

## Prospective Evaluation of Critically ill Patients With Therapeutic Plasma Exchange in Medical Intensive Care Unit

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### Abstract

**Background:** Therapeutic plasma exchange (TPD) is the separation of the patient's plasma for treatment purposes and the replacement of another fluid. Therapeutic plasma exchange, the use of which has expanded in recent years, is a treatment method that cleans the blood extra-corporeally and is used in many immunological and toxicological diseases. The aim of this study is to prospectively examine critical patients who are followed up in the intensive care unit and undergo therapeutic plasma exchange.

**Materials and methods:** Patients who were hospitalized in the Intensive Care Unit of Erciyes University, Faculty of Medicine, older than 18, and whose therapeutic plasma exchange (TPD) indication were included in the study. Demographic information of the patients, indication for admission to intensive care unit, and TPD indication were recorded before the procedure. Patients who were indicated for plasmapheresis were observed for side effects during the procedure.

**Result:** A total of 31 patients were included in the study. The mean age of the patients was  $46 \pm 18$  years. 52% of the patients were female and 48% were male. The hospitalization median APACHE II score (min-max: 5-40) of the patients was 20. When the patients were evaluated in terms of TPD indications in intensive care, the most common causes were 56% microangiopathic hemolytic anemia (MAHA), 13% Crimean Congo Hemorrhagic Fever (KKKA) and 10% Guillen Barre Syndrome.

**Conclusion:** The frequency of TPD indications of patients included in the study is compatible with the literature, and TPD was applied most frequently because of MAHA. The patients were younger than the normal intensive care population. This study provides clinicians with some helpful information about the intensive care clinical course before patients undergo TPD.

**Keywords:** Therapeutic plasma exchange, intensive care unit, mortality, critical disease.

### Introduction

Therapeutic Plasma Exchange (TPE) is the removal of pathological substances from the blood and reinfusion of the remaining components (such as erythrocytes, leukocytes, platelets) in the replacement fluid [1, 2]. In TPE, blood is separated from the plasma by an extracorporeal technique and the high molecular weight substances in the plasma are removed, while 5% albumin, fresh frozen plasma (FFP) or colloidal solutions are given to the patient as a replacement fluid [3]. TPE procedure aims to reduce the plasma components acting on the pathogenesis of several diseases (i.e., immune complexes, toxins, auto-allo antibodies, lipoproteins, monoclonal proteins and cryoglobulins) and thereby to prevent the related morbidity caused by pathogenic substance in the blood [4].

TPE is primarily used in treatment of hematological diseases such as thrombotic thrombocytopenic purpura (TTP), atypical hemolytic uremic Syndrome (aHUS) and

hyper-viscosity syndrome caused by multiple myeloma and Waldenström's macroglobulinemia (WM). The primary treatment in Good Pasture disease is TPE combined with immunosuppressive therapy [5]. Plasma exchange is also considered a life-saving treatment option in fatal pathologies such as immune activated conditions, sepsis, macrophage activation syndrome, thrombotic microangiopathic and disseminated intravascular coagulopathy (DIC) in intensive care unit (ICU) patients [6, 7].

This study aimed to evaluate the demographic, clinical and laboratory data of critically ill patients who were followed up in the ICU with TPE indication.

### Materials and methods

A total of 31 adult (aged >18 years) patients who were referred to ICU with TPE indication during their hospitalization at a tertiary care were included in this prospective observational study conducted between July 2018 and July 2019. All

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patients were categorized according to The American Society for Apheresis (ASFA) [8]. Written informed consent was obtained from each subject or their relatives following a detailed explanation of the objectives and protocol of the study which was conducted in accordance with the ethical principles stated in the "Declaration of Helsinki" and approved by the institutional ethics committee (Date of approval 15/01/2020, Decision no.: 2020/03).

### 2.1. Study Plan and Data Collection

Data on patient demographics (age, gender), indications for initial hospital admission, ICU admission and TPE, APACHE II scores, Glasgow Coma Scores (GCS) and the referral service (emergency room or a department in internal medicine) were recorded at initial ICU admission. In the daily follow-up of the patients, GCS, SOFA score, the amount of FFP or albumin used in the TPE procedure, whole blood count, biochemistry and coagulation tests were recorded on the days before and after the TPE procedure. The adverse effects during the TPE procedure, the length of ICU stay and patients' final status were also recorded.

### 2.2. Plasmapheresis device

TPE Procedure was performed by Fresenius-COMTEC 204 from July 2018 to March 2019 and by SpectraOptia® ApheresisSystem device after March 2019.

### 2.3. Statistics

Statistical analysis was made using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY). Chi-square ( $\chi^2$ ) test was used for the comparison of categorical data. Mann-Whitney U test and independent sample t-test were used for the parametric variables. Data were expressed as mean±standard deviation (SD), minimum-maximum and percent (%) where appropriate.  $p < 0.05$  was considered statistically significant

## Results

A total of 207 TPE sessions were applied to 31 patients. The mean±SD age of the patients was 46±18 years and 52% of patients were females. The respiratory failure (35% and 42%, respectively) and somnolence (16% and 26%, respectively) were the two most common indications for the initial hospital admission and ICU referral. The most commonly noted TPE indications were included microangiopathic hemolytic anemia (MAHA, 56%) and Crimean Congo hemorrhagic fever (CCHF, 13%). The median GCS was 11 (range, 3 to 15), SOFA score was 8 (range, 2 to 16) and APACHE II score was 20 (range, 5 to 40). Replacement fluids used during plasmapheresis were FFP in 84% of patients and albumin in 16% of patients. The length of ICU stay was median 12 days (range, 1 to 86 days), while ICU mortality rate was 48%. Detailed results are presented in Table 1.

**Table 1:** Demographic and clinical features of critically ill patients with therapeutic plasma change in medical ICU

Variable	Value (n = 31)
Age (year), mean±SD	46±18
Gender, n (%)	
Male	15(48)
Female	16 (52)
Initial hospitalization, n (%)	
Emergency service	14 (45)
Hematology ward	10 (32)
Nephrology ward	3 (10)
Gastroenterology ward	2 (7)
General surgery ward	1 (3)
Other	1 (3)
Reasons for hospitalization, n (%)	
• Respiratory failure	11 (35)
• Loss of consciousness	5 (16)
• CCHF	4 (13)
• Acute kidney failure	3 (10)
• Sepsis	3 (10)
• MAHA	3 (10)
• Pneumonia	2 (7)
Reason for ICU admission, n (%)	
• Respiratory Failure	13 (42)
• Loss of consciousness	8 (26)
• Pneumonia	3 (10)
• CCHF	3 (10)
• Multiple organ failure	2 (6)
• Liver failure	1 (3)
• Acute kidney failure	1 (3)
GCS, (min-max)	11(3-15)
SOFA score, (min-max)	8 (2-16)
APACHE II score, (min-max)	20 (5-40)
Replacement fluid used in plasmapheresis, n (%)	
• Fresh frozen plasma (FFP)	26(84)
• Albumin	5 (16)
Length of ICU stay (day) median (min-max)	12 (1-86)
ICU mortality, n (%)	15 (48)

MAHA: Microangiopathic Hemolytic Anemia; CCHF: Crimean Congo Hemorrhagic Fever; GCS: Glasgow Coma Score; ICU: Intensive Care Unit

The detailed TPE indications in patients with MAHA were TTP in 4 (13%) patients, aHUS in 3(10%) patients and other indications in 10(33%) patients. Overall, 121 TPE sessions were applied to patients with MAHA and 32 TPE sessions were applied to those with CCHF patients. One of the patients has improved to DIC syndrome. Guillain-Barre Syndrome (GBS) patients who had undergone TPE procedure constitute 10% of all patients (n=3) in the study. Detailed results are presented in Table 2.

The survivors vs. non-survivors had significantly higher GCS scores (median(min-max) 12 (3-15) vs. 8

**Table 2:** Indications for TPE application by the number of patients, ASFA category and mortality

Indications	Number of patients	ASFA Category	Mortality (n)	Cause of death
<b>Microangiopathic Hemolytic Anemia</b>	<b>17</b>			
TTP	4	I	1	sepsis
a-HUS	3	III	3	sepsis and cardiovascular diseases
other	10	III		
<b>Crimean Congo Hemorrhagic Fever</b>	<b>4</b>		1	DIC
<b>Gullian- Barre Syndrome</b>	<b>3</b>	I	2	sepsis
<b>Systemic Lupus Erythematosus</b>	<b>2</b>			
Nephritis	1	IV	0	
Alveolar hemorrhage	2	II	0	
<b>Multiple Myeloma</b>	<b>2</b>	I	2	sepsis
<b>ANCA-associated vasculitis</b>	<b>1</b>			
Alveolar hemorrhage	1	I	1	sepsis

TTP: Thrombotic Thrombocytopenic Purpura; a-HUS: Atypical Hemolytic Uremic Syndrome, DIC: Disseminated Intravascular Coagulation; ASFA: American Society for Apheresis

(3-15),  $p=0.008$ ) and significantly lower APACHE II scores (mean $\pm$ SD 17 $\pm$ 7 vs. 25 $\pm$ 9,  $p=0.02$ ). No significant difference was noted between survivors and non-survivors in terms of age (mean $\pm$ SD 43 $\pm$ 17 vs. 50 $\pm$ 18 years), SOFA scores (median(min-max) 7 (3-12) vs. 10(2-16) and length of ICU stay (median(min-max) 13(4-40) vs. 8 (1-86) days). Detailed results are presented in Table 3.

Of 31 patients who underwent TPE, 4 patients experienced adverse effects during plasmapheresis, including anaphylaxis (n=2), hypotension (n=1) and bleeding (n=1). The anaphylaxis in one patient resulted in mortality.

## Discussion

Patients who underwent TPE were examined prospectively and observationally. MAHA was the most common cause of TPE indication among these patients. When MAHA is evaluated, it was observed that TPE is an effective treatment in TTP patients. It was observed that the mean age of patients who underwent TPE in intensive care was smaller than the mean age of patients who were followed in intensive care. Our study showed that

**Table 3:** Patient's demographic and clinical outcomes of critically ill survivor and non-survivor patients with therapeutic plasma exchange in medical ICU.

	Survivor (n=16)	Non-survivor (n=15)	pvalue
Age (year), mean $\pm$ SD	43 $\pm$ 17	50 $\pm$ 18	0.342
<b>Gender, n (%)</b>			
Male	6(38)	9(60)	0.210
Female	10 (62)	6(40)	
<b>GCS, (min-max)</b>	12(3-15)	8(3-15)	<b>0.008</b>
<b>SOFA score, (min-max)</b>	7(3-12)	10(2-16)	0.064
<b>APACHE II score, <math>\pm</math>SD</b>	17 $\pm$ 7	25 $\pm$ 9	<b>0.020</b>
<b>Length of ICU stay, day (min-max)</b>	13(4-40)	8(1-86)	0.470

GCS: Glasgow Coma Score; ICU: Intensive Care Unit

mortality was high in patients with low hospitalization GCS and high hospitalization APACHE II scores.

In the current study a total of 207 TPE sessions were applied to 31 patients in a medical ICU. The mean age of the patients was 46 $\pm$ 18 years. In a previous study performed by Gündoğan et al. in 2011 at the same unit, the mean age of the patients was reported to be 61 $\pm$ 19 years[9]. The smaller age of patients in our study seems to be associated with the fact that TPE diseases are autoimmune diseases commonly observed in middle age. In our study, 52% of patients were female and 48% were male. Consistent with patient demographics reported in our study, in an ICU study by Ranganathan et al. in India in 2017, the authors reported the mean age of patients who required TPE to be 43.08 $\pm$ 16.84 years, while 59% of patients were males and 41% were females[6].

In a 10-year retrospective ICU study by Paton et al. in 2014 in Australia, total of 30 patients had undergone 135 TPE procedures, while the TPE indication included TTP in 11(36.7%) patients, liver transplantation rejection in 4(13.3%) patients, MG in 3(10%) patients, GBS in 2(6.7%) patients, anti-GBM disease in 3(10%) patients, ANCA-induced vasculitis in 2(6.7%) patients and other diseases in 5 patients[7]. In another ICU study performed by Lemaire et al. in 2017[10], 50 patients had undergone 260 TPE procedures, while TPE indications included MAHA in 29(58%) patients [TTP: 18(36%), aHUS: 10(20%) and drug induced TMA: 1(2%)], hyperviscosity syndrome in 12(24%) patients, ANCA induced vasculitis in 4(8%) patients, humoral rejection after kidney transplant in 3(6%) patients, severe cryoglobulinemia in 1(2%) patients and catastrophic antiphospholipid syndrome in 1(2%) patient. In this regard, our findings support the consideration of MAHA as the more prevalent TPE indication in ICU patients [7,10].

Considering the TTP, a type of MAHA, France and Canadian reports in the recent years showed that TPE use is increasing especially in hematological diseases since TPE

is used more commonly used for TTP [11]. TTP commonly manifests with fever, thrombocytopenia, MAHA, renal failure, and neurological findings [12, 13]. The introduction of treatments such as plasma infusion and plasma exchange, immunosuppressive treatment and antiplatelet agents caused dramatic reduction in mortality rates among TTP patients, which were about 100% by the 1960s [14, 15, 16]. The literature showed that TPE is an effective treatment for TTP and decreases mortality significantly. Likewise, our study also showed that TPE is an effective treatment for TTP.

Several studies showed that the high interleukin-10, interleukin-6, gamma interferon and tumor necrosis factor alpha levels are associated with poor prognosis [17]. TPE reduces cytokines and toxic components in the patients with CCHF [18]. It was observed that TPE is useful on survival in the critical patients with severe sepsis, and several diseases with known or suspected immune etiology [19, 20]. Few studies in the literature investigated the utility of TPE in CCHF, and TPE was considered effective for CCHF in these studies. The favorable results of TPE were also seen in our study.

In a multicentered retrospective study by Kaynar et al. in 2008, 41 GBS patients and 11 myasthenia gravis patients were evaluated by Hughes score for outcome before and after TPE [19]. The authors reported significant improvement in GBS patients after TPE [19]. However, in our study, the number of GBS patients was small and the mortality scores of the patients were high (APACHE II), therefore the results were not in line with the literature.

In a prospective study on 86 SLE patients performed by Lewis et al., 46 patients received treatment and 40 patients underwent TPE 3 times per week for 4 weeks [21]. When mortality rates of the two groups were compared, it was 13% in the treatment group, and 20% in TPE group. The decrease in serum creatinine rates was reported to be similar in both groups, however, the decrease in antibody level was faster in the TPE group. Similar to our findings, TPE was reported to be an effective treatment in the alveolar hemorrhage patients with SLE [21].

GCS and APACHE score systems are used to evaluate the treatment efficacy and to identify the mortality rate in ICU. APACHE II score is the modified version of APACHE and based on the worst values within the first 24 hours of 12 different physiological variables. The calculated score is used to predict the mortality and morbidity of the patient in the ICU [22, 23]. When these two scoring systems are evaluated together before the TPE procedure, they seem to offer a valuable data on the likelihood of post-procedure outcome in these patients.

In a 10-year retrospective ICU study by Paton et al. in 2014 in Australia, total of 30 patients had undergone 135 TPE procedures, and the authors reported that mean hospitalization period in ICU was 9.5 (3-17) days and mortality was 20% (n=6) [13]. In another ICU study

performed by Lemaire et al., 50 patients had undergone 260 TPE procedures and the authors reported that the mean hospitalization period in ICU was 6(3-9) days and mortality was 6% (n=3) [10]. When our study is compared with these two ICU studies, ICU hospitalization is longer, and mortality is higher. Small number of patients and high mortality scores of hospitalizations (APACHE II) were considered to be associated with delayed ICU hospitalization and delayed TPE initiation.

TPE procedure is a well-tolerated procedure without common adverse effects. The most common adverse effect is hypocalcemia induced by citrate use, paresthesia, cramps and these are minor adverse effects. However, adverse effects that show a mortal course may also occur. Approximately 50 fatal reactions during TPE were reported worldwide between 1978 and 1983, while 16 of them were cardiac and 14 were respiratory [24]. Mortality is associated with anaphylaxis, sepsis and DIC. In an ICU study performed in 2017 by Ranganathan et al. with 56 patients, TPE procedure was reported to be interrupted in 3 patients, due to transfusion-induced acute lung injury (TRALI), clinically significant hypotension and cardiac arrest [6]. The authors also indicated that the reported complications were TRALI in one patient with myasthenia gravis, hypotension induced by allergic reaction in one patient with possible vasculitis, and termination of the procedures because of cardiac arrest in one patient with mixed connective tissue disease. The adverse effects in our study were in line with the literature.

