

The experience of an emergency intensive care unit during the COVID-19 pandemic: A retrospective cohort study

Emergency intensive care unit experiences due to COVID-19

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Abstract

Aim: The availability of an intensive care unit in the emergency departments (EDICU) is one of the most important issues discussed recently in terms of increasing the quality of emergency patient care. In this study, we aimed to investigate the clinical characteristics and factors affecting the mortality in patients with COVID-19.

Material and Methods: This is a retrospective study of patients with COVID-19 hospitalized in EDICU. Patients were divided into mortality and survival groups, and the clinical characteristics of these groups were compared.

Results: A total of 38 patients were included; 47.4% (n = 18) were in the survival group. Oxygen saturation level was significantly different between the mortality and survival groups [78.0% (63.7-83.0) vs 88.5% (81.5-93.2), p = 0.001]. Patients in the mortality group had higher plasma levels of lactate dehydrogenase (LDH), procalcitonin, C-reactive protein (CRP), lactate, ferritin and D-dimer. Univariate regression analysis showed that oxygen saturation, LDH, CRP and endotracheal intubation (ETI) were significant markers in predicting mortality (p = 0.011, p = 0.035, p <0.001, respectively). A CRP level \geq 91.9 mg/L predicts mortality with a sensitivity of 66.6% and a specificity of 80.0% (AUC: 0.781, 95% CI: 0.617- 0.898).

Discussion: This study showed that oxygen saturation, ETI, LDH and CRP levels were significantly successful in predicting mortality. Therefore, early administration of antibiotherapy and timely use of ETI may increase the quality of patient care.

Keywords

COVID-19; Emergency Medicine; Intensive Care Unit; Mortality Rate

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Introduction

The COVID-19 virus, which caused the greatest pandemic of the last century, rapidly causes pneumonia and acute respiratory distress syndrome (ARDS), as well as high contagiousness [1]. In the first wave of the pandemic, there were patients with ARDS table waiting for intensive care beds for days in the emergency services of many European countries, especially Italy, Spain and England [2]. In order to avoid a similar picture in our country, the intensive care capacities of hospitals, especially those in Istanbul, have been increased across the country or the opening of new intensive care hospitals has been accelerated [3].

Critical care patients who are diagnosed as an emergency, might be cared for within 6 hours, sometimes more than twenty-four hours at ER, in case of intensive care units are totally in service for others [4]. In this case, emergency physicians also undertake the long-term critical care of these patients [5]. However, it is known that as the length of stay in emergency services increases, the general condition of the patients worsens [6]. Therefore, the EDICU model has been adopted in some emergency services to increase the quality of care of critical patients in emergency services and to reduce the length of stay [7]. Models, such as resource intensivist, hybrid and stand-alone, are used for EDICU [8]. EDICU has many benefits in the management of critical emergency patients, such as ensuring airway management using more advanced techniques such as bronchoscopy and more effective intervention of septic shock patients [9]. In addition, EDICU has also intensivists or emergency specialists who work for critical patients, communicate with other established ICUs, and reduce the length of stay of critical patients [10].

This study aimed to share the experiences regarding the follow-up and treatment of critical COVID-19 patients who were taken to EDICU with severe respiratory distress in the first wave of the pandemic.

Material and Methods

Study Population

This study was conducted among the patients hospitalized with the diagnosis of COVID-19 in the EDICU between March 10, 2020 and June 30, 2020, when the first case was seen in our country. EDICU serves as the first and unique intensive care unit in the emergency room in Istanbul, managed by emergency doctors. EDICU was established in order to manage the follow-up and treatment with intensive care discipline by admitting patients who have been indicated for hospitalization in the intensive care unit after the emergency examinations and treatments were performed.

EDICU is managed by emergency specialists and is mostly a stand-alone model. EDICU is an isolated separate unit with ICU beds near the emergency service main area. During the first wave of the COVID-19 pandemic, patients with ARDS who admitted to the emergency room were first managed in EDICU as long as there was available beds. Emergency physicians working in EDICU have attended critical care courses and have critical care certificates. Doctors, working in EDICU, are only responsible for this area in EDICU shifts. Emergency specialists working in EDICU work in other areas of the emergency service in the remaining shifts.

For the diagnosis of COVID-19, either positive RT-PCR test ty or Chest CT scan in favor of COVID-19 was accepted. The Chest CT report is an official document of the hospital and is made by radiologists. The definition of suspicious COVID-19 by the Ministry of Health of the Republic of Turkey was determined according to current guidelines [11].

