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ORIGINAL RESEARCH

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Use of Intravenous Lipid Emulsion Therapy to Prevent the Undesirable Effects of Midazolam

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Abstract

Objective: Midazolam is a lipophilic benzodiazepine used for moderate and deep interventional sedation and sedoanalgesia in emergency departments. It may cause undesirable outcomes such as bradycardia and hypotension when used. Intravenous lipid emulsion (ILE) therapy is performed to prevent the toxic effects of local anesthetics, β-blockers and lipophilic drugs. In this study, it was aimed to evaluate the effect of ILE infusion on undesirable outcomes such as bradycardia, hypotension and respiratory depression that may occur after midazolam infusion in rats.

Materials and Methods: For the study, 24 Sprague-Dawley rats with the same characteristics were randomly divided into four groups as follows: (1) 0.9% NaCl 16 mL/kg intravenously (IV), (2) midazolam 5 mg/kg IV bolus at an infusion rate of 5 mg/kg/h, (3) 16 mL ILE at an infusion rate of 16 mL/kg/min infusion, and (4) 16 mL ILE at an infusion rate of 16 mL/kg/min infusion for 4 min, then Midazolam 5 mg/kg IV bolus at an infusion rate of 5 mg/kg/h over 60 min. Vital parameters and mortality were monitored.

Results: Mean arterial pressure (MAP) and pulse rate was significantly lower in the midazolam-infused group compared to the other groups ($p<0.05$). In the group receiving midazolam + ILE treatment, MAP decreased at a later period and no significant difference was observed compared to the control group in the measurements after the 40th minute ($p>0.05$). The mortality rate of the midazolam group was 100%, and the survival rate of the other groups was 100%. A significant increase in respiratory rate was observed in the group receiving ILE treatment compared to the control group ($p<0.05$).

Conclusion: It has been shown that effects such as hypotension and respiratory depression that may occur after midazolam administration can be eliminated with ILE treatment and mortality can be reduced.

Keywords: Midazolam, intravenous lipid emulsion, rat

Introduction

Benzodiazepine (BdZ) group drugs are frequently used drugs due to their rapid onset of action, low toxicity potential, and sedative, anxiolytic and anticonvulsant effects [1-3].

Midazolam is a short-acting BdZ and a safe antidote agent used for moderate and deep interventional sedation analgesia in emergency departments. Due to the effect of midazolam on calcium (Ca^{2+}) and potassium (K^{+}) channels, it may have adverse effects such as bradycardia and hypotension. Its effects

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on these channels cannot be reversed by the antidote of midazolam, flumazenil. Various studies have been conducted to prevent and reverse these effects. The administration of intravenous lipid emulsion (ILE) is a attempt to these adverse effects. The first theory put forward regarding the mechanism of action of ILE is that it creates a lipid-rich compartment in the plasma (lipid sink), enabling the separation of lipophilic drugs from the target tissue [4]. As another mechanism of action, it is thought that long-chain fatty acids activate voltage-dependent calcium channels in cardiac myocytes by providing an energy source in the myocardium with high doses of free fatty acids [5]. ILE is an application that was first used to the toxic effects of local anesthetics and lipophilic drugs, and later studied in cardiac drug poisoning caused by several drugs such as beta-blockers due to its cardiac positive inotropic effect and is still under investigation. These emulsions consist of medium-chain triglyceride, long-chain triglyceride, or a combination of both. ILE in 20% formulation contains 20% soybean oil, 2.25% glycerin, 1.2% egg yolk phospholipid [6].

In our study, we investigated whether the undesirable effects that may occur on the cardiovascular and respiratory systems due to midazolam administration can be prevented by ILE administration.

Materials and Methods

This study was conducted in Yeditepe University Faculty of Medicine Experimental Animal Research Unit Laboratories, following the approval of the Ethics Committee dated 05.04.2016 and decision number 528. Rats with the same characteristics were randomly divided into four groups (n=6 in each group). Anesthesia was achieved by isoflurane administration. Treatment protocols were performed for 60 min.

Group 1: Control group, 0.9% NaCl [16 mL/kg intravenously (IV) for 60 min],

Group 2: Midazolam group (5 mg/kg midazolam IV bolus, 5 mg/kg/h IV for 60 min),

Group 3: ILE group (16 mL/kg/min IV, for 60 min),

Group 4: ILE + midazolam group (16 mL/kg/min IV for 4 min, then midazolam 5 mg/kg IV bolus, 5 mg/kg/h IV for 60 min).

Vital parameters were monitored via the pressure transducer set by cannulation of the femoral artery with a 26 G cannula.

Statistical Analysis

In the statistical analysis, IBM SPSS 22.0 (Armonk, New York) software was used. Mean, standard deviation, median, maximum, minimum, frequency, and ratio values were used in the descriptive statistics of the numeric data. The distribution of numeric variables was evaluated by the Kolmogorov-Smirnov test. Kruskal-Wallis, Mann-Whitney U tests was used to compare the independent quantitative data between the groups. For the analysis of independent qualitative data, the chi-square test was used. Fisher's exact test was used when chi-square test conditions were not met. In cases where the p value was less than 0.05 in a 95% confidence interval, the results of statistical analysis were considered as significant.

Results

The groups were evaluated in terms of mean arterial pressure (MAP), respiratory rate (RR) and pulse rate (bpm) during the implementation of selected treatment protocols. There was a statistically significant difference between the groups in terms of 0-3-minute MAP values ($p<0.05$). The MAP values at 5^{th}, 6^{th}, 8^{th}, 10^{th}, 20^{th}, and 30^{th} were found to be statistically significantly lower in group 2 compared to the other groups ($p<0.05$). In group 4, MAP values 6^{th}, 8^{th}, 10^{th}, 20^{th}, and 30^{th} were found to be statistically significantly lower compared to groups 1 and 3 ($p<0.05$). Groups 1 and 3 had similar MAP values on 5^{th}, 6^{th}, 8^{th}, 10^{th}, and 20^{th} minutes ($p>0.05$). In group 2, cardiopulmonary arrest developed in two rats on 8^{th} min, one rat on 10^{th} min, one rat on 33^{th} min, one rat on 36^{th} min, and on rat on 38^{th} min. On 40^{th} min, all rats died in group 2. Afterwards, there were no subjects left in group 2. No significant difference was found between groups 1.3 and 4 in terms of MAP values between the 40^{th} and 60^{th} minutes (Table 1).

The groups were evaluated in terms of RR. There was no statistically significant difference in RR between the groups on 0^{th} min ($p>0.05$). On mins 3, 5, 6, 8, 10, 20, and 30, RR was found to be significantly lower than the other groups in group 2 ($p<0.05$). RR was found significantly higher in group 3 compared to RRs of the groups 1 and 4 at the 6^{th}, 8^{th}, 20^{th}, 30^{th}, and 60^{th} minutes ($p=0.004$ and $p<0.05$, respectively). On mins 8, 10, 20, 30, 60, RR in group 4 was found to be significantly lower than that in groups 1 and 3 ($p=0.004$ and $p<0.05$, respectively) (Table 2).

The groups were evaluated in terms of bpm. There was no statistically significant difference in terms of the bpm between the groups on min 0 ($p>0.05$). On mins 3, 5, 6, 8, 10, 20, and 30, bpm was found to be significantly lower than the other groups in group 2 ($p<0.05$). The bpm was found to be significantly lower in group 4 compared to the groups 2 and 3 at the 6^{th}, 8^{th}, 20^{th}, and 30^{th} minutes ($p<0.05$). At min 20, 30 and 40, bpm was found to be significantly lower in group 1 than in group 3 ($p<0.05$; Table 3)

Table 1. Evaluation of MAP at mins 0, 3, 5, 6, 8, 10, 20, 30, 40, and 60 within and between groups

Min	Group 1	Group 2	Group 3	Group 4	p
	Mean ± SD	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	
0	97.5±6.75 (95)	87.5±3.94 (107)	94.17±5.46 (97)	95.67±5.28 (94.5)	**0.298***
3	99.0±8.63 (96)	87.67±10.23 (89.5)‡	94.67±3.61 (95)	95.0±5.37 (97)	**0.314**
5	98.67±6.68 (96)‡	74.5±18.01 (79)‡	96.5±5.72 (96)	93.0±3.41 (92.5)	**0.003***
6	99.67±10.48 (101)	63.17±26.29 (64.5)‡	98.83±2.93 (99)	85.17±4.12 (86)‡	**0.002***
8	100.83±8.61 (99.5)	43.0±36.87 (53.5)‡	97.17±4.96 (97)	78.67±3.5 (80)‡	**0.001***
10	96.17±3.97 (95.5)	48.0±32.44 (61)	97.17±3.06 (96.5)	75.5±4.04 (77.5)‡	**0.001***
20	94.67±6.09 (95.5)	48.0±1.73 (47)	98±6.2 (97)	83.17±3.6 (83)‡	**0.001***
30	94.33±6.19 (93.5)	35.67±2.52 (36)	95.17±3.49 (95)	89.17±3.92 (89)‡	**0.012***
40	95.83±9.06 (94)	-	93.17±5.71 (92.5)	92.17±4.49 (93.5)	-
60	94.33±6.09 (94.5)	-	94.0±3.22 (94)	92.83±2.79 (93.5)	-

Kruskal Wallis test, ‡Wilcoxon Sign test, *p<0.05, SD: Standard deviation, MAP: Mean arterial pressure

Table 2. Evaluation of the respiratory rates of the groups on mins 0, 3, 5, 6, 8, 10, 20, 30, 40, and 60 within and between groups

Min	Group 1	Group 2	Group 3	Group 4	p
	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	
0	37.5±2.66 (37.5)	41.17±2.48 (41.5)	37.5±2.07 (37.5)	38.17±2.99 (37.5)	**0.064**
3	39.0±1.1 (39)	32.83±4.26 (34.5)‡	40.5±2.07 (40.5)‡	40.67±2.25 (40)‡	**0.002***
5	37.33±3.08 (36.5)	26.33±5.5 (27)‡	43.5±1.87 (43.5)‡	44.33±1.75 (43.5)‡	**0.001***
6	37.67±2.66 (37.5)	21.17±7.41 (22)‡	47.67±2.25 (48)‡	34.0±4.29 (33.5)‡	**0.001***
8	37.17±1.47 (37.5)	13.83±11.91 (16.5)‡	50.0±2.0 (49)‡	24.33±2.25 (23.5)‡	**0.001***
10	39.33±1.97 (39)	16.75±11.44 (21)	51.67±1.37 (51.5)‡	26.67±1.37 (26.5)‡	**0.001***
20	37.0±3.58 (36.5)	16.67±2.52 (17)	55.0±1.26 (54.5)‡	31.67±2.16 (31.5)‡	**0.001***
30	36.67±2.34 (37)	11.0±1.73 (12)	57.83±2.14 (58)‡	34.67±2.16 (34.5)‡	**0.001***
40	37.17±2.79 (37)	0±0 (0)	61.67±4.13 (61)‡	38.17±2.04 (38.5)‡	**0.001***
60	37.33±1.63 (37)	-	62.17±2.86 (62.5)‡	40.17±2.4 (39.5)‡	**0.001***

Kruskal Wallis test, ‡Wilcoxon Sign test, *p<0.05, SD: Standard deviation

Table 3. Evaluation of the pulse rates of the groups on mins 0, 3, 5, 6, 8, 10, 20, 30, 40, and 60 within and between groups

Min	Group 1	Group 2	Group 3	Group 4	p
	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	Mean ± SD (median)	
0	379±24.16 (379)	381±22.76 (388)	377.5±18.78 (373.5)	387±14.63 (387.5)	**0.754**
3	357.83±23.79 (355)‡	316.17±11.25 (318.5)‡	392.33±9.97 (395)	390±11.3 (391)	**0.001***
5	374±17.12 (373.5)	249.5±43.83 (261)‡	388.83±7.31 (385.5)	394.17±7.11 (396)	**0.001***
6	362±27.79 (361)	182.5±69.66 (200)‡	391.33±9.14 (393.5)	359.33±18.05 (362)‡	**0.001***
8	373.33±27.13 (368)	119±104.5 (139.5)‡	396±4.34 (396)	333±10.86 (337.5)‡	**0.001***
10	368.67±36.64 (377.5)	125.25±88.28 (147.5)	392.83±7.78 (394.5)	324.33±16.99 (325)‡	**0.002***
20	373.17±24.15 (383.5)	124±32.19 (114)	391±9.96 (394)	345.83±16.33 (348.5)‡	**0.001***
30	364.33±9.69 (365.5)	84.67±26.39 (72)	394.17±73.6 (393.5)	358.83±18.71 (361)‡	**0.001***
40	358.17±26.45 (359.5)‡	-	391.17±16.44 (397)‡	376.17±11.94 (378.5)	-
60	362.17±18.1 (363)	-	398.33±7.03 (397.5)	388.17±8.04 (389.5)	-

Kruskal Wallis test, ‡Wilcoxon Sign test, *p<0.05, SD: Standard deviation

Discussion

Our study is the first to investigate whether ILE treatment reduces the undesirable effects of midazolam on the cardiovascular and respiratory system. The study had remarkable results. On mins 8, 10, 20, 30, 60, RR in group 4 was found to be significantly lower than that in groups 1 and 3. The bpm was found to be significantly lower in group 4 compared to the groups 2 and 3 at the 6th, 8th, 20th, and 30th minutes ($p<0.05$). At min 20, 30, and 40, bpm was found to be significantly lower in group 1 than in group 3.