## Conclusion

In conclusion, our findings revealed the microangiopathic hemolytic anemia, Crimean Congo hemorrhagic fever and Guillain-Barre syndrome to be the most frequent TPE indications in a medical ICU. Plasma exchange is a safe and generally well-tolerated procedure in ICU.

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# Role Of Fetal Umbilical And Middle Cerebral Artery Doppler Indices In Determining Intrauterine Growth Restriction In Preeclamptic Pregnancies

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## Abstract

**Background:** To investigate the utility of the umbilical artery (UA) and middle cerebral artery (MCA) Doppler indices and the ratios in determining intrauterine growth restriction (IUGR) and unfavorable birth outcomes in preeclamptic pregnancies.

**Material and methods:** This prospective study included 59 preeclamptic pregnant women and 63 healthy pregnant women (controls) at a gestational week of 31-40 who were followed up at the gynecology and obstetrics clinic of a tertiary hospital over a 16-month period. After the evaluation of normal and preeclamptic pregnancies using B-Mode ultrasonography, the Doppler index values of the UA and MCA were determined using Doppler ultrasonography. By determining the velocity-time waves for the UA and MCA, the systole/diastole ratio (S/D), resistive index (RI), and pulsatility index (PI) values were calculated following the automatic algorithm of the device.

**Results:** The S/D ( $3.47 \pm 1.29$ ) and UA RI ( $0.69 \pm 0.13$ ) values of the preeclamptic group statistically significantly differed from those of the controls ( $2.50 \pm 0.30$  and  $0.59 \pm 0.06$ , respectively) ( $p < 0.001$ ). The Doppler indices of the MCA were lower in preeclamptic pregnancies (PI:  $1.28 \pm 0.34$ , RI:  $0.73 \pm 0.09$ ), and this was more prominent in fetuses with IUGR ( $p < 0.001$ ). There were also significant differences between the preeclamptic and healthy control groups in terms of the UA/MCA and MCA/UA Doppler index ratios ( $p < 0.001$ ).

**Conclusion:** Non-invasive Doppler indices can be used in combination to increase diagnostic accuracy and prevent fetal mortality and morbidity.

**Keywords:** Preeclampsia, intrauterine growth restriction, doppler.

## Introduction

Preeclampsia is a specific complication of pregnancy, characterized by high blood pressure, proteinuria, and edema (1-3). It has an incidence of 7-8% in the general population and shows a hereditary tendency. Normal fetal growth and oxygenation depend on the adequate and appropriate perfusion of the intervillous space, which consists of uterine artery branches. An acute or chronic problem that occurs in this area prevents the growth and development of the fetus, resulting in an increase in fetal mortality and morbidity. As a result of the disruption of uteroplacental perfusion in preeclamptic pregnant women, fetal distress and intrauterine growth restriction (IUGR) develop, leading to fetal mortality and morbidity. This condition is defined as a developmental disorder in which the expected fetal weight for gestational age is below the 10% percentile (4). IUGR develops in 6-40% of pregnant women with preeclampsia.

Many methods, such as the non-stress test, biophysical

scoring, evaluation of pH in a blood sample taken from the fetal scalp, and Doppler ultrasonography (USG), are used in the diagnosis of IUGR in the fetus. Doppler USG provides information on fetal circulation and/or uteroplacental blood flow dynamics in a non-invasive manner and in a shorter time than other methods (4). In the literature, studies have compared the use of the Doppler parameters of the uterine artery, umbilical artery (UA), and middle cerebral artery (MCA) in determining IUGR and unfavorable birth outcomes (UBOs) that may develop in cases of preeclampsia (5, 6). The current study aimed to investigate the utility of the UA and MCA Doppler indices and their ratios in predicting IUGR and UBOs in preeclamptic pregnancies.

## Material And Method

This prospective study included 59 preeclamptic pregnant women and 63 healthy pregnant women (controls) at a gestational age of 31-40 weeks who were followed up at

the gynecology and obstetrics clinic of a tertiary hospital over a 16-month period. After the evaluation of normal and preeclamptic pregnancies using B-Mode USG, the Doppler index values of the UA and MCA were determined by Doppler USG using an EUB 515 (Hitachi -JAPAN) Doppler device and a 3.5-MHz convex probe. Velocity-time wave spectra for the UA and MCA were determined, and the systole/diastole ratio (S/D), resistive index (RI), and pulsatility index (PI) values were calculated following the automatic algorithm of the device.

The preeclampsia group consisted of 59 pregnant women presenting with a blood pressure above 160/110 mmHg, proteinuria (5 g /24 hours), oliguria ( $\leq 500$  ml /24 hours), cerebral and visual findings, pain in the upper abdominal region, pulmonary edema or cyanosis, elevated liver function parameters, hemolytic anemia, and fetal growth restriction. The control group was formed with healthy pregnant women whose last menstrual period was known, who had normal obstetric and B-Mode examination findings, and who had uncomplicated deliveries through repeat cesarean sections or the cervicovaginal route. In the control group, all deliveries occurred at a gestational age of 37 weeks or above, and the first- and fifth-minute Apgar scores were above 7. None of the fetuses in this group required intensive care.

The following cases were accepted as UBOs: deliveries by induction or cesarean section before the estimated date of delivery due to fetal distress according to the physician's evaluation, deliveries that occurred before 37 weeks of gestation, fetal weight below the 10% percentile according to the percentile scale, a fifth-minute Apgar score of less than 7, intensive care admission due to fetal distress, and intrauterine or neonatal death.

For measurements, the lowest pulse-repetition frequency that would not result in aliasing and a 100-Hz wall filter were used, and the sampling interval was selected as 2 mm. The normal UA diameter in a pregnant woman at term varies between 1.1 and 2.8 mm, and it is normally 2.4 mm. The MCA measurement was performed from the proximal section close to the Willis polygon where the thalamus and cavum septum pellucidum were best visualized (7).

**Statistical Analysis:** Statgraf v. 5.0 software was used in the statistical analysis of the data. Student's t-test was used to compare the two groups for parametric data, and the Mann-Whitney-U test for non-parametric data. The relationship between the measurement parameters was evaluated using linear regression analysis.

## Results

The data of preeclamptic and healthy pregnant women are given in Tables 1-3, and the results of the comparative statistical analyses of the cases are presented in Tables 4 and 5.

Diastolic flow was absent in two cases of IUGR and reversed in a further two cases. The fetuses of two pregnant

**Table 1:** Clinical and Doppler data of healthy pregnant women included in the study.

n = 63	Mean $\pm$ SD	Min-Max
Age (year)	26.58 $\pm$ 4.55	19-36
Gravida	2.25 $\pm$ 1.27	1-6
Gestational age at birth (week)	38.48 $\pm$ 1.70	37-41
Mode of delivery		
SVD	46/63 (73%)	
Repeat C/S	7/63 (11%)	
IVD	2/63 (3%)	
C/S	8/63 (12%)	
Fifth-minute Apgar score	9.14 $\pm$ 0.43	8-10
Fetal weight at birth (g)	3,245.24 $\pm$ 560.3	1,800-4,400
UA S/D	2.50 $\pm$ 0.30	1.87-3.52
UA RI	0.59 $\pm$ 0.06	0.37-0.74
MCA RI	0.79 $\pm$ 0.083	0.57-0.96
MCA PI	1.46 $\pm$ 0.36	0.85-2.44
UA RI/MCA RI	0.76 $\pm$ 0.09	0.58-0.94
MCA RI/UA RI	1.34 $\pm$ 0.19	1.06-1.71
UA PI/MCA PI	0.60 $\pm$ 0.15	0.31-1.10
MCA PI/UA PI	1.77 $\pm$ 0.43	1.08-3.22

SD: standard deviation, SVD: spontaneous vaginal delivery, C/S: cesarean section, IVD: induced vaginal delivery, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

**Table 2:** Clinical and Doppler data of preeclamptic pregnant women included in the study.

n=59	Mean $\pm$ SD	Min-Max
Age (year)	28.68 $\pm$ 5.71	18-43
Gravida	2.63 $\pm$ 2.20	1-10
Gestational age at birth (week)	36.25 $\pm$ 3.03	31-40
Mode of delivery		
SVD	16/59 (27%)	
Repeat C/S	3/59 (5%)	
IVD	13/59 (22%)	
C/S	27/59 (46%)	
Fifth-minute Apgar score	6.67 $\pm$ 3.65	0-10
Fetal weight at birth (g)	2,258.81 $\pm$ 944.99	800-4,200
NICU admission	22/59 (37%)	
Intrauterine or neonatal death	12/59 (20%)	
UAS/D	3.47 $\pm$ 1.29	1.86-6.44
UARI	0.69 $\pm$ 0.13	0.48-1.00
MCARI	0.73 $\pm$ 0.09	0.58-0.89
MCAPI	1.28 $\pm$ 0.34	0.75-2.13
UARI/MCARI	0.97 $\pm$ 0.28	0.54-1.73
MCARI/UARI	1.10 $\pm$ 0.26	0.58-1.50
UAPI/MCAPI	0.92 $\pm$ 0.46	0.40-2.57

SD: standard deviation, SVD: spontaneous vaginal delivery, C/S: cesarean section, IVD: induced vaginal delivery, NICU: neonatal intensive care unit, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

women with reversed diastolic flow and one pregnant woman with absent diastolic flow died in the intrauterine period. The other pregnant woman with no diastolic flow

**Table 3:** Comparison of the UA and cerebral Doppler data between pregnancies presenting with IUGR and healthy pregnancies.

	IUGR (n=21)	Healthy (n=63)	
	Mean ± SD	Mean ± SD	p
Fetal weight at birth (g)	1,515.29 ± 464.80	3,245.24 ± 560.3	0.03
UA S/D	4.20 ± 1.42	2.50 ± 0.30	0.03
UA RI	0.75 ± 0.14	0.59 ± 0.06	0.09
MCA RI	0.72 ± 0.09	0.79 ± 0.083	0.66
MCA PI	1.20 ± 0.36	1.46 ± 0.36	0.37
MCA RI/UA RI	1.01 ± 0.30	1.34 ± 0.19	0.20
MCA PI/UA PI	1.11 ± 0.57	1.77 ± 0.43	0.153

IUGR: intrauterine growth restriction, SD: standard deviation, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

**Table 4:** Comparison of the clinical and Doppler artery index parameters between healthy and preeclamptic pregnancies

	Healthy (n = 63) Mean ± SD	Preeclamptic (n = 59) Mean ± SD	p
Age (year)	26.58 ± 4.55	26.68 ± 5.71	0.02
Gravida	2.25 ± 1.27	2.63 ± 2.20	0.24
Gestational age at birth (week)	38.48 ± 1.70	36.25 ± 3.03	< 0.001
Fifth-minute Apgar score	9.14 ± 0.43	6.67 ± 3.65	< 0.001
Fetal weight at birth (g)	3245.24 ± 560.3	2258.81 ± 944.99	< 0.001
UA S/D	2.50 ± 0.30	3.47 ± 1.29	< 0.001
UA RI	0.59 ± 0.06	0.69 ± 0.13	< 0.001
MCA RI	0.79 ± 0.06	0.73 ± 0.09	< 0.001
MCA PI	1.46 ± 0.36	1.28 ± 0.34	0.003
UA RI/MCA RI	0.76 ± 0.09	0.97 ± 0.28	< 0.001
MCA RI/UA RI	1.34 ± 0.19	1.10 ± 0.26	< 0.001
MCA PI/UA PI	1.77 ± 0.43	1.31 ± 0.54	< 0.001

SD: standard deviation, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

had a premature delivery. Intracerebral hemorrhage was detected in one of the fetuses that died in the intrauterine period. Among the 21 cases with IUGR, the S/D ratio of the UA was pathological in 16 cases, and the RI and PI values of the MCA were pathological in nine cases each.

## Discussion

Preeclampsia is a specific complication of pregnancy, characterized by high blood pressure, proteinuria, and edema (3). Doppler USG is used in the evaluation of normal pregnancies and high-risk pregnant women, such as those with preeclampsia. Doppler evaluations of the uterine artery, UA, ductus venosus, and MCA are frequently undertaken

due to the widespread clinical use of this imaging modality and the importance of the results in terms of fetal-placental hemodynamics (8). The current study was conducted with healthy pregnant women and preeclamptic pregnant women at a gestational age of over 31 weeks, considering that UA values show high variations before the 30th gestational week.

It has been reported that placental vascular resistance decreases, end-diastolic flow velocities increase, and the UA index decreases in the advancing weeks of gestation in normal pregnancies. However, in preeclamptic pregnant women, due to the increase in vascular resistance, end-diastolic flow decreases, and the UA index increases (4,8). Divon et al. accepted a UAS/D value of greater than 3.00 to be pathological in women at a gestational age of 30 weeks and above. In our study, the mean S/D value of the UA was calculated to be 2.50±0.30 for the healthy control group and higher than normal (3.47±1.29) for pregnant women with preeclampsia. In addition, the increase in the UAS/D value was higher in cases of IUGR (4.20±1.42). In contrast, parallel with the decrease that occurs in vasodilation and vascular resistance as the gestational week progresses, the UA RI value does not decrease.

Zimmerman et al. (8) accepted the mean UA RI value of healthy pregnant women as 0.62 and pathological at above 0.62. In the current study, the mean UA RI value was (0.59 ± 0.06) for the healthy control, consistent with the commonly used cut-off value of 0.62 in the literature. We determined the UA RI value to be 0.69 in pregnant women with preeclampsia and 0.75 in cases of IUGR.

Sekizuka (9) reported the sensitivity and specificity of the UA RI value to be 61.8% and 84.6%, respectively, in the detection of IUGR. In our study, the UA RI value had higher diagnostic accuracy and sensitivity (75% and 73%, respectively) than the UAS/D value (70% and 64%, respectively) in the determination of UBOs. However, despite the higher sensitivity of the UA RI value in the detection of IUGR (80% vs. 71%, respectively), both the UA RI and the UAS/D had the same diagnostic accuracy (64%) in determining IUGR.

Abnormal UA waveforms have been described in 60% of fetuses with developmental delays. In these pregnancies, a significant decrease is observed in the end-diastolic flow velocity due to the increase in placental resistance. Diastolic flow may disappear or be reversed. In such cases, if the fetus is not delivered, fetal death may occur within the 12-24 hour period (10).

The first Doppler study in cerebral arteries was undertaken by Bada et al. in 1979, and the Doppler index values were found to be lower than normal in cases of hypoxia. During hypoxia, vasodilation develops in cerebral arteries, and the amount of blood flowing to the brain increases, which is known as the brain protection effect (11). As a result of vasodilation in cerebral arteries, vascular



**Table 5:** Diagnostic value of the fetal Doppler indices in detecting cases of IUGR among preeclamptic pregnant women.

	Sensitivity	Specificity	PPV	NPV	Diagnostic accuracy
UA S/D >1 SD	15/21 (71%)	23/38 (61%)	15/30 (50%)	23/29 (80%)	38/59 (64%)
UA RI >1 SD	17/21 (81%)	21/38 (55%)	17/34 (50%)	21/25 (84%)	38/59 (64%)
MCA RI >1 SD	10/21 (48%)	19/38 (50%)	10/29 (34%)	19/30 (63%)	29/59 (49%)
MCA PI >1 SD	10/21 (48%)	29/38 (76%)	10/19 (53%)	29/30 (73%)	39/59 (63%)
UA RI/MCA RI >1 SD	16/21 (76%)	21/38 (55%)	16/33 (48%)	21/26 (81%)	37/59 (63%)
MCA RI/UA RI >1 SD	15/21 (71%)	22/38 (58%)	15/31 (48%)	22/28 (79%)	37/59 (63%)
UA PI/MCA PI >1 SD	15/21 (71%)	22/38 (58%)	15/31 (48%)	22/28 (79%)	37/59 (63%)
MCA PI/UA PI >1 SD	15/21 (71%)	21/38 (55%)	15/32 (47%)	21/27 (78%)	36/59 (61%)

PPV: positive predictive value, NPV: negative predictive value, SD: standard deviation, UA: umbilical artery, S/D: systole/diastole, RI: resistive index, MCA: middle cerebral artery, PI: pulsatility index

resistance decreases and end-diastole flow increases. This results in a decrease in Doppler index values (RI and PI). Sekizuka (9) also found that the UA RI value increased, and the MCA RI value decreased in preeclamptic pregnant women. In the healthy pregnant group included in our study, the mean MCA RI value was  $0.79 \pm 0.083$ , with one standard deviation (SD) below the mean being calculated as 0.71, and the mean MCA PI value was  $1.46 \pm 0.36$ , with one SD below the mean being calculated as 1.10. While the UA Doppler index values are observed to be pathological in some fetuses in pregnancies with severe preeclampsia, the cerebral artery Doppler index values may be normal. In the literature, this situation is explained by the failure of the brain protection effect in fetuses affected by hypoxia (11). In our study, of the 21 cases that developed IUGR as a result of severe hypoxia, 16 had a pathological UAS/D value, nine patients had a pathological MCA RI value, and 10 cases had a pathological MCA PI value.

