination and redistribution of lymphocytes within the lymphatic system associated with an increase in apoptosis [14, 15]. Lymphopenia indicates a generalized state of immunosuppression and has been identified as a predictor of mortality in patients with chest pain and a prognostic marker in patients with coronary heart disease or advanced heart failure [14]. However, its significance in patients with AAA has not been adequate-

Corresponding Author: Mustafa BOGAN **e-mail:** mustafabogan@hotmail.com
Received: 05.07.2023 • **Accepted:** 24.08.2023
DOI: 10.55994/ejcc.1323023

Cite this article as: Demirel ME, Korkmaz UTK, Cetin O, Guldal H, Bogan M. The Effect of White Blood Cell and Platelet Values on Mortality in Patients With Abdominal Aortic Aneurysm. Eurasian Journal of Critical Care. 2023;5(2): 56-62

ly studied so far. Several studies have emphasized the role of lymphocytes in the pathogenesis of aneurysms [15]. It revealed an increase in lymphocytes in aneurysms [16].

The platelet/lymphocyte ratio (PLR) represents a marker of the systemic inflammatory response [17, 18]. The relationship with inflammatory indices has been investigated in atherosclerosis and various cardiovascular diseases[19]. In addition, studies are showing that PLR predicts 30-day morbidity in ruptured AAA[20].

Our study aimed to investigate the relationship between preoperative inflammatory markers, length of hospital stay, and mortality in patients with AAA who underwent EVAR or open surgical operation.

Materials and methods

The study was carried out in the Emergency Medicine and Cardiovascular surgery departments of Abant İzzet Baysal University. Ethics committee approval was obtained from the local ethics committee. Records of AAA cases who underwent open or endovascular repair between January 2015 and February 2022 were reviewed retrospectively.

Study Population

A total of 83 patients diagnosed with AAA were included in the study.

Inclusion criteria

Patients with a large aortic diameter (abdominal aortic diameter >5.5 cm for men and >4.5 for women), rupture detected, patients who are scheduled for emergency or elective operation (EVAR or open surgical repair).

Exclusion criteria

Patients with a previous history of hematological disease and malignancy were excluded from the study.

Demographic and clinical characteristics of the patients were noted, taking into account the patient's statements, medical records, and treatment. In all patients, the diagnosis was confirmed by computed tomography scanning, which is the gold standard diagnostic method. The patients were divided into two groups ruptured or non-ruptured aneurysms. Complete blood count(CBC) was performed on the first visit (pre-op 0-1 hour) in all patients, WBC: White Blood Cell, HGB: Hemoglobin, PLT: Platelet, RDW: Red Cell Distribution width LYM: Lymphocyte, MONO: Monocytes, NEU: Neutrophil, PDW: Platelet Distribution Width, MPV: Mean Platelet Volume, PCT: Procalcitonin, CRP: C Reactive Protein ALBM: Albumin, NLR: Neutrophil/Lymphocyte ratio, LMR: Lymphocyte /Monocytes ratio, PLR: Platelet/Lymphocyte ratio V, RDW*MP: Red cell distribution width/Mean Platelet Volume, PDW*MPV: Platelet Distribution width/Mean Platelet Volume, CRP/Alb: C Reactive Protein /Albumin values were recorded. PLR is the number of Platelets/ lymphocyte count. NLR is the neutrophil count/ lymphocyte count. The NALP score was calculated with the formula neutrophil x albumin x lymphocyte/platelet. Postoperative results such as mortality and length of stay were recorded. Data were collected using electronic or manual files. Imaging data were collected from the hospital information system. Non-ruptured cases (AAA) and ruptured cases (AAA-R) were compared.

Statistical Analysis

CBC parameters and index values of the patients in both groups were analyzed with the Mann-Whitney U test. The relationship with the length of stay was evaluated with the Spearman (rho) correlation coefficient. The performances of CBC parameters and indices for mortality estimation and diagnosis discrimination were investigated by ROC analysis. AUC values were compared with the DeLong test. R (version 4.1.0) program pROC (version 1.17.0.1) package was used for ROC analysis. Statistical software SPSS version 23 (SPSS Inc., Armonk, NY) was used for all other analyses. The significance level was determined as $p < 0.05$.

Results

The median age of AAA patients included in the study was 71 (63-77) and 80.7% (n:67) were male. There was a weak negative correlation was found between age and MPV. Higher hemoglobin [10.15 (9.32-12.53), 11.7 (10.4-13.8)], CRP [2.6 (0.23-14.25), 17.4 (3.9-35)] and CRP/Alb ratio [respectively,] in male patients than in female patients. 0.1 (0.01-0.4), 0.45 (0.1-1.09)] (respectively, p=0.029, p=0.030, p=0.048) (Table 1).

The patients presented with abdominal pain [n=34 (40%)], chest pain [and=27 (32.5%)], back pain [n=13 (15.7%)] and other reasons [n=9 (11.8%)]. 21 (25.3%) patients applied to the emergency department [rupture was detected in 15 of the patients (71.4% of ED visits), 10 of these patients died), and others admitted to the cardiovascular surgery outpatient clinic. 31 (37.3%) of the patients were treated with EVAR, while the others underwent open surgical procedures.

14.5% (n=12) of the patients died. Higher WBC [9.68 (7.61-14.9), 16.34 (12.91-22.88), respectively) and NEU (7.38 [4.57-12.6), 13.65 (8.78-20.24, respectively)] were obtained in patients who died than in surviving patients (respectively, p=0.0002, p=0.001). NALP [1.8 (0.9-2.8, 4.7 (3.4-5), respectively)] values were higher in patients who died than in surviving patients, while PLR [151.7 (99.4-247.2), 105.7 (75.8-133.3, respectively)] values were lower (p= 0.00004, p=0.008) (Table 2). The area under the curve (AUC) values were found to be 0.871 for NALP, 0.832 for WBC, 0.793 for NEU, and 0.739 for PLR (Figure 1). Although the highest AUC value was obtained for NALP, the difference between the AUC values of WBC, NEU and PLR

Table 1: Comparative data on genders

	Age		Gender		
	r	**p**	**Female** (n=16) Med (IQR)	**Male** (n=67) Med (IQR)	**p**
Hemogram					
WBC	-0.08	0.491	9.3 (5.85-15.26)	10.8 (8.03-16.26)	0.315
HGB	-0.01	0.927	10.15 (9.32-12.53)	11.7 (10.4-13.8)	**0.029**
PLT	-0.04	0.701	219.5 (160.25-245.5)	188 (153-241)	0.583
RDW	0.17	0.114	15.65 (14.03-16.88)	15.4 (13.7-16.6)	0.544
LYM	0.01	0.930	1.5 (0.52-2.32)	1.5 (0.96-2.03)	0.926
MONO	-0.12	0.284	0.59 (0.4-1)	0.64 (0.45-0.94)	0.858
NEU	-0.09	0.431	6.98 (4.4-12.02)	9.18 (4.99-13.9)	0.258
PDW	0.01	0.913	15.9 (11.13-17.43)	17.3 (12.7-18.2)	0.078
MPV	**-0.26**	**0.019**	9.64 (7.52-10.7)	8.64 (7.55-10.4)	0.544
PCT	-0.21	0.054	0.18 (0.15-0.23)	0.17 (0.13-0.22)	0.347
CRP	0.07	0.542	2.6 (0.23-14.25)	17.4 (3.9-35)	**0.030**
Albm	-0.18	0.103	31.7 (30-38)	36 (32-41)	0.164
Ratios					
NLR	-0.03	0.755	6.27 (2.17-14.94)	7.34 (2.82-12.63)	0.844
LMR	0.12	0.291	2.73 (1.02-4.09)	2.49 (1.3-3.59)	0.917
CLR	0.05	0.665	5.18 (0.16-15.28)	10.5 (2.08-32.81)	0.100
PLR	-0.05	0.658	161.36 (95.21-391.24)	135.14 (98.54-205.26)	0.426
Indexes					
RDW*MPV	-0.21	0.057	138.94 (126.89-162.35)	137.5 (118.4-147)	0.356
PDW*MPV	0.06	0.567	239.59 (177.78-284.68)	271.44 (178.56-295.48)	0.329
CRP/Alb	0.09	0.392	0.1 (0.01-0.4)	0.45 (0.1-1.09)	**0.048**
NALP	-0.07	0.542	1.59 (0.81-2.59)	2.09 (1.14-3.93)	0.170
Length of stay*	**-0.26**	**0.028**	17.5 (10-22.25)	11 (6-16)	**0.016**

IQR: Interquartile range (25th-75th percentiles).Mann-Whitney u testi, **r:** Spearman (rho) correlation coefficient.
WBC: White Blood Cell, HGB: Hemoglobin, PLT: Platelet, RDW: Red Cell Distribution width LYM: Lymphocyte , MONO: Monocytes, NEU: Neutrophil, PDW: Platelet Distribution Width, MPV: Mean Platelet Volume , PCT: Procalcitonin , CRP: C Reaktif Protein ALBM: Albumın, NLR: Neutrophil/Lymphocyte ratio , LMR: Lymphocyte /Monocytes ratio , PLR: Platelet/Lymphocyte ratio , RDW*MPV: Red cell distribution width/Mean Platelet Volume, PDW*MPV: Platelet Distribution width/Mean Platelet Volume, CRP/Alb: C Reaktif Protein /Albumın

were not statistically significant (DeLong test: p=0.238, p=0.128, p=0.073, respectively). The cut-off points for the classification of surviving and deceased patients were determined as 2.99 for NALP, 12.24 for WBC, 7.19 for NEU, and 144.52 for PLR (Table 3).

The median length of stay in surviving patients is 12 (7-18) days. There was a weak negative correlation between the age of these patients and their length of stay (r=-0.26, p=0.028). This period. Female patients were approximately 7 days [17.5 (10-22.25) - 11 (6-16)] and were hospitalized longer than males (p=0.016) (Table 1). There was a very weak negative correlation between hospitalization times and hemoglobin and platelet values, and a weak positive correlation between MPV and RDW*MPV values (r=-0.24, p=0.043, r=-0.24, p=0.044, r=0.30, p). =0.010, r=0.356, p=0.002) (Table 4).

Table 2: Effect of all parameters on mortality

	All Cases		
	Discharge (n=71)	**Exitus** (n=12)	**p**
Age, Year, Med (IQR)	69 (62-77)	72 (70.25-77.25)	0.193
GEnder - Male, n (%)	57 (80.28)	10 (83.33)	1.000[a]
Hemogram Med (IQR)			
WBC	9.68 (7.61-14.9)	16.34 (12.91-22.88)	**0.0002**
HGB	11.6 (10.20-13.30)	10.9 (7.84-13.08)	0.271
PLT	197 (157-240)	200.5 (140.5-253.25)	0.646
RDW	15.4 (13.8-16.6)	15.8 (14.38-16.75)	0.560
LYM	1.41 (0.79-2.03)	1.73 (1.22-2.61)	0.091
MONO	0.64 (0.45-0.91)	0.64 (0.46-1.14)	0.766
NEU	7.38 (4.57-12.6)	13.65 (8.78-20.24)	**0.001**
PDW	17.2 (12.7-18.1)	16.8 (11-19.2)	0.887
MPV	8.64 (7.56-10.4)	9.6 (7.02-10.85)	0.693
PCT	0.17 (0.14-0.22)	0.17 (0.1-0.26)	0.641
CRP	10 (2.2-35.7)	19 (1.68-26.23)	0.776
Albm	36 (31.5-41)	33.2 (26.48-37)	0.075
Ratios Med (IQR)			
NLR	7.1 (2.7-13.3)	10.1 (3.9-11.7)	0.560
LMR	2.5 (1.3-3.3)	2.7 (1.1-5.3)	0.468
CLR	8.5 (1.7-50.9)	12.3 (1.2-17.6)	0.669
PLR	151.7 (99.4-247.2)	105.7 (75.8-133.3)	**0.008**
Indexes Med (IQR)			
RDW*MPV	137.5 (122.5-147.6)	139.6 (117.3-164.3)	0.578
PDW*MPV	270.8 (178.6-289)	260.1 (175.4-310.1)	0.641
CRP/Alb	0.3 (0.1-1.1)	0.5 (0.1-0.8)	0.948
NALP	1.8 (0.9-2.8)	4.7 (3.4-5)	**0.00004**

IQR: Interquartile range (25th-75th percentiles).
Mann-Whitney U testi, [a]: Fisher'ın Kesin (Exact) testi.