In a study examining the effect of midazolam on blood pressure in healthy people, 0.15 mg/kg midazolam decreased systolic blood pressure by 5% and diastolic blood pressure by 10%, and increased heart rate (HR) by 18% [7]. In a study by Jones et al. [8] examining the cardiovascular effects of midazolam and diazepam on dogs, midazolam was shown to decrease MAP and increase heart HR. Yao et al. [9] stated that the mechanism of the effect on MAP is through the inhibition of sarcolemmal L-type Ca2q channels. In that study, it was shown that flumazenil was not effective in the reversal of this type of channel inhibition.

Ozturk et al. [10], in their study in which they applied midazolam to the rabbit heart and examined its effects on the cardiovascular system and they reported that flumazenil could not prevent the cardiac depressant effect of midazolam. In our study, MAP values were decreased by midazolam, which was consistent with the literature. We also observed that the ILE administration led the MAP value to occur later and normalize earlier. Bradycardia was observed in the rats receiving midazolam infusion, whereas no bradycardia was observed because of ILE administration before midazolam infusion. It was shown that ILE administration inhibited the bradycardia caused by midazolam.

Forster et al. [11], in their study conducted on healthy people, showed that there was a respiratory depression following the IV administration of 0.15 mg/kg midazolam. In our results, it was detected that the respiratory depression effect due to midazolam decreased in the group that was administered ILE before midazolam infusion. Only ILE infusion was observed to increase RR.

While 100% mortality was observed in the group that received only midazolam infusion, there was no mortality in the group that received ILE before midazolam infusion. It has been shown that mortality that may occur due to midazolam administration can be reduced by ILE administration.

Conclusion

It has been shown that undesirable side effects of midazolam, such as hypotension and respiratory depression, can be prevented by ILE administration.

Ethics

Ethics Committee Approval: Yeditepe University Faculty of Medicine Experimental Animal Research Unit Laboratories, following the approval of the Ethics Committee dated 05.04.2016 and decision number 528.

Informed Consent: Not required.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: H.A., Ö.O., T.P., F.D., R.A., Concept: H.A., Ö.O., T.P., F.D., Design: H.A., Ö.O., F.D., R.A., Data Collection or Processing: H.A., T.P., E.S., Analysis or Interpretation: Ö.O., R.A., Literature Search: H.A., T.P., R.A., E.A., Writing: H.A., Ö.O., F.D., E.A.

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ORIGINAL RESEARCH

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The Relationship Between Mindfulness and Styles of Coping with Stress and Depression in Emergency Medicine Residents Working in İstanbul

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Abstract

Objective: This study aimed to examine the relationship between mindfulness and coping styles with stress and depression in emergency medicine residents (EMR).

Materials and Methods: This cross-sectional survey study was used a socio-demographic data form, the mindful attention awareness scale (MAAS), Beck depression inventory (BDI), and the ways of coping with stress inventory. After defining mindfulness levels among physicians, univariate and multivariate logistic regression tests were used to explore its effect on depression.

Results: A total of 207 EMR residents were enrolled in the study. According to the cut-off level of BDI score (≥17), 83 (40.1%) of the participants had depression requiring treatment. Mean MAAS scores were significantly lower in the group with depression than the group without depression (median scores: 56 vs. 36, p=0.000). The multivariate logistic analysis disclosed that MAAS score was negatively associated with depression. Among ways of coping with stress, scores for self-confident, helpless, and submissive approaches were significantly higher in the group with depression than in those without depression (p=0.000 for all).

Conclusion: In addition to high depression rates, a significant relationship was observed between mindfulness and depression in EM residents. These findings suggest the potential benefits of mindfulness-based interventions in reducing the depression levels of EM residents.

Keywords: Emergency medicine residents, mindfulness, depression, stress, coping with stress

Introduction

The emergency departments (ED) create a stress source for many physicians due to the long shifts, overcrowding of the acute care areas, the necessity of proper and rapid treatment, and the high risk of being exposed to violence by patients and their relatives [1]. This leads to reduced professional satisfaction in physicians. Fatigue, stress, distraction, and the increased number of patient admissions may cause delays in recognizing and correcting fatal diseases. As a result of all these stress factors, the risk of many psychiatric disorders, especially depression, increases in physicians working in the ED, and impairment is observed in their social and occupational functionality [2]. To ensure professional functionality and satisfaction in emergency physicians, it is necessary to review their working conditions, increase their stress coping skills, and prevent depression.

Mindfulness is defined as focusing one's attention on the moment without judgment and accepting the present experiences [3]. With the ability to focus on the present, the person can become aware of what is happening here and now by avoiding the anxiety, fear, and troubles caused by negative experiences in the past, expectations for the future, and uncertainties. In many studies conducted in different groups, it has been revealed that there is a significant relationship

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between mindfulness and the ability to cope with stress and depression [4,5]. The literature reveals that stress management yields-positive effects, increased professional satisfaction, and decreased depressive symptoms thanks to mindfulness-based practices (mindfulness-based education, stress reduction programs, and cognitive therapies) [6,7]. There are very few studies in the literature examining the level of mindfulness among emergency physicians and the relationship between mindfulness and coping with stress and depression [8,9]. This study aims to examine the relationship between mindfulness and coping with stress and depression in emergency medicine residents (EMR).

Materials and Methods

This cross-sectional study was conducted between February 2019 and September 2019. There are 26 training and research hospitals, 4 city hospitals and 17 university hospitals in İstanbul. Emergency medicine clinic administrators of all these hospitals were applied for the research and 3 universities and 12 training and research hospitals that accepted the research were included in the research. An invitation letter was sent to all residents working in EM clinics who agreed to participate in the study, and all EMR who participated in the invitation and filled out the research form were included in the study. Socio-demographic information forms were handed to all participants who had given their written informed consent. Although the project was designed to reach data of 250 physicians, 219 persons were interviewed, 12 were excluded for inadequate data, and finally, data obtained from 207 physicians were included in the analysis. This form contains questions about the participants' age, sex, marital status, starting date of residency, working conditions, habits, chronic diseases, etc.

Mindful Attention Awareness Scale (MAAS)

The MAAS was used to measure the participants' awareness levels. Developed by Brown and Ryan [3] in 2003, this scale measures individual differences in being aware of instant experiences and being mindful of experiences. It is a 6-point likert-type scale (1= almost always, 2= most of the time, 3= sometimes, 4= rarely, 5= quite infrequently, 6= almost never), which consists of 15 items and gives a single total score. Higher scores on the scale indicate a high level of mindfulness. The internal consistency coefficient of the original scale was found to be α=0.82. Özyeşil et al. [10] conducted a validation study for the original questionnaire in Turkish, with high validity and internal consistency.

Beck Depression Inventory (BDI)

The BDI was used to assess the depression levels of the participants. This self-report scale is used to measure the severity and level of depression symptoms in adult patients and was developed in 1961 by Beck et al. [11]. Its Turkish validity and reliability study was conducted in 1988 by Hisli [12]. It consists of 21 items used to measure the symptoms of depression in vegetative, emotional, cognitive, and motivational areas. Each item consists of a 4-item self-assessment statement that goes from less to more and is scored between 0 and 3. The total score ranges from 0 to 63. For detecting depressive disorder patients, a score of ≥17 is defined as an optimal cut-off score with sensitivity 0.809, specificity 0.764, the positive predictive value, 0.402, and the negative predictive value 0.953. We set the cut-off value at a score of 17 [13]. The mean scores of the scale are not affected by sex, age, or education level.

Ways of Coping with Stress Inventory (WCSI)

In this study, the WCSI was used to determine individuals' styles to cope with stress. The scale is a 4-point likert-type scale consisting of 68 items, developed as the ways of coping inventory by Folkman and Lazarus [14]. It was adapted to Turkish and validated in 1992 by Şahin and Durak [15].

The WCSI, an abbreviated form of the inventory, was prepared by Şahin and Durak [15] in 1995 for university students. The final version of the scale has 30 items and consists of 5 factors: Self-confident, optimistic, seeking social support, submissive, and helpless approaches. As the scores obtained from the self-confident, optimistic, and social support-seeking approaches increase, it means the person uses effective coping strategies. On the other hand, as the scores for the helpless and submissive approaches increase, it is understood that they use ineffective, i.e., passive coping strategies [15].

Ethics Committee Approval

The Clinical Research Ethics Committee of the İstanbul Training and Research Hospital approved this study (approval number: 1629, date: 04.01.2019). All participants were informed in detail before starting the study and approval was obtained via written informed consent forms.

Statistical Analysis

Demographic and clinic characteristics were summarized using descriptive statistics. Kolmogorov-Smirnov test was used to determine whether the variables were normally distributed. The Mann-Whitney U test and the chi-square test were performed to determine factors associated with depression. Fisher's exact test was used when the conditions for the chi-squared test were not met. We used Spearman's correlation analysis to compare MAAS scores with WCSI subscale scores. Univariate and multivariate analyses were performed to assess the effect of mindfulness and other factors on depression. The level of significance was set at $p<0.05$ and the SPSS 22.0 software was utilized for the analyses.

Results

A total of 207 EMR were included in the study. One hundred fifty-nine of the participants were in the 24-30 age range (76.8%) and 81 were female (39.1%). Eighty-four of the participants were married (40.6%) and 37 (17.9%) had children. Eighty-nine (43.0%) of the participants worked as a split shift (day or night), while 118 (57.0%) had a 24-hour shift. One hundred seventy-two of the participants (83.1%) chose to be a medical doctor willingly and 157 (75.8%) chose the ED branch willingly. Ninety-three (44.9%) of the participants were smoking, while the rate of alcohol consumption was 50.7%. One hundred-nine of the participants (52.7%) found working conditions easy, 12 (5.8%) moderate, and 86 (41.5%) difficult. Twenty participants (9.7%) had a psychiatric disease and the rate of using antidepressant drugs was 7.7%. Twenty-one (10.1%) participants had a low-income level, 28 (13.5%) had a moderate-income level, and 158 (76.8%) had a high income. Seventy-five (36.2%) of the participants regularly did sports, while 159 (76.8%) had their hobbies. However, only 69 of these (33.3%) could spare time for their hobbies. According to the cut-off score for BDI, 83 (40.1%) of the participants had depression requiring treatment (BDI ≥17). Age, sex, marital status, or having children (p=0.053, p=0.464, p=0.439, p=0.667, respectively) did not differ significantly between participants with and without depression. On the other hand, there was a significant relationship between depression and starting date of the residency, choosing to be a medical doctor willingly, and choosing ED voluntarily (p=0.016, p=0.008, p=0.001, respectively). Also, patients with depression had higher rates of chronic illness (p=0.009) and psychiatric illness (p=0.004), while their income levels (p=0.047) were lower. As a remarkable finding, there was a significant association between depression and not being able to devote time to their hobbies (p=0.001) (Tables 1 and 2).