It is stated that the ratio of the fetal cerebral artery and UA indices is more effective than other indices in determining poor perinatal outcomes and is more related to IUGR (5). The MCA RI/UA RI ratio is above 1 in normal pregnancies and below 1 in preeclamptic pregnancies. We determined the MCA/UA RI ratio to be lower than normal in pregnant women with preeclampsia ( $1.10 \pm 0.26$ ). This decrease was even more prominent in cases that developed IUGR ( $1.01 \pm 0.30$ ). The MCA RI/UA RI ratio was found to be pathological in 12 of the 21 pregnancies presenting with IUGR. In our study, one SD of the mean MCA PI/UA PI ratio ( $1.77 \pm 0.43$ ) was calculated to be 1.33. The MCA PI/UA PI ratio was found to be lower than normal in preeclamptic pregnancies (1). The decrease in the ratio was more pronounced in cases of IUGR (1, 9). The MCA PI/UA PI ratio was pathological in 12 of the 21 pregnancies

that developed IUGR. In our study, there was no significant difference in the sensitivity of the MCA RI/UA RI and MCA PI/UA PI ratios in determining IUGR; however, the MCA RI/UA RI ratio had higher diagnostic accuracy (63%, 61%, respectively). No statistically significant difference was detected in the sensitivity or diagnostic accuracy of the Doppler indices in determining UBOs.




In conclusion, the umbilical and cerebral artery Doppler indices were found to be high in preeclamptic pregnant women. This elevation was more pronounced in cases of IUGR. The combined use of umbilical and cerebral Doppler indices in determining UBOs increased their sensitivity, specificity, and diagnostic accuracy. Lastly, umbilical and cerebral Doppler indices had lower diagnostic accuracy in determining IUGR, and the combined use of these indices did not result in an increase in diagnostic accuracy.

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## Evaluation of the Accuracy of The Emergency Department's Nurses' Triage Decision Using the ESI System

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### Abstract

**Background:** Emergency triage is extremely important in reducing morbidity and mortality. The aim of this study is to compare the accuracy of triage categorization decisions of triage nurses with the Emergency Severity Index (ESI) system categorization determined after the emergency room evaluation of patients.

**Methods:** In this descriptive, cross-sectional study, patients who were admitted to Akdeniz University Hospital Emergency Service Adult Triage Area between 01-14 March 2018 and then admitted to the emergency department were evaluated retrospectively.

**Result:** Triage scores of 3324 patients were analyzed. The kappa concordance value between the score of the triage nurse and the scores of the physicians using ESI was found to be 0.416. It was determined that the triage staff gave a triage score 1/4 lower than the ESI. In the presence of tachypnea, an increase in the low triage rate and a decrease in the high triage rate of the patients were found. It was determined that the most accurate triage scores were given in nephrological and cardiovascular disorders. The most faulty triage decisions were eye disorders and oncological emergencies. In patients between the ages of 18-65, statistically significantly higher triage was performed. Patients with chronic diseases and a history of continuous drug use were given lower triage.

**Conclusion:** In order to increase the accuracy of triage, it is necessary to increase the medical knowledge of the triage nurse and to provide practical training especially on real cases with a triage score of 2-4.

**Keywords:** Emergency, triage decision, patient management

### Introduction

Emergency services are one of the departments where patient admission cannot be restricted. Patients can apply to emergency services 24 hours a day, 7 days a week, with any complaint. Although the number of patient applications varies, the emergency service should be at the same level and quality at all hours of the day. There has been a significant increase in emergency room admissions in recent years. This increase in the intensity of admission causes delays in the evaluation and treatment of emergency patients and negatively affects patient satisfaction and service quality (1, 2). This situation has revealed the necessity of applying emergency room triage in order to determine the urgency of more urgent patients without delay in their diagnosis and treatment.

“Emergency Medical Triage” is an application made to separate patients who need urgent medical care due to their medical condition and those who may wait, and it is called “Triage” in short. The origin of the word triage is based on the French verb “trier” and it means “to classify, to separate” (3, 4).

The Emergency Severity Index (ESI), which is used in the USA, is the most frequently used and recommended

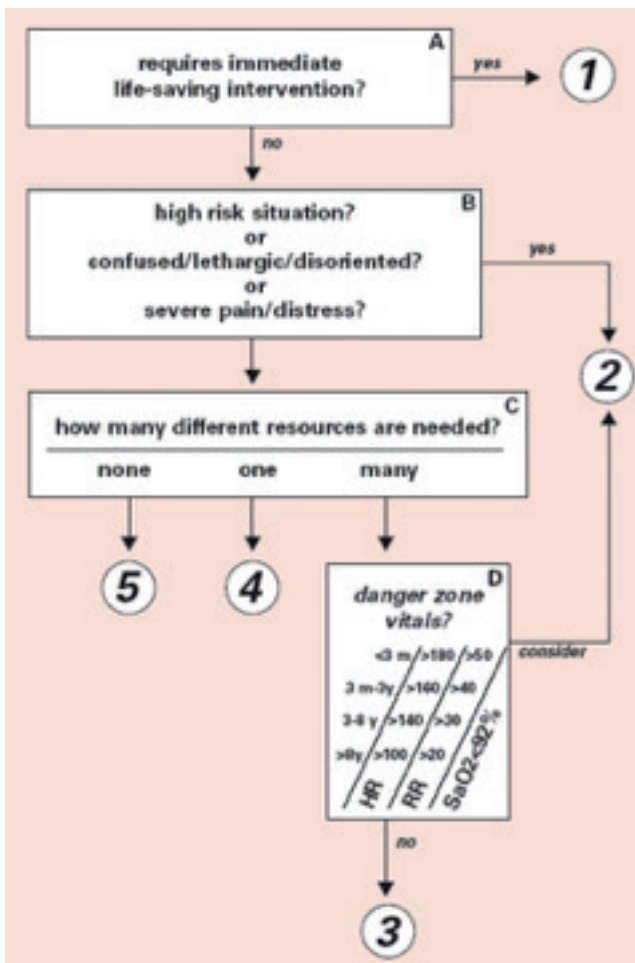
among the five-category triage systems (5). One of the most common problems encountered in the triage process is correct evaluation. The triage classification that the patient will receive with the evaluation to be made in the first care will affect the onset of the treatment, survival, waiting period and discharge.

ESI, which is also used in our study, was first introduced in 1998 by Richard Wuerz and David Eitel. The last update, the 4th Version, was published in 2012 (6).

The aim of this study is to compare the triage categorization of the patients who applied to Akdeniz University Hospital Emergency Service by the triage nurse who has emergency room experience and who has been trained in triage, with the ESI system categorization determined according to the examinations, treatments and interventions performed during the evaluation of the patients in the emergency department.

### Materials ve Method

This descriptive, cross-sectional study was conducted at Akdeniz University Hospital Emergency Service, which has approximately 100,000 patient admissions annually. In



**Figure 1:** ESI Algorithm

this study, the triage categorization of all patients who were admitted to the Akdeniz University Hospital Emergency Service Adult Triage field between 01-14 March 2018 and then admitted to the emergency room were retrospectively analyzed.

During the study period, all patients who applied for emergency department adult triage were included in the study. Patients who left the emergency service without permission, refused examination or treatment, and whose data were incomplete were excluded from the study.

Age groups were classified as “**children**” for 0-17 years old, “**young**” for 18-65 years old, “**middle age**” for 66-79 years old, and “**old**” for 80 years and over.

The patients were examined in three different time periods in terms of application hours to the emergency department. They were divided into 3 groups as “**day**” between 08:00 and 15:59, “**evening**” between 16:00 and 23:59 and “**night**” between 00:00 and 07:59.

Patients admitted to the emergency department were evaluated by healthcare personnel who had at least two years of emergency service experience and received 8 hours of theoretical and practical training on emergency room triage.

Diseases such as diabetes mellitus, asthma, chronic obstructive pulmonary disease, coronary artery disease,

cerebrovascular accident, cancer, hypertension, thyroid diseases and rheumatological diseases were evaluated in the chronic diseases section.

In the comparison of the categories determined by the triage nurse with the ESI, if the triage category given by the triage nurse was higher than it should be (for example, triage category 2 instead of 3), it was considered as “**high triage**”, if low (for example, triage category 5 instead of 4) it was considered as “**low triage**”.

During the initial evaluation of the patients in the triage area, the Triage Category was determined by looking at blood pressure, body temperature, finger-tip oxygen saturation, heart rate and respiratory rate while asking the patient’s complaints and taking a short history. Blood pressure, pulse oximeter and heart rate values were measured with a monitor. Temporal thermometer was used for temperature measurement. This information was recorded in the Emergency Triage Module in Akdeniz University Hospital Hospital Information Management System (MiaMed®).

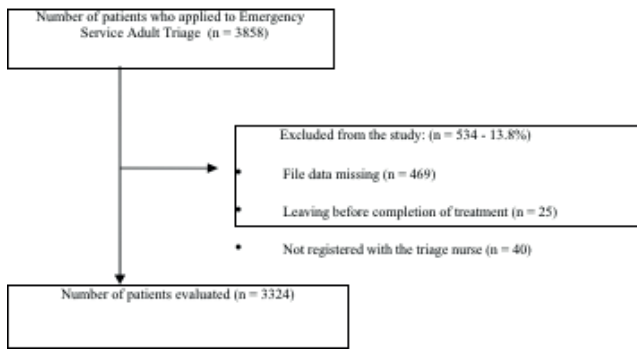
ESI categorization for each patient was determined by two emergency physicians. When there was a discrepancy between two physicians, a third emergency physician determined the ESI triage category and the determined categorization were accepted as the gold standard. The categories determined in the triage unit at the time of the patient application were compared with the ESI triage categories determined by examining the information about the patient’s entire care.

Descriptive statistics were presented with frequency, percentage, mean, standard deviation, median, minimum, and maximum values. In the analysis of categorical data, Fisher’s Exact Test (Fisher’s Exact Test) was used if the expected value was less than 5 and the cell percentage was greater than 20%, and if it was small, the Pearson Chi-Square (Pearson Chi-Square) Test was used. Differences between two dependent ratios were evaluated using the McNemar Test. Analyzes were performed using the IBM Statistical Package for the Social Sciences (SPSS) 23.0 program.  $p < 0.05$  was considered statistically significant.

## Results

Between March 1, 2018 and March 14, 2018, when the study was conducted, 3858 patients applied to Akdeniz University Hospital Adult Emergency Service. According to the records of the Hospital Information Management System, 467 patients with missing data in the patient files and 25 patients who left the emergency department before their treatment was completed were not included in the study. 40 patients, who can not be identified by whom the triage evaluation was performed were excluded from the study. The patient flow chart is shown in Figure 2.

The mean age of 3324 patients included in the study was  $40.35 \pm 18.2$  years. 1649 (49.6%) of the patients were



**Figure 2:** Characteristics of the Patient Group

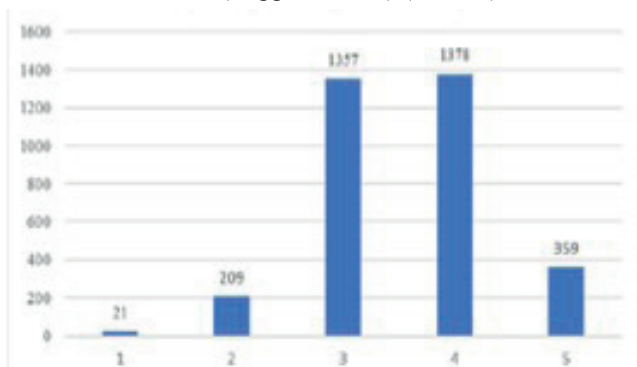
female and 1675 (50.4%) were male. While 86.7% of female patients (n = 1429) were between the ages of 18-65 (young age), this rate was found to be 86.5% (n = 1449) in men.

When the categorization of the incoming patients by triage personnel was examined, it was observed that there was an excess in Category 3 (n = 1357, 40.8%) and Category 4 (n = 1378, 41.5%) patients. While only 21 patients (0.6%) were Category 1, 209 patients (6.3%) were determined as Category 2. The category of 359 patients (10.8%) was evaluated as Category 5 by the triage nurses (Figure 3).

In the classification made by two emergency physicians according to the ESI categorization, the same ESI category was determined in 3246 of 3324 patients. The categorization of 78 patients (2.3%) who had inconsistency between the decisions of the two emergency physicians was evaluated by a third physician. According to the evaluation made by the third emergency physician, it was observed that the triage error rate of the first emergency physician was 1.41%, while the error rate of the second physician was 1.23%. When the harmony between the two physicians was examined, it was observed that there was a perfect fit (Kappa = 0.968).

In the evaluation of emergency physicians retrospectively, considering all patient information, 21 patients (0.6%) Category 1, 558 patients (16.8%) Category 2, 1178 patients (35.4%) Category 3, 987 patients (%) Category 4 and 580 patients (17.4%) were determined as Category 5 (Table 1).

When we compared the evaluation made by the triage nurse and the results of the evaluation made retrospectively according to ESI, it was observed that the harmony between them was moderate (Kappa = 0.412) (Table 1).



**Figure 3:** Number of patients according to the categorization made by the triage nurse

According to the ESI categorization accepted as the gold standard in the study, 66.0% of 558 patients determined as Category 2, 36.2% of 1178 patients determined as Category 3 and 11.8% of 987 patients determined as Category 4 it was seen that a lower category was given by the triage nurses. When the scores of triage nurses and emergency physicians were compared, significant differences were found especially in patients in category 2. Since patients with triage level 2 require urgent care and treatment, it is of great importance that they are better categorized by triage nurses, their triage level is determined correctly and they are taken to the appropriate care-treatment area more quickly. According to the ESI categorization, 62.2% of 580 patients designated as Category 5, 19.1% of 987 patients designated as Category 4, and 1.4% of 1178 patients designated as Category 3 were given a higher triage category by triage nurses (Table 1).

**Table 1:** Comparison of the triage score determined by the triage officer at the time of application with the ESI score

Triage Nurses' Score	ESI SCORE					Total
	1	2	3	4	5	
1	21 (%0,6)	0	0	0	0	21 (%0,6)
2	0	192 (%5,7)	16 (%0,4)	1 (%0,03)	0	209 (%6,3)
3	0	281 (%8,4)	836 (%25,1)	188 (%5,6)	52 (%1,5)	1357 (%40,8)
4	0	78 (%2,3)	309 (%9,2)	682 (%20,5)	309 (%9,2)	1378 (%41,5)
5	0	7 (%0,2)	17 (%0,5)	116 (%3,4)	219 (%6,5)	359 (%10,8)
<b>Total</b>	21 (%0,6)	558 (%16,8)	1178 (%35,4)	987 (%29,7)	580 (%17,4)	3324 (%100,0)

Note: The area made by the triage personnel and determined as high triage according to the ESI categorization is light turquoise; the area designated as low triage is gray in color.