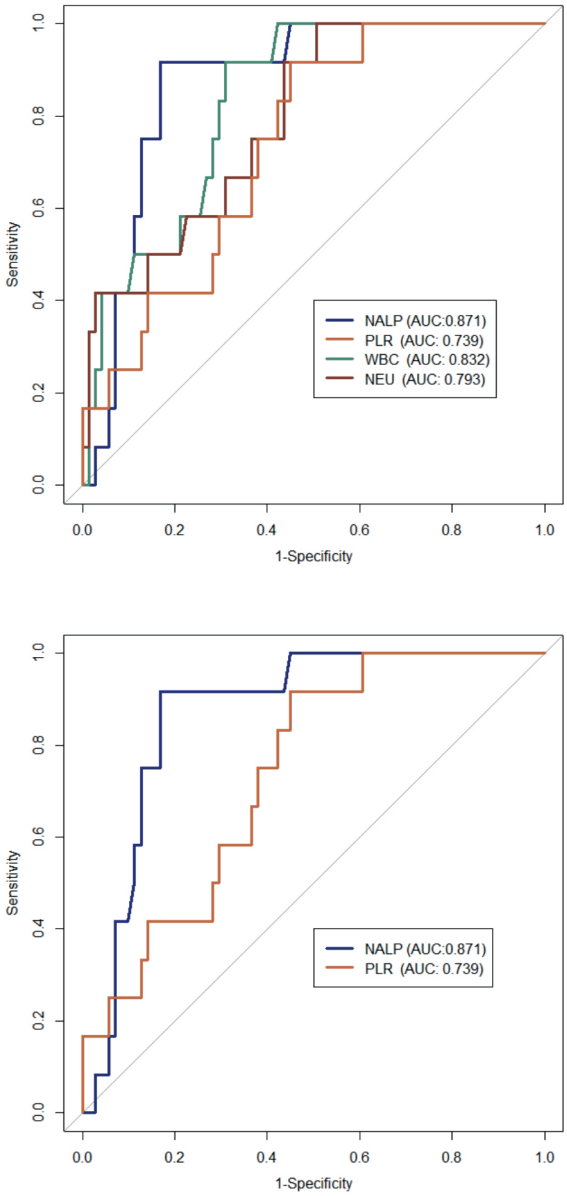


Figure 1: ROC curves and AUC values for mortality classification

There was no difference in age and gender between the AAA and AAA-R diagnostic groups, (p=0.563, p=0.724, respectively). It was observed significantly more frequently in AAA-R patients (n=10, 66.7%) than in others (p<0.01) (Table 1). Higher WBC and NALP in AAA-R patients were determined (Table 5).

Discussion

In this study, we investigated the relationship between preoperative CBC parameters, the ratios, and indices of these parameters, and postoperative mortality in AAA patients. We found higher WBC and neutrophil counts in patients with preoperative rupture and patients with postoperative death. However, we found that hemoglobin and platelet counts did not help detect preoperative rupture and predict postoperative mortality.

An aneurysm can induce an inflammatory response by leukocytosis and platelet activation [21]. Platelets can induce thrombosis and also release inflammatory molecules. Neutrophils can promote inflammatory responses, cause damage to the blood-brain barrier, and release inflammatory mediators [12]. It can interact with monocytes, platelets, and endothelial cells to support inflammatory and prothrombotic pathways [22]. In contrast, lymphocytes play an important

Table 3: Cut-off points and performance measures for mortality classification

	Cut-off	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
NALP	2.99	91.7	83.1	47.8	98.3
PLR	144.52	91.7	54.9	25.6	97.5
WBC	12.24	91.7	69.0	33.3	98.0
NEU	7.19	100	49.3	25.0	100.0

Table 4: The relationship of hemogram parameters, rates and indices with length of stay in discharged patients

	All Cases	
	r	p
Hemogram		
WBC	-0.02	0.859
HGB	**-0.24**	**0.043**
PLT	**-0.24**	**0.044**
RDW	-0.04	0.768
LYM	-0.12	0.319
MONO	-0.09	0.472
NEU	-0.01	0.939
PDW	-0.10	0.426
MPV	**0.30**	**0.010**
PCT	-0.04	0.711
CRP	-0.09	0.433
Albm	-0.19	0.111
Ratios		
NLR	0.08	0.503
LMR	0.002	0.990
CLR	-0.07	0.577
PLR	0.01	0.909
Indexes		
RDW*MPV	**0.356**	**0.002**
PDW*MPV	-0.06	0.642
CRP/Alb	-0.08	0.500
NALP	-0.02	0.849

r: Spearman (rho) correlation coefficient.

role in the anti-inflammatory response [15]. In a study conducted by Ko et al., it was shown that mortal cases in Open Repair of Abdominal Aortic Aneurysms had higher neutrophil counts and lower hemoglobin values preoperatively [23]. Nejim et al. showed that patients with a preoperative WBC value of >10000 had a larger aneurysm and were more mortal [24]. Domanovits et al. found that the CRP and WBC values of patients with ruptured AAA were not different, but hemoglobin values were lower [25]. In another study, a cohort of 252 patients undergoing thoracic endovascular aortic repair for degenerative AAA revealed that preoperative leukocytosis independently predicted the risk of late mortality [26]. In this study, higher WBC and neutrophil counts were detected in ruptured AAA cases and post-op mortal cases. However, no difference was observed between hemoglobin levels and platelet counts.

It is known that neutrophils also play a role in coagulation apart from their antimicrobial activities [25]. Activated neutrophils exhibit important procoagulant properties; neutrophils stimulate coagulation by the release of tissue factor; it has been found that they can activate platelets, factor X, factor XII, and prothrombin, and contribute to the stabilization of the fibrin clot [25]. It is seen that neutrophils play an active role in limiting bleeding that develops in this way. This information may explain the higher neutrophil monitoring in ruptured patients detected in our study.

Although there was a correlation between mortality and low PLR in our study, high PLR and decreased LMR were associated with poor clinical outcomes in some other aneurysmatic diseases [27]. Ntalouka MP et al. in the group of patients who underwent EVAR, NLR and PLR values were found to be significant in showing postoperative kidney damage and major adverse cardiovascular events (MACE) [17]. Lareyre et al. reported that high NLR values may be an indicator for a ruptured thoracic aortic aneurysm [28]. In this study, which included 83 patients with FMF, no significant difference was observed in terms of preoperative PLR value in terms of postoperative hospital stay.

Conclusion

Although the incidence and prevalence of abdominal aortic aneurysm has decreased in the last years globally, it is one of the life-threatening emergencies [29]. Therefore, new markers are needed to determine the prognosis. WBC and Neu's values were higher in AAA patients with preoperative rupture, but PLT and HB values were similar. High mortality was observed in patients with rupture. WBC and Neu's values were higher in AAA patients who died post-operatively,

Table 3: Comparison of cases with and without rupture

	AAA (n=68)	AAA-R (n=15)	p
Age, Year, Med (IQR)	70 (61.2-78)	71 (68-75)	0.563
Gender - Male, n (%)	54 (79.4)	13 (86.7)	0.724[a]
Mortality, n (%)	2 (2.9)	10 (66.7)	**<0.00001**[a]
Hemogram, Med (IQR)			
WBC	9.66 (7.61-14.11)	17.3 (13.1-23.82)	**0.00005**
HGB	11.65 (10.13-13.53)	10.9 (9.9-12.6)	0.362
PLT	186 (153.25-237.5)	234 (170-255)	0.142
RDW	15.35 (13.9-16.58)	15.8 (13.7-16.6)	0.795
LYM	1.43 (0.8-1.98)	1.63 (1.14-2.7)	0.100
MONO	0.64 (0.45-0.93)	0.59 (0.45-1.32)	0.767
NEU	7.23 (4.63-10.96)	15.2 (9.7-21)	**0.0001**
PDW	17.15 (12.7-18.08)	17.4 (10.2-18.9)	0.657
MPV	8.72 (7.6-10.5)	8.99 (6.94-9.85)	0.459
PCT	0.17 (0.14-0.21)	0.2 (0.13-0.26)	0.442
CRP	11.35 (2.2-35.93)	16.7 (2.2-22.1)	0.519
Albm	9.66 (7.61-14.11)	17.3 (13.1-23.82)	0.145
Ratios, Med (IQR)			
NLR	6.72 (2.62-13.22)	9.62 (3.49-11.8)	0.344
LMR	2.53 (1.23-3.52)	2.48 (1.43-3.72)	0.661
CLR	8.69 (1.76-52.25)	11.95 (0.77-15.08)	0.485
PLR	146.84 (98.77-239.12)	124.29 (85.89-172.66)	0.115
Indexes, Med (IQR)			
RDW*MPV	138.56 (122.98-150.09)	129.69 (115.2-147)	0.326
PDW*MPV	268.66 (179.23-288.91)	288.84 (144-313.74)	0.485
CRP/Alb	0.28 (0.06-1.33)	0.4 (0.09-0.7)	0.636
NALP	1.75 (0.9-2.83)	4.71 (2.09-6.17)	**0.0001**

IQR: Interquartile range (25th-75th percentiles).
Mann-Whitney U test, a: Fisher's Exact tests.

but PLT and HB values were similar. Normal or near-normal HB and PLT values that will be seen in the first examination of AAA cases in the emergency department may mislead clinicians or cause them to display a more optimistic attitude. Therefore, high WBC and Neu values should alert clinicians to possible rupture or mortality.

References

1. Michel JB, Martin-Ventura JL, Egido J, et al. Novel aspects of the pathogenesis of aneurysms of the abdominal aorta in humans. Cardiovasc Res. 2011;90(1):18-27.
2. Kessler V, Klopf J, Eilenberg W, Neumayer C, Brostjan C. AAA Revisited: A Comprehensive Review of Risk Factors, Management, and Hallmarks of Pathogenesis. Biomedicines. 2022;10(1):94.
3. Wei L, Bu X, Wang X, Liu J, Ma A, Wang T. Global Burden of Aortic Aneurysm and Attributable Risk Factors from 1990 to 2017. Glob Heart. 2021;16(1):35.
4. Svensjö S, Björck M, Gürtelschmid M, Djavani Gidlund K, Hellberg A, Wanhainen A. Low prevalence of abdominal aortic aneurysm among 65-year-old Swedish men indicates a change in the epidemiology of the disease. Circulation. 2011;124(10):1118-1123.
5. Macaluso CR, McNamara RM. Evaluation and management of acute abdominal pain in the emergency department. Int J Gen Med. 2012;5:789-797.
6. Chaikof EL, Dalman RL, Eskandari MK, et al. The Society for Vascular Surgery practice guidelines on the care of patients with an abdominal aortic aneurysm. J Vasc Surg. 2018;67(1):2-77.e2

