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ORIGINAL RESEARCHES

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Önder Yeşiloğlu; Gaziantep, Turkey



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Effect of SARS-CoV-2 Variants on the Progression of COVID-19 Disease: A Retrospective Analysis From a Pandemic Hospital

Adem Çakır¹, Kemal Şener², Nuran Karabulut³, Banu Arslan², Ertuğrul Altuğ², Gökhan Eyüpoğlu², Ramazan Güven²

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Abstract

Objective: Severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) is an agent of the pandemic coronavirus disease-2019 (COVID-19). New variants that have emerged throughout these pandemic presented new challenges and made the disease control process even more difficult. In our study, we aimed to investigate the effect of variants on the progression of COVID-19 and add value to the medical literature by providing valuable information.

Materials and Methods: The current study was designed as a retrospective and single-center study. Three thousand and a hundred and ninety-three patients whose SARS-CoV-2 polymerase chain reaction tests came positive between June 1, 2020, and June 1, 2021, were included in the study. Demographic data and the medical history of patients were collected and recorded. The statistical significance level sought was $p < 0.05$.

Results: Fifty percent of the cases were male and the mean age was 39.5 years. Among the variant types, the lowest median age was observed in the beta variant. Alpha is the most contagious SARS-CoV-2 variant, and the highest mortality was seen in the delta variant. Considering all SARS-CoV-2 variants, the most common patient complaints were dyspnea and fever. In fatal cases, blood pressure and saturation levels were low, whereas pulse rate and body temperature was higher. Additionally, compared to the non-fatal cases, the median age was higher in fatal cases, 39 years to 55 years. Most of the fatalities occurred in patients who required intensive care unit (ICU) admission. The mortality was low in people with double-dose vaccination, regardless of the variant types.

Conclusion: In this study, SARS-CoV-2 alpha variant was found to be more contagious, and the delta variant appeared more fatal. Patients with delta variant could be at a high risk of morbidity and mortality. Therefore, meticulous patient care should be delivered to patients with the delta variants, no history of the double-dose of vaccination, patients with unstable vital parameters, and patients who were admitted to the ICU.

Keywords: COVID-19, SARS-CoV-2, variants, pandemic, mutation

Introduction

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), has had a devastating impact on the world since it emerged in Wuhan, China in 2019 and continues to do so. It has become the most catastrophic health event that emerged until today, after the Spanish flu pandemic of 1918 that resulted in 5.4 million deaths worldwide. Ever since the World Health Organization (WHO) declared the novel COVID-19 outbreak a pandemic in 2020, the virus has continued to be catastrophic. Several countries are still suffering from multiple waves of COVID-19 infections.

Adaptive mutations in the virus genome changes pathogenicity of the virus. Even a single amino acid change can lead the virus to gain the ability to evade the immune system [1]. While some evidence suggests that SARS-CoV-2 may adapt to the human host through recurrent mutations over time, as in other RNA viruses, it seems possible that these mutations may lead to the emergence of new variants by producing characteristics [2].

In the first half of the 2020, mutations in the genomic structure of SARS-CoV-2 were identified in some studies. Several new variants have emerged and been identified by genomic data analysis. Koyama et al. [3] examined 10,022 genomes in four



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different databases from 68 countries between February 1st and May 1st. In July 2020, they reported that several variants of the SARS-CoV-2 genome exist. Additionally, they noted that there were 5,775 distinct genomes, 2,969 of which contained missense mutations. Later, multiple researchers verified that the virus had acquired several mutations [3]. In late 2020s, some evidence revealed that the number of cases associated with some of these mutations had inclined, and these mutations were observed more frequently in the spike protein (S-protein) regions. With this altered spike protein, some variants become more contagious than others [4]. The WHO and the center for disease control reported the SARS-CoV-2 variants with high infectivity (such as the variant with D614G mutation) as the variants of concern (VOC) or variants of interest (VOI) [2,4,5].

Five major VOCs were recorded in three different parts of the world; the lineage B.1.1.7 in the UK (20I/501Y.V1-Alpha variant); the lineage B.1.351 (20H/501Y.V2-Beta variant) in South Africa; P.1 lineage in Brazil (20J/501Y.V3-Gamma variant); the lineage B.1.617.2 (Delta variant) in India and the lineage B.1.1.529 (Omicron variant) in South Africa. Additionally, WHO announced eight VOIs; the B.1.427/1.429 variants (Epsilon) detected in California/USA, the B.1.525 variant (Eta) and the B.1.526 variant (Iota) in New York/USA, the S.2 lineage (20J variant-Zeta variant) in Brazil, the P.3 lineage (Theta variant) in Japan and the Philippines, the B.1.617.1 (Kappa variant) in India, lineage C.37 (Lambda variant) in South Africa and the B.1.621 lineage (Mu variant) in Columbia [6,7].

Some evidence has suggested that some of these VOCs and VOIs causes an increase in the infectivity of virulence, decrease in neutralization that was elicited with natural or vaccinated antibodies, and change in the ability to evade detection and fatality.

In our study, we assessed the progression of COVID-19 based on variant types in patients with positive polymerase chain

reaction (PCR) tests and provide some valuable information for future studies.

Materials and Methods

This single-center retrospective study was conducted on emergency department patients with suspected COVID-19 between June 1, 2020, and June 1, 2021. Three thousand one hundred and ninety three patients whose PCR test results were positive and met the inclusion criteria were included in the study.

The study hospital, University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital, is an urban research and teaching hospital with a level I trauma center. It is the largest academic hospital in the western region of İstanbul with a bed capacity of 2,682. We accept most critically ill patients on the European side of İstanbul and nearby cities since our hospital involves the most critical units such as interventional radiology, cardiovascular intensive care unit (ICU), cardiac catheterization labs, etc. The average number of admissions per day to our emergency COVID-19 outpatient clinic was around 1,800 patients during the study period.

The hospital automation system, in other words hospital information management system (HIMS) was searched for the ICD10 code of “U07.3-COVID-19”. According to the search results, 4,782 patients with positive SARS-CoV-2 PCR were identified. These patients were subjected to PCR test for having COVID-19 symptoms. Among these patients, patients under the age of 18, pregnant women, patients with chronic respiratory diseases, patients with multi-pathogen detected in respiratory tract tests, and subjects with missing data (unknown outcomes, unidentified variants, etc.) were excluded from the study (Figure 1). Overall, 3,193 patients were finally included in the study.

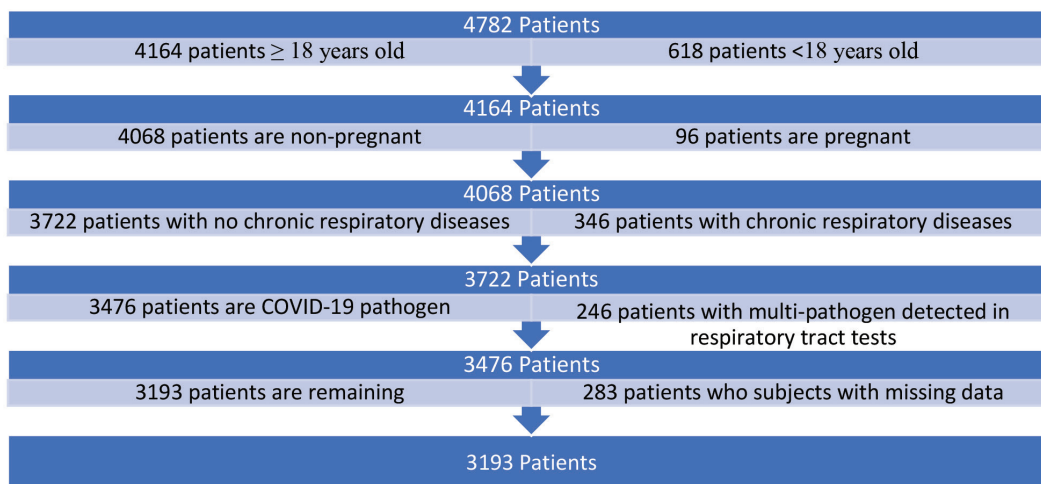


Figure 1. Flowchart of the cases included in the study
 COVID-19: Coronavirus disease-2019

Patient demographics (age, sex, and vaccination history) and clinical characteristics (main complaints at admission, vital signs including systolic and diastolic blood pressure, pulse, fever, and saturation levels, the requirement for hospitalization, the clinical unit that patient was admitted to, clinical outcome, and re-admission rates) were assessed through HIMS, and study data were recorded in a study form. Epicrisis reports and consultation notes were also examined in the study. Patients with missing data were excluded from the study.

Ethics Committee Approval

The study protocol was approved by the Ethic Committee of University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital (ethics committee meeting and decision dated 14.04.21 and ethics committee no: KAEK/2021.04.81) and followed the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. Voluntary consent was obtained from all patients.

Statistical Analysis

Study data were analyzed using SPSS Statistics for Windows®, version 23.0 (IBM Inc. Chicago, IL, USA). Descriptive data were presented with number, percentage, mean, standard deviation, median, minimum, and maximum. Kolmogorov-Smirnov test was applied to determine whether study data were normally distributed. The Pearson chi-square test and Fisher's Exact test were used to compare categorical data. T-test was used to compare two independent numerical data and Kruskal-Wallis test was used to compare triple numerical data. In this study, $p < 0.05$ was accepted as the level of significance.

Results

The study included 3,193 patients positive SARS-CoV-2 PCR test. When demographic data were examined; 50% ($n=1,596$) of the patients were female and 50% ($n=1,597$) of them were male. The median age was identified as 39.5 years in males and 39.0 years in females, with no statistically significant difference between the two groups. The most common complaints in both genders were noted as dyspnea and fever. In terms of patient complaints on admission, there was no statistically significant difference between the two groups. Vital parameters were used for emergency department admission are shown in Table 1. Our data analysis revealed no significant difference between the median values of vital parameters between the two genders. According to the oropharyngeal/nasopharyngeal swab results, the most identified SARS-CoV-2 variant was the alpha variant (UK variant) in both genders. The history of PCR positivity and history of COVID-19 vaccine in the patient's family are shown in Table 1. There was no significant difference in two genders of history of PCR positivity and history of COVID-19 vaccine in patients' families.

The clinical outcomes were assessed after each case was diagnosed, treated, and finalized. Follow-up records revealed that 3,126 patients were discharged from the hospital, and sixty-seven patients died. When vital parameters on admission were evaluated based on the clinical outcomes, it was found that systolic blood pressure, diastolic blood pressure and saturation levels were significantly lower in non-survivors. However, heart rate and body temperature were found to be significantly higher than survivors. Additionally, our data analysis demonstrated that there was no significant difference between survivors and non-survivors in terms of patient complaints on admission, SARS-CoV-2 variant types, and history of PCR test positivity in the family. However, the history of double-dose COVID-19 vaccine was found to be less in the non-survivor group and 61.2% ($n=41$) of these patients were hospitalized to the ICU (Table 2).

The median age based on the SARS-CoV-2 variants were 40.0 years (50-30 years) in the alpha variant; 26.0 years (30-22 years) in the beta variant; 42.0 years (55-36.5 years) in the gamma variant; 35.0 years (42-26 years) in the delta variant and 55.0 years (61.5-49.0) in the other variants. According to our statistical analysis, there was a statistically significant difference between the median age and the SARS-CoV-2 variants. The lowest the median age was observed in the beta variant group, other variant types had the highest median age ($p < 0.001$), 26 years and 55 years, respectively.

There was no statistically significant difference between variant types and patient complaints on emergency department admission ($p > 0.05$). Moreover, no statistically significant relationship was identified between variant types and current vaccination status.

Discussion

Since its emergence in Wuhan, China, in late 2019, SARS-CoV-2 has undergone several genomic mutations that resulted in different lineages and variants appearing in different parts of the world. Some of these mutations result in high transmission rates, complex clinical presentations, and increased severity of the disease [8,9]. It was observed that variants identified in patients with positive SARS-CoV-2 PCR test peaked in certain periods and increased the contagiousness and mortality in populations. With this study, we aimed to evaluate the contagiousness and mortality risk of variants detected in emergency patients and to provide valuable evidence to the literature and future studies.