Study Design and Data collection

For the data of this retrospective study, U06.0 and U07.3 International Classification of Disease (ICD) diagnosis codes from the hospital automation system and EDICU's archive were used. The patients included in the study were examined in two groups according to the mortality. The first group was the patients who were discharged directly from the intensive care unit as a result of the improvement of the medical condition (survival group), and the second group was the mortality group in the intensive care unit. This study was approved by the local ethics committees and the Ministry of Health with a clinicaltrial.gov ID of NCT04480060.

This retrospective, multi-center, observational study was approved by the Institutional Review Board of Kanuni Sultan Suleyman Research and Training Hospital in Istanbul, Turkey (no. 2020-KSSH-1331). The Advisory Board on Coronavirus Research of the Turkish Ministry of Health approved the study with a clinicaltrial.gov ID of NCT04479137.

Statistical analysis

All statistical analyses (sensitivity, specificity, negative predictive value, positive predictive value) were performed on MedCalc Statistical Software version v19.4.1 (MedCalc Software, Ostend, Belgium). The data of the patients are expressed as median (quartiles) for distributed data and percentage for categorical variables. The normality of the distribution of continuous variables was examined by the Shapiro-Wilk test. Between-group comparisons of normally distributed parameters were conducted by Student's t-test; the Mann-Whitney U-test was applied for non-normally distributed parameters.

Results

Eighty-one patients were admitted to EDICU between the study dates; of them, 38 patients were included in the study because 43 patients were hospitalized for reasons other than COVID-19. Among those included in the study, 65.8% (n = 25) were male, with the median (quartiles) age of 70.0 (55.0-83.5) years, 34.2% (n = 13) were female, with the median (quartiles) age of 64.0 (42.5-85.5) years. While 47.4% (n = 18) of these 38 patients were discharged from EDICU and/or transferred to the service (survival group), 52.6% (n = 20) resulted in death (mortality group). When the RT-PCR results of the patients included in the study were examined, it was seen that 43.8% of the mortality group (n = 7) were positive, 18.8% of the survival group (n = 3) were positive, and 6 patients were inadequate or inappropriate specimen collection. Among the application complaints of the patients included in the study, 68.4% (n = 26) had shortness of breath, 36.8% (n = 14) had cough, 31.6% (n = 12) had unconsciousness, 18.4% (n = 7) malaise and malaise, 10.5% (n = 4) had fever (> 38 ° C). When the vital signs of the patients included in the study were examined, the systolic blood pressure median (quartiles) value was 120.5 (102.0-

Table 1. Biochemical measurement values of study groups

	Mortality Group (n=20)	Survival Group (n=18)	p value
WBC count, ($\times 10^3$ per μ L)	11.18 (8.7-15.0)	6.72 (5.3-11.0)	0.031
Platelet count, ($\times 10^3$ per μ L)	199.0 (130.0-303.0)	200.00 (166.5-252.0)	0.977
Neutrophil count, ($\times 10^3$ per μ L)	8.74 (7.0-13.4)	4.97 (3.6-9.2)	0.015
Lymphocyte count, ($\times 10^3$ per μ L)	0.90 (0.6-1.4)	1.0 (0.6-1.4)	0.529
BUN, mg/dL	24.3 (19.8-58.6)	16.8 (8.6-28.7)	0.007
LDH, U/L	511.0 (319.5-669.0)	300.0 (215.5-411.5)	0.007
Albumin, g/L	24.9 (19.6-27.7)	30.9 (28.3-33.5)	0.245
CRP, mg/L	157.1 (76.3-289.6)	52.8 (19.6-134.1)	0.003
Procalcitonin, ng/mL	0.24 (0.09-1.24)	0.07 (0.04-0.13)	0.015
Lactate, mmol/L	1.54 (1.27-2.12)	1.07 (0.76-1.60)	0.022
Base excess, mmol/L	-0.8 (-5.2-3.0)	0.4 (-5.8-2.3)	0.884
Ferritin	909.4 (501.3-1654.0)	229.0 (66.6-751.7)	0.007
D-Dimer, mg/L	2.61 (1.5-5.5)	1.37 (0.7-2.3)	0.019
Kalsiyum, mg/dL	8.3 (7.7-8.4)	8.5 (8.0-8.9)	0.446
Potassium, mEq/L	4.4 (4.0-4.9)	3.9 (3.6-4.5)	0.067
Sodium, mEq/L	137.0 (133.5-142.5)	136.0 (133.0-138.0)	0.454
Prothrombin time, sec	12.9 (12.0-17.2)	12.7 (11.7-15.2)	0.781
Partial thromboplastin time, sec	24.0 (21.3-29.0)	23.9 (22.0-29.4)	0.502