The number of patients who underwent low triage by triage nurses was 808 (24.3%), and the number of patients who underwent high triage was 566 (17.0%). It was determined that these differences between triage increased in Category 3 and Category 4. When looking at the difference between age groups and gender, no significant difference was found. The majority of the patients (86.6%) were between the ages of 18-65.

In the examination performed among the age groups of the patients, it was found that the high triage rate was higher in younger patients (p = 0.000) (Table 2).

It was learned that 65.2% (n = 2170) of the patients who applied to the emergency department did not use medication continuously. It was observed that the low triage rate increased, while the high triage rate decreased in patients using medication (p = 0,000).

**Table 2:** Relationship between triage accuracy and age group

Age Groups	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
Children	6 (%15,0)	28 (%70,0)	6 (%15,0)	40 (%1,2)
Young	712 (%24,7)	1646 (%57,2)	520 (%18,1)	2878 (%86,6)
Middle age	69 (%21,7)	215 (%67,6)	34 (%10,7)	318 (%9,6)
Old	21 (%23,9)	61 (%69,3)	6 (%6,8)	88 (%2,7)
Total	808 (%24,3)	1950 (%58,6)	566 (%17,0)	3324 (%100,0)

\*Percentage of column \*\*Percentage of rows

When evaluated according to whether there was a chronic disease in the history of the patients, it was found that 59.5% (n = 1981) had at least one chronic disease. In the presence of a chronic disease, a worsening in triage categorization was observed (p = 0.000) (Table 3). When the accuracy of triage was examined, an increase in correct triage and a decrease in high triage were observed in the presence of a chronic disease. However, the presence of a chronic disease caused an increase in the number of patients undergoing low triage (Table 3).

**Table 3:** Relationship between triage accuracy and chronic disease

Chronic Disease	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
Yes	380 (%28,3)	816 (%60,7)	148 (%11,0)	1344 (%40,4)
No	428 (%21,6)	1134 (%57,3)	418 (%21,1)	1980 (%59,6)
Total	808 (%24,3)	1950 (%58,7)	566 (%17,0)	3324 (%100,0)

\*Percentage of column \*\*Percentage of rows

During the study period, it was found that the highest number of admissions to the emergency department were 32.5% during the day. There was no significant difference between the patients' admission time and triage assessment (p = 0.066) (Table 4).

**Table 4:** Evaluation of triage accuracy by application time

Application time	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
Day	369 (%25,1)	863 (%58,6)	241 (%16,4)	1473 (%44,3)
Evening	168 (%25,0)	399 (%59,3)	106 (%15,8)	673 (%20,3)
Night	271 (%23,0)	688 (%58,4)	219 (%18,6)	1178 (%35,4)
Total	808 (%24,3)	1950 (%58,7)	566 (%17,0)	3324 (%100)

\*Percentage of column \*\*Percentage of rows

The methods of applying the patients to the emergency department were examined in two separate classes: "by ambulance" and "by their own means". The number of patients admitted by ambulance was 198 (6.0%), and the number of outpatients was 3128 (94%). Category 3 patients constituted the majority of patients (n = 85) brought by ambulance. In the group of patients who came with their own means, there were more patients with Category 4 (n = 1300) (p = 0.758).

The application complaints of patients who applied to the emergency department were analyzed in 15 sub-categories. Trauma patients constituted 11.51% (n = 383) of the patients who applied to our emergency department. It was determined that the most frequent admissions were complaints related to ear, nose and throat diseases (20.5%), gastrointestinal system diseases (12.2%), traumatic conditions (11.5%) and cardiovascular system diseases (9.6%).

When the application complaints and triage accuracy rates were examined, nephrological disorders with 79.4% and cardiovascular diseases with 73.4% were determined to be the most accurately triaged disease groups. Eye diseases (43.3%) and oncological diseases (50.0%) were determined as the group with the worst triage accuracy.

Considering the vital signs obtained during the triage application of the patients included in the study, the mean systolic blood pressure was  $129.4 \pm 21.0$  mmHg, the average diastolic blood pressure was  $73.9 \pm 12.1$  mmHg, the median respiratory rate was 20 breaths / min (minimum 14 - maximum 60), the median heart rate was 91 beats / min (minimum 38 - maximum 201) and the average oxygen saturation was  $97.3 \pm 2.4\%$ .

While the correct triage evaluation was made in 86% (n = 68) of the patients with oxygen saturation below 90% (hypoxic), it was observed that this rate decreased to 58% (n = 1882) in non-hypoxic patients (Table 5).

**Table 5:** Relationship between triage assessment and hypoxia

Hypoxia	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
Yes	10 (%0,3)	68 (%2)	1 (%0,03)	79 (%2,9)
No	79 8 (%24)	1882 (%56,6)	565 (%16,9)	3245 (%97,6)
Total	808 (%24,3)	1950 (%58,6)	566 (%17,0)	3324 (100,0)

\*Percentage of column \*\*Percentage of rows

When the respiratory rate and triage accuracy were examined, it was observed that when the respiratory rate was more than 20 breaths per minute (tachypnea), there was an increase in the low triage rate and a decrease in the high triage rate (p = 0.000) (Table 6).

**Table 6:** Relationship between triage assessment and tachypnea

Tachypnea	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
Yes	167 (%33,7)	287 (%57,9)	41 (%8,3)	495 (%14,9)
No	641 (%22,7)	1663 (%58,7)	525 (%18,7)	2829 (%85,1)
Total	808 (%24,3)	1950 (%58,7)	566 (%17,0)	3324 (%100,0)

\*Percentage of column \*\*Percentage of rows

When we examined the accuracy of triage with heart rate, it was found that there was no significant change with bradycardia (heart rate <60 beats / minute) ( $p = 0.168$ ).

When the effect of blood pressure values on triage decision was examined, no significant difference was observed in terms of hypotension (systolic blood pressure <90 mmHg) ( $p = 0.628$ ) and hypertension (systolic blood pressure > 140 mmHg) ( $p = 0.086$ ).

The triage of the patients at the time of admission was performed by personnel who had at least 2 years of emergency service working period and had triage training. Of the 21 personnel who did triage, 15 were female (71.4%) and 6 were male (28.6%). No statistically significant difference was observed in the accuracy of triage in terms of gender ( $p = 0.075$ ), duration of professional training ( $p = 0.304$ ), years of employment in the profession ( $p = 0.086$ ), and years of work in the emergency department ( $p = 0.034$ ) (Table 7).

**Table 7:** Relationship between the working time of healthcare professionals in the emergency department and the accuracy of triage

Years of work in emergency department	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
2	121 (%27)	247 (%55,1)	80 (%17,9)	448 (%13,5)
3	203 (%24)	508 (%60)	135 (%16)	846 (%25,5)
4	207 (%25,9)	475 (%59,4)	118 (%14,8)	800 (%24,1)
5	56 (%23,5)	139 (%58,4)	43 (%18,1)	238 (%7,2)
6	43 (%25)	97 (%56,4)	32 (%18,6)	172 (%5,2)
7	12 (%35,3)	20 (%58,8)	2 (%5,9)	34 (%1,0)
8	77 (%20,1)	229 (%59,8)	77 (%20,1)	383 (%11,5)
9	3 (%13,6)	13 (%59,1)	6 (%27,3)	22 (%0,7)
10	85 (%22,7)	217 (%58)	72 (%19,3)	374 (%11,3)
18	1 (%14,3)	5 (%71,4)	1 (%14,3)	7 (%0,2)
TOTAL	808 (%24,3)	1950 (%58,6)	566 (%17,0)	3324 (100,0)

\*Percentage of column \*\*Percentage of rows

When the accuracy of the triage performed by the examining physician was evaluated, no significant relationship was observed between the duration of the study and the triage accuracy ( $p > 0.05$ ) (Table 8).

**Table 8:** Relation between the seniority of the emergency physician and the accuracy of triage

Seniority	Triage Accuracy			Total (Number, %*)
	Low Triage (Number, %**)	Correct Triage (Number, %**)	High Triage (Number, %**)	
Low	458 (%24,9)	1086 (%59,1)	294 (%16,0)	1838 (%55,3)
Intermediate	269 (%25,1)	607 (%56,7)	195 (%18,2)	1071 (%32,2)
Senior	81 (%19,5)	257 (%61,4)	77 (%18,6)	415 (%12,5)
Total	808 (%24,3)	1950 (%58,6)	566 (%17,0)	3324 (100,0)

\*Percentage of column \*\*Percentage of rows

## Discussion

Emergency services are among the departments where the number of patient applications cannot be known and limited in advance. Any patient who thinks that his / her complaint is urgent can apply to the emergency services for 24 hours. There is a wide scale in patients' complaints ranging from minor complaints to cardiopulmonary arrest. Applying at any time of the patients with all kinds of complaints prevents working with appointments. With the exceeding of the capacities of emergency services, the application of triage becomes obligatory. All these situations necessitated the application of effective and reliable triage.

In an ideal emergency room, every patient who applies should be examined and treated as soon as possible. Hospitals should use a triage system appropriate to the number of patients presenting to emergency services, the characteristics and resources of these patients. They can develop this system over time, as well as use triage methods, which are widely used in the world and whose validity and reliability have been proven.

The triage system determined by the Ministry of Health is used in our emergency department. Our aim in this study was to compare the triage categorization performed by experienced and trained triage personnel of the patients who applied to the emergency department with the Emergency Severity Index (ESI) system categorization determined according to the examinations, treatments and interventions performed during the evaluation of the patients in the emergency department.

The triage category of 82.3% of the patients who were admitted by the triage personnel within a two-week period

was determined as Category 3 or 4. According to ESI, this rate was 65.1%. While there was full compliance in Category 1, it was observed that healthcare personnel gave lower triage category than the ESI categorization in other categories. Prospective studies should be conducted to determine why healthcare personnel identify lower categorization. It should be evaluated whether the categorization system is a problem or a deficiency in the clinical decision of the triage personnel. Although the health personnel evaluating the patients included in the study in the triage department of the emergency department should be much more experienced, it should be ensured that the health personnel working in this department regularly receive the necessary training and certification programmed for the functioning of the emergency department, and they should receive practical and theoretical training on these issues at regular intervals.

We used the "inter-rater agreement" test, which is thought to be the most appropriate to compare two changes of this type, in order to compare the ESI category, which was formed as a result of the triage performed during the emergency admission of the patient and the evaluation of the physician examining it (7). In our study, the weighted kappa value calculated with the inter-rater consistency test was among the median limits. The weighted kappa value was calculated as 0.76 for ESI version 2 and 0.89 for ESI version 3 (8, 9). In a study conducted for ESI version 3, the weighted kappa value was determined to be 0.84-1.00 over the standard scenario (10). In another study conducted on real patients for ESI version 1, it was reported that the weighted kappa value was found to be 0.80 (11).

Rahmani et al. in their study, a significant difference was observed in the comparison between the triage personnel and the doctor and the kappa value was calculated as 0.659 (12). In another study conducted by Esmailian et al., nurse-doctor triage compliance was found to be over 90% (13). However, in the study of Goransson and von Rosen, a triage personnel success rate of 58% was observed, similar to our study (14).

Considering the excessive triage and low triage rates, the acceptable high triage rate suggested in the American Committee of Trauma Surgeons (ACSCOT) book was stated as 50% and the low triage rate as 10% (15). In our study, the low triage rate was 24.3%, while the high triage rate was 17%. In the triage evaluation performed by healthcare personnel in our emergency department, it was found that the low triage rate was higher than the acceptable value. It was thought that it would be beneficial to use more information and case examples for these complaints in the training of triage personnel.

We found that the low triage rate was significantly higher in the triage evaluation of patients with chronic diseases and continuous medication. It can be thought that the questioning of chronic illness and continuous drug use was done inadequately by triage personnel.

It was observed that a significantly lower triage category was given by triage personnel in patients with tachypnea. A

similar situation was observed in the studies of Hinson et al. (16). In many emergency departments, health personnel working in the triage department may often ignore this parameter and may not prioritize it, but perhaps the parameter that should be paid the most attention in triage is respiratory rate. According to our last assessment, which is considered to be the gold standard, it was thought that vital signs should be taken more seriously by triage personnel. It was observed that the respiratory rate parameter used in triage assessment was one of the most important parameters in the evaluation of the triage score of the patient and the triage score was low especially in tachypnoea cases.

It has been observed that triage success increases when patients are hypoxic. We evaluated this situation, which is similar to ESI, as the deterioration in the patient's vitals increased the attention of the triage nurses.

When the time of admission to the emergency service and the way of admission were examined, no significant differences were observed. While the number of admissions to our emergency department during the daytime was high, Rahmani et al. in their study, unlike our study, reported that there was an increase in patient admissions during the night time (12).

In the study conducted by Källberg et al., it was stated that the biggest reason for triage errors was the tenure of the triage personnel in the emergency department (17). However, as in our study, it has been reported in many studies that the experience of triage personnel is not related to triage errors. In our study, it may be that the duty period of the triage personnel in the emergency department did not make a difference in the triage decision and that the health personnel in our emergency department started to triage after 2 years of experience. This situation suggests that the 2-year period is sufficient in terms of experience.

When the correct triage rates are examined, it is seen that the most correct triage is done in nephrological diseases with 79.4% and cardiovascular diseases with 73.4%. Eye diseases (43.3%) and oncological diseases (50.0%) are the worst triage diseases. The reason for this situation may be the negligence of the triage personnel for chronic diseases such as cancer and the lack of knowledge of the branch where emergency medicine practice is less, such as eye diseases. According to the results of the study, the high triage accuracy rate of patients presenting with cardiovascular symptoms is a positive result, but the triage accuracy rate of patients presenting with oncological diseases is low. In some regions of our country, the elderly population is densely populated and there is a significant increase in the number of individuals with oncological diseases every day, and the possible emergencies of oncological diseases in such patients are also increasing and most of them require urgent follow-up, treatment and hospitalization. Therefore, triage procedures of patients admitted to the emergency department due to oncological diseases should be carried out carefully like other important situations.



## Limitations

Our study had some limitations. The pain scale, which has an important place in the ESI triage scale, was excluded from the evaluation because it was not entered into the system by the triage staff and by the attending physician many times simultaneously. Failure to evaluate triage adequacy in pediatric patients can be seen as a limitation of the study, since patients over the age of 18 and pediatric traumas were admitted to our emergency department.

Since our study was conducted in a health center where the number of outpatient admissions is relatively low compared to the emergency departments of training-research hospitals and university hospitals in other large cities, the importance of the professional experience of triage personnel in terms of triage accuracy could not be statistically revealed. A multicenter study can be conducted on this subject or more data can be obtained by keeping the study population larger.

If age groups and age ranges could have been determined more realistically and in accordance with the scientific study, more significant differences in triage scores between age groups could have been detected.

In addition to the parameters used in ESI Triage scoring, assessments such as finger prick blood glucose and brief neurological assessment can also be evaluated depending on the patient's medical history and may be useful in triage assessment.

## Conclusion

As a result of our study, it was seen that triage personnel gave a lower triage category than expected, although they had an acceptable triage success in general. In order to increase the accuracy of triage, it is necessary to increase the medical knowledge of the triage nurse and to provide practical training on real cases, especially about patients with triage category 2-4. In order to eliminate the triage errors due to the deficiencies in the anamnesis and vital signs, it is necessary to extend the triage time allocated for each patient and to increase the number of triage units in rush hours.

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# Acute Poisoning Cases Admitted to a Tertiary Hospital Emergency Department: A Prospective and Discriptive Study

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## Abstract

**Background:** Acute poisoning, characterized by exposure to toxic substances for less than 24 hours, is a significant public health issue worldwide. Factors leading to poisoning vary by region, customs, and socioeconomic level. To prevent this, countries and regions should analyze etiological and demographic characteristics of poisoning and take precautions. This study aimed to determine demographic, etiologic, and clinical characteristics of acute poisoning cases.

**Material and Method:** The study analyzed sociodemographic factors, clinical outcomes, and the causes of poisoning. Patients who attempted suicide were consulted by psychiatry at the end of their follow-up. The data was analyzed using Windows SPSS 21.0, with  $p < 0.05$  considered statistically significant.