With the rapid spread of SARS-CoV-2 variants across the globe, several COVID-19 waves have been observed in the last two years. Generally believed that transmission rates, mortality, and dominant clinical features vary during these waves. The literature reports valuable data regarding clinical presentations,

Table 1. Patient demographics and characteristics based on gender

Characteristics	Male n (%) / mean (IQR)	Female n (%) / mean (IQR)	p
Total	1596 (50)	1597 (50)	-
Age (years)	39.5 (49.5-30.0)	39.0 (50.0-29.0)	0.891*
Vital signs on admission			
Systolic blood pressure (mmHg)	120.0 (125.0-109.0)	118.0 (125.0-104.0)	0.627*
Diastolic blood pressure (mmHg)	65.0 (71.5-62.0)	63.0 (72.0-60.0)	0.527*
Saturation (%)	94.0 (96.0-92.0)	94.0 (96.0-92.0)	0.837*
Pulse (beats/min)	85.0 (94.0-77.0)	86.0 (94.0-76.0)	0.758*
Temperature (°C)	36.7 (37.2-36.2)	36.8 (37.3-36.2)	0.907*
Main presenting complaints			
Cough	184 (48.5)	195 (51.5)	0.644**
Shortness of breath	600 (49.6)	609 (50.4)	
Fever	374 (52.4)	340 (47.6)	
Diarrhea	142 (47.7)	156 (52.3)	
Nausea-vomiting	204 (48.8)	214 (51.2)	
Malaise/body aches	92 (52.6)	83 (47.4)	
SARS-CoV-2 variants			
Alfa (UK)	1189 (49.1)	1232 (50.9)	0.120**
Beta (South Africa)	56 (48.7)	59 (51.3)	
Gama (Brazil)	112 (48.3)	120 (51.7)	
Delta (India)	183 (56.1)	143 (43.9)	
Others	56 (56.6)	43 (43.4)	
Family history of positive SARS-CoV-2 PCR test			
Present	641 (49.2)	662 (50.8)	0.458**
None	955 (50.5)	935 (49.5)	
History COVID vaccine			
None	239 (47.7)	262 (52.3)	0.310**
One dose	683 (49.4)	699 (50.6)	
Two doses	674 (51.5)	636 (48.5)	

*Mann-Whitney U test is used, **Pearson χ^2 test is used, PCR: Polymerase chain reaction, IQR: Interquartile range, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, COVID: Coronavirus disease

transmission rates and mortality of the SARS-CoV-2 pathogen when it first emerged in Wuhan, China. Based on these data, the effects of VOCs were evaluated. Mallavarpu Ambrose et al. [10] stated that the new variants identified in England, USA, India, and South Africa were more transmissible but less fatal compared to the SARS-CoV-2 detected in Wuhan. Davies et al. [11] reported that the UK variant (lineage B.1.1.7-Alpha variant) had higher transmission rates than existing variants in England. In our study, we demonstrated that the alpha variant (UK-B.1.1.7) was the most detected variant (75.8%) among our subjects. Additionally, the highest risk of mortality was in the delta variant (India- B.1.617.2) (4.0%). Regarding transmissibility, our results agreed with Davies et al. [11]. Among all SARS-CoV-2 variants, the most common complaints in our study were dyspnea and fever. Even though patient complaints on admission are not

statistically significant among variants, patients with the delta variant should be meticulously evaluated since the mortality appears higher in this group.

The COVID-19 pandemic has led to the development of new treatment regimens and vaccines at an unprecedented pace. The emergence of new variants requires scientists to apply new studies and develop new generations of vaccines and treatments. In this rapidly evolving chaotic environment, the importance of vaccination and vaccine studies has shown itself once again. Literature has reported mixed results regarding the protection of neutralizing antibodies against SARS-CoV-2 variants. Although studies have indicated that the efficacy of current vaccines against emerging SARS-CoV-2 variants continues, some studies have emphasized the requirement of new vaccines [7,12,13].

Table 2. Clinical characteristics based on patient outcomes			
Characteristics	Survivors n (%) / mean (IQR)	Non-survivors n (%) / mean (IQR)	p
Total	3126 (97.9)	67 (2.1)	-
Age (years)	39.0 (49.0-29.0)	55.0 (63.0-49.5)	<0.001*
Vital signs on admission			
Systolic blood pressure (mmHg)	120.0 (125.0-110.0)	88.0 (125.0-78.0)	<0.001*
Diastolic blood pressure (mmHg)	65.0 (72.0-62.0)	47.0 (66.0-42.5)	<0.001*
Saturation (%)	94.0 (96.0-92.0)	86.0 (92.0-82.0)	<0.001*
Pulse (beats/min)	85.0 (94.0-76.0)	104.0 (122.0-91.50)	<0.001*
Temperature (°C)	36.7 (37.2-36.2)	36.8 (37.7-36.5)	0.001*
Main presenting complaints			
Cough	376 (99.2)	3 (0.8)	0.232***
Shortness of breath	1178 (97.49)	31 (2.6)	
Fever	691 (96.8)	23 (3.2)	
Diarrhea	295 (99.09)	3 (1.0)	
Nausea-vomiting	411 (98.3)	7 (1.7)	
Malaise/body aches	175 (100.0)	0 (0.0)	
SARS-CoV-2 variants			
Alfa (UK)	2370 (97.9)	51 (2.1)	0.927***
Beta (South Africa)	114 (99.1)	1 (0.9)	
Gama (Brazil)	230 (99.1)	2 (0.9)	
Delta (India)	313 (96.0)	13 (4.0)	
Others	99 (100.0)	0 (0.0)	
Family history of positive SARS-CoV-2 PCR test			
Present	1274 (97.8)	29 (2.2)	0.677**
None	1852 (98.0)	38 (2.0)	
History COVID-19 vaccine			
None	482 (96.2)	19 (3.8)	<0.001**
One dose	1341 (97.0)	41 (3.0)	
Two doses	1303 (99.5)	7 (0.5)	
Type of follow-ups			
Outpatient follow-up	2854 (99.99)	3 (0.01)	<0.001**
Hospitalization	216 (89.6)	24 (10.4)	
ICU admission	56 (57.3)	40 (42.7)	

*Mann-Whitney U test is used, **Pearson χ^2 test is used, ***: Fisher's Exact test is used. PCR: Polymerase chain reaction, ICU: Intensive care unit, IQR: Interquartile range, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2, COVID-19: Coronavirus disease-2019

Our results demonstrated that 15.7% of the emergency patients with positive SARS-CoV-2 PCR were unvaccinated. 43.3% of these patients had a history of single-dose, and 41.0% had a double-dose of COVID-19 vaccine. There was no statistical difference between variant type and the history of vaccine in non-survivors. However, the mortality rate was 0.5% in patients with a history of the double-dose of the COVID-19 vaccine and it was higher in patients with a history of single-dose and unvaccinated patients,

3.0%, and 3.8%, respectively. Our results conclude that vaccine studies are significantly important in preventing mortality regardless of variant types.

Our study demonstrated that the median age was higher in non-survivors. Clinicians should be extremely careful in assessing the mortality risk in patients with unstable vital parameters on emergency department admission and patients requiring early ICU admission.

Study Limitations

There are some limitations to the present study. First, this was a retrospective study conducted through HIMS search. Even though we could access every single patient's medical record who was admitted to the emergency department with COVID-19 symptoms and offered a positive SARS-CoV-2 PCR, some of these files had missing study data that had us to exclude several patients from the study. Second, patient medical records involved the status of the COVID-19 vaccine, however type of vaccine or vaccine (Sinovac, Biontech, etc.) was not recorded. Lastly, our study did not include data on the omicron variant since the emergence of the variant comes across the time, we had completed the study.

Conclusion

The current study demonstrated that the alpha variant was the most contagious, and the mortality was seen as the highest in the delta variant. Additionally, we showed that a double-dose of COVID-19 vaccine can be protective against mortality regardless of SARS-CoV-2 variants. Our results emphasize that clinicians should provide meticulous care to COVID-19 patients with advanced age, unstable vital parameters on emergency admission and no history of double-dose of COVID-19 vaccines. We believe that future studies on this subject can provide valuable information for emergency doctors and clinicians who frequently encounter COVID-19 patients and guide them in improving pandemic patient management.

Acknowledgment

We would like to express our deepest gratitude to all healthcare workers and scientists who work devotedly, often putting themselves and their families in the back despite all challenges arising from the COVID-19 pandemic. Your efforts will not be forgotten.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ethic Committee of University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital (ethics committee meeting and decision dated 14.04.21 and ethics committee no: KAEK/2021.04.81) and followed the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.

Informed Consent: All patients were reached and voluntary consent was obtained. Consent was obtained from first-degree relatives in patients with a mortal course.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.Ç., K.Ş., N.K., B.A., E.A., G.E., R.G., Concept: A.Ç., B.A., G.E., R.G., Design: A.Ç., K.Ş., E.A., R.G.,

Data Collection or Processing: A.Ç., K.Ş., N.K., E.A., G.E., Analysis or Interpretation: A.Ç., R.G., Literature Search: A.Ç., N.K., B.A., G.E., R.G., Writing: A.Ç., N.K., B.A.

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Demographic and Clinical Characteristics of COVID-19 Cases at the 112 Emergency Call Centers in İstanbul

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Abstract

Objective: The study aims to present calls received at the 112 Emergency Calls Centers in İstanbul. Algorithms were applied to analyze the demographic and clinical characteristics of coronavirus disease-2019 (COVID-19) cases.

Materials and Methods: Incoming calls at the 112 Emergency Call Centers of the European and Anatolian regions of the metropolitan city of İstanbul were assessed. In the retrospective study, the period under investigation was from March 11 to May 1 of 2020.

Results: Patients with suspected severe acute respiratory syndrome-coronavirus-2 pneumonia (n=35,443) were analyzed. The mean age of the patients was found to be 50.6±22.3. Of this total, 16,902 (47.7%) cases were female. Ambulance response times for these cases were reported as 10.2 (7.0-16.3) minutes. In terms of clinical symptoms, 18,958 (53.50%) of the cases had fever, 18,359 (51.86%) had a cough, and 21,121 (59.60%) had shortness of breath. The district with the highest number of cases was Gaziosmanpaşa with 1,256 cases, 42.16 people per square meter.

Conclusion: Prehospital health services are an important link in the chain of survival. Ambulance services act as a bridge between individuals in the community and hospital care services in cases of disasters such as earthquakes, floods, pandemics. The structural establishment of a robust system to meet the incoming demands, the construction of applicable algorithms, building the optimal infrastructure for ambulances in accordance with the population intensity, will both protect the system and help to improve the quality of health services delivery.

Keywords: Command and control centers, prehospital health services, ambulance, pandemic, SARS-CoV-2, COVID-19 pneumonia

Introduction

A pneumonia cluster with unknown cause appeared in Wuhan, China, in December 2019 [1]. The National Health Commission of the People's Republic of China announced later that a new coronavirus, named severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) by World Health Organization (WHO), was responsible for the coronavirus disease-2019 (COVID-19) outbreak [2-4]. The virus spreads rapidly around the world and in January 2020, WHO declared COVID-19 a global public health emergency [5]. The pandemic continues to threaten lives and economies globally [6]. On April 21, 2020, more than 2.4 million

people tested positive for SARS-CoV-2 and the outbreak caused more than 165,000 deaths [7]. The Turkish Ministry of Health confirmed that the first COVID-19 case in Turkey was diagnosed on March 11, 2020. National and private ambulance services took safety precautions in handling potential cases, including the filtering of cases from incoming calls to 112 Emergency Call Centers, identification of potential, suspected, confirmed COVID-19 cases, dispatching teams with fully secure personal safety equipment, correct and appropriate use of the protective supplies and apparatus, compliance with safety procedures during sample-taking and transport, assuring that patients wear surgical masks, decontamination, and cleaning of the



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ambulances following transportation. These precautions were important measures in terms of the safety of patients, healthcare workers, and the general community.

The study analyzes and presents features regarding the incoming calls at the 112 Emergency Calls Centers in the metropolitan city İstanbul. In the period when emergency calls surged in İstanbul during the coronavirus outbreak, algorithms were applied to define the demographic characteristics of the COVID-19 cases from the call centers' case records. The demographic and clinical characteristics of COVID-19 cases are hereby presented.

Materials and Methods

Incoming calls at the 112 Emergency Call Centers of the European and Anatolian regions of the metropolitan city of İstanbul were assessed. In the retrospective study, the period under investigation was from March 11 to May 1 of 2020. A total of 980 healthcare staff were employed in the two call centers, where 245 personnel worked daily, on a 24-hour-a-day basis. A total of 3,432 staff were employed at 286 stations altogether, in 39 districts, at 112 Ambulance Services of İstanbul.

The Ethics Committee of University of Health Sciences Turkey, İstanbul Bagcilar Training and Research Hospital approved the research application, dated May 6, 2020 with document #EY.FR.26.

The triage questions to 112 emergency call centers were as follows:

1. Do you have a cough?
2. Do you have difficulty breathing or respiratory distress?
3. Do you have fever or a history of fever?
4. Have any of your relatives been hospitalized within the last 14 days due to respiratory disease?
5. Have any of your relatives been diagnosed with COVID-19 within the last 14 days?

These five questions were asked and if the answer to at least two of these questions were "yes", the case was considered potential COVID-19. If the answers to the first two questions were "yes", it was recommended for 112 personnel to wear N95/FFP2 masks and goggles/face protectors. In handling the remaining cases, it was recommended for them to wear medical masks and goggles/face protectors. While attendants were not allowed in the ambulances for adult patients, as mandatory exceptions, they were required to wear medical face masks.

Call data from 112 Emergency Call Centers calls were reviewed retrospectively and analyzed. WHO recommendations were followed for contact tracing. Fever, cough, shortness of breath

complaints, comorbid diseases, malignity, thorax-computed tomography (CT) results were noted. History-taking included the question of whether anyone was diagnosed with COVID-19 in the household; and if that was the case, international travels was questioned.

To assess the pattern and trend of COVID-19 spread, the calls corresponding to the same period in 2018 and 2019 were recorded, and the increase rate for calls for in 2020 was calculated using simulation methods. Simulations were then run for 2020, to compare actual numbers in the existence of COVID-19 and results if the disease did not exist.

Statistical Analysis

Statistical analysis was performed using data obtained retrospectively from case records. Data were recorded and analyzed using SPSS 24.0 (Armonk, NY: IBM Corp.) software. Data were expressed as numbers and percentages for categorical variables and as mean ± standard deviation (SD) for continuous variables. Continuous data are given as mean ± SD and median (25th-75th).