(Data are expressed as median (quartiles) Abbreviations: WBC: White Blood Cell, CRP: C-reactive protein)

Table 2. Bacterial infection development rates and significance levels of the treatments administered between mortality and survival groups

	Mortality group (n=20)	Survival group (n=18)	p value
Secondary bacterial infection	19 (95.0)	12 (66.7)	<0.001
ETI, % (n)	16 (80.0)	1 (5.6)	<0.001
High Flow*, % (n)	20.0 (4)	11.1 (2)	0.663
NIMV (CPAP) *, % (n)	25.0 (5)	11.1 (2)	0.128
Prone position*, % (n)	10.0 (2)	0.0 (0)	0.488
High flow*, % (n)	20.0 (4)	11.1 (2)	0.663
ECMO*, % (n)	15.0 (3)	0.0 (0)	0.232
Hydroxychloroquine, % (n)	100.0 (20)	100.0 (18)	1.000
Steroid*, % (n)	15.0 (3)	11.1 (2)	1.000
Plasma*, % (n)	10.0 (2)	0.0 (0)	0.488
Linezolid*, % (n)	20.0 (4)	11.1 (2)	0.663
Vancomycin*, % (n)	25.0 (5)	0.0 (0)	0.048
Levofloksasin, % (n)	75.0 (15)	55.6 (10)	0.207
Piperacillin-Tazobactam, % (n)	70.0 (14)	55.6 (10)	0.357
Meropenem, % (n)	40.0 (8)	16.7 (3)	0.113
Oseltamivir, % (n)	70.0 (14)	38.9 (7)	0.054
Favipiravir*, % (n)	95.0 (19)	77.8 (14)	0.170
Tocilizumab*, % (n)	15.0 (3)	0.0 (0)	0.232
Anticoagulant therapy*, % (n)	95.0 (19)	88.9 (16)	0.595

*Fisher exact test

(Data are expressed as median (quartiles). Abbreviations: ETI:Endotracheal intubation, NIMV (CPAP): Non invasive mechanical ventilation (continuous positive airway pressure), ECMO: Extra Corporeal Membrane Oxygenation, ARDS: Acute Respiratory Distress Syndrome)

Table 3. Effects of various variable on mortality of Covid-19 intensive care patients in univariate and multivariate logistic regression analyses

Variable	Univariate logistic regression analyses		Multivariate logistic regression analyses	
	OR (95% CI)	P value	Adjusted OR(95% CI)	P value
Age (years)	1.032 (0.992-1.074)	0.120		
Gender	1.485 (0.386-5.707)	0.565		
DM	0.857 (0.218-3.371)	0.825		
HT	1.250 (0.348-4.486)	0.732		
Admission Oxygen saturation (%)	0.864 (0.772-0.967)	0.011	0.933 (0.800-1.088)	0.377
SOFA score	1.186 (0.935-1.505)	0.159		
APACHE II score	1.057 (0.975-1.145)	0.177		
WBC count, ($\times 10^3$ per μ L)	1.057 (0.952-1.172)	0.300		
Neutrophil count, ($\times 10^3$ per μ L)	1.075 (0.960-1.205)	0.079		
BUN, mg/dL	1.023 (1.997-1.050)	0.083		
LDH, U/L	1.004 (1.000-1.009)	0.035	1.000 (0.994-1.006)	0.990
CRP, mg/L	1.010 (1.002-1.018)	0.011	1.007 (0.995 -1.020)	0.242
Procalcitonin, ng/mL	0.980 (0.930-1.034)	0.462		
Lactate, mmol/L	1.102 (0.778-1.560)	0.585		
Ferritin	1.001 (1.000-1.002)	0.114		
D-Dimer, mg/L	1.096 (0.972-1.235)	0.134		
ETI	68.000 (6.850-674.988)	<0.001	28.770 (2.543-337.402)	0.007

(Abbreviations: OR: Odds Ratio, CI: confidence interval, HT: Hypertension, DM: Diabetes Mellitus, WBC: White Blood Cell, BUN: Blood Urea Nitrogen LDH: Lactate Dehydrogenas, CRP: C-reactive protein, ETI: Endotracheal intubation)