The participants had a median MAAS value of 47.0 (minimum 15-maximum 79). The MAAS scores were significantly lower in the group with depression (p=0.000) than the group without depression. Among coping styles with stress, self-confident approach was significantly higher, while helpless and submissive approaches scores were significantly lower in the group with depression than those without depression (p=0.000 for all). Optimistic approach (p=0.241) and social support-seeking approach scores (p=0.063) did not differ significantly between the groups (Table 3).

In the univariate analysis performed to determine the factors affecting depression, choosing to be a medical doctor willingly [hazard ratio (HR): 2.86, 95% confidence interval (CI): 1.34-6.11, p=0.007], choosing the ED willingly (HR: 2.74, 95% CI: 1.41-5.32, p=0.003), having a chronic illness (HR: 2.84, 1.26-6.39, p=0.011), having a psychiatric illness (HR: 3.99, 95% CI: 1.46-10.86, p=0.007), spending time for hobbies (HR: 2.80, 95% CI: 1.47-5.32, p=0.003), working conditions (HR: 1.97, 95% CI: 1.11-3.47, p=0.019), and MAAS score (HR: 0.88, 95% CI: 0.85-0.91, p=0.000) were significant factors. Among the coping styles with stress, self-confident (HR: 0.39, 95% CI: 0.22-0.70, p=0.002), optimistic (HR: 0.35, 95% CI: 0.20-0.60, p=0.000), helpless (HR: 3.51, 95% CI: 1.95-6.31, p=0.000), and submissive approaches (HR: 1.71, 95% CI: 1.01-2.89, p=0.043) were significant as well. In the multivariate analysis after adopting the factors that were found to be significant in the univariate analysis, spending time for hobbies, helpless approach, and MAAS score obtained significant results. The correlation between MAAS scores and styles of coping with stress was examined. There was no significant (p=0.118) correlation between MAAS scores and the optimistic approach score. However, there was a significant (p=0.001) negative correlation between MAAS scores and self-confident approach score and significant positive correlations between MAAS scores and helpless, submissive, and social

Table 1. The relationship between depression and clinical characteristics*

		Depression (+)		Depression (-)		p
		n	%	n	%	
Specialization time	1-6 months	26	21	26	31.3	0.016
	7-12 months	12	9.7	7	8.4	
	13-24 months	33	26.6	10	12.0	
	25-36 months	29	23.4	13	15.7	
	More than 36 months	24	19.4	27	32.5	
Working hours	Split shift	55	44.4	34	41.0	0.629
	24-hour shift	69	55.6	49	59.0	
Chose to be a medical doctor willingly	(+)	11	88.7	62	74.7	0.008
	(-)	14	11.3	21	25.3	
Chose the emergency department willingly	(+)	10	83.9	53	63.9	0.001
	(-)	20	16.1	30	36.1	

*Chi-square test (Fisher's exact test)

support-seeking approaches scores (p=0.001, p<0.001 and p=0.03, respectively) has been observed (Table 3).

Discussion

Our study revealed the prevalence of depression among EMR and the factors affecting it, especially their coping with stress and mindfulness. We found that increasing mindfulness levels can be an important protective factor against depression. In studies on the prevalence of depression both in ED and in other departments, a wide range of results have been obtained depending on factors such as the test chosen, the cut-off value of the test, specialization time, and the country in which the study was conducted [2,16,17]. In our study, according to the BDI, 83 (40.1%) of the participants had depression requiring treatment. Depression rates were significantly lower in those who chose the medical school and ED voluntarily than those who made their decisions randomly, which is consistent with the literature [18]. The rate of chronic illnesses was found to

Table 2. The relationship between depression and other socio-demographic characteristics*

		Depression (+)		Depression (-)		p
		n	%	n	%	
Chronic illness	(+)	11	8.9	18	21.7	0.009
	(-)	113	91.1	65	78.3	
Smoking	(+)	52	41.9	41	49.4	0.290
	(-)	72	58.1	42	50.6	
Alcohol use	(+)	57	46.0	48	57.8	0.094
	(-)	67	54.0	35	42.2	
Working conditions	Easy	57	46.0	52	62.7	0.062
	Moderate	8	6.5	4	4.8	
	Difficult	59	47.6	27	32.5	
Psychiatric illness	(+)	6	4.8	14	16.9	0.004
	(-)	118	95.2	69	83.1	
Use of antidepressants	(+)	7	5.6	9	10.8	0.170
	(-)	117	94.4	74	89.2	
Income level	Low	10	8.1	11	13.3	0.047
	Int.	12	9.7	16	19.3	
	High	102	82.3	56	67.5	
Being involved in sporting activities	(+)	50	40.3	25	30.1	0.134
	(-)	74	59.7	58	69.9	
Hobbies	(+)	101	81.5	58	69.9	0.053
	(-)	23	18.5	25	30.1	
Spending time for hobbies	(+)	52	41.9	17	20.5	0.001
	(-)	72	58.1	66	79.5	

*Chi-squared test (Fisher's exact test)

Table 3. Relationship of depression with MAAS and WCSI subscale scores*

	Depression (-)	Depression (+)	p
	Mean ± SD	Mean ± SD	
MAAS score	55.2±12.0	37.3±11.4	0.000
Self-confident approach	1.1±0.5	1.5±0.6	0.000
Optimistic approach	1.1±0.5	1.2±0.6	0.241
Helpless approach	0.3±0.6	0.0±0.5	0.000
Submissive approach	1.3±0.4	1.0±0.4	0.000
Social support-seeking approach	0.7±0.3	0.6±0.4	0.063

*Mann-Whitney U test.

SD: Standard deviation, MAAS: Mindful Attention Awareness Scale, WCSI: Ways of Coping with Stress Inventory

be significantly higher in the group with depression, in line with the literature [19]. The rate of psychiatric illness was significantly higher in the group with depression than in the group without depression, which is also consistent with the literature [20]. The loss of interest and pleasure is one of the most prominent depressive symptoms and social isolation and distancing from activities and hobbies that people were previously interested in are common among people with depression [21]. In the present study, the rate of devoting time to hobbies was significantly lower in the group with depression than the group without depression, in line with the literature. The inability to spare time for hobbies was one of the influential factors on depression in univariate and multivariate analyses. Mindfulness is the awareness of one's feelings, thoughts, internal and external stimuli, and experiences. The mind does not aim to stand on something or move away from it; it just observes, does not judge, and accepts it as it is. This makes the person more receptive, alert, peaceful, and happy. For this reason, there have been many studies examining the relationship between mindfulness and depression [5]. Studies are frequently conducted among individuals with chronic diseases (especially cancer patients), occupational groups with heavy stress load (especially teachers and healthcare professionals), and students, and a significant portion of these studies show that there is an inverse relationship between mindfulness level and depression. Depressive symptoms seem to decrease with such interventions [22-24]. Therefore, mindful awareness-based training has started to take place in medical schools in some countries [25]. In another study, a 4-week mindfulness-based training program was applied to medical students during their EM clerkship and a significant positive effect was observed on their behaviors and attitudes [9]. In our study, in accordance with the literature, the mindfulness score was significantly lower in the group with depression than the group without depression. It was also observed that the mindfulness score was effective on depression in both univariate and multivariate analyses. Based on these findings, we think that an increase in mindfulness may be a factor to decrease depression. Another issue that ED professionals should focus on is stress management and coping skills. When the literature is examined, more emotional and passive coping styles are seen in depressive individuals [26]. In our study, WCSI was used to investigate the styles of coping with stress. According to this scale, coping styles are discussed under two main headings as active and passive coping. Accordingly, "self-confident approach", "optimistic approach" and "seeking social support approach", which are sub-dimensions of the scale, are considered active methods of coping with stress. In contrast, "helpless approach" and "submissive approach" are passive methods [14]. In our study, the helpless and submissive approach scores were significantly higher in the group with depression than the group without depression, consistent with the literature. Besides, self-confident and optimistic approaches among active coping styles and helpless and submissive approaches among passive coping styles were determined as effective factors on depression in the univariate analysis. In the multivariate analysis, only the helpless approach was found to be effective on depression. According to these results, we think that depression is higher in individuals who use passive coping styles. Looking at the relationship between coping with stress and mindfulness, studies have found that mindfulness was positively associated with the self-confident, optimistic, and social support-seeking approaches. It has been negatively associated with the helpless and submissive approaches [27]. Again, many studies have shown the positive effects of mindfulness-based practices, such as mindfulness-based stress reduction program, mindfulness-based cognitive therapy, and dialectical behavior therapy on coping with stress and stress factors [27-29]. In this study, a significant positive correlation was observed between MAAS scores and social support-seeking sub-scale scores, an active coping style, in line with the literature. While no significant relationship was observed between MAAS scores and optimistic approach subscale scores, another active coping style, a negative correlation was observed between MAAS scores and self-confident subscale scores, contrary to expectations. One of the potential reasons for this may be the low number of participants. Another reason can be the characteristic of WCSI since it is a self-report scale. The use of author-reported scales can provide more meaningful results.

Study Limitations

Limitation of our study, apart from what we have mentioned before, is that it was conducted in a cross-sectional design, as the causal relationship between variables may not have been adequately revealed. Since the study included only residents, most of the participants were young and healthy individuals, and this prevented generalization of the findings to different age groups. Additionally, the fact that the study consisted of EMR prevents us from extrapolation of the findings to emergency physicians and other branch residents and specialists. Another limitation is utilization of self-report scales to measure the major endpoints, which may have represented a source of bias for each participant.

Conclusion

In EMR; increasing mindfulness levels can be an important protective factor for depression. Depression rates were significantly lower in those who chose the medical school and ED voluntarily than in those who made their decisions randomly. Depression is higher in individuals who use passive coping styles. According to the findings we have obtained, studies aimed at increasing mindfulness will positively affect the coping skills of EMR and will reduce depressive symptoms.

However, further studies with larger sample groups are needed to confirm this conclusion.

Ethics

Ethics Committee Approval: The Clinical Research Ethics Committee of the İstanbul Training and Research Hospital approved this study (approval number: 1629, approval date: 04.01.19).

Informed Consent: Informed consent was obtained from the all patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.F.O., E.A.O., Ö.K., Concept: A.F.O., E.A.O., Ö.K., Design: A.F.O., Ö.K., Data Collection or Processing: A.F.O., Analysis or Interpretation: A.F.O., S.Y., E.A.O., Literature Search: A.F.O., S.Y., E.A.O., Writing: A.F.O., S.Y., Ö.K.

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ORIGINAL RESEARCH

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Does the Percentage of Immature Granulocytes Predict the Severity and Mortality of the Disease in Patients with Acute Pancreatitis Presenting to the Emergency Department?

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Abstract

Objective: In this study, it was aimed to investigate the percentage of immature granulocytes (IG) and other hemogram parameters in the early period in predicting severe disease, in-hospital and short-term mortality in patients with acute pancreatitis (AP).

Materials and Methods: Our study was designed as a retrospective observational clinical study. Patients admitted to the emergency department with the diagnosis of AP between 01.01.2017 and 31.12.2021 years were included in the study. Hemogram parameters were compared according to mortality and the Balthazar severity index.

Results: We found that the percentage of IG was not statistically significant for mortality and disease severity. We found that the mean age of the group with mortality was statistically significantly higher than that of the group without mortality (p=0.012). We found that the lymphocyte count was statistically significantly lower in the group with mortality compared to the group without mortality. When we grouped the patients according to the Balthazar severity index, 366 (85.12%) of the patients were evaluated in the mild group, 61 (14.19%) in the moderate group, and 3 (0.69%) in the severe group. Among the groups; we found significant differences in hemoglobin, white blood cell (WBC), neutrophil, length of stay, and Balthazar severity index.

Conclusion: The IG percentage does not have a predictive value for the severity of the disease and the mortality process, particularly in patients with mild AP. A decrease in lymphocyte count can be considered a marker for mortality and long-term hospitalization. In patients with AP, WBC count and neutrophil count can be used to predict the severity of the disease on the first admission to the emergency department.

Keywords: Immature granulocyte, mortality, pancreatitis

Introduction

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas and the mortality rate of the disease can vary between 3 and 17% depending on the severity of the disease and complications [1,2]. AP is inflammation caused by damage to the acinar cells of the exocrine pancreas. It is thought to result from the activation of early enzymes in the pancreas [3]. The severity of the disease can range from mild pancreatic edema to systemic inflammation leading to pancreatic necrosis, organ failure, and death [4].