Results

Patients with suspected SARS-CoV-2 pneumonia (n=35,443) were analyzed. The mean age of the patients was found to be 50.6±22.3. Of this total, 16,902 (47.7%) cases were female, while 502 (1.4%) of the cases were of foreign nationality. Geriatric patients, older than 65 years, constituted 10,948 (30.9%) of the cases (Table 1). Ambulance response times for these cases were reported as 10.2 (7.0-16.3) minutes, the median (25th-75th). In terms of clinical symptoms, 18,958 (53.50%) of the cases had fever, 18,359 (51.86%) had a cough, and 21,121 (59.60%) had shortness of breath. The district with the highest number of cases was Gaziosmanpasa with 1,256 cases, 42.16 people per square meter. While 29,729 (83.9%) of the calls received were emergency calls, 5,704 (16.1%) of them were transport calls. Of the transport cases, 288 (5.0%) were transferred to intensive care units, and 197 (68.4%) of these cases were intubated.

Characteristic		Mean ± SD
Age (year)		50.6±22.3
	Age group	n (%)
	0-14	2208 (6.2)
	15-49	14315 (40.4)
	50-64	7962 (22.5)
	≥65	10948 (30.9)
Sex	Female	16902 (47.7)
	Male	18531 (52.3)

SD: Standard deviation, SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2

The distribution of these cases according to hospital type is presented in this study (Table 2). The distribution of the cases with fever, cough and shortness of breath complaints is presented graphically (Figure 1). In terms of the symptoms, 9,619 cases had all three symptoms, 18,958 (53.50%) cases had fever, 18,359 (51.86%) cases had cough, and 21,121 (59.60%) cases had shortness of breath. Of 35,433 suspected or potential COVID-19 cases transported, shortness of breath was present in 28,075 (79.2%) and 3,065 (8.65%) cases were thorax CT positive. While 3,428 (9.7%) of the cases had a history of contact, 363 (1.0%) had a history of traveling to abroad. The district with the lowest number of cases in İstanbul was Sile with 128 cases, 0.5 people per square meter; the district with the highest number of cases was Gaziosmanpasa with 1,256 cases, 42.16 people per square meter. A statistically significant correlation was found between the population per square meter and the rate of cases in the districts of İstanbul ($p < 0.001$, $r = 0.636$).

Simulations were run for 2020, to compare actual numbers in the existence of COVID-19 and results if the disease did not exist. Calls from the same period in 2018 and 2019 were recorded and compared for the assessment (Figure 2a-d). Sanitizing and disinfecting the ambulance after transporting a COVID-19 patient is important; a key step is the disposal of medical gowns worn by staff. Sterilization procedures for ambulances are applied at the stations after each case. In the transportation of 35,433 cases, 180,708 gowns (5.1 per case), 163,992 N95/FFP2 masks and goggles (4.6 per case) for each personnel, 77,953 surgical masks (2.2 per case) and many gloves were used.

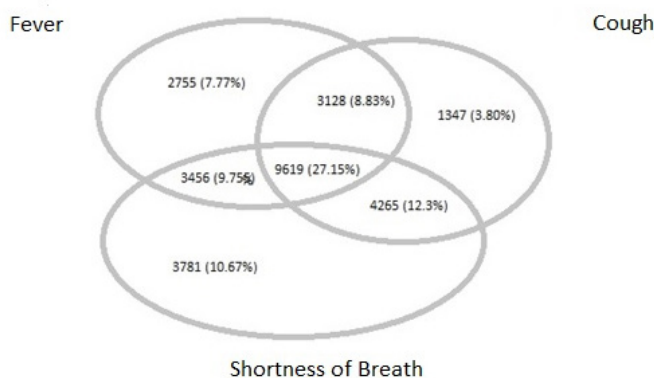


Figure 1. Intersecting sets of fever, cough, shortness of breath complaints of the SARS-CoV-2* suspected calls

*SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2

Discussion

This research is one of the first studies to present data, analysis, and experiences in prehospital patient services during the COVID-19 pandemic. The authors conclude that, for quality service in disasters such as the COVID-19 pandemic, feasible algorithms should be created. Another finding of the study was that the adequacy of personal protective equipment, along with the safety of a healthy work environment, increased the quality of health service delivery. It was observed that individuals in the population were late in adopting the measures taken and early in giving up.

In Choi’s [8] study, the median age was found as 77 years of age (range 35-93 years), and the female-to-male ratio was found as 44:56. Lian et al. [9] found mean age was 45 (5-88) and ages were mostly between the range of 15 and 49. In this study, while the average age was 50.6 ± 22.3 (mean \pm SD), ages were in the range of 15 to 49, in compliance with current literature. The female-to-male ratio in the current study was 48:52.

In the general population, the most frequent symptoms were fever (98%), cough (76%), dyspnea (55%) and myalgia or fatigue (up to 44%) [1,10]. In a study conducted on 21 critical patients with SARS-CoV-2 infection, the most frequent symptoms were shortness of breath (76%), fever (52%) and cough (48%) [11]. Studies have shown that complaints are variable, depending on the severity of the cases. The distribution of the complaints showed close numbers in this research. The most frequent symptom was shortness of breath in Arentz et al.’s [11] study. In the station assessment study by Venkatraman et al. [12] found “call received” to “arrived at the scene” 17.0 (7.0-60.0) minutes. In this study, although wearing protective gear increased ambulance response time in the cases reported as suspected or potential by the command and control center, the time was found as 10.2 (7.0-16.3). This finding can be explained by the fact that the metropolitan city of İstanbul is surrounded by a network of 112 stations.

Thorax CT is a critical tool in the initial screening of COVID-19 pneumonia. Shi et al. [13] analyzed the CT images of 81 patients with COVID-19 pneumonia and found that in chest CT scan, COVID-19 pneumonia mostly presented with bilateral and sub-pleural ground glass opacities. Ai et al. [14] showed that diagnostic results of CT images were consistent with reverse-transcriptase polymerase chain reaction analyses for the diagnosis of COVID-19 pneumonia. Additionally, they

Table 2. Characteristics of suspected SARS-CoV-2 calls and distribution of the hospitals the cases were transported to			
	State hospital n (%)	University hospital n (%)	Private hospital n (%)
Emergency	26372 (88.7)	553 (1.9)	2804 (9.4)
Transport	3420 (60.0)	119 (2.1)	2165 (38.0)
SARS-CoV-2: Severe acute respiratory syndrome-coronavirus-2			

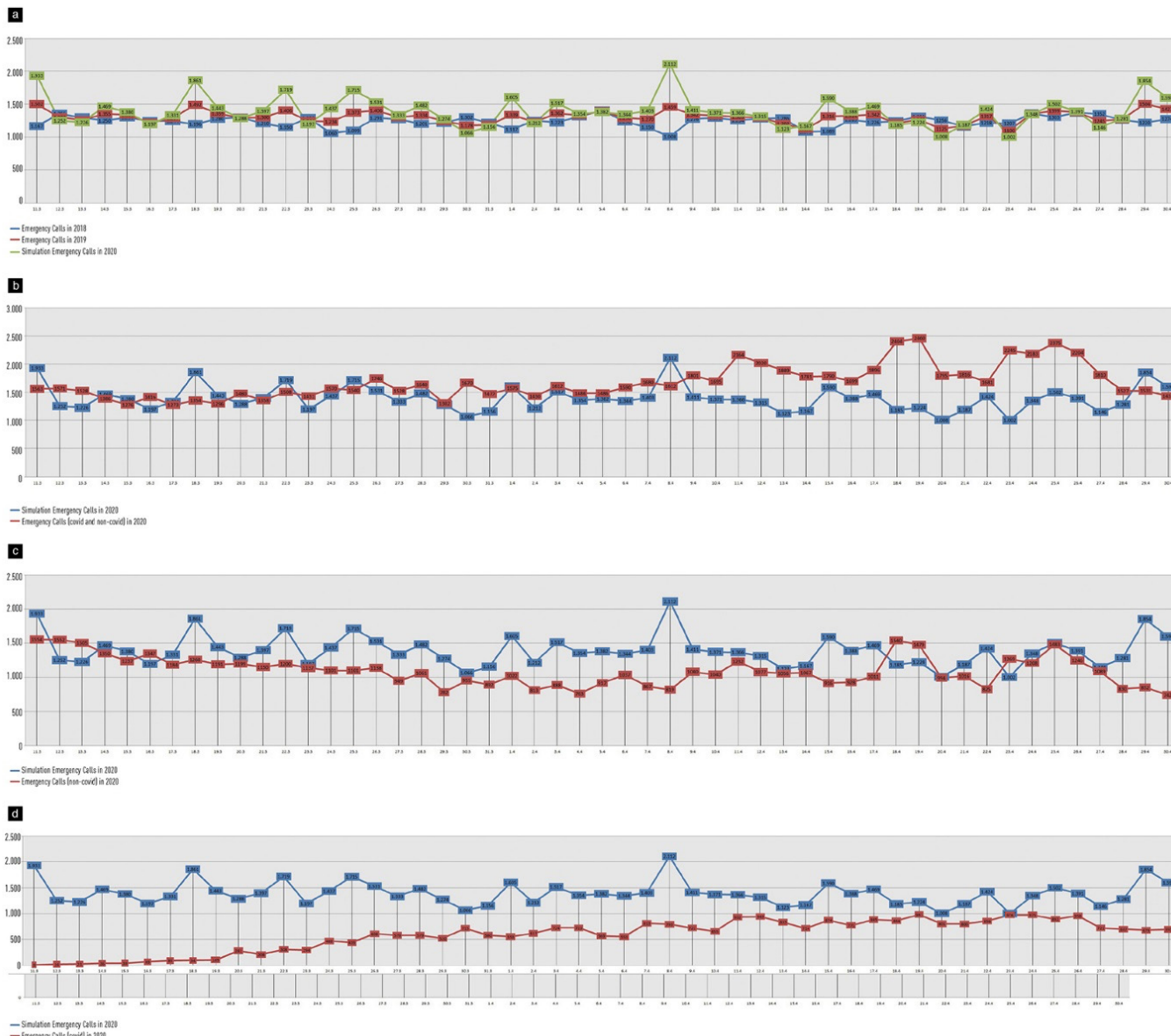


Figure 2. Timeline of calls to the emergency call center

found that CT has a very high sensitivity for the diagnosis of COVID-19 pneumonia [14]. Although CT images show a great potential in the diagnosis of COVID-19 pneumonia, currently radiographic features of COVID-19 pneumonia should be defined manually from all thin layer CT images (an average of 300 layers per patient) by trained radiologists. This will significantly increase the work load of radiologists and delay diagnosis [15]. CT is recommended for COVID-19 patients with initial moderate to severe symptoms and with advancing clinical symptoms [16]. CT also plays a role in predicting the severity of COVID-19 and guiding clinical management. For instance, CT results can provide an estimate of the proportion of unaffected, normally ventilated lungs associated with better outcomes [17]. A comprehensive analysis should be conducted

on the potential benefits of examination against financial costs and being exposed to ionizing radiation. The radiation dose, movement artefacts and beam hardening artefacts can be reduced significantly by using modern CT scanners [18]. Notably a negative chest CT does not exclude COVID-19, especially when it is performed within the first few days after the symptoms start [19-21]. CT rate was found to be low in our study since diagnosis is first made with tomography and then test and clinic and since contacts are tracked.

Studies conducted have reported that the COVID-19 pandemic is observed intensely in crowded societies or mass living or working centres [22,23]. In our study, the number of calls evaluated as potential or suspected cases was found to be high

in our districts with high intensity of population. Additionally, social distancing adjustments were made quickly and safe working areas were created in 112 Emergency Call Centers with a crowded working environment.

Although it varies from society to society, especially during the pandemic period, it takes time for the population to perceive the risks and make the necessary behavioral adjustments, to put the recommended precautions into action, to practice and sustain safe healthy lifestyle measures. During the pandemic, while the number of regular calls decreased after March 11, 2020 with the rise of calls received for COVID-19, calls for other cases began to increase again as of April 9, 2020 (Figure 2d).

Conclusion

Prehospital health services are a bridge between individuals in the community and hospital care services in cases of disasters such as earthquakes, floods, pandemics. The structural establishment of a robust system to meet the incoming demands, the construction of feasible algorithms, building the optimal infrastructure for ambulances in accordance with the population intensity, will both protect the system and help to improve the quality of health services delivery.

Ethics

Ethics Committee Approval: TR MoH Bagcilar Research and Training Hospital Ethics Committee approved the research application, dated May 6, 2020 with document #EY.FR.26.

Informed Consent: Standard patient informed consent requirements were met before the research was initiated.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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

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Comparison of Gum Elastic Bougie and Macintosh Laryngoscope in Pre-hospital Pediatric Airway Management; A Randomized, Prospective Study

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Abstract

Objective: Endotracheal intubation (ETI) in children requires good techniques and experience. Gum elastic bougie (GEB) is a practical, inexpensive, easy-to-use airway method in the adult airway. Through GEB, ETI is a method that can be learned after a short training. We evaluated the effectiveness of this method, which has not yet been validated in pediatric patients in prehospital pediatric airway applications.

Materials and Methods: This study was designed as a study simulating the prehospital period with a mannikin. Practitioners were asked to perform intubation by conventional intubation or GEB.

Results: This study was conducted with 48 emergency medical technicians and paramedics. Four (8.3%) of the practitioners had experience using GEB. In terms of first-pass success, no difference was found between ETI via GEB and Macintosh blade conventional ETI [91.7% (44/48), 93.8% (45/48), respectively, $p=1.000$]. Use of GEB increased ETI time [28.6 ± 6.0 sec vs. 17.1 ± 4.0 sec, mean df: 11.3 sec (95% CI: 9.7-12.8), $p<0.001$]. While 87.6% of the practitioners evaluated the use of GEB as very easy and easy, 83.3% of the practitioners evaluated the traditional method as very easy and easy ($p=0.914$).