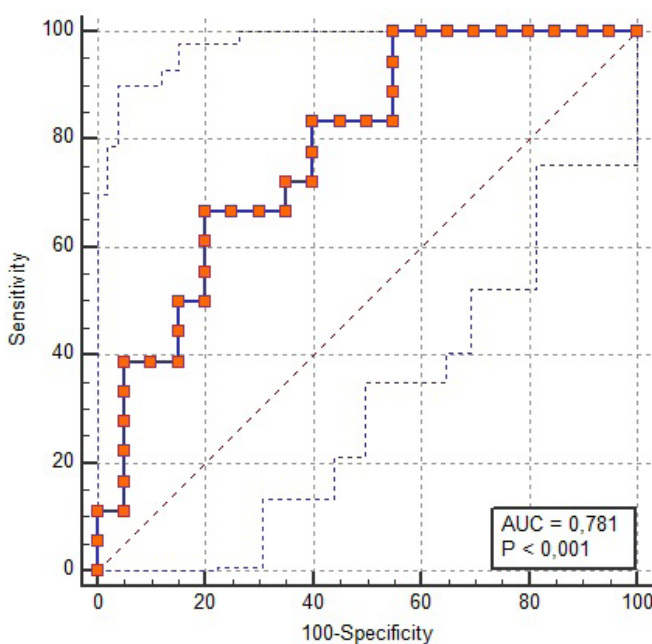


Figure 1. ROC (Receiver-operating characteristic) curve analysis of CRP (C-reactive protein) for predicting mortality

135.7) mmHg, diastolic blood pressure median (quartiles) value 76.0 (64.7-82.2) mmHg, the median (quartiles) value of the pulse measured per minute was 92.0 (76.7- 115.5), oxygen saturation median (quartiles) value was 82.5% (74.5-91.2), body temperature median (quartiles) 37.1°C (36.1-37.6). Hypertension in 47.4% (n = 18) of patients, diabetes mellitus in 31.6% (n = 12), congestive heart failure in 21.1% (n = 8), coronary artery disease in 15.8% (n = 6), 15.8% (n = 6) had chronic obstructive pulmonary disease, 13.2% (n = 5) had renal failure, and 13.2% (n = 5) had previous cerebrovascular disease. The rates and significance levels of the characteristics of the study population according to the study groups (mortality group vs survival group) were examined. There was no significant difference in age (median, quartiles; 72.0 (56.2-85.7) vs 61.5 (44.0-78.5, $p = 0.128$) and sex (male; 70.0% (n = 14) vs 61.1% (n = 11), $p = 0.564$) between the mortality group and the survival group. Considering the significance level of the difference between mortality group and survival group according to the presence of comorbidity, those in the mortality group had a significantly higher rate of renal failure than the survival group (25.0% (n = 5) vs 0.0% (n = 0), $p = 0.048$). Only the baseline oxygen saturation level was significantly different between the groups (mortality vs survival) (78.0% (63.7-83.0) vs 88.5% (81.5-93.2), $p = 0.001$) among vital signs. While there was no significant difference in the application APACHE II score (20.0 (11.5-30.0) vs 15.5 (10.7-18.2), $p = 0.203$) in the mortality group compared to the survival group, the admission SOFA score (3.0 (3.0-6.0) vs 2.0 (2.0-3.0), $p = 0.034$) was higher in the mortality group.

The levels and intergroup significance levels of the first laboratory parameters taken during admission to intensive care according to the study groups are shown in Table 1.

The distribution and significance levels of the interventions and treatment by groups are shown in Table 2. Accordingly, it was observed that patients who required endotracheal intubation (ETI) resulted in mortality at a high significance level (16 (80.0) vs 1 (5.6), $p < 0.001$). In the mortality group, 95% of the patients had secondary bacterial infection ($p < 0.001$).

The results of univariate and multivariate logistic regression analysis applied to determine the independent risk factors (age, sex, vital signs, comorbidities, laboratory parameters, interventions) affecting mortality of patients hospitalized in EDICU with the diagnosis of COVID-19 are shown in Table 3.

Univariate regression analysis demonstrated that admission oxygen saturation, LDH, CRP and ETI were significant markers in predicting mortality ($p = 0.011$, $p = 0.035$, $p < 0.001$, respectively). In order to distinguish the mortality group from the survival group, when the cut-off value of the CRP level was taken as 91.9 mg / L in the ROC curve, the sensitivity was 66.6%, specificity 80.0%, positive likelihood ratio 3.3, negative likelihood ratio 0.4 (AUC: 0.781, 95% CI: 0.617- 0.898) (Figure 1).