**Result:** A study of 236,464 patients admitted to the adult emergency department within a 6-month period found that 432 (0.18%) were diagnosed with acute poisoning. The most common cause of acute poisoning cases was suicide attempts. The most common exposure agents were analgesics and antidepressants. The proportion of females (75.2%) in suicide attempts and males (89.5%) in abuse was statistically significantly higher. Of the 286 patients with suicide attempts, 212 (74.1%) underwent psychiatric consultation in the emergency department. The predominant psychosocial factors contributing to suicide attempts were familial issues and socioeconomic insufficiency. The overall mortality rate in patients followed up for acute poisoning was 0.46%.

**Conclusion:** The most common cause is intentional poisoning, particularly suicidal. Therapeutic drugs and food poisoning are the most common toxic agents. Family problems and socioeconomic inadequacy are common reasons for suicide attempts.

**Keywords:** Acute poisoning, epidemiology, emergency department, suicide.

## Introduction

Poisoning remains a common cause of morbidity and mortality worldwide (1). Acute poisoning is characterized as exposure to a toxic substance for a short period of time, typically less than 24 hours (2). In many parts of the world, acute poisoning is a big public health problem that can be avoided and leads to illness and death (3,4). In the past, statistics on patients poisoned in emergency departments in Turkey were quite scarce. However, improved records and data on acute or emergency poisoning cases through the Turkish Statistical Institute (TUIK) and the 114 National Poison Call Center have helped us understand the importance of this health problem (5,6). In many countries, acute poisoning due to drugs and chemicals is among the most common reasons for admission to emergency departments. In the United States of America (USA), a developed country, the annual incidence of poisoning cases has been reported at 0.68 (7). In studies conducted in our country on acute poisonings, the annual incidence of admissions to emergency departments due to poisoning was found to be between 0.7% and 10.1% (8-12).

The factors leading to poisoning may vary according to the region of residence, the customs and traditions of the society, and the socioeconomic level. For this reason, each country and even each region should conduct studies analyzing the etiological and demographic characteristics of poisoning and take precautions. Obtaining the latest up-to-date information on acute poisoning is also important for the planning of health and education services.

The aim of this study was to determine the demographic, etiologic, and clinical characteristics of acute poisoning cases admitted to the Emergency Department of Kayseri Education and Research Hospital (KEAH), to determine the risk factors leading to poisoning, and to determine the follow-up periods of these cases in the emergency department and intensive care unit.

## Material and Method

This prospective study included patients aged 18 years and older who were admitted to the emergency department of KEAH with acute poisoning during the 6-month period

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between April 15, 2014 and October 15, 2014. This observational cross-sectional study was initiated with the decision of the Education Planning Committee of Kayseri Training and Research Hospital dated 07/04/2014 under number 28.

### Study Design

This descriptive study was planned prospectively to include cases of acute poisoning in individuals aged 18 years and older who were admitted to the KEAH Emergency Department. The resident physicians entered patient data into the pre-established database. Patients who consented to participate in the study were included in the study. In addition, patients with incomplete data were excluded from the study. The study was conducted in accordance with the ethical rules of the helsinki declaration. This study is a publication produced from a thesis.

### Analyzed Data

The study examined various sociodemographic factors of the patients in the database, including age, gender, educational attainment, marital status, occupation, and monthly family income level, as well as the specific details regarding the nature and type of intoxication. The evaluation of the patients' level of consciousness upon their arrival at the emergency department was conducted using the Glasgow Coma Scale (GCS). This study assessed acute poisoning clinical outcomes (discharge, admission to the critical care unit or ward, transfer to another hospital, voluntary departure from the clinic, or death). Mortality rates and discharge times from the intensive care unit were also analyzed in the study. In determining the type of poisoning, information was obtained from the patients themselves or their relatives who were present at the time of admission to the emergency department and the causes of poisoning due to suicide, accidental ingestion or abuse or addiction of toxicological substances were investigated. Patients who attempted suicide were consulted by psychiatry at the end of their emergency department follow-up. In this way, it was possible to distinguish between real suicide attempts and impulsive suicide attempts. Biopsychosocial factors underlying suicidal ideation were also investigated.

### Statistics

The data were analyzed using the Windows SPSS 21.0 statistical package program. In descriptive statistics, qualitative data were expressed as rates and percentages. Chi-square test was used to compare categorical variables between two groups, one-way analysis of variance (Anova, F test) was used to compare more than two group averages, and Tukey HSD method was used as 'post-hoc' method in multiple comparisons made after analysis of variance. Normally distributed quantitative data were expressed as mean±Standard deviation; non-normally distributed

quantitative data were expressed as median (minimum-maximum). Kolmogorov-Smirnov test was performed for normality test. All data were analyzed at 95% confidence interval and  $p < 0.05$  was considered statistically significant.

## Results

Among a total of 236,464 patients admitted to the adult emergency department within a 6-month period, 432 (0.18%) patients aged 18 years and over were followed up with a diagnosis of acute poisoning. Demographic data for 432 patients is shown in Table 1. In our study, 150 (34.7%) of

**Table 1:** Sociodemographic characteristics of poisoning cases

Variables	Count (N:432)	Percentage (%)
<b>Sex</b>		
Male	150	34.7
Female	282	65.3
<b>Age Groups (years) - mean age: 30.93±12.88</b>		
18-25	194	44.9
26-35	105	24.3
36-44	70	16.2
45-54	34	7.9
55-64	19	4.4
65-81	10	2.3
<b>Marital status</b>		
Married	264	61.1
Single	146	33.8
Widowed/divorced	22	5.1
<b>Education Status</b>		
Illiterate	20	4.6
Primary (elementary-middle school)	281	65
High School	108	25
University	23	5.3
<b>Place of Residence</b>		
City	388	89.8
District	25	5.8
Town	7	1.6
Village	12	2.8
<b>Job Status</b>		
Working	126	29.2
Unemployed	66	15.3
Housewife	175	40.5
Retired	18	4.2
Student	40	9.3
Military Personnel	7	1.6
<b>Monthly income level (TL) mean income: 1239.76± 709.58</b>		
0-950	134	31.0
951-1900	217	50.2
1901-3800	77	17.8
3801-5000	4	0.9

the patients admitted with the diagnosis of acute poisoning were male, and 282 (65.3%) were female. The mean age of the patients was  $30.93 \pm 12.88$  years. Considering the age distribution of the patients, the highest number of applications was found in the 18–25 age group, with a rate of 44.9%. Most of the applications were made by those living in the city center, with a rate of 89.8%. When the cases were analyzed according to marital status, it was observed that a higher proportion of the patients were married (61.1%). In addition, according to educational status, the majority of the patients (65%) were primary and secondary school graduates. When compared according to the monthly income level of the household, it was found that the highest number of visits to the emergency department were among patients with low income levels (the minimum wage was calculated as 950 TL

The manifestation and causes of acute poisoning cases are summarized in Table 2. Accordingly, out of 432 patients, 286 (66.2%) were poisoned due to suicide attempts, 127 (29.4%) due to accidents, 19 (4.4%) due to abuse or addiction, 273 (63.2%) due to drugs, 19 (4.4%) due to chemical gas, 23 (5.3%) due to pesticides, 25 (5.8%) due to corrosive agents, 53 (12.3%) due to food, and 39 (9.3%) due to other causes.

The median Glasgow Coma Scale (GCS) value of the patients upon their arrival at the emergency department was 15, with a minimum value of 4 and a maximum value of 15. The number of intoxications with a single drug was 176 (64.5%), and the number of multiple drug exposures was 97 (35.5%) (N = 273). The most common cause and percentage of poisonings are summarized in Table 3. The most common exposure agents were analgesics with a rate of 31.3% (NSAIDs 21.6%; paracetamol 9.7%) and antidepressants with a rate of 22.2%. Carbon monoxide (CO) was identified as the causal agent in all 19 patients (100.0%) who were affected by chemical gas poisoning. Among the cases of acute pesticide poisoning, a majority of 60.9% (n=14) were attributed to insecticides, while 30.4% (n=7) were caused by rodenticides. Herbicides accounted for a smaller proportion of cases at 8.7% (n=2). Among 15 patients poisoned with

**Table 3:** The most common agents and their percentages in acute poisonings

Type of Poisoning		Most common agent	Percent(%)
Drugs	Analgesics (n:176)	Analgesics	%31.3
	Paracetamol+NSAIDs (n:97)	Paracetamol + NSAIDs	%13.40
Chemical Gas (n:19)		Carbon Monoxide	% 100.0
Pesticides (n: 23)		Organophosphate	% 34.78
Corrosive Agent (n:25)		Bleach	% 64.0
Food (n:53)		mushrooms	% 58.5
Other* (n: 39)		Scorpion bite/sting	% 20.51

\*(15 patients with poisonous animal bites or stings, 9 patients with drugs, 7 patients with alcohol, and 8 patients with more than one type of exposure)

insecticides, the causative organophosphate was found in 8 patients (53.3%). The predominant cause of foodborne illness was attributed to the consumption of mushrooms, accounting for 58.5% of reported cases. Among the cases of poisoning involving caustic compounds, it was observed that 16 patients, including 64% of the total, experienced hazardous exposure specifically due to bleach. In the venomous animal bites/stings group, scorpion stings (53.3%) were the most common animal contact poisoning. Besides, ethanol was found to be the most common agent in 6 out of 7 patients (85.7%) with alcohol-only poisoning. Out of the 11 individuals who were admitted to the emergency department due to illicit drug use, it was seen that 6 patients (54.5%) reported the use of synthetic cannabis, specifically bonzai and its derivatives. Additionally, 3 patients (27.3%) acknowledged the use of cannabis, while 2 patients (18.2%) reported the use of heroin.

When gender was compared according to poisoning types, it was found that the proportion of females (75.2%) in suicide attempts and males (89.5%) in abuse was statistically significantly higher ( $p < 0.001$ ). In addition, when the age, GCS and length of stay in the intensive care unit were compared according to the type of intoxication, the mean age was found to be lower in the suicide attempt group than in the accidental and substance abuse group, and the mean GCS was found to be lower in the substance abuse group. And this difference was found to be statistically significant ( $p < 0.001$ ). On the other hand, no significant difference was found when the types of poisoning were compared according to the duration of intensive care unit stay ( $p = 0.47$ ). This relationship is shown in table 4.

Of the 286 patients with suicide attempts, 212 (74.1%) underwent psychiatric consultation in the emergency department. As a result of psychiatric consultation, 71 (33.5%) and 141 (66.5%) of the 212 patients were evaluated as real and impulsive suicide attempts, respectively. The predominant psychosocial factors contributing to suicide attempts were identified as familial issues (57.3%) and socioeconomic insufficiency (9.1%). Among the suicide attempts evaluated by a psychiatrist in the emergency

**Table 2:** Types and manifestation of acute poisoning

		Count	Percent (%)
Types	Drugs	273	63.2
	Chemical Gas	19	4.4
	Pesticide	23	5.3
	Corrosive Agent	25	5.8
	Nutrients	53	12.3
	Other*	39	9.3
	Total	432	100.0
Manifestation	Suicide attempt	286	66.2
	Accident	127	29.4
	Abuse/addiction	19	4.4

**Table 4:** Comparison of gender, age, GCS, length of stay in intensive care unit according to the type of intoxication

Variables		Type of poisoning				P value
		Accidental	Abuse	Total		
Suicide Attempt		*mean ± SD	*mean ± SD	*mean ± SD		
Gender n (%)	Male	71 (24.8)	62 (48.8)	17 (89.5)	150 (34.7)	<0.001**
	Female	215 (75.2)	65 (51.2)	2 (10.5)	282 (65.3)	
*Age		27.66 ± 9.92	37.59 ± 15.78	35.63 ± 12.69	30.93 ± 12.88	<0.001***
*GCS		14.87 ± 0.72	14.99 ± 0.08	12.89 ± 2.94	14.82 ± 0.94	<0.001***
*Length of Stay in the Intensive Care Unit		3.06 ± 1.16	2.73 ± 0.45	3.50 ± 2.12	3.00 ± 1.07	0.47***

\*mean±SD, \*\*chi-square analysis, \*\*\*One-way ANOVA analysis

department (n=212), 45 patients (21.22%) were under psychiatric follow-up in the last 6 months. In addition, 34 of 212 patients (16.03%) had suicidal ideation. The rate of actual suicide attempts was higher than impulsive suicide attempts in patients with suicidal ideation who were under psychiatric follow-up in the last 6 months, and this difference was statistically significant (p<0.001). This relationship is shown in table 5. Finally, 47.9% of the patients were discharged, 23.4% left the emergency department voluntarily before the end of the follow-up period, 13% were admitted to in-hospital wards, 8.6% were admitted to in-hospital intensive care units, 6.9% were referred to the intensive care units of another institution and 1 patient (0.2%) died. Of the 67 patients hospitalized in the intensive care unit due to poisoning, 66 (98.5%) were discharged from the unit, and 1 patient (1.5%) also died. The overall mortality rate (n=2) in patients followed up for acute poisoning was 0.46%.

## Discussion

In studies conducted in different centers, there are differences in the rates of poisoning cases admitted to the emergency department (13,14). This is due to the fact that in the regions

**Table 5:** Comparison of gender, age, GCS, length of stay in intensive care unit according to the type of intoxication

Variables		Real n (%)	Impulsive n (%)	Total n (%)	P value
Psychiatric follow-up in the last 6 months	Yes	28 (62.22)	17 (37.78)	45 (100.0)	<0.001
	No	43 (25.75)	124 (74.25)	167 (100.0)	
	Total	71 (33.49)	141 (66.51)	212 (100)	
Suicidal thoughts again	Yes	30 (88.23)	4 (11.77)	34(100.0)	<0.001
	No	41(23)	137 (77)	178 (100.0)	
	Total	71(33.49)	141 (66.51)	212 (100)	

where hospitals are established, the sociodemographic characteristics, customs, and traditions of the people in that region differ between regions and even countries. The annual incidence of acute poisoning cases admitted to emergency rooms in Turkey varies between 0.7% and 2.4% (8-12), according to studies published in the literature. This rate was determined to be 0.18% in our study. In comparison to other research conducted in Turkey, this rate was found to be low. We believe that the fact that green area patients make up the majority of annual emergency department visits (50.7%) and that the emergency department is used as an outpatient clinic has a significant impact on this. In studies conducted in Turkey, it is observed that poisoning cases are mostly in women and young people (15-17). Similar results were also obtained in our study. In addition, when the age distribution of the patients was analyzed, it was observed that most of the applications were in the 18-25 age group. Consistent with findings from previous research conducted in our country and neighboring Iran (18-20), which are considered developing nations, the majority of acute poisoning cases in our study consisted of individuals residing in urban areas (89.8%). Furthermore, a significant proportion of these cases were primary school graduates (65%), individuals with low income levels (81.2%), married individuals (61.1%), and housewives (40.5%). In our study, the most common agent taken for poisoning was high dose drug intake (63.2%). This rate is similar to the results of studies conducted in other regions of Turkey (21,22). According to the reports of other country studies, drugs were found to be the most commonly ingested agent in acute poisonings (13,14,23). However, drugs may not be the most common agent in countries with a high rate of agriculture. For example, in a study conducted in Thailand, pesticides (41.5%) were found to be the most common agent (24). In our study, analgesics (NSAIDs 21.6%; paracetamol 9.7%) and antidepressants (22.2%) were the most common agents in single drug poisonings, respectively. The ranking remains unchanged for all drug poisonings, including combinations. We think that this is due to the easy access and widespread use of analgesics and antidepressants. Unlike benzodiazepines, antidepressants, which can be dispensed from pharmacies even without a prescription, are considered to be the most frequently used agents in acute poisonings due to their unintentional consumption as 'feel-good' drugs. For this reason, we believe that trainings should be provided to raise awareness among the public about these drugs and their side effects in order to be aware of the side effects that can be caused by high doses of these drugs, especially paracetamol, which seems innocent, and we strongly recommend that antidepressant drugs should be given by pharmacies against prescription in order not to be consumed off-label. While paracetamol was the most common analgesic agent in some studies conducted in some regions of Turkey (9,11), NSAIDs were found to be the most common agent in some studies including our study

(8,22,25). In our study, the mortality rate was found to be 0.46 % in patients admitted with acute poisoning. Eddlestone et al. reported that mortality rates due to poisoning varied between 0% and 50% (26). In the same study, the reasons for the wide range of mortality rates were shown to be the severity of the poisoning, the ingestion of lethal or nonlethal agents and the fact that serious cases resulting in death occurred before hospitalization. In our study, deaths were due to methanol (abuse) and organophosphate ingestion (suicide attempt) and the gender of the patients was male in both deaths.