Today, many classifications are used to determine the severity of the disease. There are many scorings such as Ranson criteria, the Accuracy of Acute Physiology and Chronic Health Evaluation II scoring, Bedside index of severity in AP scoring and Balthazar computed tomography (CT) scoring. However, these scores are still insufficient to predict the severity of the disease at the patient's first admission to the emergency department [5]. Therefore, the search for parameters that can predict serious disease in AP patients continues.

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Immature granulocytes (IG) are not normally found in the peripheral bloodstream. Recent studies have shown that IG are markers of inflammation in diseases such as sepsis, AP, and acute appendicitis [6-8].

However, studies on IG are limited. This study, was aimed to investigate the percentage of IG and other hemogram parameters in the early period in predicting severe disease, and in-hospital and short-term mortality in patients with AP.

Materials and Methods

Research Design

In the study, the data of patients who applied to the emergency department with the diagnosis of AP between 01.01.2017 and 31.12.2021 were recorded retrospectively from the hospital information management system. All patients over the age of 18 who were diagnosed with AP based on examination findings, laboratory tests and imaging methods in the emergency department were included in the study. The study was conducted by collecting data between 10.02.2022 and 10.04.2022. In the study, patients' age, gender, additional disease information, hemoglobin (Hgb), hematocrit level (Hct), white blood cell (WBC), neutrophil count, lymphocyte count, platelet count, imaging results [CT, ultrasonography (USG)], hospitalization information, length of hospitalization, clinical outcome, and short-term mortality information were recorded.

In the study, 542 AP patients admitted to the emergency department from January 2017 to the end of December 2021 were screened. Since recurrent pancreatitis could not be differentiated from chronic pancreatitis retrospectively, it was excluded in the study (Figure 1).

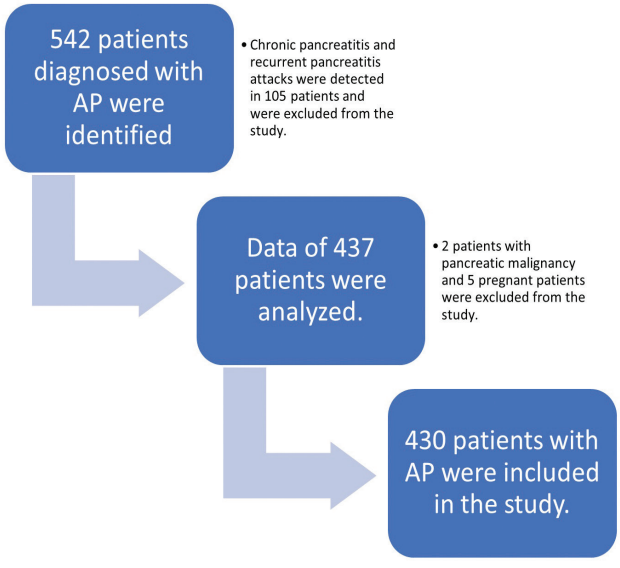

Figure 1. Flowchart of the cases included in the study

In the analysis of the data, the patients were divided into various groups. These groupings are as follows.

Patients with gallstones or biliary sludge detected by USG or CT were included in the biliary pancreatitis group, and patients without gallstones or biliary sludge were included in the non-biliary pancreatitis patient group. All the patients who were not discharged were included in the hospitalization group and compared with the discharged patients. Using the Balthazar CT severity index, patients were divided into three classes: Mild, moderate and severe pancreatitis. Patients with mortality within one month (detected by the E-nabız system and hospital information management system) were included in the mortality group, and patients without mortality within 1 month were included in the non-mortality group.

Exclusion Criteria

- Patients whose information cannot be accessed in the hospital information management system,
- Patients presenting with chronic and recurrent pancreatitis attack,
- Patients under 18 years of age,
- Patients with pancreatic malignancy,
- Pregnant patients,
- Patients with hematological diseases,
- Patients with a history of immunosuppression.

Statistical Analysis

The data obtained were analyzed in SPSS Statistics 24.0 (IBM Inc., New York, USA) program. Categorical data were presented as numbers and percentages. To test the normality of continuous variables, Kolmogorov-Smirnov and Shapiro-Wilk tests and skewness and kurtosis values were used. Data that fit the normal distribution were shown as the arithmetic mean and standard deviation and those that did not fit were shown as the median and interquartile range. Pearson chi-square and Fisher's Exact test were used in the analysis of categorical variables, and independent sample t-test and Mann-Whitney U test were used in the comparison of continuous variables. All statistical analysis were performed at the 95% confidence interval and values less than 0.05 were considered significant for the p value.

Results

A total of 430 patients, 260 (60.5%) women, and 170 (39.5%) men, were included in our study. Descriptive statistics of the study group are given in Table 1. Considering the distribution of the patients according to their clinical results, 261 (60.7%) patients were admitted to the service and 10 (2.3%) patients to the intensive care unit. One (0.2%) patient died in the emergency

Table 1. General characteristics of the research groups

		Non-biliary	Biliary	p
		n	n	
Gender	Woman	100	160	**0.018**
	Man	85	85	
Diabetes mellitus	Present	42	51	0.638
	Absent	143	194	
Hypertension	Present	47	75	0.236
	Absent	138	170	
Cholelithiasis	Present	22	27	0.778
	Absent	163	218	
Alcoholism	Present	2	1	0.396[a]
	Absent	183	244	
Hyperlipidemia	Present	15	15	0.424
	Absent	170	230	
Malignancy	Present	3	5	0.523[a]
	Absent	182	240	
Mortality	Present	1	6	0.121[a]
	Absent	184	239	
Clinical outcome	Discharged	60	98	0.107
	Hospitalization	125	147	

[a]: Fisher's Exact test

department and 158 (36.7%) patients were discharged from the emergency department. When the 1 month mortality of the patients was examined; we found that 7 (1.6%) patients died within 1 month and 423 (98.4%) patients did not experience mortality.

When we grouped the patients according to pancreatitis types; we found that the mean age of patients with biliary pancreatitis was statistically significantly higher than that of non-biliary patients (p=0.013). In patients with non-biliary pancreatitis, lymphocytes and length of hospital stay was statistically significantly higher than in patients with biliary pancreatitis. We found that platelet-lymphocyte ratio (PLR) values in patients with biliary pancreatitis were significantly higher than those in patients with non-biliary pancreatitis (p<0.01). We did not find a statistically significant difference in other parameters (Table 2).

When we grouped the patients according to their discharge status; we found that the Hgb, Hct, Balthazar score, WBC, neutrophil-lymphocyte ratio (NLR), and PLR values of the hospitalized patients were statistically significantly higher than the values of the discharged patients (p<0.01). Lymphocyte levels were statistically significantly higher in discharged patients compared in hospitalized patients (p<0.01). We did not find a statistically significant difference in other variables. In the grouping made according to mortality; we found that the mean age of the group with mortality was statistically significantly higher than that of the group without mortality (p=0.012). We found that the lymphocyte value was statistically significantly lower in the group with mortality compared to the group without mortality (p<0.01). We did not find a statistically significant difference between the groups in any other parameters (Table 3).

When we grouped the patients according to the Balthazar severity index, 366 (85.12%) of the patients were evaluated in the mild group, 61 (14.19%) in the moderate group, and 3 (0.69%) in the severe group. In the analysis of intergroup variables; we found significant differences in Hgb, WBC, neutrophil, length of hospital stay, and Balthazar severity index. Since the number of patients in the severe group is insignificant, in the double group analysis made by adding it to the moderate severity group; we found significant differences in Hgb, WBC, neutrophil, length of hospital stay, and Balthazar severity index (Table 4).

Discussion

IG (including promyelocytes, myelocytes, and metamyelocytes) are early granulocytes released from the bone marrow during infection and inflammatory conditions. The presence of IG in peripheral blood indicates leukopoiesis and indicates infection, inflammation, and bone marrow stimulation. When leukocytes are used peripherally, the bone marrow produces more leukocytes in response. As a result, an "left upper shift"

Table 2. Analysis of variables by pancreatitis types

	Pancreatitis	Mean	SD	p value
Age	Non-biliary	54.95	17.54	**0.013**
	Biliary	59.34	18.69	
Hemoglobin	Non-biliary	13.48	1.96	0.050
	Biliary	13.10	1.97	
Hematocrit	Non-biliary	39.46	5.07	0.152
	Biliary	38.72	5.51	
Balthazar score	Non-biliary	1.63	1.47	0.301
	Biliary	1.48	1.51	
		Median	**IQR**	
White blood cell	Non-biliary	12110	6120	0.133
	Biliary	11325	5587.50	
IG %	Non-biliary	0.40	0.30	0.826
	Biliary	0.40	0.20	
Neutrophil	Non-biliary	9200	6600	0.516
	Biliary	9210	5422.50	
Lymphocyte	Non-biliary	1500	1200	**<0.01**
	Biliary	1200	1000	
Platelet	Non-biliary	245000	119000	0.396
	Biliary	261000	103500	
Neutrophil-lymphocyte ratio	Non-biliary	5.73	9.23	0.172
	Biliary	6.43	8.42	
Platelet-lymphocyte ratio	Non-biliary	154.62	144.19	**<0.01**
	Biliary	189.69	166.82	
Length of hospital stay (day)	Non-biliary	5.0	8.0	0.020
	Biliary	3.0	6.0	

Student's t-test, Mann-Whitney U test, SD: Standard deviation, IQR: Interquartile range, IG: Immature granulocytes

occurs. Although its predictive value in sepsis and many infections has been investigated recently, it is thought that it is not a sufficient parameter alone despite positive results. In our study, the percentage of IG was not found to be statistically significant for 1 month mortality, disease severity, and inpatient treatment. In a study by Çıldır and Kocaoğlu [9], IG % levels were found to be significantly higher in patients with severe AP, and in-hospital mortality. However, Doğan and Gürleyen [10] in research conducted in 2022, it was found that the percentage of IG in patients with acute perforated appendicitis was significantly higher than in patients without perforation. In a study conducted on patients with sepsis in 2019, Ayres et al. [11] found the IG percentage was significant in demonstrating sepsis. Jeon et al. [12] found that the percentage of IG was moderately significant in demonstrating sepsis in patients who developed sepsis after burns in 2021. Karon et al. [13] in 2017, found that the percentage of IG was moderately significant in showing sepsis in sepsis patients. Türkmen et al. [14] in 2022, the percentage of IG in sepsis patients was found to be higher in the sepsis group than in the control group, and the difference was statistically significant. Ha et al. [15] in 2014, did not find the percentage of IG significant in demonstrating the 28 day mortality in sepsis patients. In our study, it was thought that the reason for the low IG % value was that most of our patients were patients with mild pancreatitis and that we could have caught patients in the early stages of leukopoiesis.