7. Parkinson F, Ferguson S, Lewis P, Williams IM, Twine CP; South East Wales Vascular Network. Rupture rates of untreated large abdominal aortic aneurysms in patients unfit for elective repair. J Vasc Surg. 2015;61(6):1606-1612.
8. Patel SR, Ormesher DC, Smith SR, et al. A risk-adjusted and anatomically stratified cohort comparison study of open surgery, endovascular techniques and medical management for juxtarenal aortic aneurysms-the UK COMPlex AneurySm Study (UK-COMPASS): a study protocol. BMJ Open. 2021;11(11):e054493
9. Dahl M, Frost L, Søgaard R, Klausen IC, Lorentzen V, Lindholt J. A population-based screening study for cardiovascular diseases and diabetes in Danish postmenopausal women: acceptability and prevalence. BMC Cardiovasc Disord. 2018;18(1):20.
10. Davis FM, Rateri DL, Daugherty A. Mechanisms of aortic aneurysm formation: translating preclinical studies into clinical therapies. Heart. 2014;100(19):1498-1505.
11. Bhutta H, Agha R, Wong J, Tang TY, Wilson YG, Walsh SR. Neutrophil-lymphocyte ratio predicts medium-term survival following elective major vascular surgery: a cross-sectional study. Vasc Endovascular Surg. 2011;45(3):227-231.
12. Siminiak T, Flores NA, Sheridan DJ. Neutrophil interactions with endothelium and platelets: possible role in the development of cardiovascular injury. Eur Heart J. 1995;16(2):160-170.
13. Haumer M, Amighi J, Exner M, et al. Association of neutrophils and future cardiovascular events in patients with peripheral artery disease. J Vasc Surg. 2005;41(4):610-617.
14. Ommen SR, Gibbons RJ, Hodge DO, Thomson SP. Usefulness of the lymphocyte concentration as a prognostic marker in coronary artery disease. Am J Cardiol. 1997;79(6):812-814.
15. Zhang L, Wang Y. B lymphocytes in abdominal aortic aneurysms. Atherosclerosis. 2015;242(1):311-317.
16. Lv BJ, Li J, Cheng X. T lymphocytes and aortic aneurysms. Sci China Life Sci. 2014;57(8):795-801.
17. Ntalouka MP, Nana P, Kouvelos GN, et al. Association of Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratio with Adverse Events in Endovascular Repair for Abdominal Aortic Aneurysm. J Clin Med. 2021;10(5):1083
18. Yıldız S, Kazğan A, Tabara M, Atmaca M. The Relationship Between Impulsivity Level and Neutrophil / Lymphocyte Ratio, Platelet/ Lymphocyte Ratio and Mean Platelet Volume in Individuals Diagnosed with Gambling Disorder. Medical Records. 2021; 3(3): 177-183.
19. Balta S, Celik T, Mikhailidis DP, et al. The Relation Between Atherosclerosis and the Neutrophil-Lymphocyte Ratio. Clin Appl Thromb Hemost. 2016;22(5):405-411.
20. Lareyre F, Carboni J, Chikande J, et al. Association of Platelet to Lymphocyte Ratio and Risk of 30-Day Postoperative Complications in Patients Undergoing Abdominal Aortic Surgical Repair. Vasc Endovascular Surg. 2019;53(1):5-11.
21. Kasius KM, Frijns CJ, Algra A, Rinkel GJ. Association of platelet and leukocyte counts with delayed cerebral ischemia in aneurysmal subarachnoid hemorrhage. Cerebrovasc Dis. 2010;29(6):576-583.
22. Yun S, Yi HJ, Lee DH, Sung JH. Systemic Inflammation Response Index and Systemic Immune-inflammation Index for Predicting the Prognosis of Patients with Aneurysmal Subarachnoid Hemorrhage. J Stroke Cerebrovasc Dis. 2021;30(8):105861.
23. Ko DE, Yoon HJ, Nam SB, Song SW, Lee G, Ham SY. Preoperative Neutrophil to Lymphocyte Ratio, Platelet to Lymphocyte Ratio, and Mean Platelet Volume as Predictors of 1-Year Mortality in Patients Undergoing an Open Repair of Abdominal Aortic Aneurysms: A Retrospective Study. J Clin Med. 2021;10(22):5410.
24. Nejim B, Chau M, Ramirez Castello C, Aziz F, Flohr TR. Preoperative leukocytosis among female patients predicts poor postoperative outcomes following endovascular aneurysm repair for intact infrarenal abdominal aortic aneurysms. J Vasc Surg. 2021;74(6):1843-1852.e3.
25. Morotti A, Phuah CL, Anderson CD, et al. Leukocyte Count and Intracerebral Hemorrhage Expansion. Stroke. 2016;47(6):1473-1478.
26. Chung J, Corriere MA, Veeraswamy RK, et al. Risk factors for late mortality after endovascular repair of the thoracic aorta. J Vasc Surg. 2010;52(3):549-555.
27. Tao C, Wang J, Hu X, Ma J, Li H, You C. Clinical Value of Neutrophil to Lymphocyte and Platelet to Lymphocyte Ratio After Aneurysmal Subarachnoid Hemorrhage. Neurocrit Care. 2017;26(3):393-401.
28. Lareyre F, Raffort J, Le D, et al. High Neutrophil to Lymphocyte Ratio Is Associated With Symptomatic and Ruptured Thoracic Aortic Aneurysm. Angiology. 2018;69(8):686-691.
29. Çelik K, Demirel ME. Aort anevrizmaları. Yürümez Y.(Editor). Cardiovascular Emergencies. 1. Edition. Ankara: Türkiye Klinikleri; 2022. p.96-102.

Letter to Editor
Eurasian Journal of Critical Care

The New Biomarkers for Acute Coronary Syndrome

Ozkan A[1], Ozdemir S[1],
[1] Department of Emergency Medicine, University of Health Sciences Bagcilar Training and Research Hospital, Istanbul, Turkey

Dear editor

We read your article prepared by Doğan and Taşlıdere, titled "Investigation of Panic Attack Patients Presenting to the Emergency Department of Bezmialem Vakıf University with Chest Pain" and published in the first issue of your magazine in 2023, with great interest (1). We would like to thank the authors and editorial board for this article, guides the effective use of resources in health. We would like to thank again to the authors for their efforts to clarify this situation, that is a clinical dilemma in the emergency department and that clinicians find difficult to manage We congratulate them. However, we would like to point out a few points that will contribute to the discussion of the study.

The diagnosis of acute coronary syndrome (ACS) is made by history, electrocardiography (ECG) and positive cardiac markers. However, the fact that all of them are negative does not exclude the diagnosis of ACS. Interestingly, 2-5% of patients with ACS are improperly discharged from the emergency department each year (2). This situation leads to long follow-up and examination processes in the emergency services, thus causing both time and financial loss. For this reason, many ACS risk scoring systems have been developed. By identifying low-risk patients in a short time, they can be discharged faster, which results in a reduction in the intensity and financial losses in the emergency department. At the same time, it allows high-risk patients to be identified in a short time and to give these patients more time and opportunities.

EDACS (Emergency Chest Pain Score Evaluation), Vancouver chest pain scoring system, HEART (History, ECG, Age, Risk factors, Troponin), TIMI (Thrombolysis in Myocardial Infarction) and GRACE (Global Registry of Acute Coronary Events) are among the scoring systems used to calculate the risk of 30-day major adverse cardiac events in the patient population presenting with chest pain in the emergency department. The purpose of risk scoring is to both predict possible complications and guide emergency physicians for safe and rapid discharge of patients (3).

Clinical evaluation is not sufficient to diagnose or exclude ACS in patients presenting to the emergency department with chest pain without ST segment elevation on ECG. Therefore, laboratory tests are useful in the evaluation of ACS. The most used biomarker in the evaluation of ACS is troponin. Cardiac troponins are proteinaceous molecules in the cytoplasm of cardiac myositis cells and required for cardiac contraction (4).

SCUBE-1 molecules are stored in alpha granules in inactive platelets. After activation by thrombin, it translocates to the platelet surface. It is secreted in the form of small soluble fragments and is incorporated into the thrombus. SCUBE-1 accumulation was detected immunohistochemically in the subendothelial matrix of advanced atherosclerotic lesions in humans. SCUBE-1 is thought to be a new platelet adhesion molecule (5). Recent studies have revealed that SCUBE-1 expression is increased in patients with acute coronary syndrome and acute large vessel atherothrombotic stroke. Immunohistochemically it has been shown that SCUBE-1 is collected in the subendothelial matrix of the atheroma plaque (6). However, the biological function of SCUBE-1 in atherosclerosis or thrombus formation is still unclear. In a study from Taiwan, they found that SCUBE1 was increased in patients with ACS (7). On the other hand, in a study from Turkey, it was reported that there was no relationship with SCUBE1 in patients with unstable angina pectoris (8).

Aspirosin is a fasting hormone that promotes hepatic glucose production. Aspirosin in plasma crosses the blood-brain barrier and directly activates orexigenic agouti-related peptide neurons in a cyclic adenosine monophosphate-dependent pathway. This signaling results in appetite stimulation and the urge to accumulate fat and body weight in a gamma aminobutyric acid-dependent manner of down-

Corresponding Author: Abuzer Ozkan **e-mail:** ebuzerozkan@gmail.com
Received: 16. 05. 2023 • **Accepted:** 24.08.2023
DOI: 10.55994/ejcc.1297849

Cite this article as: Ozkan A, Ozdemir S. The New Biomarkers for Acute Coronary Syndrome. Eurasian Journal of Critical Care. 2023;5(2): 63-64

stream anorexigenic pro-opiomelanocortin neurons (9). In a study from Turkey, it is reported that aspirosin can be used as a biochemical marker in the evaluation of prognosis and mortality in ischemic heart disease (10).

Meteorin like is a poorly characterized small molecular weight secreted protein produced by activated macrophages. The main cellular sources are epithelial cells in the mucosa and fibroblasts in the skin (11). In another study from Turkey, it is found that negative correlation between the level of meteorin like and troponin in the emergency department (12).

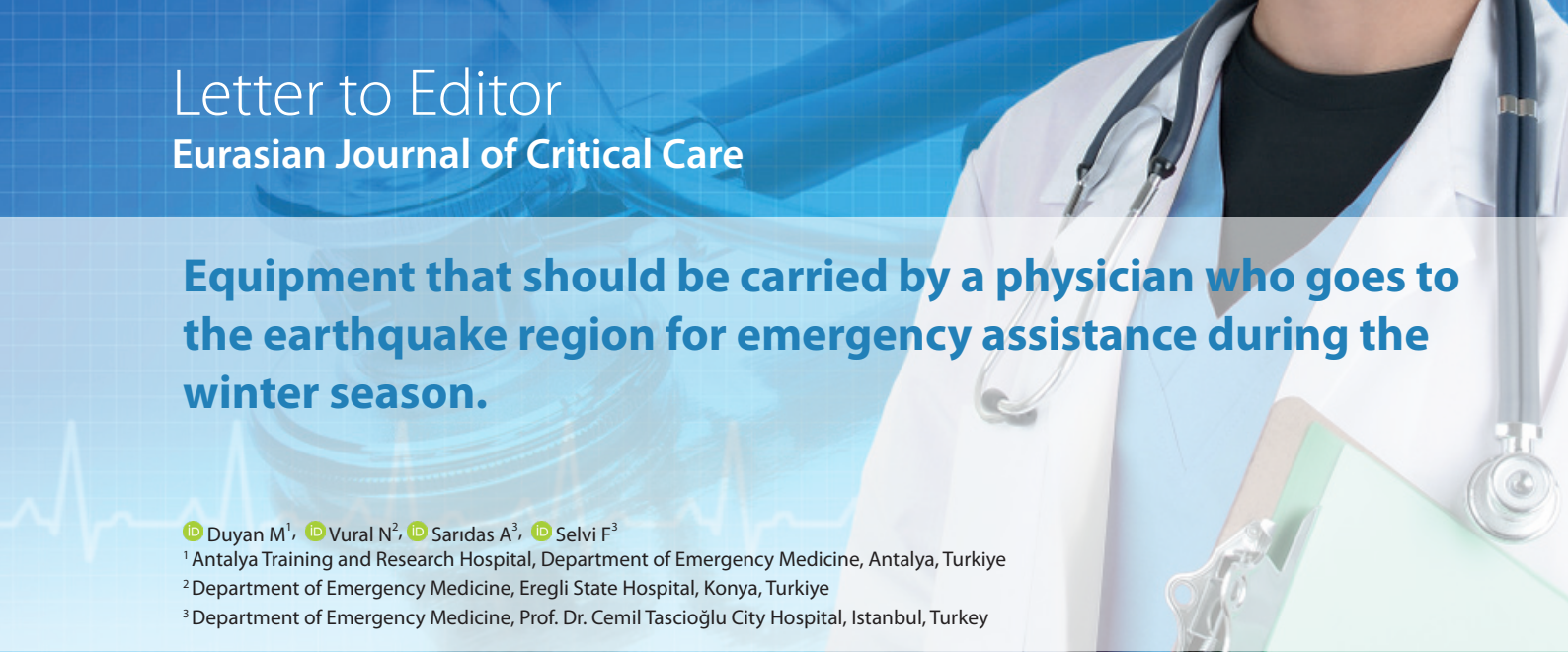
Ischemia-modified albumin (IMA) occurs when changes in cellular size caused by ischemia reduce the binding capacity of the N-terminal region of albumin for cobalt, copper, and nickel. Because of this mechanism, changes in the level of IMA in clinical pictures with ischemia have been a frequently researched subject in recent years. Thus, IMA is a newly defined marker of ischemia (13). In another study from India, it is recommended that Ima can be used as a role out marker of ACS in patients with inconclusive diagnosis in emergency department (14).

As a result, ACS is an important cause of mortality and morbidity in developed and developing societies. Researchers should be encouraged to develop new biomolecules and markers and treatment options in this area.