When the biopsychosocial reasons for suicide attempts were analyzed, familial problems were the most common reason (57.3%). It has been reported that 80%-90% of the cases of self-harm in England are between 80% and 90% and 50% of these cases are due to family problems (27). Furthermore, in a multicenter study conducted by Schmidtke et al. investigating the sociodemographic characteristics of suicide attempts in European countries, it was reported that suicide attempts were mostly in the low social class; were most common in women aged 15-25 years and least common in the group aged 55 years and older; were mostly among the unmarried (singles and widows) and in cases with low education level; unemployment in men and economic independence in women was an important risk factor and previous suicide attempts were common in suicide attempt cases (28). Given that the majority of the participants in our study were married individuals and housewives, 66.5% of whom attempted impulsive suicide, it is reasonable to assume that the suicidal act was motivated by psychological distress due to household problems, as well as a desire to escape from adverse circumstances or to obtain secondary benefits. In addition, socioeconomic inadequacy was the second most common cause of suicide attempts. Upon comparing the preexisting chronic diseases or addictions of individuals who had attempted suicide with the nature of their suicide attempts, it was noted that those with underlying psychiatric disorders, substance and alcohol dependencies, and chronic illnesses exhibited a higher frequency of real suicide attempts. Our findings are consistent with previous studies (28,29). Besides, Schmidtke et al. reported that an average of 15% of suicide attempters under observation made one or more suicide attempts (28). In our study, similar to the literature, it was found that 16.8% of suicide attempters continued to have suicidal ideation. Therefore, in order to minimize the rate of suicide attempts in the future, such patients should definitely be consulted by psychiatry in emergency departments and treatment and follow-up of the patients should be planned.

### Limitations

The biggest limitation of this study is that it was a single-center study and the study period was short (6 months). The fact that the study period did not include the winter months

may have caused the rates of some types of poisoning (CO poisoning) to be lower. In this respect, it may not be appropriate to say that our findings fully reflect the rates of acute poisoning in the general population.

## Conclusion

The present data provide additional information on the epidemiology of acute poisoning in Kayseri province. The findings showed that the incidence of acute poisoning was 0.18%. Females outnumbered males and poisoning was most common in young adults aged 18-25 years. We also observed that most cases of poisoning were intentional, especially suicidal. Our study showed that therapeutic drugs were the most common group of toxic agents, followed by food poisoning. In our study, acute poisoning cases were mostly urban dwellers, primary school graduates, people with low income, married and housewives. CO poisoning is still a serious problem in Turkey, especially in winter. Scorpion stings are the most common type of venomous animal bites or stings. In this respect, protective measures should be taken. Alcohol and substance abuse is still a serious problem in Turkey. In our study, one out of two deaths in acute poisoning cases is due to alcohol poisoning. Family problems and socioeconomic inadequacy were found to be the most common biopsychosocial reasons for suicide attempts. In order to reduce the rate of suicide attempts, risk factors should be identified through multicenter studies and measures should be taken accordingly; family support lines and social education programs should be established to minimize family problems.

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## Examination Of Neutrophil/Lymphocyte (NLR), Monocyte/Lymphocyte (MLR), And Platelet/Lymphocyte (PLR) Ratios Between Alzheimer's Disease and Vascular Dementia

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### Abstract

**Background:** The present study aims to investigate whether proinflammatory marker ratios in whole blood differ in these two dementia diseases.

**Material and Method:** This study will involve Alzheimer's disease (AD) and vascular dementia (VaD) patients who were treated as outpatients in the outpatient clinic and inpatients in the ward of the Neurology Department of Adnan Menderes University Hospital. The patients' diagnoses will be scanned in the hospital information system. The admission blood results of patients who presented between January 2018 and September 2020 will be included, and the patients' hemogram results will be scanned retrospectively. Neutrophil/lymphocyte, monocyte/lymphocyte, and platelet/lymphocyte ratios in the hemogram results will be calculated and recorded.

**Result:** In the AD-VaD comparison of the patients participating in the study, a significant difference was identified between the variability of platelet/lymphocyte (PLR) and NLRs (NLR) ( $p < 0.001$ ). Moreover, a significant difference was found between the mean ages of patients with vascular dementia and those with Alzheimer's dementia ( $p < 0.0001$ ).

**Conclusion:** While proinflammatory markers obtained secondary to inflammation are significant in AD since it is a chronic and progressive process, the use of these markers is limited due to the gradual course after an acute event in vascular dementia. Furthermore, there is a need for additional studies on peripheral blood cells to identify the potential prodromal biomarkers of AD.

**Keywords:** Alzheimer's dementia, NLR, proinflammatory markers, vascular dementia.

### Introduction

Alzheimer's disease (AD) is a neurodegenerative disease that arises with irreversible loss of neurons in the hippocampus and cortex regions of the brain. Memory impairment in Alzheimer's disease often takes place as the inability to learn new information, which is characterized by short-term memory loss. Language disorders (left hemisphere posterior heteromodal) are also evident in Alzheimer's disease (1).

The pathology of AD consists of abundant senile amyloid plaques, neurofibrillary tangle structure, significant synapse and cholinergic losses, and neuron atrophy in certain regions of the brain (2).

It is known that Alzheimer's patients have synaptic loss, especially in the hippocampus, at a rate of 45-55% (3).

Alzheimer's disease, the most common cause of dementia, is reported to be found in 5 million cases over the age of 65 nowadays, according to studies conducted in the United States of America (USA) (4).

The term dementia is a persistent, frequently progressive clinical picture that leads to impairment in mental functions

and inadequacy in a person's activities of daily living. The use of the Diagnostic and Statistical Manual for Mental Disorders fourth edition (DSM-IV) diagnostic criteria has been recommended to diagnose dementia (5). The DSM-IV criteria for dementia are as follows:

Development of multiple cognitive impairments, including memory impairment and at least one of the following: (I). Aphasia, apraxia, agnosia, disruption of executive functions (II). Cognitive impairments should meet the following criteria (III). They must be severe enough to cause deterioration in professional or social functions (IV). A decrease must be observed compared to the previous high level of function (V). Dementia cannot be diagnosed if cognitive impairments develop only during delirium (VI). However, if dementia is experienced when there is no delirium, both dementia and delirium can be diagnosed. (VII). Dementia may be etiologically related to general internal conditions, substance abuse (including toxin exposure), or a combination of these factors.

Another cause of dementia is vascular dementia (VaD). VaD is characterized by loss of clinical and

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cognitive functions as a result of ischemic, hemorrhagic, or hypoperfusion damage to the brain (6). Multi-infarct dementia develops as a result of large vessel disease, whereas subcortical small vessel disease is observed in Binswanger's type VaD. Tissue loss of around 100 ml in the cortical and subcortical areas leads to dementia. In addition to tissue loss, in other words, infarct volume, the localization of the lesion is also important. The thalamus, mesial temporal area, hippocampus, frontobasal areas, and angular gyrus areas are important for these areas (7).

The present study aims to investigate whether proinflammatory marker ratios in whole blood differ in these two dementia diseases.

## Materials And Methods

The current research is a hospital-based cross-sectional study. It will involve AD and vascular dementia patients who were treated as outpatients in the outpatient clinic and inpatients in the ward of the Neurology Department of Adnan Menderes University Hospital. The patients' diagnoses will be scanned in the hospital information system. The admission blood results of patients who presented between January 2018 and September 2020 will be included, and the patients' hemogram results will be scanned retrospectively. Neutrophil/lymphocyte, monocyte/lymphocyte, and platelet/lymphocyte ratios (NLR, MLR and, PLR) in the hemogram results will be calculated and recorded. Patients diagnosed with dementia other than Alzheimer's disease and vascular dementia and healthy controls will not be included in the study. If the study group exhibits a normal distribution, continuous data will be evaluated with Student's t-test. If it does not, the Mann-Whitney U test will be used. Categorical data will be evaluated with the chi-square test. Besides, a multivariate regression analysis was performed to compare the results between Alzheimer's dementia and vascular dementia patients. The study covers 33 months between January 2018 and September 2020.  $p < 0.05$  will be considered for statistical significance.

## Results

A total of 104 patients were included in the study. Of them, 60 were male and 44 were female, 66 had Alzheimer's dementia, and 38 had vascular dementia. Of male patients, 34 had Alzheimer's dementia, and 26 had vascular dementia. Of female patients, 32 had Alzheimer's dementia, and 12 had vascular dementia.

The mean age of the patients included in the study was 73.51 years, and the lowest age was 59 years, while the highest age was 84 years. It was determined that the mean age of male patients was 72.76 years, the lowest age was 59 years, and the highest age was 82 years. The mean age

of female patients was 74.54 years, the lowest age was 66 years, and the highest age was 84 years. The mean age of patients with Alzheimer's dementia was 75.53 years, the lowest age was 68 years, and the highest age was 84 years. The mean age of patients with vascular dementia was 70.03 years, the lowest age was 59 years, and the highest age was 78 years. A significant difference was revealed between the mean age of patients with vascular dementia and patients with Alzheimer's dementia ( $p < 0.001$ ).

In the evaluation of the patients' PLRs, the mean PLR was found to be 148.14, the lowest value was 104, and the highest value was 188.24. Concerning the platelet/lymphocyte ratio of Alzheimer's dementia patients, the mean platelet/lymphocyte ratio was 155.85, the lowest platelet/lymphocyte ratio was 131, and the highest was 188. In patients with vascular dementia, the mean platelet/lymphocyte ratio was 134.75, the lowest platelet/lymphocyte ratio was 104, and the highest platelet/lymphocyte ratio was 181. A significant difference was determined between the patients' diagnoses and the variability of PLRs ( $p < 0.001$ ).

In the evaluation of the patients' NLRs the mean NLR was 9.15, the lowest value was 3.05, and the highest value was 18.20. The mean NLR of patients with Alzheimer's dementia was 10.42, the lowest NLR was 4.5, and the highest NLR was 18.2. In patients with vascular dementia, the mean NLR was 6.95, the lowest NLR was 3.5, and the highest NLR was 15.3. A significant difference was identified between the patients' diagnoses and the variability of NLRs ( $p < 0.0001$ ).

In the evaluation of the patients' MLRs, the mean MLR was 238.81, the lowest value was 217, and the highest value was 264. It was revealed that the mean MLR value was 238.6, the lowest MLR value was 217, and the highest MLR value was 264 in patients with Alzheimer's dementia. In vascular dementia patients, the mean MLR value was 239.15, the lowest MLR value was 224, and the highest MLR value was 256. No significant difference was found between the patients' diagnoses and the variability of MLRs ( $p = 0.81$ ).

The mini-mental test (mmt) mean value of patients was found as 19.78, the lowest mmt score as 17, and the highest value as 23. The mean mmt value of patients with Alzheimer's dementia was 20.03, the lowest mmt score was 7, and the highest mmt value was 23. The mean mmt score of patients with vascular dementia was 19.36, the lowest mmt score was 17, and the highest score was 23. There was a significant weak difference between the patients' diagnoses and the variability of the mmt ratios ( $p = 0.049$ ) (Table 1).

Significant regression results were obtained between Alzheimer's dementia and vascular dementia patients when the results of logistic regression analysis were compared with age ( $p < 0.0001$ ), neutrophil/lymphocyte (0.008), platelet/lymphocyte (0.006), and mini-mental test (0.002) (Table 2).

**Table 1:** Comparison of inflammatory markers, age and mini-mental values between Alzheimer's dementia and vascular dementia

	Alzheimer's dementia		Vascular dementia		Statistical analysis		
	Mean	SD	Mean	SD	F	df	p
Age	75.53	3.90	70.02	4.10	0.075	102	<0.0001
Monocyte/lymphocyte	12.85	1.58	6.72	1.09	22.40	102	0.807
Neutrophil/lymphocyte	10.41	3.07	6.95	2.89	0.176	102	<0.0001
Platelet/lymphocyte	155.84	16.89	134.76	20.14	1.292	102	<0.0001
	Mean	SD	Mean	SD	U	Z	p
Mini-mental test	20.03	1.66	19.36	1.49	969.500	-1.966	0.049

**Table 2:** Logistic regression analysis results between Alzheimer's dementia and vascular dementia patients

Independent variables	B	S.E	Exp. (B) %95 CI	p
Age	-0.561	0.136	0.570 (0.437-0.744)	<0.0001
Neutrophil/lymphocyte	-0.353	0.133	0.945 (0.907-0.984)	0.008
Platelet/lymphocyte	-0.057	0.021	0.703 (0.542-0.912)	0.006
Minimental test	-1.009	0.322	0.365 (0.194-0.685)	0.001
Constant	71.868	16.542	1.629	<0.0001

## Discussion

Studies comparing patients with AD and healthy individuals of the same age showed that immune functions were more impaired in AD (8-10). It has been asserted that increased immune aging, in other words, chronic oxidative inflammatory stress, may be an effective factor in the development of AD (9). Since immune functions are a good indicator of the aging rate, the analysis of these functions can be used in the early diagnosis of premature and rapid aging in humans (11,12).

In the study conducted with patients with cerebral hemorrhage, patients whose condition worsened in the first week had higher total white blood cell count, higher neutrophil count, and lower lymphocyte count. This refers to a higher NLR calculation. NLR was independently associated with neurological deterioration and was determined to be the best discriminating variable for predicting negative outcomes. In a retrospective analysis of patients with acute intracerebral hemorrhage (ICH), NLR values obtained 24-48 hours and 5-7 days after the onset of symptoms were significantly higher in deceased patients, whereas they remained relatively stable in patients who survived (13). The mean age of the patients included in the study was found to be 73.51 years. In the study by Shigemizu, D et al., a total of 271 AD patients were included, the male/female ratio was 1:2.15, and the mean age of the AD patients included in the study was 79.55. It is possible to make a comment that there is a compatibility between our study and the literature in terms of mean ages, and the high age of patients is known as a risk factor in AD cases (14).

In the study, 66 patients had AD, and 38 had VaD. Of the patients with AD, 34 were male, and 32 were female.

Of the cases with vascular dementia, 26 were male, and 12 were female. In the study by Claire Thompson et al., female dominance was found to be 61.5% in the AD group, and male dominance was found to be 66.2% in the VaD group (15,16). In other words, the rate of women in AD dementia is 72.7%, whereas the rate of men is 57.6%. In our study, the rate of men in vascular dementia is 43.4%, while the rate of women is 27.3%. These results were found to be consistent with the literature. This difference is explained by the long life expectancy in women (17).

In the study by Carmen Vida et al., a mini-mental test was applied to assess cognitive findings in AD cases. In the study, the value of 23 was considered as the threshold value for AD. In our study, the lowest mini-mental ratio of AD patients was 7, and the highest ratio was 23. The mini-mental test mean value of AD patients in our study was found to be 20.03. In terms of the test used, compatibility was observed between our research and the literature (18). Additional studies can be conducted to check whether there is any correlation between mini-mental values and proinflammatory markers. Neutrophil, lymphocyte, and platelet ratios in the peripheral blood of the patients were evaluated in our study. Researchers performed biomarker evaluation in peripheral blood in many diseases, including AD (19-21).

Neutrophils have been identified in the brain parenchyma of patients with Alzheimer's disease (22). In the study, neutrophil homeostasis in peripheral blood was observed to shift toward proinflammatory properties in AD patients at the later stages. Cognitive decrease in AD patients was also found to be proportional to these changes. It can be assumed that the increased levels of circulating cytokines in AD patients may be associated with cytokine production

increased by previously reported activated monocytes and lymphocytes in patients with Alzheimer's disease.