When we looked at the other hemogram parameters of AP patients, a relationship was found between the WBC count and neutrophil count and the severity of the disease in our study. Additionally, a relationship was found between lymphocyte count and mortality and length of hospital stay. In a study in which AP patients were divided into two according to the Ranson score; WBC, mean platelet volume, and NLR were found to be higher and statistically significant in the group with a high Ranson score, and the differences in PLR values were not statistically significant [16]. In a study by Keskin [17] in patients with AP in 2020, WBC, neutrophils, lymphocytes,

Table 3. Analysis of variables in clinical outcome and mortality status

	Clinical outcome	Mean	SD	p value	Mortality	Mean	SD	p value
Age	Discharged	56.78	17.30	0.552	Present	78.57	16.21	**0.012**
	Hospitalization	57.85	18.89		Absent	57.10	18.15	
Hemoglobin	Discharged	12.82	1.85	**<0.01**	Present	12.96	1.08	0.480
	Hospitalization	13.53	2.00		Absent	13.27	1.98	
Hematocrit	Discharged	37.93	5.11	**<0.01**	Present	38.90	3.49	0.921
	Hospitalization	39.68	5.35		Absent	39.04	5.36	
Balthazar score	Discharged	1.21	1.37	**<0.01**	Present	1.71	1.70	0.796
	Hospitalization	1.74	1.52		Absent	1.54	1.49	
		Median	**IQR**			**Median**	**IQR**	
WBC	Discharged	10610	5505	**<0.01**	Present	12530	5030	0.435
	Hospitalization	12220	5950		Absent	11515	5945	
IG %	Discharged	0.40	0.20	0.238	Present	0.50	0.30	0.418
	Hospitalization	0.40	0.30		Absent	0.40	0.30	
Neutrophil	Discharged	8060	5410	**<0.01**	Present	11410	5625	0.117
	Hospitalization	9960	6270		Absent	9100	579750	
Lymphocyte	Discharged	1600	1100	**<0.01**	Present	800	550	**<0.01**
	Hospitalization	1200	1000		Absent	1300	1075	
Platelet	Discharged	260500	103000	0.272	Present	229000	50500	0.199
	Hospitalization	249000	113000		Absent	254500	109500	
NLR	Discharged	4.66	4.99	**<0.01**	Present	14.51	14.64	**<0.01**
	Hospitalization	7.96	11.09		Absent	6.24	8.50	
PLR	Discharged	155.38	122.48	**<0.01**	Present	271.11	136.36	0.020
	Hospitalization	198.46	196.58		Absent	181.79	169.96	
Length of hospital stay (day)	Discharged			**<0.01**	Present	4.0	9.50	0.948
	Hospitalization	6.0	5.0		Absent	4.0	7.0	

Student's t-test, Mann-Whitney U test. SD: Standard deviation, IQR: Interquartile range, IG: Immature granulocytes, WBC: White blood cell, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

NLR, and PLR were found to be higher in severe pancreatitis. In a case-control study, the lymphocyte level was found to be statistically significantly lower in the patient group [18]. We think that the decrease in lymphocyte count is due to consumption due to the effect of inflammation. We believe that the decrease in lymphocyte count is associated with prolongation of hospital stay and mortality and can be used in the emergency room for the prognosis of the patient.

In studies showing the relationship between the female gender and AP; the rate of female patients was determined as 49.3%, 53%, and 57.5% [19,20]. In the study of Williams et al. [21], it was reported that the rate of female patients was 1.4 times higher than that of males. Biliary pancreatitis is the most common type of pancreatitis, although it varies regionally. Biliary pathologies are more common in female patients than in males, so a higher rate can be expected in female patients. This relationship was considered the reason for the high rate of female patients in our study.

In previous studies in our literature review; biliary etiology was determined in different values such as 53.46%, 60.9%, 22.7%, and 80.9% in AP patients [22-25]. As seen in the literature, biliary tract pathologies were found to be the most common etiology in our study. Our study is also compatible with the literature.

In a study by Hayran [26] in 2015, 20% of the patients diagnosed with AP were discharged from the emergency department, 58% were hospitalized in the service and 22% were hospitalized in the intensive care unit. Bayındır [27] in a study conducted on 229 patients in 2018, it was stated that 98.7% of the patients were admitted to the ward and 1.3% of the patients were admitted to the intensive care unit. In the

Table 4. Analysis of variables with the Balthazar computed tomography severity index

	Mild (n=366)	Moderate (n=61)	Severe (n=3)	p	p^2
	Median (IQR) (minimum-maximum)				
Age	57.00 (28)	54.00 (31.5)	47.00 (23-54)	0.278	0.406
Hemoglobin	13.20 (2.60)	13.65 (2.40)	14.00 (13.10-16.10	**0.031**	**<0.01**
Hematocrit	39.20 (6.50)	40.10 (6.25)	41.50 (38.0-48.20)	0.130	0.061
Balthazar CT severity index index	1 (2)	4 (0.0)	10	**<0.01**	**<0.01**
White blood cell	11395 (5810)	12495 (5765)	13140 (12800-16600)	**<0.01**	**<0.01**
IG %	0.40 (0.30)	0.40 (0.30)	0.40 (0.30-2.30)	0.887	0.781
Neutrophil	8775 (5590)	10215 (5760)	11160 (9800-13800)	**<0.01***	**<0.01***
Lymphocyte	1350 (1075)	1300 (1100)	1200 (900-2100)	0.996	0.968
Platelet	255500 (108500)	229000 (110500)	292000 (244000-803000)	0.254	0.469
NLR	6.05 (8.41)	8.33 (10.04)	11.50 (4.67-12.40)	0.248	0.104
PLR	180.71 (171.35)	185.85 (172.23)	271.11 (139.05-669.17)	0.563	0.881
Length of hospital stay (day)	4.0 (6.0)	7.0 (6.25)	0 (0-3.0)	**<0.01**	**<0.01**

*Kruskal-Wallis test, p^2: Calculated for mild and moderate + severe groups, Mann-Whitney U test. IQR: Interquartile range, IG: Immature granulocytes, WBC: White blood cell, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, CT: Computed tomography

results of our study, we determined that most patients (63%) were planned for inpatient treatment, and this was consistent with the literature.

In an AP study by Aktaş [28] with 138 patients; mortality was observed in the 1 month period in 3.3% of the patients participating in the study. Knudsen et al. [29] in the Danish population, the 30 day mortality rate was 10% in 1988-1992, the 30 day mortality rate was 6.3% in 2013-2017, 4.2%, and 3.9% in the study of Miller et al. [30]. In the study of Yurt [22] it was reported as 7.2%. Our 30 day mortality rate was low compared to the literature. We believe that the inclusion of milder cases according to the Balthazar severity index resulted in a lower mortality rate.

Study Limitations

There are some limitations to our research: The most important of these limitations is the retrospective and single-center planning of the study. The information of the patients was obtained from the hospital electronic database and files in the hospital archive. The very unequal distribution of patient groups according to the Balthazar severity index can be counted as another limitation of the study.

Conclusion

The IG value does not have a predictive value for the severity of the disease and the mortality process in patients with AP. We think that leukocyte count, lymphocyte, and neutrophil count are useful markers in predicting the severity of the disease in patients with AP at the first admission to the emergency department.

Ethics

Ethics Committee Approval: Ethics Committee of University of Health Sciences Turkey, İstanbul Kanuni Sultan Suleyman Training and Research Hospital (subject number: KAEK/2022.02.39).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.K., B.Y., Concept: S.K., S.D., Design: S.K., S.D., A.E., U.M.K., Data Collection or Processing: S.K., S.D., A.E., B.Y., U.M.K., Analysis or Interpretation: S.K., S.D., A.E., Literature Search: S.K., S.D., Writing: S.K., S.D., B.Y., U.M.K.

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ORIGINAL RESEARCH

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The Impact of Ambulance Disinfection Methodology on 112 Emergency Health Care Parameters, During the COVID-19 Pandemic in İstanbul

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Abstract

Objective: This study aims to analyze the effects of the coronavirus disease-2019 (COVID-19) pandemic on the preparation process of the first responder teams in emergency medical services. Ambulance station response times, command and control centers' response times, and case response times are reported and compared with current literature. Research findings elaborate on how the procedures for corrective actions in the disinfection process affected these main parameters in a 24-hour period in prehospital care.

Materials and Methods: The comparison was made for ambulance times, after the transportation of COVID-19 cases, between the March 2020 period when the ambulances were disinfected in five centers in the hospital yards and the April 2020 period when the disinfection devices were placed in all ambulances.

Results: The total number of cases per ambulance per day was 10.1 (8.5-11.6) in the March group and 10.8 (8.8-13.2) in the April group ($p<0.001$). While the number of COVID-19 cases per ambulance per day was 1.7 (1.3-2.1) in the March group, it was 3.2 (2.4-4.1) in the April group. While the ambulance disinfection time per COVID-19 case was 51.9 (27.7-73.0) minutes in the March group, it was 11.0 (6.0-24.1) minutes in the April period ($p<0.001$).

Conclusion: During the pandemic process, ambulance disinfection and wearing personal protective clothing-prolonged preparation times. In March 2020, ambulances had to travel to common sites for cleaning and disinfection. Changing this procedure to self-cleaning at the ambulances' own station locations in April 2020, decreased both the ambulance disinfection time and the ambulance response time, in spite of the increase in the number of COVID-19 cases.

Keywords: 112 emergency call center, ambulance response time, prehospital transport, infection control, pandemic, communicable disease, outbreak

Introduction

Urban growth, with the rise in urbanization and population explosion, poses challenges globally. Estimates indicate that, by 2050, 6.29 billion people will populate urban areas, which is approximately 68% of the world population [1,2]. An increasing proportion of people living in large cities. Consistently, increasing numbers of heart attacks, drownings, traffic accidents, and other serious events occurring with firearms are consistently observed ubiquitously. The process of urbanization promotes and infects disaster risks. Higher levels of susceptibility and vulnerability are encountered to the social, economic, environmental impacts of hazards, such as landslides, floods, earthquakes [3]. Urban development proportionally reflects on health care costs worldwide. Health care spending reached an estimate of 17.6% in 2010, with emergencies constituting 5%-10% of health expenditures [4,5]. Shifting rural populations to urban areas have to inevitably rely on existing reserves and resources are scarce. The demand for transport causes serious congestions, delays, accidents, environmental problems in metropolitan areas around the world [6], which places a significant burden on ambulance services. Ambulance response time (ART) is overall the main indicator. ART defines the period between the

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notification of the event and the arrival of the ambulance at the scene. According to the World Health Organization, ART is ideally under 8 minutes [7]. Regarding the definition of ART, Lawner et al. [8] draw attention to secondary results which include changes in other metrics, such as the average ART range and the overall out-of-service interval. The ART range is the time that passes between the referral of the ambulance to arrival at the scene. The out-of-service interval is the amount of time that an ambulance is not available to respond to other incidents.

Protecting people and societies in an era where lives are profoundly changed, presents new issues to health care providers, as pandemics continue to threaten lives and economies [9]. It is widely accepted that the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) was first identified in China in December 2019 [10,11]. In Turkey, the first patient with coronavirus disease-2019 (COVID-19) was documented on March 11, 2020. Following the index case, the number of cases increased from 15,679 on April 1st to 120,204 on April 30th [12]. By June 28, 2020, the total number of cases in Turkey reached 198,284, of which 108,749 were documented in İstanbul [13]. Disinfection units were created for the teams in March 2020 and disinfection devices were purchased, in order to avoid delays due to the prehospital disinfection protocols. Disinfection devices distributed for the teams to conduct their own disinfection procedures are among examples of good practice. For ambulances, high pressure washers were provided at the 112 transportation units.

The aim of the study is to analyze and compare with current literature, how the COVID-19 pandemic affected the preparation process of emergency medical services (EMS) responders' in prehospital care. Ambulance station response times, command and control center's (CCC) response times, and ARTs are reported. Researchers share their experiences with the international scientific community, regarding how the disinfection process and the period of preparation for cases affected outcomes and propose solutions from recent practices.

Materials and Methods

In the metropolitan city of İstanbul, incoming calls at the Anatolian and the European 112 Emergency Ambulance Services' call centers were analyzed retrospectively, for the period of March 11-May 1, 2020. CCC response times, ambulance response times, the number of cases per ambulance, and ambulance disinfection times were recorded. In the March 2020 group, ambulances were disinfected in five centers after the transfer and transport of suspected or probable COVID-19 cases. In the April 2020 group, disinfection devices were placed in all ambulances and disinfection procedures were performed in the hospital yards, immediately following the transfer and transport of COVID-19 cases. The study design is based on a comparison of the two groups.

Ethics Committee Approval

The Clinical Research Ethics Committee of the Republic of Turkey Ministry of Health (TR MoH) University of Health Sciences Turkey, Bağcılar Research and Training Hospital approved the research application, dated May 7, 2020 with document #2020.05.1.23.055. Written informed consents were obtained from the COVID-19 Coordination Center of İstanbul.

Statistical Analysis

Categorical data were recorded and measured as numbers and percents, while continuous measurements were the recorded as average and standard deviation. Normality distribution of the continuous variables was analyzed with Kolmogorov-Smirnov test. For comparing the two groups, Student's t-test was used for normally distributed parameters, while the Mann-Whitney U test was used for parameters which were not normally distributed. Chi-square test was used in the analysis of the categorical variables. A $p<0.05$ value was considered statistically significant.

Results

At the time of study, a total of 3,432 employees worked at 112 İstanbul Emergency Ambulance Services. There were 286 stations in total in the 39 districts of İstanbul.

Before dispatch for cases evaluated by the CCC as suspected or probable COVID-19 patients, each one of the 3,432 ambulance personnel wore protective overalls, goggles, gloves, N95 masks, in compliance with the algorithms released by the TR MoH Coronavirus Scientific Advisory Board.