Conclusion: GEB does not make any difference in pediatric airway management in terms of first-pass success. However, the use of GEB in terms of ETI durations increases the duration of ETI. Besides, the use of GEB is seen as a method that can be applied more efficiently, even in inexperienced groups.

Keywords: Airway control, gum elastic bougie, pediatric, pre-hospital

Introduction

Endotracheal intubation (ETI) in children requires good techniques and experience. Since the pediatric airway is more sensitive to trauma, repetitive intubation attempts should be avoided [1]. The correct selection of the tube size, the laryngoscope's blade, and the pediatric airway anatomy knowledge are essential. Gum elastic bougie (GEB) is a practical,

inexpensive, and easy-to-use airway method in the adult airway [2,3]. ETI through GEB is a method that can be learned after a short training [4]. The use of this method in pediatric patients has not yet been confirmed.

Pediatric and adult airways have distinct anatomical differences (prominent occiput, large tongue, etc.). These differences should be known in airway management.



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The American Society of Anesthesiologists defined a difficult airway as the inability to insert the endotracheal tube in three or more attempts with direct laryngoscopy or more than 10 minutes [5]. Tests and evaluation methods used for difficult intubations are generally not appropriate or practical for children [6]. The difficult airway is defined as the clinician’s difficulty during ventilation, laryngoscopy, and intubation [7]. The difficult airway is a significant cause of brain damage, cardiac arrest, and death in pediatric patients [8]. However, studies have which the success rate at the first attempt in difficult intubation with direct laryngoscopy in pediatric patients is 3% [9].

It would be appropriate to use a high first entry success method, rapid application, easy to learn, and inexpensive method in ensuring airway safety of pre-hospital pediatric patients.

This study compares the first entry success and intubation times of Macintosh laryngoscope and GEB applications on a pediatric airway model after pre-hospital healthcare workers’ pediatric airway training. It is predicted that GEB will increase the chances of success.

Materials and Methods

This study was designed as a randomized, prospective crossover ambulance simulation study using mockups. Kocaeli University Non-Interventional Clinical Research Ethics Committee approval was obtained for our study (2018/202).

Emergency medical technicians (EMT) and paramedics working in emergency health services were included in this study. The study was conducted in a training hall environment with 48 participants during the 10th and 11th months of 2018. EMT and paramedics, who will perform the ETI intervention, were given general information about the study, but they were blinded to its specific purpose. Before the study, the participants were given theoretical training on the ETI procedure and GEB by an emergency medicine specialist. Later, the participants were allowed to practice on the mannequin with both the Macintosh blade and the GEB when they felt sufficient (approximately 30 min each), and practical training was given (Figure 1). Written consent was obtained from those who wanted to participate in the study. In the study, “Advanced Child Airway Management Trainer with Stand LF03762U life/form the USA” a model of an 8-year-old child that allows ventilation with BVM suitable for human anatomy was used. PlusMed brand number 2 Macintosh blade, 12 Fr, 65 cm long VBM Medizintechnik brand GEB, Beybi brand 5.5 mm ETT, BVM, lubricant were used.

Participants were randomized after obtaining written consent. For both groups, an equal number of cards were created for each group with 1 or 2 on the same scale. The cards were folded in half, and each card was placed in a dark envelope. Envelopes were mixed in a bowl and participants were asked

to select an envelope. Participants who chose one were asked to do ETI with a Macintosh blade first and then via GEB, and those who chose two were asked to do ETI via GEB first and then with a Macintosh blade.

A camera was placed in the study room to see the stretcher and participant. Throughout the study, the participants were informed that the video would be recorded. The data related to the video were transferred to pre-prepared data entry forms. Since the participants made their attempts in the ambulance in a sitting position, they were allowed to attempt the same position as the ambulance stretcher and the same height as the ambulance practitioner seats in a sitting position. The lubricant was applied to the endotracheal tube before ETI. Holding the laryngoscope by the practitioner was considered the start time of the intervention. The end time was determined when intubation on the model was observationally successful (ventilation of the lungs with BVM after ETI). Each participant was given 2 min for each method. Regardless of which method the participants started randomly, they were asked to try the same method again in case of unsuccessful attempts. Participants’ first login success, ETI durations, a number of attempts, ETI experiences were recorded. After all, attempts were completed, the participants were asked to evaluate the difficulty levels of the intervention methods according to the Likert scale as 1- very easy, 2- easy, 3- neutral, 4- difficult, and 5- very difficult. The responsible researchers regularly checked the data collection and recording processes.

The primary outcome variable of the study was defined as initial success. Secondary outcome variables; ETI time, the number of trials for ETI, and difficulty rating according to the Likert scale.

Statistical Analysis

The study’s data were analyzed using the “SPSS for Windows, Version 20.0” package program. The study’s data were presented

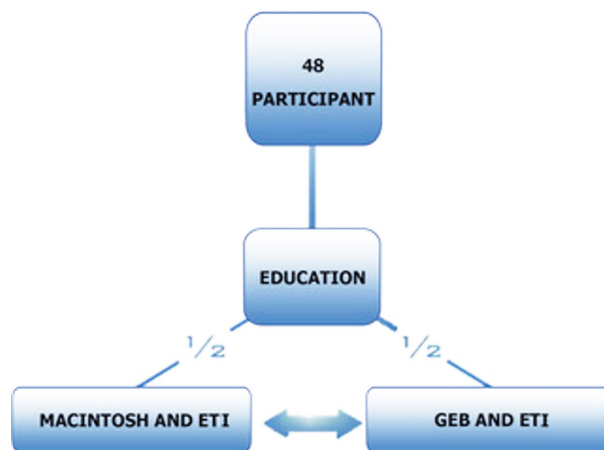


Figure 1. Study shema
 GEB: Gum elastic bougie, ETI: Endotracheal intubation

with the mean value 0.005 standard deviation (\pm SD), number, and percentage values. A 5 second difference in 20 seconds ETI time was considered significant. When alpha error probability was accepted as 0.05 and beta error probability as 0.2, the number of samples required for each group was calculated as 23. The Kaplan-Meier test was used to evaluate the average ETI times between the Macintosh and GEB groups. The McNemar test was used to compare ETI success rates between the GEB and Macintosh groups. Qualitative data were evaluated with a mean \pm SD and percentile values. Statistical significance was taken as $p \leq 0.05$.

Results

The average age of the practitioners participating in the study was 24, and 26 (54.2%) of the 48 practitioners were women. Four (8.3%) of the practitioners had previous experience of using GEB. Practitioners' experience in the pediatric age group was limited. While 38 of 48 practitioners stated that they had never intubated pediatric patients before, all participants stated that they performed pediatric airway intubation on a manikin at least once. All participants had completed the pediatric advanced life support training program, which is available in service training programs.

No statistically significant difference was found between ETI via Macintosh blade and ETI via GEB in first-pass success. ETI success was 91.7% (44/48) via GEB, and 93.8% (45/48) with a macintosh blade, $p=1.000$ (Table 1). While 75% (3/4) of the

participants using GEB were successful in the second attempt, 100% (3/3) were successful in the second attempt when using the Macintosh.

However, the average successful ETI time was longer in ETI via GEB than using only macintosh blades. The average successful ETI time via GEB was found to be 28.6 ± 6.0 sec, the average successful ETI time with the Macintosh blade was 17.1 ± 4.0 sec, mean df: 11.3 sec (95% CI: 9.7-12.8), $p < 0.001$ (Figure 2).

Practitioners reported no implementation difficulties between using GEB and using macintosh blades. 43.8% (21/48) of the participants evaluated the use of GEB as very easy, 43.8% (21/48) as easy, 10.4% (5/48) moderately difficult and 2.1% difficult (1/48). While 39.6% (19/48) of the participants evaluated the Macintosh usage as very easy, 43.8% (21/48) as easy, 12.5% (6/48) moderately difficult, and 4.2% (2/48) difficult ($p=0.914$) (Figure 3). This difference was not statistically significant.

Discussion

One of the essential duties of the first and emergency personnel is to ensure airline safety. Although some different methods and tools have emerged with developing technology to ensure airway safety, traditional ETI with direct laryngoscopes, especially before the hospital, is frequently applied. Conventional ETI can be quite challenging when the degree of laryngoscopic view is suboptimal [10]. Pediatric airway management is as challenging and essential as it is in adult patients. There are fewer studies on pediatric airway

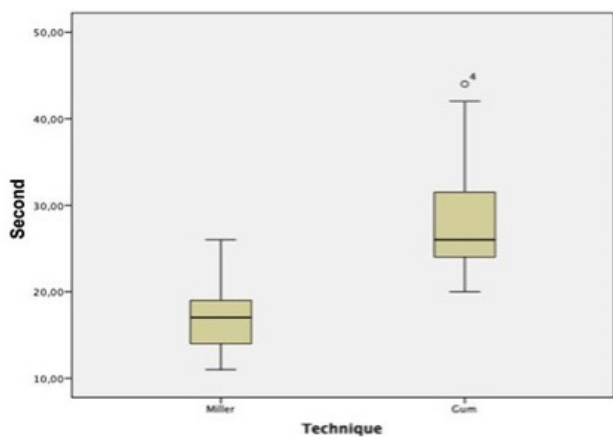


Figure 2. Success ETI time
ETI: Endotracheal intubation

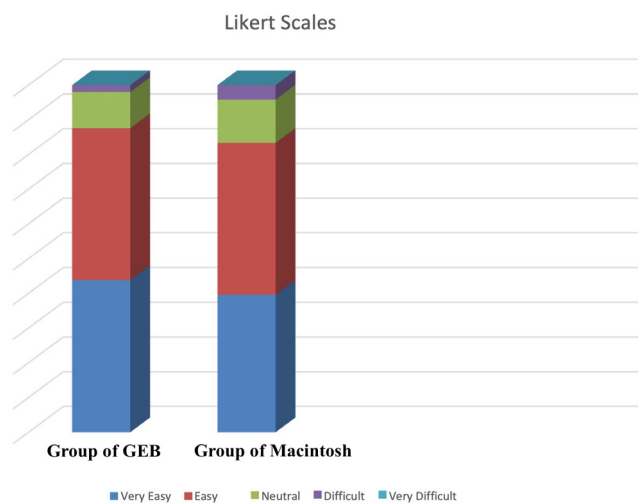


Figure 3. Distribution of groups according to Likert scales

Table 1. Successful ETI rates and average ETI times			
	GEB (n=48)	Machintosh (n=48)	p value
First success rate (m, %)	44 (91.7)	45 (93.8)	1.000
Mean ETI time (s, m)	28.6 (6.0)	17.1 (4.0)	<0.001

ETI: Endotracheal intubation, GEB: Gum elastic bougie

management than are adult airway management. Therefore, studies on pediatric airway management are needed. GEB is recommended in various guidelines in the first steps of difficult airway management [11,12]. Due to the unique difficulties of pre-hospital airway management (lack of staff experience, not always optimal environment provided, equipment limitation, etc.), various delays can be experienced, especially in the pediatric age group, and quite fatal results are observed. Therefore, GEB, one of the recommended equipment for difficult airway management, especially in the pre-hospital and pediatric age groups, may help manage airway management. We carried out this study to hypothesize that GEB can be beneficial in terms of the first entry success in ETI in pre-hospital ambulance simulation, pediatric airway model.

The practitioners recruited to our study have advanced airway intervention licenses. ETI's decision and implementation of are decided by EMTs and paramedics outside the hospital, who constitute the first step of the emergency health services. For this reason, we included EMTs and paramedics as practitioners in this study, which we designed as an ambulance simulation. However, especially in some countries, ETI can only be performed by a physician or under a physician's supervision. In a field study by Jabre et al. [4] in France, GEB was used by physicians in difficult intubation, and it was shown to be beneficial.

In our study, there was no statistically significant difference between the two groups in terms of first pass success.

We obtained overlaps with some of the previous studies that were frequently conducted on adult patients or models. In our study, the average successful ETI time was longer in ETI than using only Macintosh blades via GEB. The average successful ETI time was 28.6 ± 6.0 sec via GEB and 17.1 ± 4.0 sec with the Macintosh blade. In a model study by Ohchi et al. [13] no difference was found between ETI groups in intubation with a Macintosh blade with and without using GEB in terms of ETI success. However, in the same study, the presence of stomach contents in the airway was simulated. ETI via GEB was found to be statistically more successful in the presence of stomach content. In terms of time, in the usual scenario, GEB extended the ETI time. However, when the presence of stomach contents in the airline was simulated, ETI via GEB shortened the successful intervention time compared with ETI with only Macintosh.

In a model study by Komasaawa et al. [14] no difference was found between ETI groups in intubation with a Macintosh blade with and without using GEB in terms of ETI success. However, ETI via GEB was statistically more successful when chest compression was applied to both groups' models. No

significant difference was found in either scenario in terms of duration.

An infant model was used in another model study by Komasaawa et al. [15]. In this study, no difference was found between ETI groups in normal (Cormack Lehane 1-2) and cervical stabilization (Cormack Lehane 3), using a Macintosh blade, with and without GEB. When the model was in anteflexion (Cormack Lehane 4), ETI was found to be more successful through GEB. No difference was found in terms of duration in the normal state terms of duration, but GEB shortened the duration of successful ETI in cervical stabilization and anteflexion.

In the model study by Maruyama et al. [16] successful ETI time via GEB significantly prolonged the time in all different scenarios (average, chest compression, cervical stabilization) compared to intervention with only Macintosh, and this situation is consistent with other studies in the literature [17-19]. However, using a single model in our study may make it difficult to compare it with other studies on this subject.