Discussion

In this study, the experiences of managing critical COVID-19 patients admitted to the emergency department in EDICU and the factors affecting mortality were evaluated. In this study, which was examined in two groups as mortality and survival, it

was observed that only the oxygen saturation level of the vital signs showed a significant difference between the groups (78.0 (63.7-83.0) vs 88.5 (81.5-93.2), $p = 0.001$), and low oxygen saturation level increased the risk of mortality (OR 0.864; 95% CI 0.772-0.967; $p = 0.011$). Among laboratory parameters, CRP was found to differ significantly between the groups (157.1 (76.3-289.6) vs 52.8 (19.6-134.1), $p = 0.003$) and high CRP was the best laboratory marker for predicting mortality (OR: 1.010; 95% CI 1.002-1.018; $p = 0.011$). A higher rate of secondary bacterial infections was found in the mortality group ($p < 0.001$). All interventions that had a role in the literature in the pandemic period, such as ECMO, high flow oxygen and plasma, were used for the patients hospitalized in EDICU. It was observed that ETI was the best marker for predicting mortality, and 95% (19/20) of patients who received ETI died. A study conducted on patients hospitalized with COVID-19 defined 5 predictors of intensive care admission included LDH, procalcitonin, pulse oxygen saturation, smoking, and lymphopenia, and concluded that there are 7 predictors of mortality: heart failure, chronic obstructive pulmonary disease (COPD), heart rate, and age [12]. In a meta-analysis investigating the relationship between laboratory parameters and the severity of COVID-19 and mortality, the increase in D-dimer and procalcitonin levels was reported to be associated with poor prognosis and was one of the important markers of mortality [13]. In this meta-analysis, ferritin and CRP were parameters that are indicators of mortality and poor prognosis. In our study, the elevation of procalcitonin, ferritin, D-Dimer and CRP was significantly higher in the mortality group. However, among the laboratory parameters only CRP was significant in predicting mortality in regression analysis. Although a sensitivity rate of 66.6% was obtained for the CRP level of 91.9 mg/L in predicting mortality in EDICU, it had a better specificity rate of 80.0%. In a study investigating laboratory parameters of mild-to-moderate COVID-19 patients, progressing from non-severe to severe condition, it was concluded that procalcitonin and lymphocyte did not have a significant effect in distinguishing non-severe and severe groups, and CRP had high level of discrimination [14]. We suggest that the reason why CRP predicted the mortality best, might be associated with the higher rate of secondary bacterial infection in the mortality group compared to the survival group.

One of the controversial issues in critical COVID-19 patients is the timing of the application of ETI. In this regard, there are different opinions about whether early ETI gives better results or ETI should be reserved for patients who had no improvement after having high flow nasal cannula (HFNC) and/or continue noninvasive mechanic ventilation [15]. In patients followed up in EDICU, the ETI decision was made according to the clinical status and blood gas results.

A total of 80% (n = 16) of the patients in the mortality group and 5.6% (n = 1) of the survival group were required ETI during follow-up. Prospective multi-center studies are needed to define when and what criteria ETI should be applied in critical COVID-19 patients. In a case series of 24 patients referred to ICU from 9 hospitals in Seattle-area hospitals, 50% of the patients followed in ICU died in the first 18 days [16]. In a retrospective observational study conducted in China in the first months of the

pandemic, the mortality rate of COVID-19 patients followed in ICU was 61.5% [17]. In our study, the mortality rate was 52.6%. The COVID-19 pandemic, which started in China in December 2019, was seen for the first time in our country in March 2020. Despite the possibility of increasing the need for intensive care in the emergency, the number of EDICU beds doubled, as well as the number of nurses and mechanical ventilation.

Limitations

The limitations of this study can be defined as it was a single-center study, and the other limitation was that the statistical method used to calculate the differences between groups of treatments was the Fisher Exact test instead of the Pearson Chi-Squared test, due to the small sample size. It is thought that this was the reason, even if there was a difference between the groups, it could not be shown by statistical analysis.

Conclusion

In conclusion, EDICU had similar mortality rates and similar results with ICUs of other hospitals. Secondary infection risk should be taken into consideration for patients followed up in ICU and it should be considered that this may be related with mortality. Therefore, early antibiotics may be recommended. CRP can be used to predict mortality in patients with ICU. A standard protocol is needed to be developed regarding when ETI should be applied. In the COVID-19 pandemic, EDICU is shown to be effective in improving the quality of care by reducing the length of stay of critical patients in the emergency room.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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