Table 1 the compares of 112 ambulance times for March and April 2020, shows the distribution median, range values, and significance-level p values. The differences were found to be statistically significant for all values of between the March and April groups. While hospital delivery time increased in the April group, the other parameters were found to decrease. Additionally, CCC response time, station response time, ART, prehospital on-scene intervention time, and hospital delivery time median values were calculated as 7.11 (4.11-14.11), 1.65 (0.93-2.95), 10.23 (7.00-16.26), 12.15 (7.98-18.55) and 15.33 (10.00-25.00) minutes, respectively.

In terms of working times, CCC response and station response times were statistically significantly lower, and hospital delivery and intervention times were higher in women. While 112 Emergency Ambulance Services ambulances were cleaned in five centers in March 2020, three on the European and two on the Anatolian sides (Figures 1A, B). In compliance with the TR MoH Coronavirus Scientific Advisory Board algorithms, each

ambulance performed their own cleaning procedures in April 2020 (Figures 2A, B).

Table 2 shows the number of cases per ambulance per day, disinfection time in minutes per ambulance, a number of COVID-19 cases per ambulance per day, disinfection time in minutes per COVID-19 case. The number of cases and disinfection times in minutes per ambulance were recorded for March and April 2020 groups, in terms of median, range, and p values.

Table 1. The comparison of 112 ambulance times for March and April 2020 (median, range, p values)

Ambulance times (minutes)	March 2020 group	April 2020 group	p value
	Median (range)	Median (range)	
Command response time	8.56 (5.00-19.83)	6.88 (4.01-13.48)	<0.001
Station response time	1.76 (0.96-3.91)	1.65 (0.91-2.86)	<0.001
Time from call to arrival at the scene	24.68 (17.25-40.00)	18.98 (12.71-30.00)	<0.001
Ambulance response time	13.26 (8.71-20.33)	9.96 (6.81-15.47)	<0.001
On-scene intervention time	14.00 (9.00-21.48)	12.00 (7.76-18.00)	<0.001
Hospital delivery time	13.86 (9.00-20.90)	16.00 (10.00-26.00)	<0.001
Busy time	107.50 (77.00-140.00)	69.20 (51.00-97.68)	<0.001

Figure 1. A, B) Photograph showing collective disinfection at a common spot in March 2020

Figure 2. A, B) Photograph showing the disinfection of each ambulance in the hospital yard after each case is taken to the hospital

Table 2. Number of cases and disinfection times in minutes per ambulance, March and April 2020 (median, range, p values)

	March 2020 group	April 2020 group	p value
	Median (range)	Median (range)	
Number of cases/ambulance/day	10.1 (8.5-11.6)	10.8 (8.8-13.2)	<0.001
Disinfection time in minutes/ambulance	8.6 (4.3-12.3)	3.3 (1.7-7.6)	<0.001
Number of COVID-19 cases/ambulance/day	1.7 (1.3-2.1)	3.2 (2.4-4.1)	<0.001
Disinfection time in minutes/COVID-19 case	51.9 (27.7-73.0)	11.0 (6.0-24.1)	<0.001

COVID-19: Coronavirus disease-2019

Table 3. Ambulance times for March and April 2020, in minutes (median, range, p values)

Ambulance times (minutes)	March 2020 group	April 2020 group	p value
	Median (range)	Median (range)	
Time at the hospital	75.9 (58.3-115.7)	102.3 (71.4-171.4)	<0.001
Disinfection time	81.4 (38.1-117.2)	36.1 (18.8-74.0)	<0.001
Total time with the case	134.9 (118.2-152.7)	115.1 (98.6-132.3)	<0.001
Ambulance maintenance time, for breakdowns, repairs, other needs	271.7 (180.7-348.4)	324.9 (279.3-398.5)	<0.001
Case intervention patient time	245.1 (184.6-331.3)	328.0 (247.4-411.2)	<0.001

Table 3 shows ambulance times in minutes for March and April 2020, in terms of median, range, and p values. Waiting time at the station, time at the hospital, disinfection time, total time with the case, round trip transportation time, ambulance maintenance time for breakdowns, repairs, and other needs, case intervention patient time were recorded.

Discussion

This research, conducted in the metropolitan city of İstanbul, is one of the first studies to analyze a 24 h time period in prehospital care and to share case data from 112 Emergency Ambulance Services at the onset of the COVID-19 pandemic. At times, disasters and local events in the community make it necessary to modify the routines, in order to keep up with changing needs and conditions. In March 2020, ambulances were cleaned at five common locations. In April 2020, with guidance from the TR MoH Coronavirus Scientific Advisory Board and the CCCs of İstanbul, each ambulance was cleaned at their station locations in April 2020. Despite the fact that the total number of cases increased, ambulance disinfection time and ART both decreased in April (Tables 1-3). This positive outcome was attributed to disinfection devices which were purchased for the teams, in order to avoid the delays from the disinfection procedures. Teams conducting their own disinfection operations are hereby shared as good practice in ambulance service communicable disease prevention. Worthy of notice is that high pressure washers were provided for ambulances at the 112 transportation units.

The average ART recorded in Vienna, Austria in 2015 was 15 minutes, this value varied with traffic intensity and weather events that impacted the roads at different locations. In Belo Horizonte, Brazil, the average ART was approximately 21 minutes in 2010 [14]. In the city of São Paulo, Brazil, ART in EMS was 27 minutes in 2007 [15]. Takeda et al. [16] discussed EMS act in the United States, which determined the standards that 95% of the emergency requests should be served within 10 minutes in urban areas and within 30 minutes in rural areas. There are similar regulations in other parts of the world. The regulation in Montreal, Canada states that 95% of the requests should be answered within 10 minutes in urban areas and within 14 minutes in rural areas. In London, United Kingdom, the standard is set for 70% of the requests to be responded to within 7 minutes, and for 50% in 8 minutes [8,17,18]. The average ART is shorter in Asia (7.3 minutes), followed by Oceania (8.0 minutes), where Australia is the only country to report EMS response times, from the city of Melbourne. Only Ghana in West Africa, where the average ART is 19 minutes in the cities of Kumasi, Accra and Tamale, is the only country to report EMS response times. America has a median response time of 9 minutes; in Europe, this value is 11 minutes [3,19]. The median ART was measured as 10.23 minutes during the timeframe of the current COVID-19 research. There was a significant decrease in ART from 13.26 (8.71-20.33) in March 2020 to 9.96 (6.81-15.47) in April 2020 (Table 1). Improvements, in the practice of the disinfection process, in April shortened ART. Compared to March 2020, ambulances no longer had to travel from their stations to different sites for clean-up. As a result, they were able to reach the cases faster in April 2020. The ART value in April 2020 was close to those recorded before the occurrence of COVID-19. The first responder teams' preparation incorporates wearing personal protective clothing,

such as medical masks, overalls, goggles or face protectors, in addition to preparing for patient transfer with the necessary equipment and supplies. Considering that this preparation is also included in ART, this is remarkable performance.

In March 2020, five ambulance disinfection sites were established, in the hospital yards close to CCCs. With guidance from TR MoH Coronavirus Scientific Advisory Board and the CCCs of İstanbul in April 2020, the method of cleaning was changed to cleaning and disinfection procedures to be carried out with devices, for ambulances to use at their own station locations. Although the median number of cases per ambulance increased to 10.8 (8.8-13.2) from 10.1 (8.5-11.6) and the number of COVID-19 cases per ambulance increased to 3.2 (2.4-4.1) from 1.7 (1.3-2.1) from March to April, both disinfection time per ambulance and disinfection time per COVID-19 case decreased significantly (Table 2). This was reflected in the measurements as a reduction in ART. The mileage, time spent, and fuel used in liters spent by the ambulances while going to and coming back from the cleaning centers in March were found to decrease in April.

Going to cases outside of the routine, especially going to cases that require preparation before patient transfer, such as the COVID-19 cases, leads to prolonged intervention time in the assessment of the case. Factors associated with a probable or a suspected COVID-19 case, including comorbidities, prolong intervention time and require choosing an adequate hospital for the patient. However, with the implementation of TR MoH Coronavirus Scientific Advisory Board algorithms and with the guidance of the CCCs of İstanbul, starting from the first day of the pandemic, even though the number of cases increased, patient intervention time decreased significantly from 14.00 (9.00-21.48) in March 2020 to 12.00 (7.76-18.00) in April 2020. The increase in delivery time from 13.86 (9.00-20.90) in March 2020 to 16.00 (10.00-26.00) in April 2020 results from the fact that the patients were not admitted to emergency rooms at hospital arrival, but to the inpatient services directly (Table 1).

In the intensity of the pandemic, an incoming call regarding a new case while the ambulance is at a case or is delivering a case to the hospital, is a factor that contributes to the increase in ART measurement. Contrariwise, a factor that contributes to the decrease in ART in April was the fact that the CCCs of İstanbul determined the hospitals locally according to the features of the COVID-19 cases. As a result, the time spent in cases decreased significantly from 134.9 (118.2-152.7) minutes in March 2020 to 115.1 (98.6-132.3) minutes in April 2020 (Table 3). At 112 İstanbul Emergency Ambulance Services, this shortened the time spent with the cases. Ambulances were ready for new cases earlier than before, resulting in a decrease in ART.

Conclusion

In EMS health care provision, challenges occur every day due to local and environmental factors. In regular times, heavy traffic in urban areas and land conditions in rural areas cause problems. During the pandemic period, preparations, which including wearing personal protective clothing, cleaning up and disinfecting the ambulances, and preparing for patient transfer with the necessary equipment and supplies, prolong response times. A change from common cleaning sites in March 2020 to cleaning and disinfecting the ambulances at their own station locations in April 2020 led to noticeable decreases in both ambulance disinfection time and ART, in spite of the fact that the number of cases increased in the same time period. Both CCCs of İstanbul guiding 112 Emergency Ambulance Services based on both cases and hospitals and the Science Board guiding this center caused a decrease in ART despite an increase in cases. This performance was accomplished through guidance from TR MoH Coronavirus Scientific Advisory Board, supervision and case-based evaluations from the CCCs of İstanbul, including the selecting adequate hospitals for patient transfer.

The COVID-19 pandemic presents global issues for 112 İstanbul Emergency Ambulance Services personnel and their colleagues that creating adaptive strategies in a complex, changing world is critical for health care provision.

Ethics

Ethics Committee Approval: The Clinical Research Ethics Committee at the Republic of Turkey Ministry of Health (TR MoH) University of Health Sciences Turkey, Bağcılar Research and Training Hospital approved the research application (approval number: #2020.05.1.23.055., date: 07.05.2020).

Informed Consent: Written informed consents were obtained from the COVID-19 Coordination Center of İstanbul.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: Y.A., V.T., Ş.Ö.H., İ.Ö., G.E., Design: Y.A., G.E., V.T., Data Collection or Processing: Y.A., Ş.Ö.H., Analysis or Interpretation: Y.A., İ.Ö., G.E., Literature Search: Y.A., G.E., Writing: Y.A., G.E.

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CASE REPORT

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Left-sided Acute Appendicitis in a Case of Situs Inversus Totalis

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Abstract

The displacement of all thoracic and abdominal organs is called situs inversus totalis (SIT). Its incidence is 0.01% and it is characterized by abnormal anatomy but normal organ functions. It is a benign condition with a normal life expectancy and an asymptomatic course. Situs inversus; causes difficulties in the diagnosis and treatment of all internal organ pathologies. Having detailed information about human structure and anatomical variations is of great importance in daily clinical practice and particularly in emergency medical interventions and surgeries. Anatomical variations can be fatal in routine patient evaluations and emergency interventional procedures. Acute appendicitis is the most common pathology requiring emergency surgery and constitutes 4%-8% of all emergency department admissions. Although it can be easily diagnosed by clinical examination without the need for imaging studies due to typical symptoms such as pain migration, there is difficulty in definitive diagnosis in patients with anatomical variations such as SIT. The symmetrical localization of the appendix in situs inversus cases causes acute appendicitis to be included in the differential diagnosis of left lower quadrant pain. The differential diagnosis of left lower quadrant appendix vermiformis with gynecopathology, such as ovarian cyst rupture, causes more difficulties in female patients with SIT. The differential diagnosis of left lower quadrant pain is more difficult in women than in male patients. SIT is mostly diagnosed incidentally. The different anatomical location of the organs from normal healthy individuals causes the patient management to take a very careful situation in the applications of patients with situs inversus in cases requiring emergency intervention. When these patients present to the emergency department with acute abdomen findings, both the diagnosis and consultation process to the necessary branches should be clearer than other patients. A definitive diagnosis should be avoided without clarification of organ localization.