In our study, we used the Likert scale to evaluate the application status of the use of GEB and the practitioners' traditional methods of intubation subjectively. We asked all participants to perform this scale, regardless of whether they performed both applications successfully or unsuccessfully. According to the Likert scale, the use of GEB may cause problems for the participants both in terms of intubation experience and difficulty of use. However, 16.7% of the practitioners stated that the method was moderately difficult or difficult according to the Likert scale in ETI made using only the Macintosh blade. Even if there is no statistically significant difference between the two groups, these results can be interpreted differently, considering that 87.5% of the participants had intubation experience with the Macintosh blade. However, only 8.3% of the participants have experience with GEB. Although using GEB is an easy-to-learn method, this difference in experience may have affected the results. In some previous studies, it has been reported that the use of GEB has shown limited success in increasing the success of ETI in emergency physicians who have not applied the method before [20,21]. In contrast, in the study conducted by Driver et al. [17] physicians preferred to use GEB in 435 (80%) of 543 ETI interventions performed in an emergency room where the use of GEB is common, and they achieved first-pass success in 95% of these cases [16]. ETI may be possible via the GEB application to provide a more successful airline management in case of improvements in user experience.

Although GEB is a recommended method in adults with difficult airway conditions, information about its use in the pediatric age group is limited. Difficult intubation is relatively rare (3%), and it should be kept in mind that the procedure may be difficult due to anatomical differences in the pediatric age group [4].

Study Limitations

Our study has several limitations. These include the fact that the study is a manikin study and the absence of chest compression, cervical collar, airway secretion, blood, and stomach content, which may be present in real patients, complicating the ETI procedure. In cases where these factors were present, GEB could be more beneficial in terms of both the duration and the first pass's success [22,23]. Besides, most of the study practitioners were inexperienced with GEB. As stated in the study's methodology, although the training was given before the study, the practitioners may have felt inadequate about the experience. Another limitation is the absence of an ambulance simulation to better simulate the ambulance environment.

Conclusion

Our study found that the success of ETI through GEB, which has strong recommendations for its use in difficult airway management in the literature, was not different from the success of traditional Macintosh blade-mediated intubation in standard pediatric airway management. However, in terms of ETI durations, the duration was found to be statistically longer in the GEB group. We believe that if manipulations make airway management difficult, GEB can shorten the ETI time and increase the first entry's success. In our study, most of the practitioners' application of GEB was considered an easier method, although there was no statistically significant difference. Additionally, using a single model in our study may be a limitation that affects our results. We believe that if pre-hospital practitioners gain similar application experience in using GEB, more successful results in airway management can be achieved.

Ethics

Ethics Committee Approval: Kocaeli University Non-Interventional Clinical Research Ethics Committee approval was obtained for our study (2018/202).

Informed Consent: Written consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

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

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

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The Predictive Value of CURB-65 and Pneumonia Severity Index in Patient with COVID-19 Pneumonia and Correlation with Laboratory Parameters

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Abstract

Objective: Coronavirus disease-2019 (COVID-19) pneumonia is a disease with a high mortality rate caused by the severe acute respiratory syndrome-coronavirus-2 virus. Therefore, it is essential to identify patients at risk for mortality. This study aims to determine the ability of pneumonia scores to predict mortality and correlation with laboratory parameters.

Materials and Methods: A total of 312 pneumonia patients with positive polymerase chain reaction results were included in this single-center retrospective study conducted between 10.03.2020 and 10.06.2020. All data obtained from the hospital database, confusion, urea, respiratory, blood pressure, 65 or older (CURB-65) and Pneumonia Severity Index (PSI), scores were calculated. Receiver operator characteristics (ROC) curve analysis was performed for the prognostic value.

Results: The demographic data followed as; 175 (56.1%) of 312 patients were male and 137 (43.9%) were female; mean age was 58.2±16.1 years. The mortality rate was 16% (n=50). The length of hospital stay was 10.6±6.4 day. CURB-65, PSI, and PSI risk class was found to be higher in cases that resulted in mortality compared to those without mortality (p<0.001). CURB-65, PSI, PSI risk classification were positively correlated with, D-dimer, ferritin, and neutrophil lymphocyte ratio. The area under the ROC curve was 0.851 [95% confidence interval (CI): 0.803-0.899] for PSI, 0.833 (95% CI: 0.779-0.888) for PSI risk class score and 0.795 (95% CI: 0.725-0.865) for CURB-65. In determining mortality; optimal cut-off values were ≥1 for CURB-65 (sensitivity 86.0% specificity 61.1%), ≥6.5 for PSI (sensitivity 82%, specificity 70.6%), and ≥4 for PSI risk classification (sensitivity 76.0%, specificity 72.9%).

Conclusion: CURB-65, PSI, and PSI risk classifications were found eligible for use in COVID-19 and combining these scores with laboratory parameters can be useful to determine the prognosis.

Keywords: CURB-65, ferritin, D-dimer, NLR, COVID-19 pneumonia, PSI

Introduction

Coronavirus disease-2019 (COVID-19) is an infectious respiratory disease caused by the severe acute respiratory syndrome-coronavirus-2. It was first discovered in 2019 in Wuhan, China, and has since spread worldwide, leading to the 2019-2020 coronavirus pandemic [1]. Since the pandemic began, there have been approximately 400 million cases of COVID-19 and more than 5 million deaths worldwide [2]. The clinical manifestations of the disease range from asymptomatic to acute respiratory failure. The symptoms are dry cough, fever,

chills, malaise, myalgia, pleuritic chest pain and shortness of breath [3]. The mortality of the disease is associated with older age and comorbidities [4-6].

It is important for healthcare providers to diagnose COVID-19 pneumonia, identify patients with a high risk of mortality and to decide whether to treat patients as outpatients or inpatients under pandemic conditions. In particular, some objective criteria have been defined to help the physician decide on hospitalization. Many treatment guidelines, updated recently, recommend confusion, urea, respiratory, blood pressure, 65 or



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older (CURB-65) and Pneumonia Severity Index (PSI) scoring in this regard [7]. CURB-65 was defined by the British Thoracic Society in 2002 and is useful in classifying patients at high risk of mortality. Variables of CURB-65 are confusion, blood urea nitrogen, systolic blood pressure, respiratory rate, and age. Patients with a score of 3 and above have high mortality rates. Due to the small number of variables, it can be easily used in emergency and primary care, as it allows us to quickly predict the requirements and duration of hospitalization, discharge, or intensive care hospitalization of the patients [8,9]. PSI has 19 parameters and classifies patients into 5 different groups in terms of risk factors. The primary purpose of this score is more closely related to the question of which patients should be hospitalized rather than mortality. The main parameters in this scoring are; age, comorbidity, and abnormalities in vital signs. Additionally, laboratory tests, blood gas, chest X-ray are also needed for PSI. PSI class of I-III was reported to represent a low risk of death. Patients who had a PSI class of \geq IV were defined as being at a high risk of death [10]. Details of these scores are in the Supplemental File.

In addition to these scoring systems, some laboratory parameters are considered be associated with mortality. These are D-dimer, ferritin, neutrophil lymphocyte ratio (NLR) and lactate [11-13]. Tools for predicting mortality in patients with COVID-19 pneumonia still remain unclear. This study aims to determine the prognostic values of CURB-65, PSI scores and laboratory parameters in patients hospitalized for COVID-19 pneumonia.

Materials and Methods

Patients

This single-centered and retrospective study was conducted out between 10.03.2020-10.06.2020 at Şişli Hamidiye Etfal Training and Research Hospital, Clinic of Emergency, which is a pandemic hospital. Patients who were admitted to the emergency department with positive COVID-19 real time-polymerase chain reaction (RT-PCR) test, clinical and radiological pneumonia findings were included in the study. All pneumonia patients with RT-PCR positive hospitalized. A total of 312 patients with complete data were enrolled in the study.

Data Collection and Processing

During the study period, age, gender, date of admission to the clinic of emergency, hospitalization (service or intensive care unit), Glasgow Coma scale at the time of admission, comorbidities, laboratory findings (NLR, D-dimer, ferritin, lactate), vital signs, COVID-19 PCR results, radiological imaging and mortality status was obtained from the hospital database system. CURB-65 and PSI scores were calculated, and the results were recorded in the study form. Details of the scores are shown in the Supplemental File.

Ethical Approval

This study was approved by the Local Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital and was conducted in accordance with the Helsinki Declaration (decision no: 1527, date: 02.06.2020).

Statistical Analysis

For statistical analyses, the SPSS 22.0 Windows program was used. Number and percentage were used as categorical variables. Mean, standard deviation, minimum, maximum and median were used as numerical variables. Rates in independent groups were compared with the chi-square test. Since the numerical variables did not meet the normal distribution, comparisons of two independent groups were performed using the Mann-Whitney U test. Relations between numerical variables were preformed with Spearman correlation analysis since parametric test condition was not met. Cut-off analysis were performed using receiver operating characteristic (ROC) curve analysis. The statistical alpha significance level was accepted as $p < 0.05$.

Results

A total of 312 patients participated in the study and 175 (56.1%) of the patients were male, 137 (43.9%) were female. While 185 (59.3%) patients did not have any comorbidities, 127 (40.7%) patients had various comorbidities. The most common comorbidity was hypertension 72 (23.1%). Demographic characteristics of the patients, laboratory results, CURB-65, PSI scores and clinical outcomes are shown in Table 1.

A positive correlation was found between CURB-65, PSI score, PSI risk classification, and age, D-dimer, ferritin, NLR, and hospitalization time. CURB-65, PSI score was found to be negatively correlated with the day of mortality Table 2. CURB-65, PSI score, PSI risk classification level were statistically significantly higher in those with comorbidity than in those without comorbidity (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$). CURB-65, PSI score, PSI risk classification level was higher in those with hypertension (HT) than in those without HT (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$). Likewise, CURB-65, PSI score, and PSI risk classification level was higher in patients with coronary artery disease (CAD) compared with those without CAD (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$). In those with diabetes mellitus (DM) and congestive heart failure (CHF), the PSI score and PSI risk classification level were higher than those without DM and CHF. In terms of mortality, there was a statistical difference between the CURB-65, PSI, PSI risk classes of patients with and without mortality (respectively $p < 0.001$, $p < 0.001$, $p < 0.001$) Table 3.

ROC analysis of CURB-65, PSI, and PSI classifications is shown in Figure 1. Area under the curve (AUC) was 0.795 [95% confidence interval (CI): 0.725-0.865], 0.851 (95% CI: 0.803-0.899), 0.833 (95% CI: 0.779-0.888), respectively.

Youden's index was used to determine the optimal cut-off point in determining mortality. Accordingly, CURB-65 ≥ 1 has 86.0% sensitivity, 61.1% specificity, PSI score ≥ 86.5 has 82.0%

sensitivity, 70.6% specificity, PSI risk classification ≥ 4 has 76.0% sensitivity, 72% specificity Table 4.

Table 1. Demographic, clinical and laboratory characteristics

Age mean \pm SD (min-max)		58.2 \pm 16.1 (22-97)	
Sex n (%)	Male	175 (56.1)	
	Female	137 (43.9)	
Comorbidities n (%)	No	185 (59.3)	
	Yes	127 (40.7)	
	DM	50 (16.0)	
	HT	72 (23.1)	
	CAD	27 (8.7)	
	COPD	21 (6.7)	
		CKD	18 (5.8)
		CHF	6 (1.9)
		CvD	4 (1.3)
		Malignancy	4 (1.3)
	Others	34 (10.9)	
CURB-65 mean \pm SD (min-max)		0.79 \pm 1.01 (0-5)	
PSI score mean \pm SD (min-max)		79.6 \pm 39.9 (16-204)	
PSI risk class mean \pm SD (min-max)		2.65 \pm 1.44 (1-5)	
PSI risk class n (%)	1	101 (32.4)	
	2	55 (17.6)	
	3	47 (15.1)	
	4	70 (22.4)	
	5	39 (12.5)	
D-dimer mean \pm SD (min-max)		955.4 \pm 1.779.7 (2.2-21.200)	
Ferritin mean \pm SD (min-max)		329.9 \pm 475.7 (4-5.032)	
Lactate mean \pm SD (min-max)		1.97 \pm 5.35 (0.62-93)	
NLR mean \pm SD (min-max)		4.71 \pm 4.77 (0.55-32.64)	
Mortality n (%)	No	262 (84.0)	
	Yes	50 (16.0)	

Results are expressed as count (%) for categorical variables and as mean (standard deviation minimum-maximum) for quantitative variables. DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CKD: Chronic kidney disease, CHF: Congestive heart failure, CvD: Cerebrovascular disease, NLR: Neutrophil lymphocyte ratio, PSI: Pneumonia Severity Index, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older

Table 2. Correlation of CURB-65, PSI score and PSI risk class with age, D-dimer, ferritin, NLR, lactate, hospital stay and mortality in patients with COVID-19 pneumonia

	CURB-65		PSI score		PSI risk class	
	r	p	r	p	r	p
Age	0.710	<0.001	0.793	<0.001	0.687	<0.001
D-dimer	0.410	<0.001	0.430	<0.001	0.419	<0.001
Ferritin	0.317	<0.001	0.376	<0.001	0.324	<0.001
Lactate	0.071	0.218	0.103	0.075	0.101	0.082
NLR	0.322	<0.001	0.333	<0.001	0.310	<0.001
Hospital stay	0.221	0.001	0.295	<0.001	0.269	<0.001
Mortality day	-0.464	0.004	-0.333	0.044	-0.298	0.073

NLR: Neutrophil lymphocyte ratio, PSI: Pneumonia Severity Index, COVID-19: Coronavirus disease-2019, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older

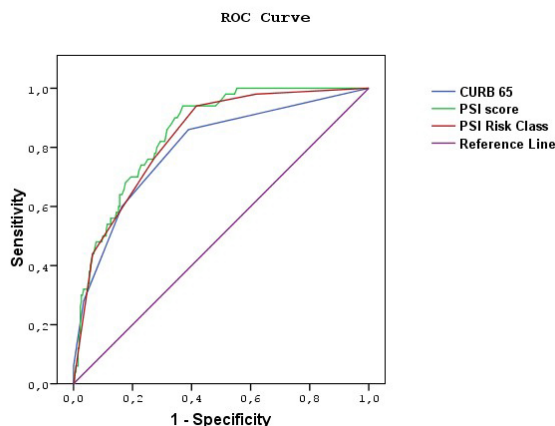


Figure 1. ROC analysis of CURB-65, PSI and PSI risk class

ROC: Receiver operator characteristics, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, PSI: Pneumonia Severity Index

Discussion

This infection, which affects the whole world, causes many deaths as well as many economic, social and psychological effects. Therefore, it is important to determine the course of the infection well managing for the disease. The analysis of demographic, epidemiological and clinical data is important to develop right strategies against COVID-19.