References

1. Dogan AB, Taslidere B. Investigation of Panic Attack Patients Presenting to the Emergency Department of Bezmialem Vakıf University with Chest Pain. Eurasian j Crit Care. 2023; 5(1): 13-16.
2. Sonmez E, Turkdogan KA, Karabacak M, Civelek C, Yilmaz C, Ozer OF, et al. The diagnostic role of signal peptide-C1r/C1s, Uegf, and Bmp1-epidermal growth factor domain-containing protein 1 in non-ST-elevation acute coronary syndrome. Am J Emerg Med. 2015 Jan;33(1):21-4. doi: 10.1016/j.ajem.2014.09.047.
3. Dur A, İsmailoğlu Z, İsmailova M, Akbay D, Uysal O, Metin H, et al. Relationships among markers of inflammation, neutrophil-to-lymphocyte ratio, and syntax severity score in the early phase of acute coronary syndrome. Bezmialem Sci. 2017;5(2):56-60. doi: 10.14235/bs.2016.790.
4. Kumar A, Cannon CP. Acute coronary syndromes: diagnosis and management, part I. Mayo Clin Proc. 2009 Oct;84(10):917-38. doi: 10.1016/S0025-6196(11)60509-0.
5. Yılmaz C, Gülen B, Sönmez E, Akbay D, Söğüt Ö, Özdemir S, Özer ÖF. Serum SCUBE-1 Levels and Return of Spontaneous Circulation Following Cardiopulmonary Resuscitation in Adult Patients. Avicenna J Med. 2022 Sep 5;12(3):148-153. doi: 10.1055/s-0042-1755389.
6. Akça HŞ. SCUBE-1 as a novel predictor of thromboembolic event. J Exp Clin Med. 2023; 40(1): 197-198.
7. Dai DF, Thajeb P, Tu CF, Chiang FT, Chen CH, Yang RB, et al. Plasma concentration of SCUBE1, a novel platelet protein, is elevated in patients with acute coronary syndrome and ischemic stroke. J Am Coll Cardiol. 2008 Jun 3;51(22):2173-80. doi: 10.1016/j.jacc.2008.01.060.
8. Özkan A, Sönmez E, Özdemir S, Özer F, Muharrem N, Gülen B, et al. The Diagnostic Value of SCUBE1 in Unstable Angina Pectoris Patients. Eurasian J Emerg Med. 2016;15:167-171. doi: 10.5152/eajem.2016.83997.
9. Keser MG, Ünüsan N. Asprosin ve Glikoz Metabolizması Üzerine Etkileri. Turk J Diab Obes. 2021; 5(1): 89-95. doi: 10.25048/tudod.840549.
10. Algin A, Özdemir S, Akça HŞ, Hökenek NM, Kokulu K, Erdoğan MÖ, et al. The assessment of plasma asprosin levels in acute coronary artery disease and its correlation with HEART score. J Clin Med Kaz. 2022;19(2):43-7. doi: 10.23950/jcmk/11939.
11. Uzun M, Ilhan YS, Bozdag A, Yilmaz M, Artas G, Kuloglu T. Asprosin, irisin, and meteorin-like protein immunoreactivity in different stages of colorectal adenocarcinoma. Pathol Res Pract. 2023 May;245:154432. doi: 10.1016/j.prp.2023.154432.
12. Giden R, Yasak IH. Meteorin-like protein decreases in acute coronary syndrome. Eur Rev Med Pharmacol Sci. 2023 Jan;27(1):208-214. doi: 10.26355/eurrev_202301_30873.
13. Can Ü, Yosunkaya Ş. A New Marker for Ischemia: Ischemia-modified Albumin. Koşuyolu Heart J. 2017;20(2):148-152. doi: 10.5578/khj.10257.
14. Bhakthavatsala Reddy C, Cyriac C, Desle HB. Role of "Ischemia Modified Albumin" (IMA) in acute coronary syndromes. Indian Heart J. 2014 Nov-Dec;66(6):656-62. doi: 10.1016/j.ihj.2014.12.005.

Letter to Editor
Eurasian Journal of Critical Care



Equipment that should be carried by a physician who goes to the earthquake region for emergency assistance during the winter season.

Duyan M[1], Vural N[2], Sarıdas A[3], Selvi F[3]
[1] Antalya Training and Research Hospital, Department of Emergency Medicine, Antalya, Turkiye
[2] Department of Emergency Medicine, Eregli State Hospital, Konya, Turkiye
[3] Department of Emergency Medicine, Prof. Dr. Cemil Tascioğlu City Hospital, Istanbul, Turkey

Dear editor

It was experienced on February 6, 2023, by two consecutive earthquakes in southern and central Turkey and northern and western Syria 1. It occurred at 04:17 Turkey Time (01:17 UTC), 34 km (21 mi) west of Gaziantep city, with a minimum moment magnitude scale of Mw 7.8 and a maximum Mercalli intensity XI (Extreme). An unusually strong Mw 7.7 aftershock centered 95 km (59 mi) north-northeast in Kahramanmaraş province nine hours after the mainshock2. Matching the 1939 Erzincan earthquake, possibly surpassed only by the 1668 North Anatolian earthquake, it is one of the strongest earthquakes ever experienced in Turkey3,4. According to the latest data, it resulted in at least 50,500 deaths and 107,204 injuries in the ten most affected provinces in Turkey, and these numbers are increasing with each passing hour5. At least 13.5 million people and 4 million buildings were affected. Thousands of people were trapped under the rubble when the buildings collapsed5. Rescue efforts in this earthquake, named " "the disaster of the century," are still ongoing, and the number of injured and killed is expected to rise.

Turkish Disaster and Emergency Management Presidency (AFAD) personnel, Turkish Armed Forces personnel, and the civilian population fought hard to save those under the rubble and the injured. In addition, volunteer physicians and other health personnel from almost every region of the country within the body of the National Medical Rescue Team (UMKE) immediately went to the disaster area to intervene in the rescued injured.

In this article, we wanted to discuss the personal and medical equipment that a physician who goes to an earthquake-prone area should bring.

It is very difficult to obtain these equipment from the disaster area. We can put this equipment into a classification. The equipment required for patient care is as follows; stethoscope, trauma scissors, flashlight, and headlamp (for power outage situation), safety glasses, scrubs (spare), mask, medical gloves, regularly used drugs (such as decongestants, antibiotics, analgesics), battery, hospital ID, notepad, pen.

Personal equipment that is not necessary for patient care is as follows; backpack (with name tag), power bank (to keep in touch), list of basic contact numbers, thermos (for tea and coffee), enough ready-made food to last at least three days (dry foods, energy, and protein bars, instant sachet soup, etc.), water bottle, fork, spoon, glass, garbage bag, whistle, work gloves, ear protection, sleeping bag and mat (tent if possible), personal hygiene items (soap, toothbrush, toothpaste, wet wipes, napkins). In addition, since the earthquake occurs in the winter season, winter boots, thermal clothes, thick coats, thin raincoats, berets, scarves, gloves, loose underwear and socks, spare clothes, and hand-face moisturizing creams are required. Since banks and automatic teller machines do not work in the region, some cash should be kept. It is useful to download the maps to your smartphone beforehand, as there is a high probability of not having internet access. The climate of the region and, if any, the recommendations of the teams that went to the area before you should be considered.

The data in this article have been written based on personal experience. It will guide the physicians who will be sent to the region urgently in future disasters and prevent them from being caught unprepared. Furthermore, it will meet the needs of field physicians until professional equipment support arrives.

References

1. Live updates: Turkey-Syria earthquake kills thousands. https://web.archive.org/web/20230207044338/https://www.cnn.com/middleeast/live-news/turkey-earthquake-latest-020623/index.html. [accessed 13 Feb 2023]

Corresponding Author: Murat Duyan **e-mail:** drmuratduyan@gmail.com
Received: 14. 04. 2023 • **Accepted:** 04.07.2023
DOI: 10.55994/ejcc.1283562ORCID

Cite this article as: Duyan M, Vural N, Sarıdas A, Selvi F. Equipment that should be carried by a physician who goes to the earthquake region for emergency assistance during the winter season. Eurasian Journal of Critical Care. 2023;5(2): 65-66

2. Larson E, Ekström G, Nettles M (2011) Global CMT Search Results. https://www.globalcmt.org/cgi-bin/globalcmt-cgi-bin/CMT5/form?itype=ymd&yr=2023&mo=2&day=6&oyr=2023&omo=2&oday=7&jyr=1976&jday=1&ojyr=1976&ojday=1&otype=nd&nday=1&lmw=7&umw=10&lms=0&ums=10&lmb=0&umb=10&llat=-90&ulat=90&llon=-180&ulon=180&lhd=0&uhd=1000&lts=-9999&uts=9999&lpe1=0&upe1=90&lpe2=0&upe2=90&list=0. [accessed 13 Feb 2023]

3. Impact of Turkey earthquake on local population, economy will be "massive": Expert - CNA. https://web.archive.org/web/20230206155841/https://www.channelnewsasia.com/world/turkey-syria-earthquake-aftershocks-local-population-economy-impact-3257776. [accessed 13 Feb 2023]

4. Historic Worldwide Earthquakes. https://web.archive.org/web/20090825081330/http://earthquake.usgs.gov/regional/world/historical.php/. [accessed 13 Feb 2023]

5. 2023 Turkey–Syria earthquake - Wikipedia. https://en.wikipedia.org/wiki/2023_Turkey–Syria_earthquake#Damage_and_casualties. [accessed 14 april 2023]

Case Report
Eurasian Journal of Critical Care

A Case Report of Kounis Syndrome Developing Anaphylaxis Secondary to Vitamin B and C Infusion

Tanriogen I[1], Akgun DE[1], Safak O[1]
[1] Balıkesir University, Department of Cardiology, Balıkesir, Turkiye

Abstract

Kounis syndrome is a condition characterized by temporary coronary spasm, reduction in coronary blood flow and myocardial ischemia by activated mast cells as a result of an abnormal immune reaction to a drug or molecule. It is also called allergic angina and allergic myocardial infarction. It was first described by Kounis and Zarvas in 1991(1). Kounis syndrome can be observed in all age groups regardless of the history of coronary artery disease. Kounis syndrome may occur due to environmental factors such as drugs, intracoronary stent implantation, foods, insect bites, bee stings, pollen, latex exposure etc. In our case report, acute coronary syndrome occurring during anaphylaxis secondary to vitamin B and C infusion, which is frequently used in clinical practice, will be explained.

Case Report

A 26-year-old female patient with no known disease was admitted to the emergency department with complaints of widespread body pain, weakness, and fatigue. The Covid 19 PCR test performed on the patient was negative. Vitamin B complex and vitamin C infusion were started in saline solution for hydration and support. The patient described numbness in the arm, feeling unwell, flushing on the face, and difficulty in breathing within the first minute after starting the infusion. The infusion was terminated, and the patient was monitored. Progression in dyspnea was observed. As the patient was hypotensive and tachycardic, 0.5 mg adrenaline was administered intramuscularly with the preliminary diagnosis of anaphylaxis. Simultaneously, the patient developed vomiting and palpitation. In the ECG, T wave negativity was observed in d2-d3 avF and V3-6. (figure 1) The control ECG, which was taken at the 15th minute after the medical treatment, was found to be normal. (Figure 2) IV hydration was applied to the patient who was hypotensive and tachycardic in the follow-ups. Progressive increase in troponin values was observed. The 1st troponin was 62 ng/L, the 3rd hour troponin 1100 ng/L, and the 6th hour troponin 1200 (upper limit of normal 11.6 ng/L) Kounis syndrome was considered in the patient with ECG change, left arm pain and increased troponin. 300 mg acetyl salicylic acid, 600 mg clopidogrel and 6000 IU enoxoparin were administered in medical treatment. In the follow-up of the patient in the coronary intensive care unit, angina and arrhythmia did not develop, and no additional changes were detected in the control ECGs. A decrease in troponin value was observed at the 14th hour (650 ng/L) and at the 30th hour troponin 140 ng/L. The echocardiographic evaluation was totally normal. The patient, who had no known atherosclerotic history, was discharged after 72 hours of monitored follow-up in the coronary intensive care unit without coronary angiography due to the patient's disapproval. No additional pathology or symptoms were detected in the outpatient follow-up at the 1st month.

Discussion

Vitamin supplements are commonly used, often without a doctor's recommendation. Triggering anaphylaxis and subsequent progression to acute coronary syndrome in a patient without any known allergy history, risk factors and disease shows the importance of preventing unnecessary use of these molecules. Although the pathophysiology of Kounis

Corresponding Author: : İbrahim Tanrıöğen **e-mail:** ibrahimtanriogen@hotmail.com
Received: 07.05.2023 • **Accepted:** 10.08.2023
DOI: 10.55994/ejcc.1293720

Cite this article as: Tanriogen I, Akgun DE, Safak O. A Case Report of Kounis Syndrome Developing Anaphylaxis Secondary to Vitamin B and C Infusion. Eurasian Journal of Critical Care. 2023;5(2): 67-69