In our study, the monocyte/lymphocyte ratio was found to be  $10.41 \pm 1.58$  in the AD group and  $6.72 \pm 1.09$  in the VaD group when patients in the AD group and patients in the VaD group were compared. There was no significant difference between the two groups in terms of monocyte/lymphocyte ratio ( $P > 0.05$ ), but the high ratio obtained in the AD group is consistent with the hypotheses in the literature. In our study, the NLR was  $10.41 \pm 3.07$  in AD patients and  $6.95 \pm 2.89$  in VaD patients, and the significant difference between the two groups in terms of NLR ( $P < 0.001$ ) was found to be consistent with the literature. In the study conducted by Yuan Dong et al. (2018), blood samples collected from patients with dementia and Alzheimer's disease indicated neutrophil hyperactivation associated with increased reactive oxygen production and elevated neutrophil levels. Moreover, the same study strongly suggests that it may be a prognostic blood biomarker in patients with Alzheimer's disease. In our study, the PLR was  $155.84 \pm 16.89$  in AD patients and  $134.76 \pm 20.14$  in VaD patients, and the significant difference between the two groups in terms of PLR ( $P < 0.001$ ) was found to be consistent with the literature (22).

In the study performed by Kuyumcu et al., NLR was significantly higher in AD patients compared to controls. Although NLR values in the normal population are around 1-3, the NLR identified in AD cases was found to be  $10.41 \pm 3.07$  in the study we conducted in line with the literature (23).

## Conclusion

AD is a degenerative disease. It takes time for symptoms to appear and develop. Inflammation is known to emerge earlier in AD and contribute to neurodegeneration and pathogenesis at later stages. Inflammation is continuous in AD, whereas the neurodegenerative process is not prominent in vascular dementia as in AD. In our study, proinflammatory blood parameters, which are used in many areas, were found to be significantly different in AD and VaD, as predicted. The markers obtained secondary to inflammation are therefore significant in AD, while a significant difference was determined between AD and VaD since an acute inflammation was observed in 37 vascular dementia patients but the course was not progressive and chronic, as in AD. Furthermore, there is a need for additional studies on peripheral blood phagocytes, function in lymphocytes, and oxidative-inflammatory stress changes to identify potential prodromal biomarkers of AD.


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## Exploring the Role of Bispectral Index in Interrupting CPR for ROSC Diagnosis: A Call for Further Research

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### Abstract

The current approach in cardiopulmonary resuscitation (CPR) involves interrupting the chest compressions to assess the pulse and diagnose Return of Spontaneous Circulation (ROSC). This critical step is essential for determining the effectiveness of resuscitation efforts. However, the interruption of CPR poses a challenge, prompting researchers to explore alternative methods for diagnosing ROSC without compromising the ongoing resuscitation process.

One potential solution proposed in the literature is the use of the Bispectral Index (BIS). BIS is a numerical value derived from processed electroencephalogram data, providing a measure of the depth of anesthesia or sedation. Some studies have reported an increase in BIS values following successful ROSC during CPR. This observation suggests that monitoring BIS levels could offer real-time information about cerebral perfusion and neurological status, eliminating the need for pulse checks that require CPR interruption.

Despite these promising indications, it is crucial to acknowledge the limited existing literature on the subject. The evidence supporting the use of BIS in diagnosing ROSC during CPR is not yet robust, and further research is warranted. Researchers are encouraged to delve into this unexplored area, conducting comprehensive studies to assess the reliability and effectiveness of BIS as a tool for continuous monitoring during resuscitation efforts.

In conclusion, while the concept of using BIS to diagnose ROSC during CPR holds potential, it remains an area that requires substantial research attention. The limited existing literature underscores the need for more extensive investigations to determine the feasibility and reliability of integrating BIS into the CPR protocol. As technology advances, exploring innovative approaches for continuous assessment during resuscitation becomes imperative for improving outcomes in cardiac arrest scenarios.

**Keywords:** Cardiopulmonary resuscitation, Return of Spontaneous Circulation, Bispectral Index, Pulse checks, Cerebral perfusion, Neurological status, Resuscitation monitoring, Continuous assessment, Resuscitation outcomes.

### Cardiopulmonary resuscitation

Cardiopulmonary resuscitation (CPR) is the immediate and critical response to cardiopulmonary arrest. The primary goal of CPR is to maintain a minimal level of blood flow to vital organs, particularly the brain, until the normal heart rhythm can be restored. This is achieved through a combination of chest compressions and rescue breaths. The American Heart Association and other relevant medical organizations provide guidelines for the correct application of CPR techniques (1). In the event of witnessing someone experiencing cardiopulmonary arrest, the first step is to call for emergency medical assistance. Simultaneously, the initiation of chest compressions is crucial. Chest compressions help circulate oxygenated blood throughout the body, sustaining essential organ function (2). Additionally, rescue breaths, which involve providing breaths to the patient, play a role in delivering oxygen to the lungs. This is especially important because the interruption of normal breathing is

a hallmark of cardiopulmonary arrest. The combination of chest compressions and rescue breaths constitutes basic life support (BLS) and is vital in maintaining oxygen supply to the body's tissues (3).

Alongside CPR, advanced cardiac life support (ACLS) may be required, involving interventions such as defibrillation, administration of medications, and airway management. Defibrillation, the delivery of an electrical shock to the heart, is particularly effective in restoring a normal heart rhythm, especially in cases of ventricular fibrillation (4). Return of spontaneous circulation (ROSC) is the ultimate objective in cardiopulmonary resuscitation. ROSC occurs when the heart regains an effective and sustainable rhythm, leading to the restoration of spontaneous blood circulation. Achieving ROSC is a critical milestone as it indicates that the interventions have been successful in reviving the patient (5). The chances of achieving ROSC are significantly influenced by the timeliness and effectiveness of the interventions. Early initiation of CPR,

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prompt defibrillation, and coordinated advanced life support measures substantially increase the likelihood of ROSC. However, even with successful ROSC, the underlying cause of the cardiac arrest must be identified and addressed to prevent a recurrence (4,5).

Healthcare providers use various methods to assess ROSC. One primary indicator is the presence of a palpable pulse, indicating that the heart is pumping blood effectively. The assessment of adequate blood pressure and spontaneous, purposeful movements also contributes to confirming ROSC. Additionally, the return of spontaneous breathing is a crucial sign that the patient is regaining autonomous respiratory function (6). Technological aids, such as cardiac monitoring and capnography, are valuable in the ROSC evaluation process. ECG monitoring helps healthcare providers observe the heart's electrical activity, confirming the reestablishment of a coordinated rhythm. Capnography, which measures exhaled carbon dioxide, provides an indirect but reliable indicator of cardiac output, aiding in the assessment of circulatory status (7,8).

Despite these indicators, it's important for healthcare providers to remain vigilant, as certain factors may mimic signs of ROSC without genuine circulation restoration. Therefore, a comprehensive and multifaceted approach, incorporating both clinical and technological assessments, is essential in accurately determining ROSC and guiding further interventions (9).

Regular reassessment is crucial, as the patient's condition can change rapidly. Continuous monitoring, along with adherence to established protocols, ensures that any deterioration or recurrence of cardiac arrest is promptly addressed. Overall, the thorough evaluation of ROSC is integral to the post-resuscitation care process, influencing subsequent treatment decisions and the overall prognosis of the individual who has undergone cardiac arrest (10).

## Bispectral Index

Bispectral Index (BIS) is a numerical value that quantifies the depth of anesthesia by analyzing electroencephalographic (EEG) signals. It is a crucial monitoring tool in anesthesia management, providing real-time feedback on a patient's level of consciousness during surgical procedures (11). The BIS is derived from the analysis of the patient's EEG, which reflects the electrical activity of the brain. By processing this EEG data, the BIS produces a numerical value between 0 and 100, where lower values indicate a deeper level of anesthesia and higher values suggest increased consciousness. This information helps anesthesiologists and healthcare providers optimize anesthesia administration, tailoring it to the patient's individual needs (12).

The advantages of using BIS include its ability to minimize the risk of awareness during surgery, optimize drug dosages to prevent over-sedation or inadequate

anesthesia, and enhance the overall safety of the anesthesia process. BIS monitoring is particularly valuable in surgeries where precise control of the depth of anesthesia is critical, such as cardiac procedures or neurosurgery (13). Healthcare providers interpret the BIS values in conjunction with other clinical signs to ensure comprehensive patient care. While BIS is a valuable tool, it is essential to consider other factors, such as the patient's response to stimuli and vital signs, for a complete assessment (14).

## Bispectral Index and Return of Spontaneous Circulation

During cardiac arrest or CPR situations, the focus is usually on restoring the patient's cardiac functions and supporting vital functions. Therefore, other types of monitoring and assessment tools are typically employed in these emergency situations. The primary focus during CPR includes actions such as chest compressions, respiratory support, and defibrillation.

However, in post-cardiac arrest situations where the patient has achieved ROSC and the condition stabilizes, monitoring tools like BIS may be used in later stages of treatment for assessing consciousness and controlling the depth of anesthesia.

In their case study, Azim and Wang demonstrated that BIS monitoring showed a parallel decline with blood pressure before cardiac arrest, reaching zero, and subsequently increasing during CPR, highlighting its potential use in assessing cerebral perfusion dynamics in cardiopulmonary arrest (15). In another case presentation of a patient experiencing arrest in the emergency department, it was reported that the patient's BIS value increased from the moment ROSC was achieved (16). In the case presentation by Chakravarthy et al., BIS monitoring was concluded to be an additional tool to confirm the adequacy of CPR. A BIS value of approximately 40 was generally established as the desired level, requiring efforts not only to achieve an adequate mean arterial pressure but also emphasizing that low BIS values should not be considered as a sole reason to terminate CPR (17). In the case presentation involving two patients by Nitzschke et al., they argued that numerical processed parameters such as BIS and Patient State Index, derived during CPR based on EEG recordings, would be affected by artifacts from chest compressions, rendering them incapable of providing useful information regarding the adequacy of cerebral oxygenation during CPR (18). In Shibata et al.'s study, BIS monitoring was conducted on 10 patients admitted to the intensive care unit after experiencing sudden cardiac death with successful ROSC. The average BIS values of four patients who achieved positive neurological outcomes reached >80 within the first 30 minutes after admission. In contrast, patients who





did not survive after ROSC attained only an average BIS of 9.7(19). In Liu et al.'s study, BIS monitoring was conducted on patients who received cerebral protective treatment after ROSC. In the surviving group, the BIS values were significantly higher compared to the group that resulted in death. Additionally, a positive correlation was observed between Glasgow Coma Scale and BIS (20). In Çetinkaya Ünal's study, when examining the correlation between the elapsed time during CPR and the BIS value, a negative correlation was observed. Similarly, when investigating the correlation with the duration and signal complexity index value, a positive correlation was noted (21). This indicates that as time passes, the BIS value tends to decrease.

As a result, we interrupt CPR to assess the pulse for diagnosing ROSC during CPR. BIS could be a suggestion to address the issue of interrupting CPR; however, the existing literature is not sufficient to establish this. Researchers should be encouraged to delve into this matter.

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## A Race Against Time In Emergency Department: Necrotizing Fasciitis

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### Abstract

Necrotizing fasciitis is an important disease caused by multiple bacteria resulting in necrosis of the skin and soft tissue. Swelling, discoloration and bullae formation may be observed in the affected area. The presence of crepitation under the skin on palpation is a warning sign for necrotizing fasciitis. In our case, necrotizing fasciitis was considered as a preliminary diagnosis after a comprehensive systemic examination in a patient admitted to the emergency department with hyperglycemia. The diagnosis was confirmed by imaging, but the patient died before treatment could be started. Since the mortality rate is quite high, rapid diagnosis and initiation of treatment is very important.

**Keywords:** Necrotizing fasciitis; Soft tissue infection; Diabetes mellitus.

### Introduction

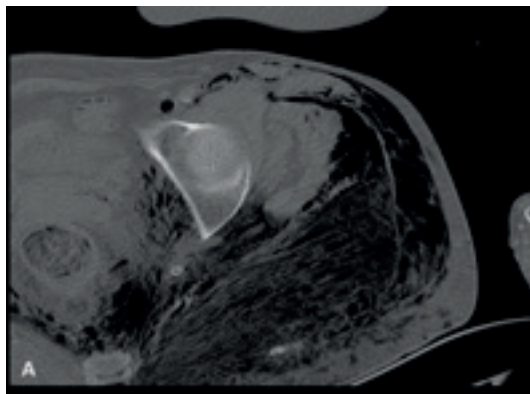
Necrotizing fasciitis is a rare, rapidly progressive infection that causes extensive necrosis of fascia and subcutaneous tissue (1). In most cases, the causative agent is the virulent form of group A streptococci (2). Cellulitis and erysipelas are more common in the emergency department. Necrotizing fasciitis differs from these diseases by its rapid spread and the presence of systemic and laboratory disorders. LRINEC score is used as an important marker in distinguishing necrotizing fasciitis from other soft tissue infections. Treatment includes debridement of necrotic tissues, broad spectrum antibiotics, hyperbaric oxygen, heparin, ultraviolet, intravenous immunoglobulin and supportive therapy. In this case, we tried to emphasize the importance of detailed systemic examination in patients presenting to the emergency department with a different prediagnosis and how this serious condition can be fatal. It is known that blood sugar regulation is impaired in sepsis, so sepsis should be kept in mind in patients presenting to the emergency department with hyperglycemia.

### Case Report

An 81-year-old woman was admitted to the emergency department with complaints of high blood glucose. She had

a history of hypertension, diabetes mellitus and coronary artery disease. At the time of admission, blood pressure was 112/63 mmHg, pulse 103/min, SpO<sub>2</sub> 98%, temperature 36.4 °C, and fingerstick blood glucose 379 mg/dL. In the physical examination of the patient; GCS was 15 and muscle strength in the left lower extremity was 3/5. There were no acute pathologic findings in other neurologic examinations. On examination of the left lower extremity, tenderness and subcutaneous crepitation were detected from the distal thigh to the left lower quadrant wall of the abdomen on palpation. When the patient's anamnesis was deepened and history of trauma was questioned, it was learned that the patient felt pain in his left leg after falling from the same level 2 days ago. Appropriate laboratory and radiologic investigations were ordered. Based on the examination findings of the patient, necrotizing fasciitis was considered in the preliminary diagnosis and the LRINEC score was calculated. The patient's LRINEC score was 11. To confirm the diagnosis, the patient underwent radiological imaging without waiting for the results of the blood tests. Allergy was questioned and antibiotherapy was started immediately. There were no acute pathologic findings on brain CT. CT scan of the thigh and abdomen showed emphysema and edema findings compatible with diffuse necrotic myofasciitis in the left gluteal and thigh skin, subcutaneous and muscle planes, perineum and extending to the right (Figure A, B, C). Air densities extending from the left iliac veins to the vena

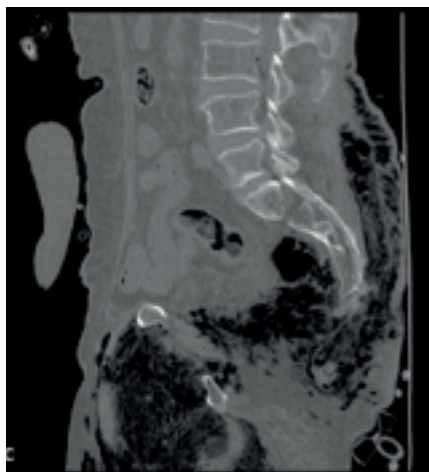




**Figure A:** Wide spread subcutaneous intraabdominal and intravascular air densities (Axial section)



**Figure B:** Wide spread subcutaneous and intraabdominal air densities (Coronal section)



**Figure C:** Wide spread subcutaneous air densities (Sagittal section)

cava inferior were observed. No fractures were observed in bone structures. Laboratory tests revealed pH:7.31 lactate:8 mmol/L WBC:31.1  $10^3/\mu\text{L}$  NEU:28.9  $10^3/\mu\text{L}$  Glucose:368 mg/dL AST:159 U/L CRP:310 mg/L and other laboratory values were within normal limits. Although the patient was sent for imaging immediately after the physical examination, the patient developed cardiac arrest after the CT scan was completed. There was no response to CPR in the resuscitation area and the patient was considered ex.