Table 4. Prognostic accuracy of CURB-65, PSI, PSI risk class with optimal cut-off values

	Sensitivity	Specificity	PPV	NPV
CURB-65 ≥ 1	86.0%	61.1%	29.7%	95.8%
PSI score ≥ 86.5	82.0%	70.6%	34.7%	95.4%
PSI risk class ≥ 4	76.0%	72.9%	34.9%	94.%

CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, PSI: Pneumonia Severity Index, PPV: Positive predictive value, NPV: Negative predictive value

Table 3. Relationship between comorbidities and scores

Comorbidity	Minimum Mean \pm SD (min-max)	Maximum Mean \pm SD (min-max)	p
CURB-65	0.65 \pm 0.98 (0-5)	0.98 \pm 1.02 (0-4)	0.001
PSI	70.0 \pm 38.1 (16-194)	93.5 \pm 38.4 (22-204)	<0.001
PSI risk class	2.3 \pm 1.4 (1-5)	3.2 \pm 1.3 (1-5)	<0.001
DM			
CURB-65	0.76 \pm 1.04 (0-5)	0.90 \pm 0.84 (0-3)	0.078
PSI	76.8 \pm 40.1 (16-204)	94.3 \pm 35.2 (42-188)	0.001
PSI risk class	2.5 \pm 1.5 (1-5)	3.3 \pm 1.1 (1-5)	<0.001
HT			
CURB-65	0.69 \pm 1.00 (0-5)	1.11 \pm 0.97 (0-3)	<0.001
PSI	73.3 \pm 38.8 (16-194)	100.6 \pm 36.0 (40-204)	<0.001
PSI risk class	2.4 \pm 1.4 (1-5)	3.5 \pm 1.1 (2-5)	<0.001
CAD			
CURB-65	0.73 \pm 0.99 (0-5)	1.37 \pm 1.01 (0-3)	<0.001
PSI	76.5 \pm 38.8 (16-204)	112.2 \pm 37.1 (57-188)	<0.001
PSI risk class	2.5 \pm 1.4 (1-5)	3.9 \pm 0.9 (2-5)	<0.001
COPD			
CURB-65	0.80 \pm 1.01 (0-5)	0.62 \pm 0.97 (0-3)	0.389
PSI	79.6 \pm 39.9 (16-204)	79.1 \pm 40.8 (22-165)	0.899
PSI risk class	2.6 \pm 1.4 (1-5)	2.8 \pm 1.4 (1-5)	0.654
CHF			
CURB-65	0.78 \pm 1.01 (0-5)	0.83 \pm 0.75 (0-2)	0.602
PSI	79.1 \pm 40.0 (16-204)	105.3 \pm 24.5 (66-132)	0.047
PSI risk class	2.6 \pm 1.4 (1-5)	3.8 \pm 1.0 (2-5)	0.040
Mortality			
CURB-65	0.59 \pm 0.84 (0-3)	1.82 \pm 1.17 (0-2)	<0.001
PSI	71.4 \pm 35.1 (16-204)	122.7 \pm 35.7 (60-194)	<0.001
PSI risk class	2.4 \pm 1.3 (1-5)	4.1 \pm 1.0 (1-5)	<0.001

Results are expressed as mean (standard deviation minimum-maximum) for quantitative variables.
 DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, COPD: Chronic obstructive pulmonary disease, CHF: Congestive heart failure, PSI: Pneumonia Severity Index, SD: Standard deviation, CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older

The mean age and gender distribution of the patients participating in the study are similar those the studies in the literature [14,15]. As it is known, studies have shown that additional diseases such as HT, DM, CAD and older age are risk factors for mortality in COVID-19 pneumonia. In our study, mortality rates were found to be higher, especially in patients with HT and DM [16]. The Chinese Center for Disease Control and Prevention reported that the overall mortality rate was 2.3% in 44,672 cases. When only severe and critical illness groups were included in the evaluation, the mortality rate was 12.4% [17]. In our study mortality rate was 16%. The reason for this high rate is that our study was conducted in a tertiary hospital. Sharifpour et al. [18] showed that elevated C-reactive protein and procalcitonin are potential predictors of COVID-19 disease severity. There are also studies showing that high D-dimer levels, high ferritin levels, lymphopenia and hypoalbuminemia are risk factors for the severe COVID-19 disease and mortality [19,20]. Liu et al. [21] showed that NLR is an independent risk factor for determining the severity of the disease and mortality in hospitalized patients, and its height is effective in predicting critical illness. In our study, there was a significant positive correlation with laboratory parameters (D-dimer, ferritin, and NLR) and CURB-65, PSI score, PSI risk classification ($p < 0.001$, in all). The use of scoring systems together with these parameters may be effective in demonstrating the severity of COVID-19.

Bradley et al. [22] showed that the CURB-65 score was not a guide for discharge, but patients with a high CURB-65 score were at risk of mortality. PSI is also a well-known scoring system for assessing the severity of community-acquired pneumonia, and its efficacy has also been confirmed in viral pneumonia and there is a significant association between PSI and mortality [23,24]. Satici et al. [25] showed that the PSI score was a better predictor than CURB-65 with a higher AUC. In the same study, the optimal cut-off value is ≥ 2 for CURB-65, while it is ≥ 4 for PSI. Likewise, in our study, the PSI score was found to be better than CURB-65 with an AUC of 0.851 (95% CI: 0.803-0.899). In the study by Fan et al. [24], the optimal cut-off value for CURB-65 was found to be ≥ 1 , the optimal cut-off for PSI risk class was ≥ 3 and the sensitivity of the PSI score was found to be higher than CURB-65. In our study, it was determined as the optimal cut-off for PSI risk classification ≥ 4 for mortality. On the other hand, CURB-65 ≥ 1 was found to be a good predictor with 86% sensitivity. Although there are differences between the scores, both scores appear to be good predictors, especially in identifying high-risk patients in terms of mortality.

Study Limitations

The main limitations were the study was; single-centered and retrospective, the sample size was limited, the scores and laboratory parameters were calculated only at the admission,

repeated measurements of patients during follow-up were not calculated.

Conclusion

In conclusion, addition to older age and comorbidities in COVID-19 patients, D-dimer, ferritin and NLR that can be used to predict the severity of the COVID-19 pneumonia. Additionally, it has been demonstrated that high CURB-65, PSI score, and PSI risk classification values are useful for determining the severity of the disease and mortality at the admission. It is thought that the creation of new scoring systems by adding biomarkers may better guide clinicians.

Ethics

Ethics Committee Approval: This study was approved by the Local Ethics Committee of Şişli Hamidiye Etfal Training and Research Hospital and was conducted in accordance with the Helsinki Declaration (decision no: 1527, date: 02.06.2020).

Informed Consent: Prospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.A., E.A., Design: H.A., E.A., Data Collection or Processing: H.A., Y.E.A., Analysis or Interpretation: H.A., Y.E.A., Literature Search: E.A., Writing: H.A., Y.E.A.

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

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Supplemental File. CURB-65	
Parameters	Score
Confusion	1
BUN >20 mg/dL (7 mmol/L) or urea > 42.8 mg/dL	1
Respiratory rate ≥30/min	1
Systolic blood pressure <90 mm/Hg or diastolic blood pressure <60 mm/Hg	1
Age ≥65 year	1

CURB-65 score [8]. CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, BUN: Blood urea nitrogen

Pneumonia severity index	
Demographic factors	Point
Age- male	Age in years
Age- female	Age in years-10
Nursing home resident	10
Comorbidities	
Neoplastic disease	30
Liver disease	20
CHF	10
Cerebrovascular disease	10
Renal disease	10
Physical examination findings	
Altered mental status	20
Respiratory rate ≥30/min	20
Systolic blood pressure <90 mmHg	20
Temperature <35 °C or ≥40 °C	15
Heart rate ≥125/min	10
Laboratory and radiological findings	
Arterial pH <7.35	30
BUN ≥30 mg/dL	20
Sodium <130 mEq/L	20
Glucose >250 mg/dL	10
Hematocrit <%30	10
PaO2 <60 mm/Hg or SaO2 <%90	10
Pleural Effusion	10

CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, BUN: Blood urea nitrogen

PSI risk classification	
Class	Point
1	<50 years no comorbidity
2	<70
3	71-90
4	91-130
5	>130

PSI and PSI risk classification [9,10]. PSI: Pneumonia Severity Index

Optimal cut-off points of scores			
Test	Results	Sensitivity	Specificity
CURB-65	-1.0	1.000	0.000
	0.5	0.860	0.611
	1.5	0.600	0.836
	2.5	0.280	0.966
	3.5	0.060	1.000
	4.5	0.020	1.000
	6.0	0.000	1.000
PSI score	81.5	0.880	0.668
	82.5	0.860	0.683
	83.5	0.840	0.687
	84.5	0.820	0.691
	85.5	0.820	0.695
	86.5	0.820	0.706
	87.5	0.800	0.718
	88.5	0.780	0.721
	89.5	0.780	0.725
	90.5	0.760	0.729
	92.0	0.760	0.740
	93.5	0.760	0.748
	94.5	0.740	0.760
95.5	0.740	0.763	
96.5	0.740	0.771	
97.5	0.720	0.779	
PSI risk class	0.0	1.000	0.000
	1.5	0.980	0.382
	2.5	0.940	0.584
	3.5	0.760	0.729
	4.5	0.440	0.935
	6.0	0.000	1.000

CURB-65: Confusion, urea, respiratory, blood pressure, 65 or older, PSI: Pneumonia Severity Index

Left Paraduodenal Hernia: A Rare Case Report of Internal Herniation

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Abstract

Internal herniation is a rare cause of acute abdomen. If it is not diagnosed and treated in time, it can cause death. This case report discusses the clinical findings and surgical treatment of a case of left paraduodenal hernia, a rare cause of internal herniation. The diagnosis and treatment process of a 24-year-old female patient with ileus findings was retrospectively evaluated and presented in the literature. The patient was operated on with a preliminary diagnosis of internal herniation and the definitive diagnosis was made intraoperatively. At laparotomy, it was observed that almost all of the small intestines herniated posteriorly from the left paraduodenal region. Small intestinal loops were reduced and the hernia sac defect was primarily repaired. The patient was discharged on the fifth postoperative day with complete recovery. Left paraduodenal hernia is a type of internal herniation that should be considered in the differential diagnosis of patients with recurrent abdominal pain and intestinal obstruction. Surgical reduction and primary repair of the defect is an appropriate treatment.

Keywords: Emergency department, emergency surgery, internal herniation, intestinal obstruction, paraduodenal hernia

Introduction

An internal herniation is defined as a herniation of the small intestine from the mesenteric defect in the abdominal cavity [1]. Internal herniation is a rare cause of acute abdomen and if it is not diagnosed and treated in time, it can cause intestinal obstruction and ischemia. It can even cause death [2,3]. Internal herniation accounts for 0.6-5.8% of intestinal obstruction cases [4-6]. Paraduodenal hernias cause approximately 50% of internal hernias and are responsible for approximately 1% of all small bowel obstructions. Left paraduodenal hernia is observed 3 times more often than right [2,3,5-9]. It is most commonly observed between the 4th and 6th decades. It is three times more common in men than in women [3,5,6,9]. About half of the life-long cases are at risk of intestinal obstruction or strangulation, while the other half may take a quiet course [5]. Here, we share a case report that we operated for left paraduodenal hernia.