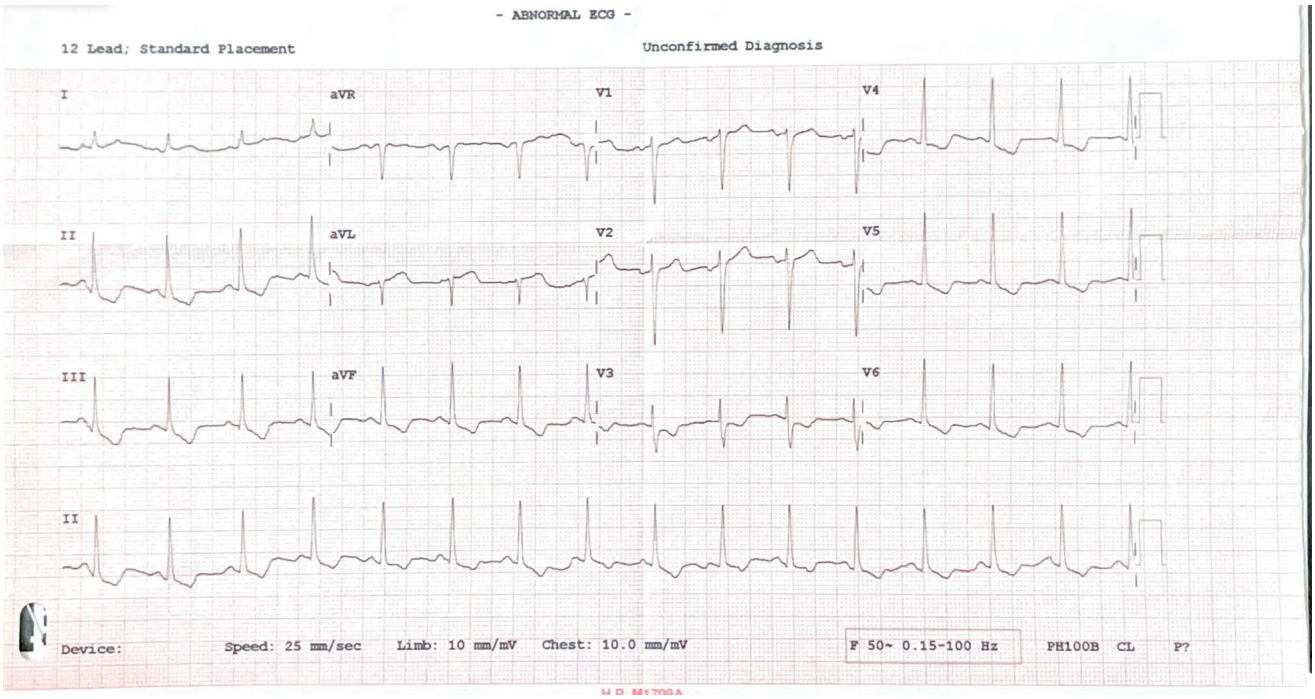


Figure 1

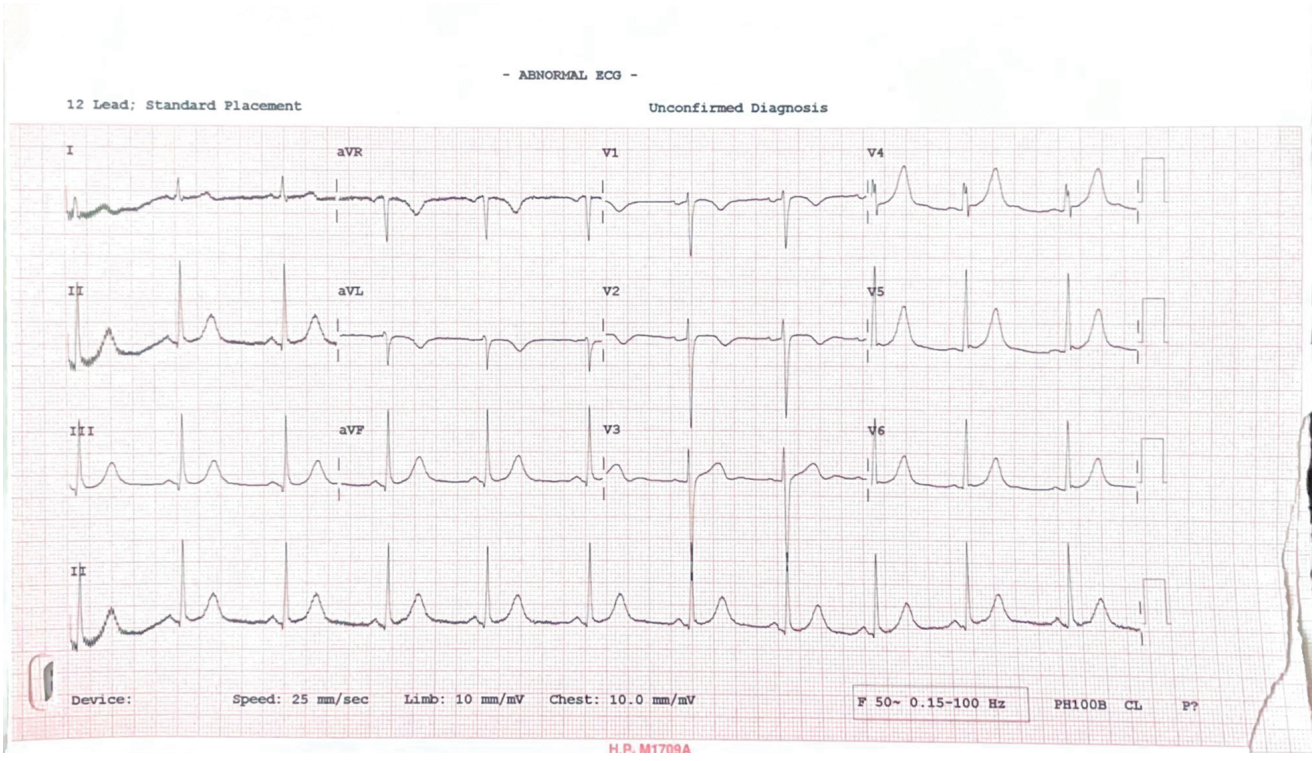


Figure 2

syndrome is not clearly defined, the most likely cause is activation of mast cells secondary to allergic stimuli and triggering of coronary spasm, plaque rupture and plaque erosion by vasoactive mediators such as histamine, tryptase, chymase, paf, cytokines, prostaglandins and leukotrienes released from these cells is considered (2). In addition, hypotension, which is one of the main clinical consequences of anaphylaxis, also plays a triggering role in the decrease in coronary blood flow and triggers myocardial ischemia. Angina, ECG changes, myocardial wall movement disorders, and cardiac enzyme elevations, especially troponin, can be detected in patients with acute coronary syndrome.

Kounis syndrome is basically classified into 3 types: Type 1 kounis syndrome is also called allergic vasospastic angina. Patients have normal coronary arteries or noncritical coronary artery disease. Depending on the severity of the clinic, an increase in troponin can be detected. In the treatment, nitroglycerin and calcium channel blockers can be used in patients who do not have hypotension in addition to intramuscular adrenaline (3,4). Type 2 kounis syndrome is an acute coronary syndrome triggered by coronary spasm or plaque erosion in individuals with asymptomatic coronary artery disease. In type 3 Kounis syndrome, stent thrombosis is observed. Activation of mast cells, which are densely located in atherosclerotic areas, triggers thrombosis (5). If the thrombus is stained with Giemsa and Hematoxylin eosin, the presence of eosinophils and mast cells can be demonstrated. Thrombus aspiration or stent implantation is the appropriate treatment option in these patients (6). Intramuscular adrenaline is recommended for the initial treatment, especially in patients presenting with anaphylaxis. However, the use of intravenous adrenaline is also recommended in patients with persistent symptoms despite intramuscular adrenaline therapy. It should be kept in mind that the effect of adrenaline is limited, especially in patients using beta-blockers, and the use of glucagon should be considered. In our case, we describe a 26-year-old young patient who developed anaphylaxis and concurrent acute coronary syndrome symptoms in the first minute of the infusion. In our patient, intramuscular adrenaline was administered for anaphylaxis due to the development of hypotension, tachycardia and airway obstruction. After symptomatic treatment, the patient's complaints regressed. Simultaneously, an improvement was detected in the ECG. Due to limited access to mast cell activation markers such as histamine, tryptase, and chymase some tests could not be performed. Angiography could not be performed because the patient's complaints regressed and did not accept coronary angiography. Although it is currently thought that the patient has Type 1 Kounis syndrome, the possibility of alpha receptor-mediated coronary vasoconstriction secondary to the effect of adrenaline cannot be excluded. In the case report of a 15-year-old who developed angioedema after exposure to cats and dust but developed ST elevations on the ECG after iv administration of epinephrine, it could not be distinguished whether the cardiac pathology was secondary to an allergic reaction or due to a side effect of epinephrine, similar to our case. However, while cardiac symptoms developed after epinephrine administration in this case, the fact that the onset of allergic reaction and the onset of cardiac symptoms were simultaneous in our case shows that our case is primarily compatible with Kounis Syndrome (7). Adrenaline, one of the cornerstones of anaphylaxis treatment, acts on both alpha- and beta-adrenergic receptors, causing vasoconstriction, positive chronotropic and inotropic effects, and bronchodilation. It also suppresses histamine and histamine-related mediators released from mast cells. However, it may cause transient myocardial ischemia with its coronary vasoconstriction effect. At this stage, a great dilemma is observed in making the treatment decision of the patients. The use of nitroglycerin and calcium channel blockers is recommended due to their effects on coronary vasospasm, especially in Kounis syndrome cases without hypotension (8).

References:

1. Kounis, N. G., and G. M. Zavras. "Histamine-induced coronary artery spasm: the concept of allergic angina." The British journal of clinical practice 45.2 (1991): 121-128.
2. Brown, Simon GA. "Cardiovascular aspects of anaphylaxis: implications for treatment and diagnosis." Current opinion in allergy and clinical immunology 5.4 (2005): 359-364.
3. Kounis, Nicholas G. "Kounis syndrome: an update on epidemiology, pathogenesis, diagnosis and therapeutic management." Clinical Chemistry and Laboratory Medicine (CCLM) 54.10 (2016): 1545-1559.
4. Nikolaidis, Lazaros A., Nicholas G. Kounis, and Alan H. Gradman. "Allergic angina and allergic myocardial infarction: a new twist on an old syndrome." The Canadian journal of cardiology 18.5 (2002): 508-511.
5. Chen, Jack P., et al. "Drug-eluting stent thrombosis: the Kounis hypersensitivity-associated acute coronary syndrome revis-ited." JACC: Cardiovascular Interventions 2.7 (2009): 583-593.
6. Fassio, Filippo, and Fabio Almerigogna. "Kounis syndrome (allergic acute coronary syndrome): different views in allergo-logic and cardiologic literature." Internal and emergency medicine 7.6 (2012): 489-495.
7. Ongun, Ebru Atike, et al. "Diagnostic Dilemma in Allergy and Coronary Syndromes: Kounis Syndrome or Adrenaline Effect?." Cocuk Acil ve Yogun Bakım 5.1 (2018): 25.
8. Giovannini, Mattia, et al. "Kounis syndrome: a clinical entity penetrating from pediatrics to geriatrics." Journal of Geriatric Cardiology: JGC 17.5 (2020): 294.

Case Report
Eurasian Journal of Critical Care

A Rare Mechanical Cause of Extubation Failure After Short-Term Intubation and Outgoing with the Stridor Clinic: A Case Report

Ernur D[1], Gokmen AN[1]
[1] Dokuz Eylul University Faculty of Medicine, Department of Internal Diseases, Izmir, Turkiye
[2] Dokuz Eylul University Faculty of Medicine, Department of Anesthesia and Reanimation, Izmir, Turkiye

Abstract

Stridor after extubation is generally a clinical symptom that may indicate laryngeal edema or vocal cord injury due to intubation, and hoarseness may accompany this.The presence of stridor may cause reintubation due to upper airway obstruction, a risk factor for patient mortality and morbidity.Laryngeal edema and vocal cord damage are mostly seen as the cause of stridor.In this case, OFTP (Obstructive fibrinous tracheal pseudomembrane) and stridor in the lower line of the vocal cords, which are rarely seen during short-term intubation, are presented.

Keywords: Obstructive fibrinous tracheal pseudomembrane;post extubation stridor;fiberopticbronchoscopy;medical intensive care unit

Introduction

Stridor may cause reintubation due to upper airway obstruction, which is a risk factor for patient mortality and morbidity[1,2].The incidence of stridor and hoarseness after extubation ranges from %1.5 to %26.3 [3].Studies have shown that female gender, long-term intubation status, increased number of intubation attempts, younger age, trauma, and being hospitalized in the ICU (Intensive care unit)are risk factors for the development of laryngeal edema stridor after extubation[4-7].OFTP (Obstructive fibrinous tracheal pseudomembrane) is a rare and little- known complication of endotracheal intubation that presents with stridor.In this case, OFTP in the lower line of the vocal cords and stridor, which are rarely seen during short-term intubation, are presented. Written informed consent was obtained from the patient for the case report.

Case report:

A 42-year-old female patient was admitted to the Anesthesia ICU in the postoperative period after McKeown esophagectomy operation by the general surgery clinic due to esophageal squamous cell carcinoma.After the routine examinations of the patient who was followed up with right lung tube thoracostomy and arterial blood gas detection, sedative agents were discontinued and spontaneous breathing trials were performed.The patient was extubated on the 5th postoperative day without any problems. After extubation, the patient was followed up with an 8L/min oxygen mask with SaO2 %95 and in the arterial blood gas,pH:7.48 PaO2:60mmHg PaCO2:36 mmHg HCO3:26 mmol/L SaO2:%94. It was observed that approximately 48 hours after the patient's extubation, respiratory distress was observed, and accessory respiratory muscles were involved in respiration.The arterial blood gas of the patient whose respiratory rate was 20-22/min,showed pH:7.52 PaCO2 :41 mmHg PaO2 :58 mmHg HCO3 :33 mmol/L, SaO2: %.94. Intravenous 1mg/kg methylprednisolone, inhaler beta-2 agonist and inhaler steroid treatment was started to the patient. However, in the follow-up, the patient's oxygen demand and respiratory distress increased significantly despite medical treatment,and thorax computed tomography was performed. Computed tomography sections showed a lesion that could be a pseudomembrane extending towards the lumen, narrowing the tracheal lumen by more than 50%, just below the vocal cords (Figure 1).