## Discussion

Necrotizing fasciitis is a rare soft tissue infection with a fulminant course that can lead to limb amputation or death in patients and requires urgent medical attention. Risk factors for necrotizing fasciitis include old age, smoking, alcohol abuse, obesity, diabetes, peripheral vascular disease, liver disease, tumors, and long-term high-dose steroid use, of which diabetes is the most common risk factor (3). Hyperglycemia affects innate immunity, causes mitochondrial abnormalities, and also increases apoptosis through toxic pathways. Glucose variability (standard deviation of the average glucose level) is high in septic patients.(4) It is especially important to differentiate it from cellulitis, which has relatively less clinical severity. Using biochemical parameters, the LRINEC score (laboratory risk indicator for necrotizing fasciitis) (Table 1,2) can be calculated to differentiate necrotizing fasciitis from other soft tissue infections (5,6). The overall morbidity and mortality rates are around 70-80%. One of the most important determinants of mortality is delayed diagnosis of necrosis; therefore, computed tomography plays a vital role in early diagnosis to start treatment rapidly (7). Early diagnosis, rapid and aggressive surgical debridement, antibiotic therapy and supportive care are the basic principles to be relied upon for a better prognosis (8). In this case, the delay in presentation to the emergency department and the absence of any history of diagnosis and treatment after previous trauma increased mortality. When a patient presents to the emergency

**Table 1:** The laboratory risk indicator for necrotizing fasciitis score

Variable	Value	Score
C-Reactive protein (mg/L)	≤150	0
	>150	4
Total white blood cell count (1000 cells/ $\mu\text{L}$ )	<15	0
	15-25	1
	>25	2
Hemoglobin (g/dL)	>13.5	0
	11-13.5	1
	<11	2
Sodium (mmol/L)	≥135	0
	<135	2
Creatinine (mg/dL)	≤1.6	0
	>1.6	2
Glucose (mg/dL)	≤180	0
	>180	1

**Table 2:** LRINEC risk assessment.

Risk Category	LRINEC Points	Probability for Presence of NF
Low	≤5	<50%
Medium	6–7	50–75%
High	≥8	>75%

NF: Necrotizing fasciitis

department with any complaint, all systemic examinations other than the system of the presenting complaint should be performed and other diagnoses of the patient should be taken into consideration. In cases where necrotizing fasciitis is thought to be the diagnosis as a result of clinical evaluation and imaging tests, antibiotic treatment should be started immediately and emergency surgery should be planned (9). Since the mortality rate is quite high, emergency physicians should differentiate and prioritize these patients. Similarly, rapid consultation of these cases to the relevant specialties is also important.

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### Warfarin-induced Sublingual Swelling: A Case of Pseudo-Ludwig Angina

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#### Abstract

Pseudo-Ludwig angina is a swelling that develops generally due to a cause other than an infection and can lead to fatal conditions such as severe respiratory obstruction. Due to anticoagulant use is rarely reported in the literature. This study presented a patient whose INR value was within the normal range and who developed sublingual swelling after dental treatment (intraoral trauma). A 68-year-old female patient was admitted to the emergency department complaining of increasing intraoral swelling on examination with a sublingual 3x5 cm hematoma. Warfarin was stopped, and she was monitored for possible intubation risk in the service. The patient did not develop respiratory distress and was discharged 4 days later. The INR range within which intraoral interventions can be performed safely is still unclear. The dentist should keep in mind that such complications may develop and be prepared for bleeding complications before treatment using warfarin patients.

**Keywords:** Warfarin, Pseudo-Ludwig Angina, Bleeding

#### Introduction

Ludwig's angina is submandibular cellulitis that occurs after an oral infection such as gingivitis. Pseudo-Ludwig angina is a swelling that develops generally due to a cause other than an infection, and can lead to fatal conditions such as severe respiratory obstruction. Pseudo-Ludwig's angina due to anticoagulant use is rarely reported in the literature.

The target International Normalized Ratio (INR) level for patients receiving warfarin therapy varies depending on the underlying condition but is typically recommended to be between 2.0 and 3.5. Case reports of high doses of anticoagulants in the context of the etiology of pseudo-Ludwig angina have been presented in the literature.<sup>1-3</sup> This manuscript presented a patient whose INR value was within the normal range and developed sublingual swelling after dental treatment (intraoral trauma).

#### Case Report

A 68-year-old female patient was admitted to the emergency department complaining of increasing intraoral swelling. On examination, the general condition was good, with a sublingual 3x5 cm hematoma and an approximately 5x2 cm ecchymosis from the front of the mandible to the neck (Figure 1). There was no dyspnea or stridor. There was mild submental oedema. No palpable mass was detected on neck examination, and there

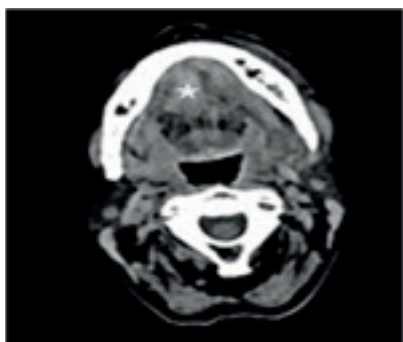


**Figure 1:** Sublingual hematoma

was no lymphadenopathy. Blood pressure was measured as 130/80 mmHg, pulse 82/minute, saturation 99, and respiratory rate 12-15/minute. The patient stated that she had applied for a dental procedure three days ago. She had no history of smoking. She used warfarin for 30 years due to mitral and aortic valve replacement and atrial fibrillation (AF). She had a history of heart failure and chronic anemia.

In the examinations taken in the emergency room, hemoglobin was 13.3 g/dl, hematocrit was 40%, leukocyte was  $6.65 \times 10^9/l$ , INR ratio was 2.54, prothrombin time was 33, and the ECG showed atrial fibrillation.

Neck tomography was requested, and the images showed a hyperdense lesion with a diameter of 3x1.5 cm, compatible with a hematoma, at the level of the genioglossus muscle at the floor of the mouth (Figure 2).



**Figure 2:** Axial non-contrast computed tomography scan shows hyperdense lesion compatible with hematoma at the level of the genioglossus muscle.

The cardiologist and otolaryngologist evaluated the patient. Warfarin was stopped, and she was monitored in the service for respiratory tract monitoring and possible intubation risk. Low molecular weight Heparin, antibiotics, diuretics, and beta blockers were administered. At discharge, the hematoma had regressed entirely. The patient did not develop respiratory distress and was discharged 4 days later. The patient was followed up at the cardiology outpatient clinic at one-week intervals, and it was determined that the INR level reached the target level after 5 weeks (2.32 ratio).

## Discussion

Pseudo-Ludwig cases developing after high INR levels following intentional or unintentional intake of oral anticoagulants have been reported in the literature.<sup>2, 3</sup> Still, cases with normal INR, as in this study, are rare.

A study by Visser et al.<sup>4</sup> stated that in patients with heart disease and long-term use of warfarin, metabolism will deteriorate, possibly affecting the hepatic veins, and the INR level and bleeding risk will increase. This may explain why bleeding even though our patient's INR value was normal.

The most feared situation when developing pseudo-Ludwig's angina is the mechanical obstruction of the airway. Intubation may be difficult, and interventions such as tracheostomy and emergency cricothyroidotomy may be needed. In addition to treating the obstruction, the clinician must also consider the risk of aspiration. Appropriate medications can be added to the treatment against the risk of oedema and allergies that may develop after an intraoral procedure. In case of bleeding, intravenous (IV) vitamin

K, fresh frozen plasma (FFP), and prothrombin complex concentrates (PCC) treatment should be given.<sup>5</sup> Our case did not require intubation. Although there was a history of chronic anemia, profound anemia did not develop, and a rapid response was obtained to the conservative treatment.

## Conclusion


The most common and feared side effect of Warfarin is bleeding, which may develop with a minor trauma (it can even be seen while brushing your teeth) or spontaneously. Bleeding is seen in various organs, but sublingual hematoma is rare and may cause obstruction in the airway. Many guidelines state that if INR is  $<3.5$ , simple intraoral interventions can be performed without discontinuing warfarin.<sup>6</sup> Although, in our case the level of INR was in the lower limit the recommended range of 2.5 to 3.5, bleeding was developed. Based on this experience, individualisation of the INR limit may be considered, especially in elderly patients, to perform a safe intraoral intervention.

*Patient consent was obtained for this study.*

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## Prognostic Biomarkers in Sepsis

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### Abstract

Broca aphasia is a non-fluent aphasia in which spontaneous speech output is markedly diminished, and normal grammatical structure is lost. We report a case of aphasia presenting different features of aphasia following cerebral hemorrhage in the left frontoparietal lobe, which includes Broca's area. A 25-year-old man presented to our emergency department with a headache, Broca aphasia, and difficulty in vision that started two days ago. Bilateral hemorrhagic areas were seen in dilated fundus examination. A CT scan was performed and showed multiple intracranial hemorrhages. Although stroke is considered a disease of the elderly, it can also be present among young people. An underlying malignancy may be the trigger for hemorrhagic ischemia. Injury to the frontal regions of the left hemisphere impacts how words are strung together to form complete sentences. This can lead to Broca's Aphasia.

**Keywords:** Broca's aphasia, Stroke, Hemorrhage

### Dear editor

We read with great interest the article titled "Evaluation and Diagnostic Effectiveness of Hemogram, Biochemistry and Inflammatory Markers (Immature Granulocyte, Procalcitonin, CRP, NLR, PLR) in Patients with Sepsis" prepared by Gedik and Çiftçioğlu and published in the second issue of your journal in 2023 (1). We would like to thank the authors and the editorial board for this descriptive study sharing data from a tertiary hospital in Kahramanmaraş province. However, we would like to touch upon a few points that may contribute to the discussion of the study about prognostic values of biomarkers.

Early recognition of sepsis, which is life-threatening organ dysfunction caused by an unregulated host response to infection, is of utmost importance. Intensive monitoring and intensive care are often required for the management of septic patients (2). Early detection of critically ill patients is important for the effective use of healthcare resources and especially intensive care unit beds. To this end, early warning systems such as qSOFA, REMS, RAPS, and MEWS, which are based on vital parameters, and more complex scoring systems such as APACHE II, which are based on vital parameters and laboratory parameters, are being used up till now (3,4). Nevertheless, despite advancing technology, newly discovered drugs, and the increasing number of

intensive care unit beds, the mortality of septic patients in the intensive care unit remains around 15% (5).

In order to recognize sepsis early, inflammatory biomarkers have been studied primarily based on the involvement of dysregulated host response in its pathogenesis. Furthermore, acute phase reactants have also shown promise in prognosticating septic patients (6). Neutrophil-lymphocyte ratio (NLR), also presented in the study of Gedik and Çiftçioğlu, is one of the first investigated inflammation-related markers. NLR was shown as a predictor of septic shock and mortality in critical care patients with prolonged intensive care unit stay. NLR have some prognostic value in septic patients reflected by an area under the curve (AUC) of 0.695 with the cut-off value of 23.8 (Sensitivity: 81.3%, Specificity: 53.6%) (7).

CRP is a liver-derived positive acute phase reactant and is a frequently used biomarker in evaluating the response to antibiotics in patients with bacterial infection (8). Among critically ill patients admitted to the emergency department, the mortality group has high initial CRP values. In emergency department patients with sepsis large amounts of inflammation reflected by increased CPR was associated with early mortality (AUC of 0.68) and late mortality (AUC of 0.64) (9). Elevated CRP concentrations (> 100 mg/L) appear to be associated with higher mortality rates (odds ratio of 55.75, 95% confidence interval: 2.8-1108.8) (10).

Procalcitonin is the precursor of the calcitonin hormone and is normally secreted from thyroid C cells. However, in case of bacterial infection, its release from all parenchymal tissues in the body increases and its serum level increases. It is thought that the rapid PCT elevation that develops after the injection of bacterial endotoxins is closely related to the induction of proinflammatory cytokines (11). The increase in procalcitonin after intravenous injection of bacterial endotoxin follows the increase in TNF- $\alpha$  and IL-6, similar to CRP. Procalcitonin levels appear to be related with mortality and severity in emergency department septic patients although with a modest prognostic value (AUC of 0.68) (12).

Another important point for all these inflammatory markers is the timing of testing. Inflammation increases starting from the early stages of sepsis and becomes an exaggerated host response. Initial test and day of death tests may have different prognostic values. For example, in an intensive care unit study, the AUC for the CRP value on the first day of hospitalization was found to be 0.57, and the AUC for the CRP value on the third day was 0.72 (13).

Apart from easily accessible NLR, CRP and procalcitonin in sepsis, there are many prognostic biomarkers that are still under study, with or without demonstrated prognostic value. For example, studies on adipocytokines continue. While the poor prognostic value of leptin is revealed (AUC of 0.56), good prognostic values are reported for adiponectin (AUC of 0.68) and resistin (AUC of 0.68) (14,15). The cardiovascular system is regulated by mechanisms involving various neural and hormonal factors, including vasoactive peptides. One of these vasoactive peptides is adrenomedullin (16). In this way, it has been reported that adrenomedullin may be a short-term mortality predictor in sepsis based on hazard ratio of 2.6 (17). SCUBE-1 is a peptide synthesized from platelets and associated with thrombosis, hypoxia and inflammation (18,19). Increased SCUBE-1 concentrations in the systemic circulation are associated with mortality in sepsis based on AUC of 0.813 with a specificity of 75.6%, a sensitivity of 81.3%, and a cutoff value of  $\geq 4.73$  (20).


As a result, despite scientific advances, infection-related death rates are still relatively high. Research related to sepsis and septic management continues. Research funds on this subject should be increased and researchers should be encouraged to conduct research on sepsis and septic shock.

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## Quincke Disease in Earthquake Zone

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### Dear Editor,

We are writing this article to share with you that rare cases that we have not thought of may have increased in the earthquake zone and to be aware that pollution in the region may trigger allergic reactions, including anaphylaxis. We share with you two cases of Quincke's Disease, which is a rare allergic reaction.

Quincke's Disease or isolated uvular angioedema was described in 1882 by German physician Heinrich Quincke. It is a rare angioedema that only affects the upper airway. [1] It is characterized by swelling of the uvula, which rests on the tongue. Symptoms usually include odynophagia, difficulty in managing oral secretions, retching, and a feeling of fullness in the throat. It develops due to type 1 hypersensitivity reaction. It is characterized by a recurrent, localized, ill-defined, non-itchy subcutaneous swelling that usually occurs rapidly and resolves within hours to days. Various etiological factors like food allergy, hereditary angioedema, inhalation exposure, drug reactions and trauma have been implicated. [2]

When I worked in an earthquake zone, there were 2 Quincke's disease applications within a month. Two men, aged 37 and 41, were the patients. They applied to the emergency room with a complaint of foreign body swelling in the throat. There was no fever on physical examination in both of them. Respiratory rate, blood pressure, heart rate, and oxygen saturation were normal. Both were conscious, GKS 15, oriented and cooperative. There was no exposure to any allergens or medication use. No allergy-triggering factor could be identified in their history. They did not have any disease. It was learned that one of them had previously had the same attack on Mount Ararat, while the other patient had the first attack in his life. After 2 repeated doses

of dexamethasone (8 mg), chlorpheniramine maleate and inhaled corticosteroid treatment, the patients' uvula edema resolved. Epinephrine was not administered to both patients. After eight hours of follow-up, they were discharged with a completely normal physical examination.

In the medical treatment of Quincke's edema, H1 and H2 antihistamines, inhaled and parenteral corticosteroids, and inhaled epinephrine are usually sufficient. Parenteral epinephrine may be necessary only in severe cases that do not respond to treatment.

The fact that we encountered 2 cases of Quincke edema, a rare allergic reaction, within 1 month in a district public hospital with a low number of daily patient admissions in the period after the earthquake, made us think that asbestos and other substances that increased after the earthquake could trigger Quincke edema.

In the literature, in the study conducted by Kenneth et al., published in the New England in 1994, it was observed that anaphylactic reactions developed in 5 alpine skiing athletes who received abrasion injuries on asbestos-cement ground within a two-week period. [3] This reminded us that one of our patients had his first attack on Mount Ararat and that Mount Ararat is rich in asbestos.

Asbestos, as we know, is a very powerful carcinogenic substance. We need more studies to say whether there is a triggering factor for Quincke's edema. While writing this article, we aimed to be prepared for such cases that may be encountered in the earthquake region, to differentiate it from anaphylaxis, to avoid unnecessary parenteral epinephrine administration, and to reveal that asbestos may have effects beyond what we know.

**Keywords:** Quincke disease, earthquake, asbestos, anaphylaxis



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