Keywords: Situs inversus totalis, acute appendicitis, left-sided appendicitis, ovarian cyst

Introduction

Situs inversus totalis (SIT) is a genetically originated condition in which the thoracic or abdominal structures are located symmetrically in their normal anatomical position concerning the midline [1]. The incidence of this syndrome is 0.01%, and it is characterized by abnormal anatomy with normal organ functions. It is a benign condition with normal life expectancy and it presents no clinical symptoms [2]. SIT causes difficulties in the diagnosis and treatment of all internal organ pathologies, especially pathologies that affect one side of the body, such as acute cholecystitis and appendicitis.

Having detailed information about the human body and anatomical variations is critical in daily clinical practice, and particularly in emergency interventions and surgeries. Anatomical variations can be fatal in a routine patient evaluation. Acute appendicitis is the most common pathology requiring emergency surgery and constitutes 4%-8% of all emergency department admissions [3]. Although acute appendicitis can be easily diagnosed by clinical examination without the need for imaging studies due to typical symptoms such as pain migration, finding the definitive diagnosis in patients with anatomical variations such as SIT can cause a challenging process. The differential diagnosis of left lower quadrant appendix vermiformis with gynecopathology, such as ovarian cyst rupture, causes more difficulties in female patients with SIT [4].

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In this article, we presented a case of acute appendicitis in a female patient who was newly diagnosed with SIT and presented to the emergency department with left lower quadrant pain. Also, we emphasized the importance of anamnesis, physical examination and electrocardiography (ECG) findings in the differential diagnosis of SIT considering this case.

Case Report

A 44-year-old female patient with no known chronic diseases other than an ovarian cyst and no medication use was admitted to the emergency department with abdominal pain, nausea-vomiting and fever that had started the day before the admission. After the patient's pain that started in the middle part of the abdomen was localized to the left lower quadrant a few hours later. She was conscious, cooperative and oriented. Vital signs on admission were the following; blood pressure 124/76 mmHg, heart rate 85 beats per minute, oxygen saturation 98% and body temperature 37.8 °C. On physical examination, severe tenderness, defense and rebound in the left lower quadrant were detected, and pre-op tests were requested. Since a history of ovarian cyst and the abdominal pain was located in the left lower quadrant, a gynecological consultation was requested with the preliminary diagnosis of ovarian cyst rupture. Laboratory results of the patient were as follows; white blood cell 18.66/uL, neutrophil 16.9/uL, hemoglobin 12.9 g/dL, C-reactive protein (CRP) 0.2 mg/dL, B-HCG <1.2 mIU/mL and ketone (+) was in urinalysis. Other laboratory results did not display any pathology. In the abdominal ultrasonography images, both ovaries were normal in size and a hemorrhagic cyst of 15 mm in diameter was found in the left ovary. In ECG, right axis deviation and loss of R wave progression were detected in the precordial leads (Figure 1). After confirming the placement of the electrodes several times, her ECG was interpreted as dextrocardia. Postero-anterior chest X-ray was requested to differentiate dextrocardia. On the chest X-ray, right-sided gastric air and dextrocardia were detected (Figure 2). Contrast-enhanced abdominal computed tomography (CT) was requested for differential diagnosis of newly diagnosed SIT, considering the development of symptoms and physical examination findings to be compatible with acute appendicitis. On CT images, SIT and 13.5 mm appendix vermiformis located on the left side with closed lumen were detected (Figure 3). The patient was operated with a diagnosis of acute appendicitis. Because of the operation, pathology results showed that an edematous, inflamed appendix vermiformis with a length of approximately

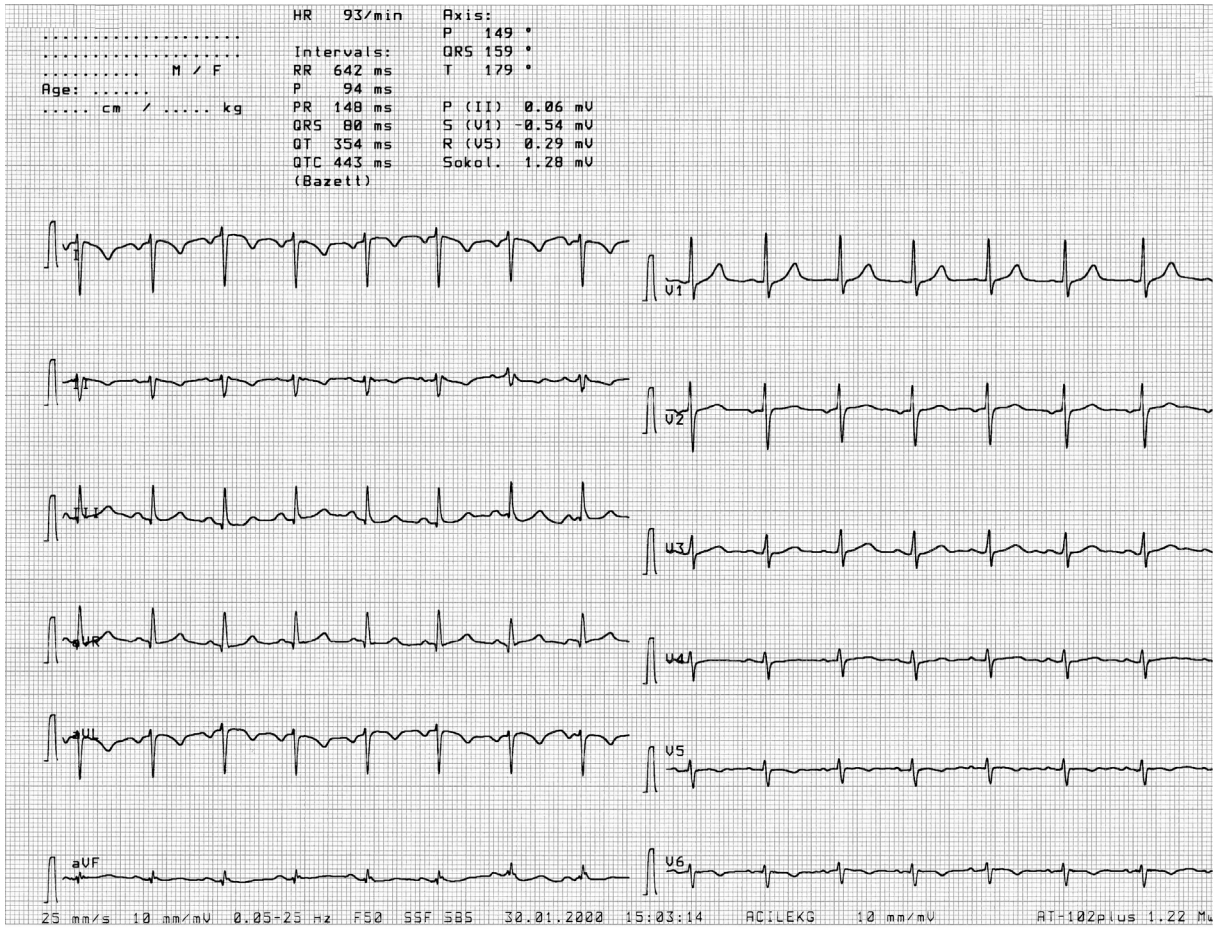

Figure 1. Right axis deviation and loss of R vawe progression in the precordial leads, compatible with dextrocardia

7 cm and a width of 1.5 cm containing fecaloid material was obtained. The patient had no additional complaints on the second post-op day and was discharged with full recovery.

Discussion

Abdominal pain is one of the most common causes of emergency department admission. The etiologic causes of the acute abdominal pain range from benign pathologies to serious pathologies with high mortality [5]. Also, complications in these patients who were applied with abdominal pain constitute a large percentage of medicolegal actions [6].

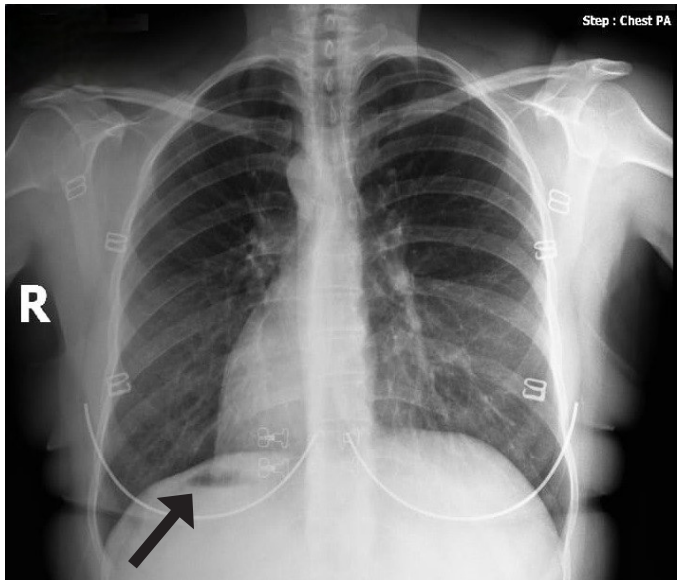

Figure 2. Right-sided gastric fundus air and dextrocardia appearance on chest X-ray (black arrow)

The causes of left lower quadrant pain include gastrointestinal and urinary system and gynecological pathologies. In the differential diagnosis; sigmoid diverticulitis, intestinal obstructions, inguinal hernia, renal colic, cystitis, pelvic inflammatory disease and epididymal, testicular, ovarian pathologies are considered. The symmetrical localization of the appendix in SIT cases causes acute appendicitis to be included in the differential diagnosis of left lower quadrant pain. The only difference in abdominal pain due to acute appendicitis in SIT compared to the normal population is that the localization of pain to the left lower quadrant instead of the right lower quadrant within 24 h of the onset of the abdominal pain in the umbilicus [7]. Because of the symmetrical location of the heart, thoracic and abdominal organs in SIT, there are some differences compared with the normal population. Right axis deviation (QRS negativity in DI and QRS positivity in aVF) due to dextrocardia is seen in ECG. Additionally, QRS wave positivity in aVR suggests the possibility of incorrectly connected electrodes. The main criterion in differential diagnosis is that the loss of R progression is seen only in the precordial leads in dextrocardia and is not seen in the case of incorrectly connected electrodes. In this study, the right axis deviation and loss of R progression on ECG were the main features that led to the diagnosis of dextrocardia instead of SIT. These ECG findings were similar to the ECG findings in the literature [8].

Identifying the leading cause of abdominal pain in female patients with SIT is similar to solving a puzzle. The main reason for the difficulty in the differential diagnosis of left lower quadrant pain in female patients with SIT is the presence of ovarian and other gynecological pathologies. Once an acute gynecopathological finding that may cause this

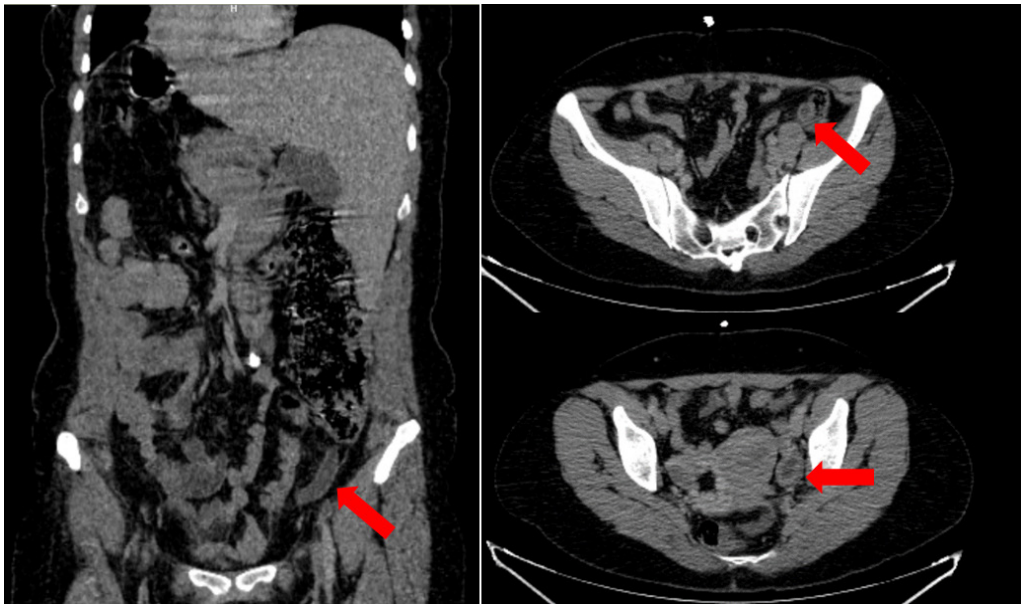

Figure 3. Appearance of 13.5 mm acute appendicitis in the coronal plane (left) and axial plane (top right) and left ovarian cyst (bottom right) with accompanying situs inversus in abdominal computed tomography examination (red arrow)

abdominal pain is detected, as in our patient, the possibility of acute appendicitis can be missed/ignored. This will delay the diagnosis of the patient and worsen her clinical features. Our case is important and special because it will change the perspective on the etiology of abdominal pain in female patients.