FOB (Fiberoptic bronchoscopy procedure) was planned for the patient in the presence of current clinical and radiological findings.The respiratory rate of the patient was 28-

Corresponding Author: Damla Ernur **e-mail:** drdamlaernur@gmail.com
Received: 09.06.2023 • **Accepted:** 15.08.2023
DOI: 10.55994/ejcc.1312037

Cite this article as: Ernur D, Gokmen AN. A Rare Mechanical Cause of Extubation Failure After Short-Term Intubation and Outgoing with the Stridor Clinic: A Case Report Eurasian Journal of Critical Care. 2023;5(2): 70-73

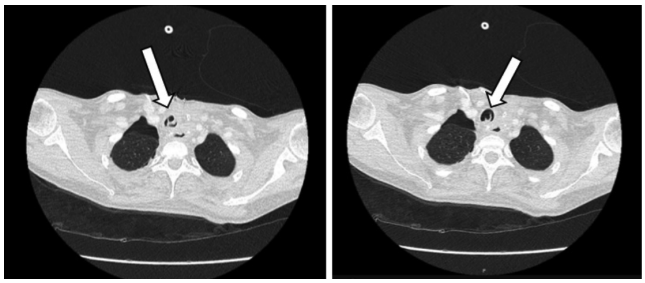


Figure 1: Pseudomembrane tissue in computed tomography

30/min, and the patient had significant dyspneic.The arterial blood gas of the patient showed that pH: 7.24 PaCO2 :79 mmHg PaO2 :72 mmHg HCO3 :27mmol/L SaO2:%88. There was a change in consciousness of the patient and elective intubation was decided. During the intubation of the patient with the intubation tube numbered 8.0 under the video laryngoscope, a yellow-grayish hard lesion was seen in the camera of the laryngoscope located just below the vocal cords, which prevented the advancement of the intubation tube and narrowed the trachea (Figure 2).

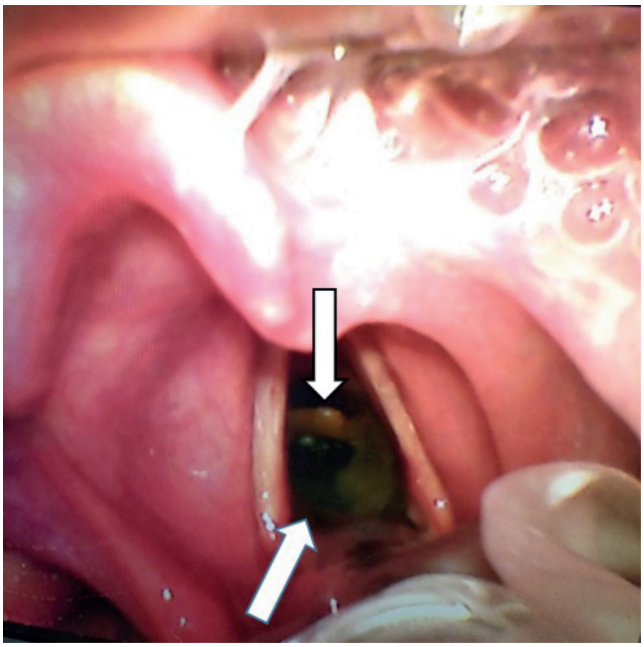


Figure 2: On the video laryngoscope camera, the appearance of a yellow-grayish hard pseudomembrane narrowing the trachea in the posterior location just below the vocal cords

The patient was intubated with the numbered 7.0 intubation tube.In order for the existing lesion not to progress to the lower part of the trachea, the balloon of the tube was inflated just below the vocal cords, and mechanical ventilation was supported.In the chest X-ray taken after intubation, it was observed that the left lung was total atelectatic(Figure 3).

In the FOB performed with the chest diseases clinic, intense purulent secretion and plug in the left lung bronchial structures were seen and aspirated.The lesion under the vocal cord was tried to be aspirated by FOB.Forceps were used

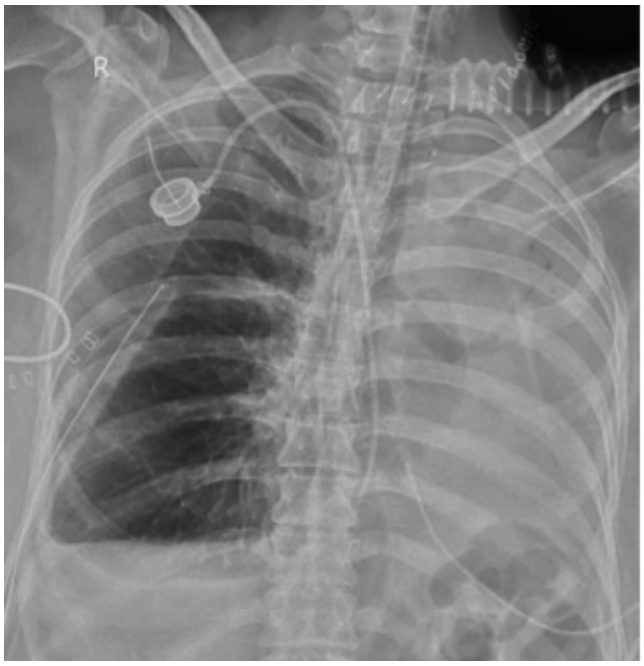


Figure 3: A/P (Antero-Posterior) chest X-ray on the left, atelectasis

to remove the lesion, which had a hardness and consistency that could not be aspirated.It was decided to terminate the FOB procedure and the patient was taken to the rigid bronchoscopy.With the rigid bronchoscopy, 5x1 cm lesion was excised from just below the vocal cord and sent to pathology (Figure 4,5).

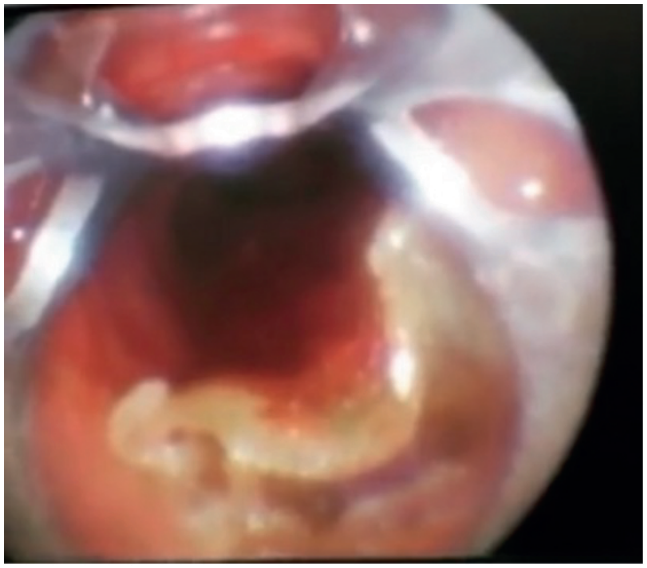


Figure 4: Image of pseudomembrane adhered to the posterior wall of the trachea in rigid bronchoscopy

Pathological examination revealed inflamed fibrin tissue and squamous cell debris.After the procedures,in the chest X-ray of the patient whose hypoxia and hypercarbia had resolved, it was observed that the atelectatic area was totally opened (Figure6).The patient who was extubated,was fol-

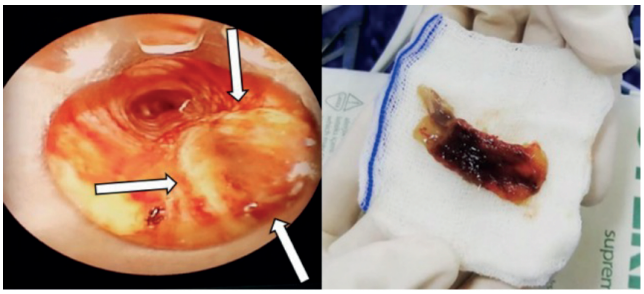


Figure 5: The appearance of the lesion after removal

lowed up under 4L/min simple oxygen mask treatment and transported to the service.After the follow-ups in the service, the patient was discharged without any problem.

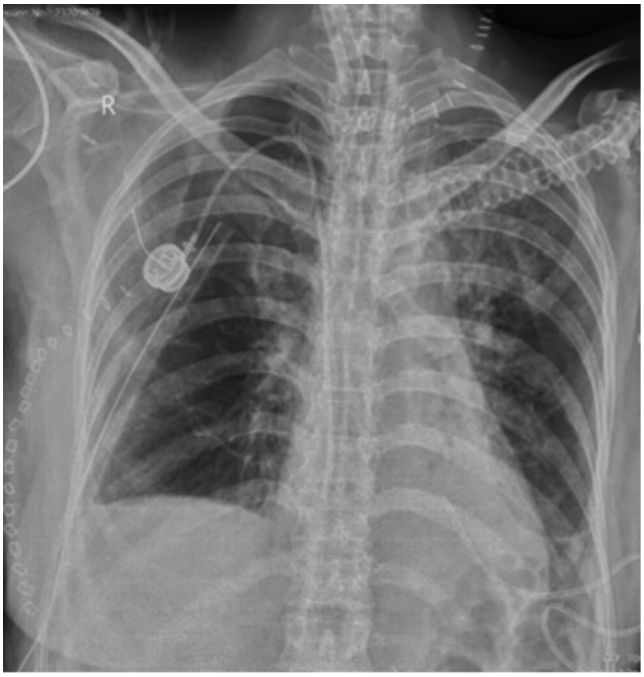


Figure 6: A/P chest X-ray taken after removal of the lesion

Discussion

Stridor after extubation are generally clinical signs that may indicate laryngeal edema or vocal cord injury due to intubation.Stridor may cause reintubation due to upper airway obstruction, with stridor after extubation ranges from %35 to %69 [8,9].In our case , after esophageal surgery,the patient was extubated in the intensive care unit as a result of suitable extubation conditions and stridor developed after extubation.

The stridor clinic of OFTP is a rare and little-known complication of endotracheal intubation.It was first reported in 1981[10].Although chest radiography and tomography are used in the diagnosis and treatment of OFTP , bronchoscopy is often preferred.In one of systematic review; rigid bronchoscopy was used in %46.3 of cases and FOB was used in %31.5 of cases in the treatment of 53 cases with OFTP development.While rigid bronchoscopy was used more frequently in adults (%56.4) to relieve airway obstruction, FOB was used more frequently in pediatric cases (%60)[11]. Lins et al.reported the use of bronchoscopy in 22 of 24 cases diagnosed with OFTP (rigid bronchoscopy in 18 cases, FOB in 4 cases) [12].In one of the review where 58 cases with signs of obstruction due to tracheal pseudomembrane were reported after extubation between 1981 and 2015, it was found that rigid bronchoscopy was used in 31 cases and FOB was used in 18 cases[13].Kang et al. primarily used FOB for the removal of the lesion in the case of OFTP they reported, and after their failure, they removed the lesion with rigid bronchoscopy[14].In our case,we primarily used FOB, but we failed because the pseudomembrane was highly adherent to the tracheal wall.

Then, we ensured the complete removal of the pseudomembrane with rigid bronchoscopy.OFTP is thought to represent the first step in a process that can lead to tracheal stenosis and is caused by ischemic injury from cuff pressure. Despite the use of a low-pressure high-volume cuff with intensive monitoring of cuff pressure in our case, we have no explanation for why OFTP occurs. We have routinely used high-volume, low-pressure endotracheal tubes for many years. After the endotracheal tube is in place, the cuff is inflated with enough air to reach a leak-free spot. Following placement of the endotracheal tube, the cuff pressure is adjusted to less than 25 cm H2O by controlling the amount of cuff leakage, as excessive cuff pressure can cause ischemia of the tracheal mucosa. The concern with increasing cuff pressure above this threshold is that mucosal blood flow is compromised, eventually resulting in subglottic stenosis. Cuff pressure is checked daily.In our case, OFTP developed at a level that endangered airway safety even during a short intubation period.It was determined that the pathology causing stridor was a pseudomembrane consisting of inflamed fibrin tissue and squamous cell fragments at the subglottic level.The lesion, which caused more than %50 intraluminal stenosis in the trachea, resulted in reintubation by causing significant dyspnea in the patient.Due to the current secretions, left lung atelectasis was added to the clinical situation in the patient.In conclusion, OFTP, a rare but potentially life-threatening complication of endotracheal intubation, requires rapid diagnosis (FOB) and treatment (usually rigid bronchoscopy).It is thought that avoiding long-term intubation of patients, avoiding high cuff pressure levels during intubation, spontaneous breathing trials and effective secretion excretion will reduce the mechanical obstruction caused by post-extubation secretions.