Case Report

A 24-year-old female patient presented to the emergency department with abdominal pain, nausea, and vomiting. On physical examination, there was widespread tenderness in the abdomen. In the examinations, the white blood cell: $8.57 \times 10^3 / \text{mm}^3$, C-reactive protein (CRP): 7 mg/L and the air-fluid level was not detected in the direct abdominal X-ray (AXR), the patient was given symptomatic treatment by applying a nasogastric tube (Figure 1). Abdominal computed tomography (CT) was performed because there was no significant regression in abdominal pain and examination findings after treatment. CT showed that “intestinal segments in the right half of the abdomen were not observed. Intestinal loops were displaced to the left and showed retraction. The calibration of the intestinal loops remaining proximal to internal herniation increased up to 33 mm. The cecum is displaced toward the midline” reported as (Figure 2). The patient, who applied to the emergency department several



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times with similar complaints, suffered from gas pain, received symptomatic treatment with unknown fluids and drugs, and whose symptoms and examination findings regressed after the treatment, was discharged from the emergency room. He stated that his pain was more severe than in his current application. He was admitted to the general surgery service and planned for symptomatic treatment and follow-up due to recurrent admissions with emergency treatment, absence of septic findings, and mild regression in signs and symptoms. The oral was closed. Daily hemogram, CRP and biochemistry values, and AXR were followed. In the follow-ups, air-fluid

level and free air were not observed in AXRs (Figure 3). There was no significant increase in white blood cell and CRP values. Abdominal pain persisted despite intermittent relief and there was no gas or stool. Although the abdominal pain was relieved intermittently, it continued, there was no gas or stool. On the second day of hospitalization, abdominal pain increased, nausea and vomiting symptoms recurred. On his examination, there were signs of tenderness, defense, and rebound, especially in the left upper quadrant, and surgical intervention was decided (Figure 4). On laparotomy, it was observed that approximately 3/4 of the intestinal segments with a hernia sac in the left upper quadrant were in the hernia sac, and the diameter of the distal segments where the proximal segments were dilated was decreased. The cecum was retracted to the midline of the abdomen. The mouth of the hernial sac was expanded and the intestinal segments were released. We



Figure 1. First standing direct abdominal X-ray

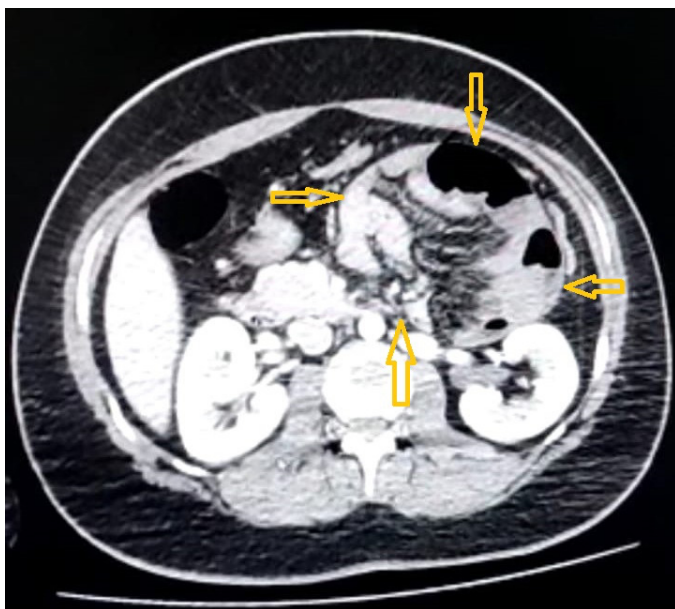


Figure 2. Computed tomography of the abdomen at first admission (yellow arrow)

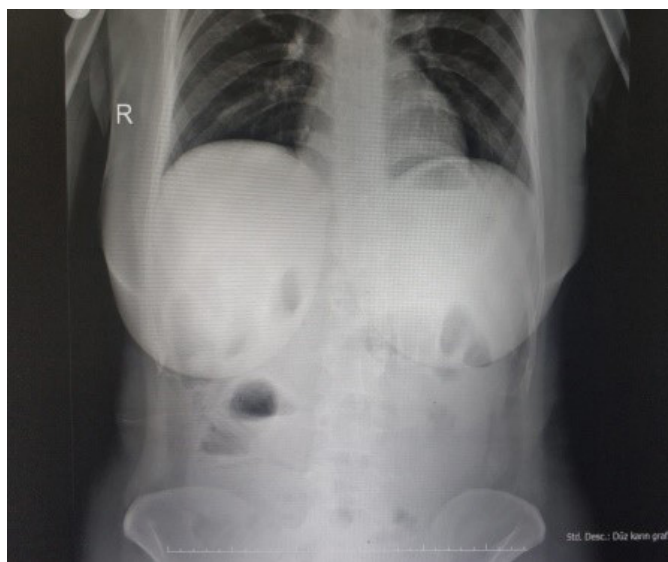


Figure 3. 1st day of hospitalization, standing direct abdominal X-ray

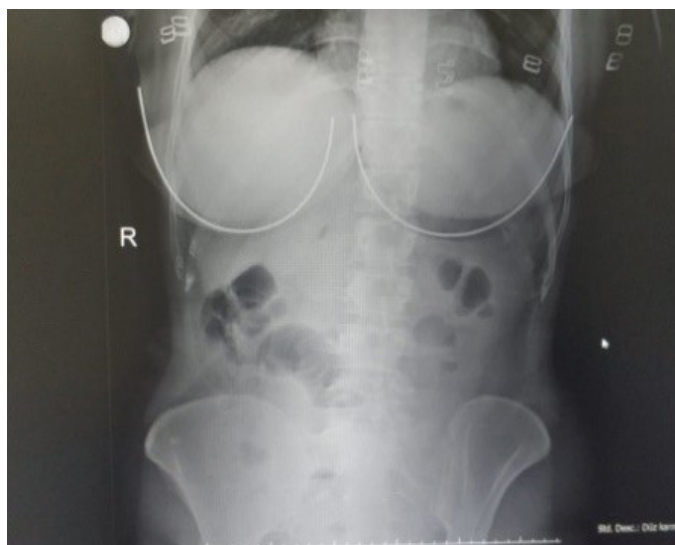


Figure 4. 2nd day of hospitalization, standing direct abdominal X-ray

observed that the hernia defect was located just adjacent and inferior to the ligament of Treitz. The defect was repaired and closed. All the intestinal segments were evaluated. Except for dilatation, no signs of ischemia or perforation were detected; small serosa defects in 2 separate regions were repaired (Figure 5-7).

Postoperative follow-up of the patient was uneventful. Stool discharge occurred on the 2nd postoperative day, oral intake was opened and continued without any problems. He was discharged on the fifth postoperative day with good recovery.

Discussion

The most accepted theory for the formation of paraduodenal hernia was described by Andrews in 1923. This theory states

that paraduodenal hernia results from the penetration of the intestines between the mesentery and the posterior abdominal wall due to the midgut rotation disorder that occurs during embryological development [1,5-7]. In the left paraduodenal hernia, the jejunal anus herniated through an opening to the left of the ligament of Treitz. The left paraduodenal fossa was first described by Landzert in 1871 and is located lateral to the fourth part of the duodenum, behind the inferior mesenteric vein and the left colic artery. The contents of the hernia consist of small intestinal loops. It does not contain the colon or omental tissue. The hernia sac may contain a loop of the small intestine a few centimeters long, or it may include all the small intestines [4,7,8]. Tong et al. [6] evaluated 32 cases and reported that 69% of the patients had chronic symptoms and 66% of the patients presented with acute obstruction or strangulation. Our patient had a similar clinical picture. She had been describing occasional abdominal pains since childhood. Collected intestinal loops and non-displaced air-

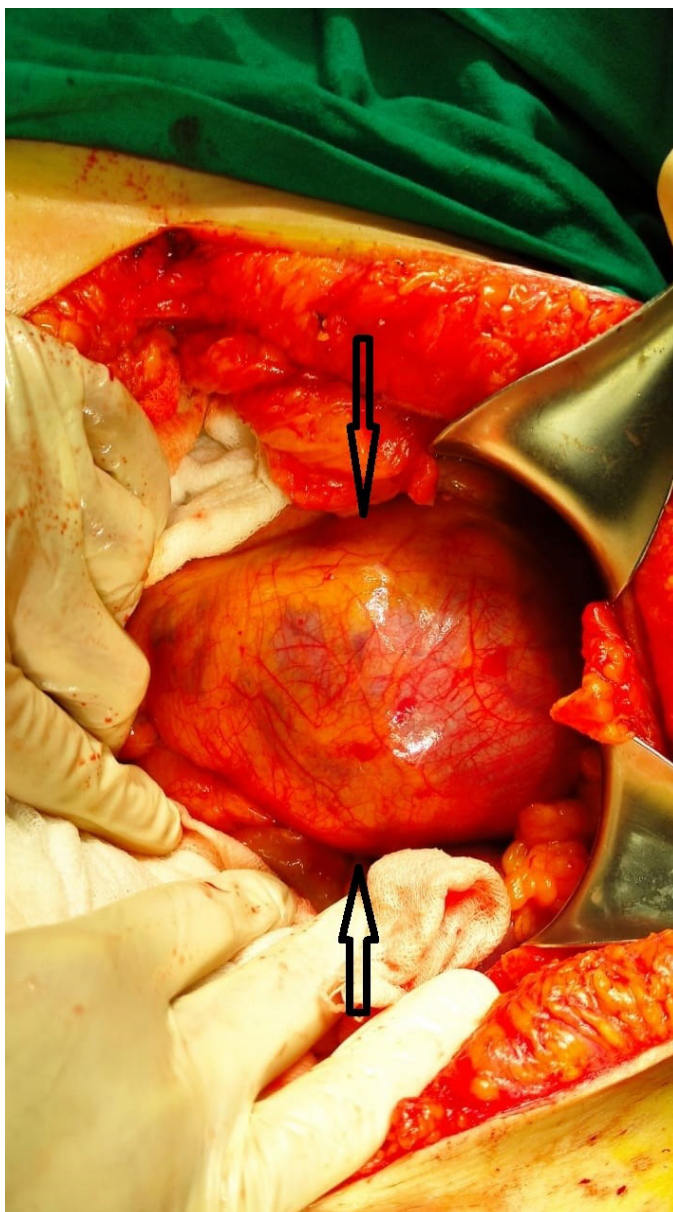


Figure 5. Hernial sac and hernia defect at the bottom (black arrow)

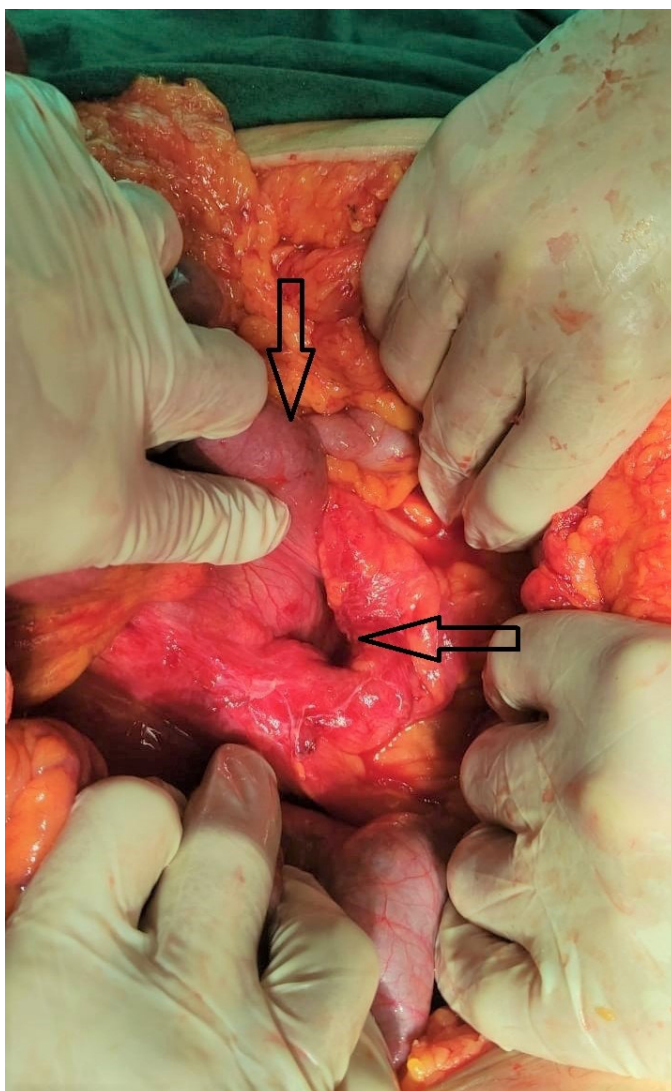


Figure 6. Treitz ligament and hernia defect (black arrow)

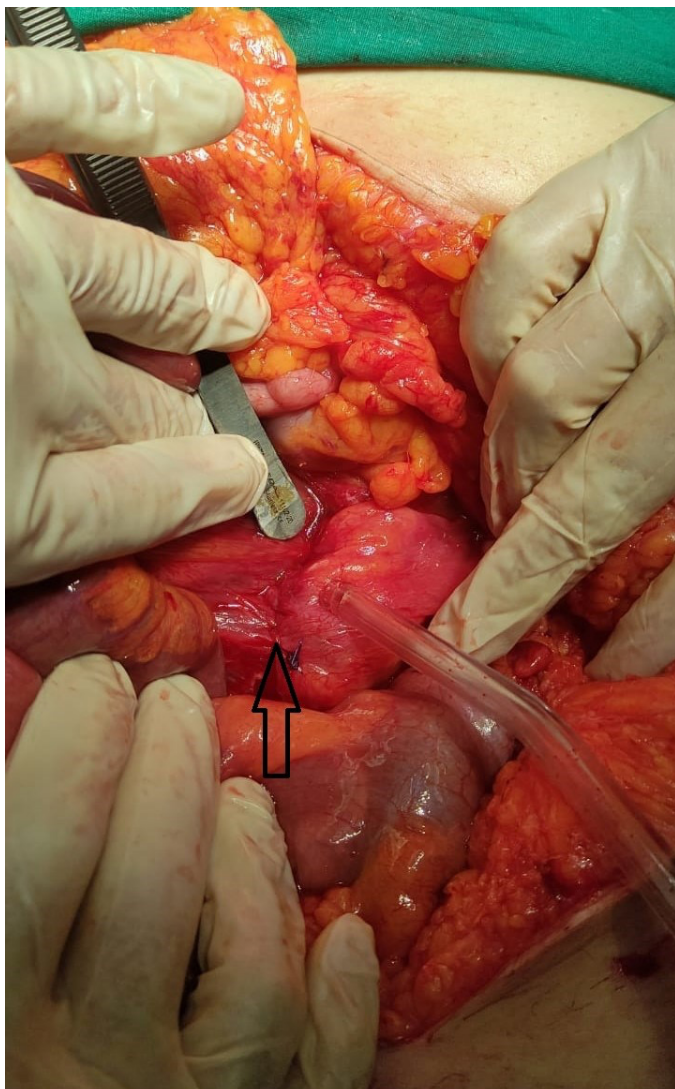


Figure 7. Hernia defect after repair (black arrow)

fluid levels can be observed in the standing direct abdominal X-ray. However, in our patient, there was no air-fluid level at the time of admission and follow-up. Observation of dilated small bowel loops clustered between the stomach, pancreas, and spleen in CT is highly diagnostic, and typically, a collective extension of the vascular structures feeding the herniated dances into the sac can be observed. CT findings similar to those in the literature were detected in this study. Complete blood count and biochemical parameters may vary depending on whether ischemia or necrosis develops in the herniated small bowel loop. The basic principles of treatment are based on the reduction of herniated small bowel loops and primary repair of the defect [1-3,5,6]. However, it may be in cases where the neck of the sac is narrow and there are adhesions and severe swelling between the intestinal loops. It is also stated that in these cases, the inferior mesenteric vessels can

be cut or the hernia sac can be reached with an incision made from the avascular plane to the left of the inferior mesenteric vein [2,3,6].