Despite successful laparoscopic appendectomy case reports, the abdominal anatomical difference in patients with SIT causes difficulties in the laparoscopic approach to acute appendicitis. This difficulty causes surgeons to prefer open surgery mostly. In the case, open surgery was preferred instead of laparoscopy.

Conclusion

SIT is a rare condition in the population, and due to its asymptomatic clinical course, it is mostly diagnosed incidentally during examination or imaging performed for any complaint. For the clinician faced with an undiagnosed female patient with SIT, this clinical evaluation can be quite a challenge. When these patients present to the emergency department with acute abdomen findings, both the diagnosis and consultation process to the necessary branches should be clearer than other patients. Before deciding on a definitive diagnosis for the patient, the localization of the organs should be confirmed by imaging.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: İ.A., B.Ö., D.T., S.D., Concept: İ.A., B.Ö., D.T., S.D., Design: İ.A., B.Ö., D.T., S.D., Data Collection or Processing: İ.A., B.Ö., D.T., S.D., Analysis or Interpretation: İ.A., B.Ö., D.T., S.D., Literature Search: İ.A., B.Ö., D.T., S.D., Writing: İ.A., B.Ö., D.T., S.D.

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

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CASE REPORT

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Could Mild Symptoms Lead to a Critical Diagnosis? Subtle Symptoms of an Aortic Dissection

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Abstract

Aortic dissection is among the rare admissions to the emergency department. Although their clinical presentation is well defined, diagnosis is difficult in patients with mild symptoms. Failure to diagnose an aortic dissection can lead to very catastrophic results. We present a case report of aortic dissection, which presented with only epigastric pain as a symptom. Using pain scales and careful follow-up in the emergency department have reached a critical diagnosis.

Keywords: Dissection, emergency medicine, pain measurement, aorta

Introduction

Aortic dissection is defined as separating the layers that make up the aortic wall. Despite advances in diagnosis and treatment methods, the mortality rate is still high [1].

Patients with acute aortic dissection typically present with sudden onset, severe, tearing chest pain [2]. The pain may spread to the neck, jaw, and interscapular region. Syncope, stroke clinic, impaired mental activity, hemoptysis, dysphagia, dyspnea, flank pain, abdominal pain, anxiety, and fear of death may accompany the course of the disease [3]. A very small group of patients present with only mild pain. These mild symptoms could be confused with a symptom of musculoskeletal disorders in the chest, groin, or back [4,5]. Thoracic aortic dissection should be considered in the differential diagnosis of all patients presenting with chest pain.

The diagnosis of acute aortic dissection initially requires a high index of suspicion. In addition to the history and physical examination, data from electrocardiogram (ECG), various laboratory markers (D-dimer, and the organ affected by end-organ damage due to dissection in general), vital signs, and symptoms related to the area affected by the dissection should be carefully evaluated.

Chest radiography, bedside ultrasonography (USG), contrast-enhanced tomography, magnetic resonance, and aortography can be used for diagnosis [6,7]. Our aim is to emphasize the importance of using USG in the emergency department in case of suspected aortic dissection.

Case Report

A 52-year-old female patient who had previously only known hypertension and gastritis was admitted to our emergency department with the complaint of abdominal pain. Our patient described the onset of pain 4 hours before she presented to the emergency department. At admission, the patient's blood pressure was 170/95 mmHg, heart rate was 79/min, oxygen saturation was 99%, and body temperature was 36.9 °C. The patient's vital signs were stable except for a high blood pressure. When questioned in detail, she complained about the epigastric region pain as a focal point and stated that the pain did not spread and was stationary. There were no other gastrointestinal system symptoms such as nausea, vomiting, or diarrhea. The

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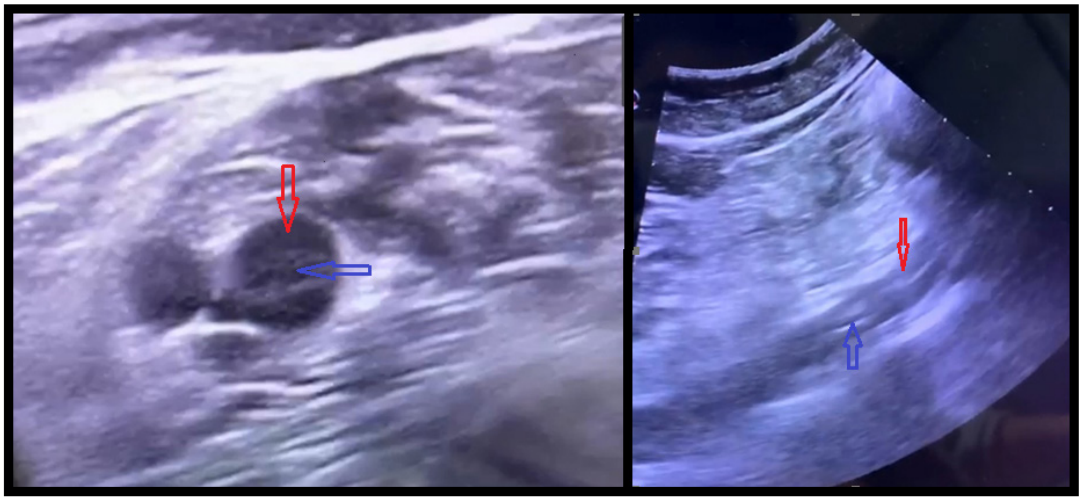

Figure 1. Abdominal ultrasound of aortic dissection. We see the longitudinal and transverse section view. Blue arrow marks true lumen, red arrow marks pseudolumen

patient's general appearance was stable, and the patient seemed comfortable. No pathological finding was detected in the physical examinations. An abdominal examination revealed epigastric tenderness. There were no acute abdomen findings. After clinical appearance and physical examination, the differential diagnosis included; peptic ulcer activation, acute coronary syndrome, pancreatitis, mesenteric ischemia, and dissection. An ECG was then taken to exclude some of these diagnoses. As laboratory tests, complete blood count, troponin level, blood gas, urea, creatinine, amylase, and lipase were sent. The ECG findings included a right bundle branch block (which was also present in previous ECGs). Laboratory results were found to be within the reference ranges.

Proton pump inhibitor, antacid, and tramadol treatment were applied to the patients in symptomatic treatment. However, there was no change in the complaints in the follow-up examinations after the symptomatic treatment, and they remained mild. Pain intensity was questioned. Although the patient seemed quite comfortable, the pain rating was 9/10 according to the "visual analog pain scale". The patient emphasized that her pain has always been the same since she applied. The patient's pain was different from that of previous peptic ulcer complaints. Because of the high pain score, critical emergencies were given priority. Blood pressure was rechecked from both arms, and while the patient was still hypertensive, there was no difference between the extremities.

Bedside transthoracic echocardiography was performed to obtain further clues for the diagnosis, such as acute coronary syndrome, mesenteric ischemia, aortic dissection, and pancreatitis. The aortic diameter was 32 mm in measurements made using a cardiac sector probe, and mild pericardial fluid was detected. When the aorta was visualized again from the abdomen using a convex probe, the aortic diameter was enlarged and there was a dissection flap (Figure 1). A diagnosis of aortic dissection was made, and computed tomography angiography was performed to clarify the type and size of the dissection. The diagnosis was reported as type 1 aortic dissection (Figure 2).

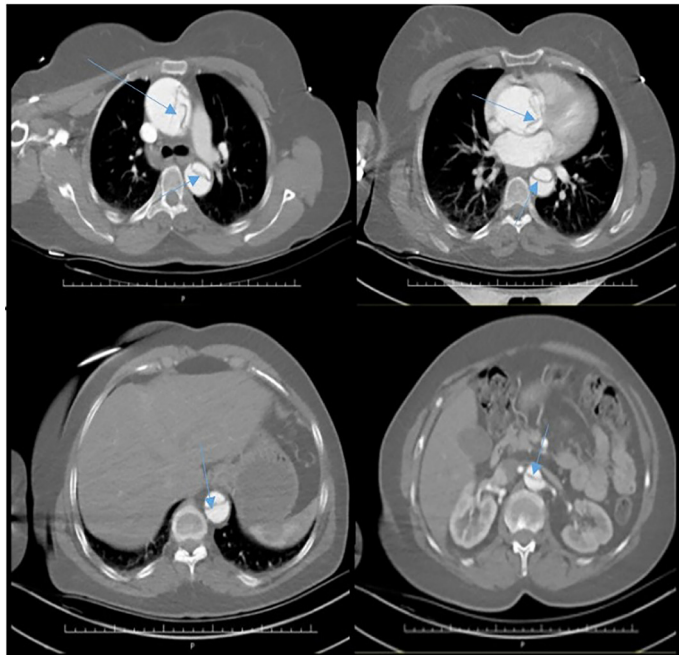

Figure 2. CT angiography image of type 1 aortic dissection. We see the dissection line in different sections (blue arrow)

CT: Computed tomography

Treatment was started to lower the blood pressure below 120/90 mmHg. The cardiovascular surgery department was consulted, and an emergent operation decision was made.

Discussion

As in many other diseases, patients with aortic dissection might admit to emergency departments with different clinical presentations [8]. The location of the pain is important in predicting where the dissection occurs. Anterior chest pain and chest pain mimicking acute myocardial infarction are generally associated with an ascended arch or aortic root dissection. This results from dissection, which cuts off flow to the coronary arteries and results in myocardial ischemia. Pain in the neck or jaw indicates that the dissection has involved the aortic arch and extends into the great vessels. A tear or tear-type pain in the interscapular region may indicate that the dissection has involved the descending aorta. Pain typically changes as the dissection develops.

The pain of aortic dissection is typically distinguished from the pain of acute myocardial infarction by its sudden onset and maximum severity at the onset. However, the presentations of the two conditions overlap to some extent and can be easily confused. Additionally, it can be confused with many different disease groups, depending on the dissection site.

Most physicians do not apply visual analog scales to every patient in daily clinical practice and often simply question if the complaints are regressed [9]. However, obtaining objective scores for pain might lead to critical diagnoses; otherwise, that would be missed, as presented in our case. Therefore, applying objective queries to the patients' complaints might diagnose life-threatening conditions.

Considering all these, dissection should be considered as a differential diagnosis in patients with different clinics who are thought to have simple preliminary diagnoses [10]. Using advanced examination methods to exclude every differential diagnosis in emergency services' chaotic and crowded environments causes a cost burden and creates various risks for patients.

Conclusion

Obtaining a good history, repeating examinations, and using emergency instruments such as bedside USG are more effective than many other tests in reaching a life-threatening diagnosis. Furthermore, the effective use of pain scales in the emergency department can be useful in detecting catastrophic conditions, as seen in our case.

Ethics

Informed Consent: Written informed consent was obtained from the patients.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.Ö., A.G., F.S., M.Ç., Design: A.Ö., E.Ş., Data Collection or Processing: A.Ö., Analysis or Interpretation: A.G., Literature Search: A.Ö., Writing: A.Ö., E.Ş.

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

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