Ethics approval and consent to participate:*The approval has been received.*

Consent for publication: *The approval has been received*

Availability of data and materials: *The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.*

Competing interests**:** *The authors declare that they have no competing interests"*

Funding: *None*

Authors' contributions: *Damla Ernur has significant contributions to the design of the work and the acquisition, analysis or interpretation of data for the study, final approval of the version to be published. She is responsible for all aspects of the work to ensure that questions regarding the accuracy or completeness of any part of the work are properly investigated and resolved.*

Ali Necati Gökmen has significant contributions to the design of the work and the acquisition, analysis or interpretation of data for the study, final approval of the version to be published. He is responsible for all aspects of the work to ensure that questions regarding the accuracy or completeness of any part of the work are properly investigated and resolved.All authors read and approved the final manuscript.

Acknowledgements: *We thank the anesthesia intensive care team for their support in treatment of the case.*

Reference

1. Frutos-Vivar, F., Esteban, A., Apezteguia, C., González, M., Arabi, Y., Restrepo, M. I., Gordo, F., Santos, C., Alhashemi, J. A., Pérez, F., Peñuelas, O., & Anzueto, A. (2011).Outcome of reintubated patients after scheduled extubation. Journal of critical care, 26(5), 502–509. https://doi.org/10.1016/j.jcrc.2010.12.015
2. Miltiades, A. N., Gershengorn, H. B., Hua, M., Kramer, A. A., Li, G., & Wunsch, H. (2017). Cumulative probability and time to reintubation in U.S. ICUs. Critical care medicine, 45(5), 835-842. https://doi.org/10.1097/CCM.0000000000002327
3. Pluijms, W.A., van Mook, W.N., Wittekamp, B.H. et al. Postextubation laryngeal edema and stridor resulting in respiratory failure in critically ill adult patients: updated review. Crit Care 19, 295 (2015). https://doi.org/10.1186/s13054-015-1018-2
4. Zochios, V., Protopapas, A. D., & Valchanov, K. (2015). Stridor in adult patients presenting from the community: An alarming clinical sign. Journal of the Intensive Care Society, 16(3), 272–273. https://doi.org/10.1177/1751143714568773
5. Lilienstein JT, Davis JW, Bilello JF, Dirks RC. risk factors associated with post -extubation stridor in the trauma intensive resort unit The American Journal of Surgery.2016;212:379-83. https://doi.org/10.1016/j.amjsurg.2016.02.010.
6. Vallés, J., Millán, S., Díaz, E., Castanyer, E., Gallardo, X., Martín-Loeches, I., Andreu, M.,Prenafeta, M., Saludes, P., Lema, J., Batlle, M., Bacelar, N., & Artigas, A. (2017). Incidence of airway complications in patients using endotracheal tubes with continuous aspiration of subglottic secretions. Annals of intensive care, 7(1), 109. https://doi.org/10.1186/s13613-017- 0331-0
7. El-Baradey, G. F., El-Shmaa, N. S., & Elsharawy, F. (2016). Ultrasound-guided laryngeal air column width difference and the cuff leak volume in predicting the effectiveness of steroid therapy on postextubation stridor in adult. Are they useful?. Journal of critical care, 36, 272– 276. https://doi.org/10.1016/j.jcrc.2016.07.007
8. Jaber, S., Chanques, G., Matecki, S., Ramonatxo, M., Vergne, C., Souche, B., Perrigault, P. F., & Eledjam, J. J. (2003). Post-extubation stridor in intensive care unit patients. Risk factors evaluation and importance of the cuff-leak test. Intensive care medicine, 29(1), 69–74. https://doi.org/10.1007/s00134-002-1563-4
9. Cheng, K. C., Chen, C. M., Tan, C. K., Chen, H. M., Lu, C. L., & Zhang, H. (2011).Methylprednisolone reduces the rates of postextubation stridor and reintubation associated with attenuated cytokine responses in critically ill patients. Minerva anestesiologica, 77(5),503–509. PMID: 21540805; PMCID: PMC3929386. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3929386/
10. Sigrist T, Dirnhofer R, Patscheider H. [Rare complications following tracheotomy and intubation (author's transl)] Anaesthesist. 1981 Oct;30(10) 523-527. PMID: 7304907. https://pubmed.ncbi.nlm.nih.gov/7304907/
11. Sehgal, I. S., Dhooria, S., Bal, A., Aggarwal, A. N., Behera, D., & Agarwal, R. (2016). Obstructive Fibrinous Tracheal Pseudomembrane After Endotracheal Intubation. Respiratory care, 61(9), 1260–1266. https://doi.org/10.4187/respcare.04662
12. Lins, M., Dobbeleir, I., Germonpré, P., Waelput, W., Pauwels, P., & Jorens, P. G. (2011). Postextubation obstructive pseudomembranes: a case series and review of a rare complication after endotracheal intubation. Lung, 189(1), 81–86. https://doi.org/10.1007/s00408-010-92632
13. Ammar, Y., Vella-Boucaud, J., Launois, C., Vallerand, H., Dury, S., Lebargy, F., Deslee,G., & Perotin, J. M. (2017). Obstructive Fibrinous Tracheal Pseudomembrane. Anesthesia and analgesia, 125(1), 172–175. https://doi.org/10.1213/ANE.0000000000001408
14. Kang, H. H., Kim, J. W., Kang, J. Y., Kim, J. S., Kim, M. S., Kim, S. S., Kim, Y. H., Lee, S. H., & Moon, H. S. (2010). Obstructive fibrinous tracheal pseudomembrane after tracheal intubation: a case report. Journal of Korean medical science, 25(9), 1384–1386. https://doi.org/10.3346/jkms.2010.25.9.1384

Case Report
Eurasian Journal of Critical Care

Successful treatment of warfarin overdose with 20% lipid solution: a case report

Ernur D[1], Yurtlu S[2], Hanci V[2]
[1] Dokuz Eylul University Faculty of Medicine, Department of Internal Diseases, Izmir, Turkiye
[2] Dokuz Eylul University Faculty of Medicine, Department of Anesthesia and Reanimation, Izmir, Turkiye

Abstract

International Normalized Ratio (INR) value monitoring is important in patients using warfarin, and it is aimed to keep it in the range of 2.5-3.5 in patients with mechanical heart valves. In the light of the management guideline of patients with heart valve disease published by the 2020 AHA/ACC, in the report prepared jointly by the American Society of Cardiology and the college, vitamin K, 4-factor prothrombin complex, administrativecuzumab and andexanet alfa are among the treatment options for reversing anticoagulation. In previous case reports, it has been observed that 20% lipid emulsion causes warfarin resistance and reduces prothrombin time. In this case report, it is aimed to present the successful treatment of a warfarin overdose case using 20% lipid emulsion for the first time in the literature.

Keywords: 20 % lipid solution, warfarin overdose,aortic valve replacement,mitral valve replacement

Introduction

Warfarin is an oral anticoagulant widely used with various indications (1). It is very important to monitor the International Normalized Ratio (INR) value in patients to follow the therapeutic effect of warfarin, and it is aimed to keep it in the range of 2.5-3.5 in patients with mechanical heart valves (2). Among the complications that can be seen are the INR values exceeding the therapeutic upper limit and causing warfarin overdose in patients due to multifactorial factors. If the INR value is above 4.5, the risk of major bleeding increases significantly, and if it is above 6.0, it increases exponentially. Therefore, an INR value of ≥ 6.0 requires rapid reversal of anticoagulation due to the risk of bleeding (3). Vitamin K, 4-factor prothrombin complex, idaricuzumab and andexanet alfa are among the treatment options for reversing anticoagulation (4). In experimental animal studies conducted in rats, 20% lipid emulsion has been shown to reduce the cardiotoxicity of local anesthetic agents, and it can be used in the treatment of some drug intoxications with a high protein binding rate (5). In previous case reports, it has been observed that 20% lipid emulsion causes warfarin resistance and reduces prothrombin time (6-8). However, there are no cases in which 20% lipid emulsion was used for the treatment of warfarin overdose. In this report, a case of warfarin overdose is presented, in which the desired decrease in INR value was achieved with 20% lipid emulsion and resulted in successful treatment.

Case report

An 81-year-old patient with a history of aortic and mitral valve replacement and using warfarin was admitted to the anesthesia intensive care unit for advanced oxygen support due to covid pneumonia. In the patient's labaratory findings, following was detected: International Normalized Ratio (INR) value, 4.15 (0.8-1.2), activated partial thromboplastin time (aPTT): 61.23 second (25.9-36.6), prothrombin time (pT): 37.90 second (10.7-12.9), fibrinogen: 5.58 g/L (1.8-3.5), D-Dimer: 2.43 ug/mL (0-0.55) detected. In the patient who did not receive any other warfarin, anticoagulant or antiaggregant treatment, INR values increased at 6-hour intervals and were found to be 4.48 and 6.31, respectively. Then, treatment was planned for the patient with the diagnosis of warfarin overdose. Considering the unavailability of 4-factor prothrombin complex, idaricuzumab and andexanet alfa in the current hospital, and the INR level may decrease to the recommended range in a long time interval with vitamin K treatment, it was planned to administer a lipid emulsion

Corresponding Author: Damla Ernur **e-mail:** drdamlaernur@gmail.com
Received: 27.07.2023 • **Accepted:** 16.08.2023
DOI: 10.55994/ejcc.1333434

Cite this article as: Ernur D, Yurtlu S, Hanci V. Successful treatment of warfarin overdose with 20% lipid solution: a case report. Eurasian Journal of Critical Care. 2023;5(2): 74-77

of 20%. After a 1.5 mL/kg IV bolus administration of 20% lipid emulsion, a maintenance infusion of 0.025 ml/kg/min was started. In the follow up of the patient whose lipid emulsion treatment was terminated 10 hours later, hypertension, hemodynamic instability and no change in consciousness were observed. The INR value of the patient was 1.33, 1,24 and 1,19 at the 4th, 16th and 24th hours after the termination of lipid emulsion therapy. Amylase, lipase and lipid plasma values were examined during, at the end and after the treatment, and no increase was found in their values. Since the INR value measured after 48 hours was 1.25, low molecular weight heparin treatment was initiated in the patient. The patient, who received antiviral, steroid and inhaler treatment for Covid pneumonia and whose oxygenation parameters improved, was transferred to the ward from the intensive care unit by taking 6-8lt/min oxygen. Appropriate written informed consent was obtained from the patient for publication of this case report.

Discussion

Warfarin acts by inhibiting the enzymes involved in the formation of a reduced form of vitamin K, which is necessary for the γ-carboxylation of glutamate residues at the amino terminus of coagulation factors II, VII, IX, and X, and the anticoagulant factors protein C and S (1). Unpredictable biological responses, including genetic polymorphisms in warfarin metabolism, can be seen in patients with mechanical valve replacement treated with warfarin, as well as increased INR and bleeding due to multiple interactions of drugs used, foods taken, and other patient-related factors. It is emphasized that if vitamin K is used in cases, it may take a long time for the INR to return to its normal value, and it has been reported that this treatment will not be sufficient in patients with bleeding risk or major bleeding (9). In the studies, it is emphasized that the effect of vitamin K begins after 6 hours, even if it is given as an infusion. The advantage of vitamin K injection is its ease of administration, widespread availability, promoting the formation of factors II, VII, IX, and X in the liver, and a sustained effect in the regulation of coagulopathy. The disadvantages of vitamin K are reported as the risk of developing anaphylaxis, which is thought to be due to the castor oil in the diluent. Warfarin resistance may also develop during vitamin K treatment (10-13). The risk of anaphylaxis has been reported at an estimated rate of 3/100,000, and to avoid these reactions, mixing vitamin K in at least 50 mL of intravenous fluid and giving it at least 30 minutes using an infusion pump are among the recommendations (12, 14). In patients with high INR without bleeding, subcutaneous administration is unreliable and it may take up to 72 hours for INR to reach a normal value (11-13). Intramuscular administration of vitamin K may cause hematoma, and it is emphasized that its consequences are unpredictable (12). Relevant guidelines published by the American College of Cardiology/American Heart Association (ACC/AHA) in 2020 recommended individualization of vitamin K supplementation on a case-by-case basis. The onset of action of vitamin K depends on the route of administration and the dose given, and maintenance therapy is recommended in the presence of active bleeding. In case of life-threatening bleeding, 10 mg intravenous vitamin K is recommended if it is not considered to start a vitamin K antagonist within 1 week (4). In addition, high doses of vitamin K can lead to "warfarin resistance" (up to 3%; 1 week or more) due to the accumulation of vitamin K in the liver, which may require later use of higher doses of warfarin to reach therapeutic INR levels.