Conclusion

Internal herniation, which is a rare cause, should also be considered in the differential diagnosis of mechanical intestinal obstruction, particularly in patients without previous abdominal surgery, and in describing recurrent episodes of intestinal obstruction. Timely diagnosis and surgical treatment are critical for preventing complications such as intestinal ischemia and necrosis.

Ethics

Informed Consent: Informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: B.B., İ.G., B.K., B.Ç., Concept: B.B., İ.G., B.K., B.Ç., Design: B.B., İ.G., B.K., B.Ç., Data Collection or Processing: B.B., İ.G., B.K., B.Ç., Analysis or Interpretation: B.B., İ.G., B.K., B.Ç., Literature Search: B.B., İ.G., B.K., B.Ç., Writing: B.B., İ.G., B.K., B.Ç.

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A Rare Cause of Orbital Compartment Syndrome: Gunshot Injury

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Abstract

To our knowledge, there are no reported orbital compartment syndrome (OCS) cases caused by a foreign body in the orbit accompanying retrobulbar bleeding after gunshot injury. A 44-year-old male patient presented to our emergency room with a gunshot injury, stating that a bullet hit his right eye approximately 20 min before the visit. A single bullet entry hole was visible on the lateral side of his right lower eyelid. Proptosis, ecchymosis, edema, conjunctival chemosis and lateral strabismus was present in the patient's right eye. The tonicity of the right eye was slightly increased on palpation and the patient was considered to have OCS. Computed tomography (CT) was performed, which revealed retrobulbar hemorrhage and a bullet fragment stuck in the orbital posterior wall. Anti-edema treatment was initiated and lateral canthotomy/cantholysis was planned for the patient. Another orbital CT showed perforation in the injured eye. The patient was re-evaluated by ophthalmology and neurosurgery specialists, and the foreign body (bullet nucleus) in the retrobulbar region was removed by neurosurgery specialist. The patient was discharged with recommendations from the neurosurgery ward after 5 days. OCS can occur as a rare complication of a gunshot injury. Eye tonicity of patients with firearm injuries to the ocular area should be evaluated at frequent intervals and the need for cantotomy or cantolysis should be considered with a multidisciplinary approach in this setting.

Keywords: Orbital compartment syndrome, emergency, gunshot, neurosurgery and ophthalmology

Introduction

Orbital compartment syndrome (OCS) is an important ophthalmological emergency that can result in permanent vision loss unless corrected [1]. Permanent vision loss depends on the severity and location of the increased pressure and may be caused by the direct compression of neurovascular structures or disruption of the perfusion membrane due to pressure [2]. Multiple studies have shown permanent vision loss within the first 60-100 min unless corrected [2,3]. Because of the high risk and early development of this complication, imaging should be postponed and diagnosis should be based on the history and physical examination of the patient primarily, to prevent any delays. Lateral canthotomy/cantholysis (LC/C) is the preferred modality for the immediate treatment of OCS and has been recommended since the early 1990s [4]. OCS is rarely seen after facial or orbital trauma, and its most common cause is traumatic retrobulbar bleeding [5]. Here we present a case with penetrating orbital trauma as a rare cause of OCS.

Case Report

A 44-year-old male patient presented to our emergency room with a gunshot injury. He stated that the bullet hit his right eye approximately 20 min before the visit. Physical examination revealed a Glasgow Coma scale score of 15 at the time of admission. His vital signs were as follows: blood pressure, 130/80 mmHg; respiration rate, 14/minute; and oxygen saturation with a pulse oximeter, 95% (in room air). A bullet entry hole was detected on the lateral side of his right lower eyelid. Proptosis, ecchymosis, edema, conjunctival chemosis and lateral strabismus was present in the patient's right eye. Pupillary light and accommodation reflexes were absent. The tonicity of the right eye was slightly increased on palpation. There was no hyphaema or hypopyon. The patient's visual acuity was decreased at a distance of 1 meter. Based on these findings, the patient was considered to have OCS. His intraocular pressure (IOP) was measured to be 55 mmHg using a tonometer. The first orbital computed tomography (CT) revealed retrobulbar hemorrhage and a bullet fragment stuck in the



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orbital posterior wall (Figure 1), pressing the optic nerve (Figure 2). The patient's eyeball was protected. Immediately after that, LC/C was planned for the patient. Anti-edema treatment with a combination of 20% intravenous mannitol (2 g/kg) and methylprednisolone (250 mg) was initiated as adjuvant treatment before the surgery. The patient was consulted by neurosurgery and ophthalmology specialists. Physical examination was repeated after 15 min, while the medication was continued. Re-examination revealed a reduction in the

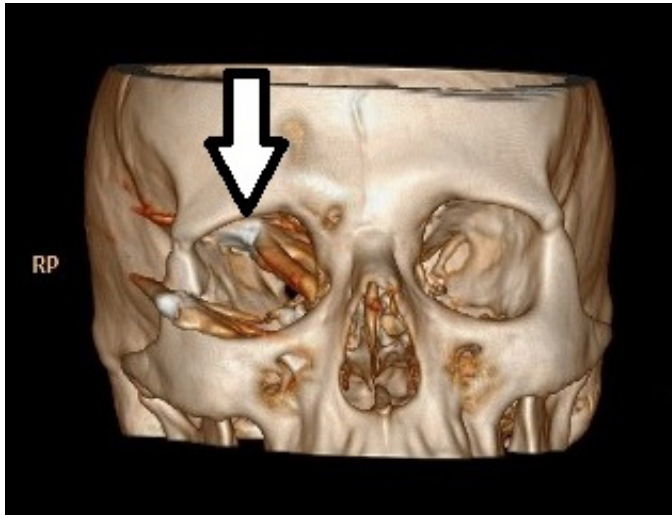


Figure 1. Three-dimensional orbital computed tomography of the patient. The arrow shows the bullet core (arrow)

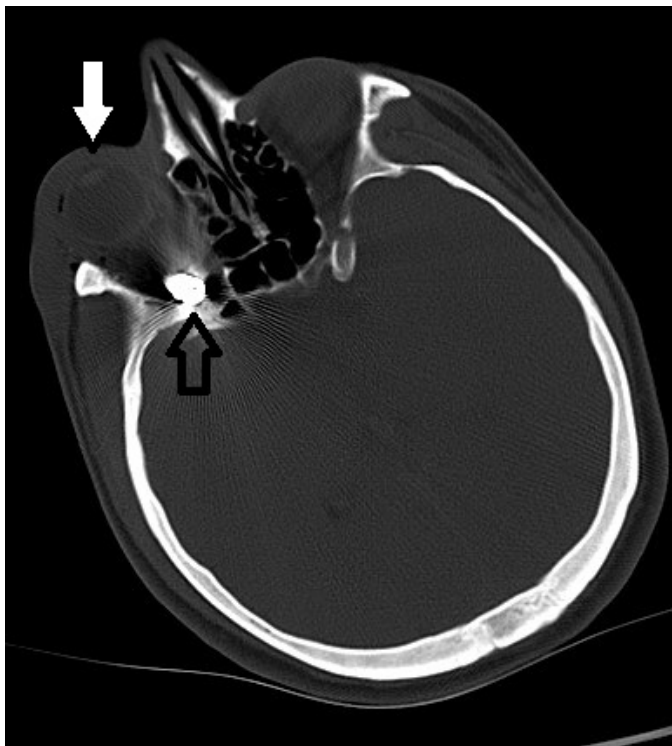


Figure 2. The bullet nucleus is seen in the retro-orbital region (black arrow). The eyeball boundaries are seen normally (white arrow) on orbital computed tomography

tonicity of the injured eye. Another orbital CT was performed immediately, which showed perforation in the injured eye. The patient was re-evaluated by ophthalmology and neurosurgery specialists, and the foreign body (bullet nucleus) in the retrobulbar region was removed by neurosurgery. The patient was discharged with recommendations from the neurosurgery ward after 5 days.

Discussion

OCS is a rare complication caused by an increase in the volume and pressure of the orbital cavity. It is a serious ophthalmological emergency, requiring urgent intervention [1,2]. The most common cause of OCS is retrobulbar hemorrhage secondary to blunt trauma to the orbital cavity or subperiosteal space [6], as IOP rarely increases after penetrating trauma to the eye [2,6]. To our knowledge, there is no reported case of OCS caused by a foreign body in the orbit accompanying retrobulbar bleeding after a gunshot injury.

The normal orbital volume is approximately 30 mL, and the normal IOP is lower than 20 mmHg (usually around 3-6 mmHg) [7]. Increases in the orbital pressure and volume can be compensated with proptosis to some degree; however, lateral and medial canthal ligaments limit this proptosis to an extent. The diagnosis of OCS is usually based on the patient history and clinical findings and does not require radiological imaging. Decreased visual acuity in the affected eye, proptosis, subconjunctival hemorrhage accompanying edema of the eyelid, ecchymosis, conjunctival chemosis, lateral strabismus and increased eye pressure (IOP >40 mmHg) with fixed enlarged pupils or an afferent pupillary defect is usually sufficient for the diagnosis of OCS after orbital and/or facial trauma [2]. All these symptoms were present in our patient.

As the intraorbital pressure exceeds the pressures of the central retinal and ophthalmic arteries, the blood flow in these vessels stops. Increased intraorbital pressure that lasts longer than 60-100 min have been shown to worsen ischemia and cause permanent vision loss. Therefore, if IOP becomes higher than 40 mmHg, LC/C should be urgently performed within the first 60-100 min [7]. In this study, IOP was measured in about 20 min and was found to be 55 mmHg, suggesting an increase in the orbital pressure due to the mass effect in the retrobulbar region by the foreign body. The decrease in the visual acuity of our patient was also thought to be caused by OCS and the bullet fragment stuck to the optic nerve.

After the diagnosis of OCS, an emergency LC/C was planned in our patient, which is the primary approach that commonly used to reduce orbital pressure [8]. The main indications for LC/C are decreased visual acuity, proptosis and IOP >40 mmHg. IOP >40 mmHg is sufficient for performing LC/C if the patient is unconscious. In addition to surgical treatment,

osmotic agents (20% mannitol, 2 g/kg) and high-dose steroids (methylprednisolone, 250 mg) can be used to suppress post-traumatic inflammation and edema [9]. In this study, initial physical examination and imaging results suggested the presence of OCS during the first examination, and emergency decompression was initially planned; however, while re-evaluating the patient, palpation of the eye revealed decreased tonicity of the injured eyeball. Therefore, another CT scan was performed, which showed perforation in the affected eye. Standard treatment methods (e.g., LC/C) were abandoned because they were contraindicated in the presence of perforation [10]. While emergency LC/C is an effective method for the treating of OCS after blunt trauma, the indications for this treatment should be re-evaluated multiple times in patients with firearm injuries with high probability of eyeball perforation. Perforation should be considered if a sudden decrease in eye tonicity is detected on repeated physical examinations. As the measurement using a tonometer is contraindicated in the presence of perforation, diagnostic imaging studies (such as orbital CT) should be repeated in the early period to detect a possible perforation [11]. We believe the necessity of a multidisciplinary approach to decide the evaluation and decompression method in patients with OCS after a firearm injury.

Conclusion

OCS can occur as a rare complication of a gunshot injury. Unlike standard emergency decompression procedures performed in patients with OCS after blunt trauma, the preferred surgical decompression method in patients with a penetrating injury should be selected by performing an eye tonicity examination at frequent intervals. The possibility of perforation should be considered if the eye tonicity is decreased, and the appropriate surgical method should be determined by a multidisciplinary approach in such patients.

Ethics

Informed Consent: Verbal informed consent was obtained from the patient(s) for their anonymized information to be published in this case report.

Peer-review: Externally peer-reviewed.

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