In the Fresh Frozen Plasma (FFP) option, the recommended dose is 15 mL/kg infusion (in the range of 10-30 mL/kg), while the average size adult has about 3-4 units of plasma, but the optimal dose is unknown (11-13). The duration of action of FFP is 10 minutes, but a few hours are required for partial reversal and at least 9 hours for a complete reversal of INR (INR<1.5) (10, 13). Other limitations in the use of FFP include fluid overload and acute lung injury due to transfusion. One of the most important reservations about FFP is the risk of viral and bacterial infection (10, 13, 14). In addition, since the plasma is frozen, it must be melted and blood group matched, which leads to a delay in its implementation.

Although FFP is widely used, four-factor prothrombin complex concentrate (PCC) has been noted to have significant benefits over FFP. One of them is that the concentration of clotting factors in PCCs is about 25 times higher than that in FFP, and that the FFP contains an insufficient concentration of factor IX (15, 16). The four-factor prothrombin complex concentrate includes factors II, VII, IX and X. The onset of action is from 5 to 15 minutes, and the duration of action is from 12 to 24 hours. It is a more specific and reliable reversal agent than fresh frozen plasma (4). The main problems limiting the use of PCC are thrombotic complications (approximately 0-7%, mean 2.3%) and the limited availability of these products (12, 14). One cause of PCC-related thrombotic risk is the high level of factor II (relative to other factors) that increases thrombin formation in PCC (15). However, in the presence of life-threatening bleeding, four-factor prothrombin complex concentrate was recommended by the 2020 American College of Cardiology/American Heart Association (ACC/AHA) guidelines (4). Intravenous use of vitamin K is recommended if active bleeding continues despite PCC administration and if vitamin K antagonsite is not started within 7 days (4). For our case, considering the concomitant diseases and COVID-19 pneumonia, although we planned the use of PCC in the foreground due to the long duration of action of vitamin K treatment in translating the effect of warfarin, the risk of infection and the volume burden that FFP may create, we used 20% lipid solution due to the lack of PCC in the local institution where we work.

Recombinant FVIIa provides a rapid and complete biochemical return in INR within 10 minutes, but has a short

half-life of < 1 hour (13). The disadvantage of rFVIIa is that it does not replace all coagulation factors and although the INR is immediately reduced, coagulation may not be reinstituted in vivo. Therefore, repeat infusions are necessary unless used with vitamin K and FFP. In a meta-analysis involving more than 4000 patients, evaluating the use of rFVIIa on the subject, it was shown that thromboembolism developed in 11.1% of the cases (17). Therefore, the most recent guidelines for the management of these patients recommend that rFVIIa be used in the treatment of warfarin-associated bleeding or in the absence of PCC or TDP (15, 18). Idarucizumab (for dabigatran) or andexanet alfa (for anti-Xa agents) is recommended for patients receiving direct oral anticoagulants and those with bioprosthetic valves or annuloplasty rings who require immediate reversal of anticoagulation due to uncontrolled bleeding (Class Of Recommendaiton 2A) (4). Idarucizumab (2.5 mg bolus infusion in two times no longer than 15 minutes) is indicated to reverse the effect of dabigatran. Andexanet alfa is administered as a bolus and 2-hour infusion and is used to reverse the effects of oral anti-Xa agents (4). On the other hand, in a systematic review of the efficacy and safety of vitamin K administration in VKA-treated patients with an INR between 4.5 and 10.0 and without bleeding, the findings suggested that the probability of benefiting from routine vitamin K administration in addition to temporary VKA cessation is low (4).

Currently, various pharmacokinetic and pharmacodynamic mechanisms have been proposed for the application of intravenous lipid emulsion as an antidote (19). Theories put forward about the mechanism of action of ILE; 1) it is the "lipid sink" theory, which assumes that it improves myocardial performance, 2) that the toxic compound is held in a lipid compartment in the bloodstream, 3) the ion channel modulation theory (5). Lipid Sink Theory describes the beneficial effects of intravenous lipid emulsion in cases of lipophilic drug toxicity, known as lipid or pharmacological "sink"; It is explained by the formation of "a lipid compartment where circulating lipophilic drugs are held" and is thought to be diffused into the new compartment by separating lipophilic toxins from the target tissues (20). With a better understanding of lipid resuscitation, intravenous liposomes have been reported as a lipid shuttle or a capture/release mechanism to transport a drug, not as a compartment for capturing and isolating the drug (21). In this regard, exogenous lipid metabolism is thought to be similar to chylomicrons (20).

In addition to its primary purpose of use, parental feeding can be used as an antidote in local anesthetic toxicity and for various purposes, including the treatment of drug overdoses (22). Significant clinical improvement in local anesthetic toxicity achieved in the treatment of poisoning with intravenous lipid emulsions and some lipophilic drugs after its use has been identified. Advantages such as the relatively easy application and low cost have led to an increase in the off-label use of lipid emulsions and paved the way for their use in the treatment of poisoning. Drug toxications that respond to treatment with lipid emulsions are bupivakain, clomipramine, verapamil, bupropion, mepivakain, ropivacaine, haloperidol, quetiapine, doxepine, carvedilol, carbamazepine, flekany, hydrochloroquine, amlodipine, propanolol and moxidectin (5).

On the other hand, some studies have suggested that lipid solutions may play a role in warfarin resistance. MacLaren et al. (6) gave 30 mg of warfarin per day to a case under propofol infusion containing 10% soybeans, but no anticoagulation was achieved (6). After the termination of propofol therapy, it was seen that after they reached effective anticoagulation, the anticoagulation was reversed when they supplemented the patient with 20% lipid solution (6). Lutomski et al. (7) described a patient with short bowel syndrome and recurrent thrombotic episodes requiring both intravenous lipid and anticoagulation. They showed that continuous infusion of a soybean oil emulsion (Intralipid) in parenteral nutrient solution interferes with the anticoagulant effect of warfarin. They achieved the desired coagulation goal by discontinuing lipid infusion and re-administration of warfarin (7).

Cotto et al. (8) added lipid infusion at varying rates to the blood samples of 23 cases with anticoagulated and prothrombin time > (1.3-2.0 x control). Lipid-free plasma and prothrombin time from lipid-containing plasma samples were compared. Average decrease in prothrombin durations; It was 0.29 seconds at 50 micrograms/ml, 0.23 seconds at 100 micrograms/ml and 0.29 seconds at 200 micrograms/ml. All concentrations showed a statistically significant decrease compared with control with the Scheffe test. This study supported the idea that lipid emulsions reduced prothrombin times in patients using anticoagulants (8). Studies conducted to date show that; patients taking lipid emulsion may have difficulty and resistance to achieving the anticoagulation target with warfarin. Most studies in the literature have pointed out that warfarin resistance develops with lipid therapy (8). In the study conducted by looking at this mechanism in reverse, a decrease in prothrombin values was detected by administering lipid emulsion (8). Warfarin binds to albumin at a rate of 98% (23) Thus, considering that it has lipophilic properties, the 'lipid sink' theory and its transport by intravenous lipid emulsion can be explained in this way.

In our hospital, due to local conditions, vitamin K was available as a therapeutic agent that could be given due to the lack of four-factor prothrombin complex, idarucizumab and andexanet alpha. We did not choose vitamin K because its effect would appear in a long time.

Considering the current cost prices of the agents used in warfarin overdose treatment, approximately; PCC was €152.2, idarucizumab €515.8, andexanet alfa €20.000, TDP €12.37,.The cost price of 20% lipid emulsion was 23.9 € and it seemed more economical than other agents. Intravenous

lipid emulsion had advantages such as faster duration of action and easy access. Although FFP is cheaper than lipid emulsion, we did not prefer it because infectious and non-infectious complications may develop.Since other agents were not available in our hospital, we considered and applied lipid emulsion as an alternative treatment.

In our case, prothrombin and INR values reached the desired value with 20% lipid emulsion and warfarin overdose treatment completed without any complications. 20% lipid emulsion, in cases of warfarin overdose can be considered as an alternative treatment option in limited geographies where the supply of first choice prothrombin complex, darucizumab and andexanet alfa is difficult. As a result, in cases of warfarin overdose or intoxication, 20% lipid emulsion can be used as an alternative treatment in socio-economically selected geographies and cases, although it is not recommended for routine treatment yet. More work is needed on this subject.

Reference

1. Sucker, C., Litmathe, J. Orale Antikoagulation mit Vitamin K-Antagonisten – ein Update. Wien Med Wochenschr 168, 121–132 (2018).
2. Daniel M. Witt, PharmD, BCPS Is It Time to Reevaluate Current International Normalized Ratio Targets for Asian Patients Following Mechanical Heart Valve Replacement? JAMA Netw Open. 2022;5(2):e2146034.
3. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2017 Sep 21;38(36):2739-2791.
4. Writing Committee Members, Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, O'Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A, Toly C. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2021 Feb 2;77(4):e25-e197. Erratum in: J Am Coll Cardiol. 2021 Feb 2;77(4):509. Erratum in: J Am Coll Cardiol. 2021 Mar 9;77(9):1275.
5. Fernandez AL, Lee JA, Rahilly L, Hovda L, Brutlag AG, Engebretsen K. (2011). The Use of Intravenous Lipid Emulsion as an Antidote in Veterinary Toxicology. Vet Emerg Crit Care. 21(4):309-20.
6. MacLaren R, Wachsman BA, Swift DK, Kuhl DA. Warfarin resistance associated with intravenous lipid administration: discussion of propofol and review of the literature. Pharmacotherapy. 1997 Nov-Dec;17(6):1331-7.
7. Lutomski DM, Palascak JE, Bower RH. Warfarin resistance associated with intravenous lipid administration. JPEN J Parenter Enteral Nutr. 1987 May-Jun;11(3):316-8.
8. Cotto MA, Lutomski DM, Palascak JE, Fant WK, LaFrance RJ. Fat emulsion effects on prothrombin time in warfarin anticoagulated patients: an in vitro study. JPEN J Parenter Enteral Nutr. 1990 Mar-Apr;14(2):201-3
9. Pernod G, Godiér A, Gozalo C, Tremey B, Sié P. French clinical practice guidelines on the management of patients on vitamin K antagonists in at-risk situations (overdose, risk of bleeding, and active bleeding) Thromb Res. 2010;126:e167–e174.
10. Chowdary GVS, Naryanan TJ, Basha PSA, Murthy TVRK, Murthy JMK. Anticoagulant-related subdural hematoma in patients with mechanical heart valves. Neurology Asia. 2005;10:13–19
11. Aguilar MI, Hart RG, Kase CS, Freeman WD, Hoeben BJ, García RC, Ansell JE, Mayer SA, Norrving B, Rosand J, et al. Treatment of warfarin-associated intracerebral hemorrhage: literature review and expert opinion. Mayo Clin Proc. 2007;82:82–92.
12. Dentali F, Ageno W, Crowther M. Treatment of coumarin-associated coagulopathy: a systematic review and proposed treatment algorithms. J Thromb Haemost. 2006;4:1853–1863.
13. Vang ML, Hvas AM, Ravn HB. Urgent reversal of vitamin K antagonist therapy. Acta Anaesthesiol Scand. 2011;55:507–516
14. Goodnough LT, Shander A. How I treat warfarin-associated coagulopathy in patients with intracerebral hemorrhage. Blood. 2011;117:6091–6099.
15. Levy JH, Tanaka KA, Dietrich W. Perioperative hemostatic management of patients treated with vitamin K antagonists. Anesthesiology. 2008;109:918–926.
16. Pabinger I, Brenner B, Kalina U, Knaub S, Nagy A, Ostermann H. Prothrombin complex concentrate (Beriplex P/N) for emergency anticoagulation reversal: a prospective multinational clinical trial. J Thromb Haemost. 2008;6:622–631.
17. Levi M, Levy JH, Andersen HF, Truloff D. Safety of recombinant activated factor VII in randomized clinical trials. N Engl J Med. 2010;363:1791–1800.
18. Morgenstern LB, Hemphill JC, Anderson C, Becker K, Broderick JP, Connolly ES, Greenberg SM, Huang JN, MacDonald RL, Messé SR, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2010;41:2108–2129.
19. Cave G, Harvey MG. (2014). Should We Consider the Infusion of Lipid Emulsion in the Resuscitation of Poisoned Patients. Crit Care. 18(5):457.
20. Robben JH, Dijkman MA. (2016). Lipid Therapy for Intoxications. Vet Clin North Am Small Anim Pract. 47(2):435-440
21. Fettiplace MR, Weinberg G. (2015). Past, Present, and Future of, Lipid Resuscitation Therapy. J Parenter Enteral Nutr. 39(1):72-83.
22. Mirtallo JM, Dasta JF, Kleinschmidt KC, Varon J. (2010). State of the Art Review: Intravenous Fat Emulsions: Current Applications, Safety Profile, and Clinical Implications. Ann Pharmacother. 44(4):688-700.
23. Tárnoky AL. Warfarin and albumin. Br Med J (Clin Res Ed). 1982 Sep 18;285(6344):812.