




## Comparison of non-COVID-19 critically ill patients between pre-pandemic and pandemic period admitted from emergency department to internal medicine intensive care unit

*Pandemi öncesi ve pandemi döneminde acil servisten iç hastalıkları yoğun bakım ünitesine kabul edilen COVID-19 dışı kritik hastaların karşılaştırılması*

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### ABSTRACT

**Aim:** During the COVID-19 pandemic, a large number of intensive care unit beds have been organized for critically ill COVID-19 patients. However, the need for intensive care for non-COVID-19 critical patients continues. In our study, we aimed to compare non-COVID-19 critically ill patients admitted to the internal medicine intensive care unit from the emergency department before and during the pandemic period.

**Materials and Methods:** Patients who were admitted to the internal medicine intensive care unit from the emergency department were grouped as pre-pandemic (March 2018-March 2020) and during the pandemic (March 2020-March 2022) and compared retrospectively in terms of the number of hospitalisations, demographic characteristics, length of intensive care unit stay and mortality.

**Results:** The number of emergency department patient admissions other than surgical reasons was 579.657 during the study period. 63.33 % of these patients were admitted before the pandemic and 36.67% during the pandemic period. The number of patients included in our study was 493 before the pandemic and 460 during the pandemic period. Median age was 61 (30) in the pre-pandemic period and 64 (26.8) in the pandemic period,  $p=0.022$ . There was no significant difference in terms of comorbidities. The main reason for hospitalization was similar and sepsis was the leading reason for hospitalization. The frequency of acute renal failure in intensive care unit was significantly higher during the pandemic period. Mortality was 25.2% before the pandemic and 24.3% during the pandemic period,  $p=0.760$ .

**Conclusion:** Although emergency department admissions decreased, the number of non-COVID-19 internal medicine intensive care unit hospitalizations did not decrease. This situation reveals the importance of organizing intensive care beds for hospitalization for non-COVID-19 reasons in order not to disrupt health services during the pandemic period.

**Keywords:** Intensive care unit, mortality, pandemic, COVID-19.

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## ÖZ

**Amaç:** COVID-19 pandemisi boyunca birçok yoğun bakım ünitesi yatağı kritik COVID-19 hastaları için ayrılmıştır. Ancak COVID-19 dışı kritik hastalar için yoğun bakım ihtiyacı devam etmektedir. Bu çalışmada pandemi öncesi ve pandemi dönemi boyunca acil servisten iç hastalıkları yoğun bakım ünitesine yatan COVID-19 dışı kritik hastaların karşılaştırılması amaçlanmıştır.

**Gereç ve Yöntem:** Acil servisten iç hastalıkları yoğun bakım ünitesine yatırılan hastalar pandemi öncesi (Mart 2018-Mart 2020) ve pandemi boyunca (Mart 2020-Mart 2022) olarak gruplanıp hasta yatış sayısı, demografik özellikler, yoğun bakım yatış süresi ve mortalite oranı açısından retrospektif olarak karşılaştırıldı.

**Bulgular:** Çalışma dönemi boyunca cerrahi neden dışı acil servis hasta başvuru sayısı 579.657 olup bu hastaların %63,33'ü pandemi öncesi, %36,67'si pandemi dönemi boyunca başvurmuştur. İç hastalıkları yoğun bakım ünitesine yatan ve çalışmaya dahil edilen hasta sayısı pandemi öncesinde 493 ve pandemi döneminde 460'tır. Medyan yaş, pandemi öncesi dönemdeki hastalarda 61 (30), pandemi döneminde ise 64 (26.8) olarak saptandı,  $p=0.022$ . Komorbiditeler açısından anlamlı fark saptanmadı. Başlıca yatış nedeni benzer olup sepsisin önde gelen yatış sebebi olduğu görüldü. Yoğun bakımda akut böbrek yetmezliği görülme sıklığı pandemi döneminde anlamlı yüksek saptandı. Yoğun bakımda kalış süresi iki grupta benzer saptandı. Mortalite pandemi öncesinde %25,2 ve pandemi döneminde %24,3 saptandı,  $p=0.760$ .

**Sonuç:** Acil servis başvuruları azalmasına rağmen COVID-19 dışı iç hastalıkları yoğun bakım hasta yatış sayısı azalmamıştır. Bu durum pandemi döneminde sağlık hizmetlerinin aksamaması için yoğun bakım alanlarının COVID-19 dışı nedenlerle yatış için de organize edilmesinin önemini ortaya koymaktadır.

**Anahtar Sözcükler:** Yoğun bakım ünitesi, mortalite, pandemi, COVID-19.

## INTRODUCTION

During the coronavirus disease 2019 (COVID-19) pandemic, intensive care beds around the world were tried to be organized for critically ill COVID-19 patients especially in the first months. One of the challenges in dealing with the pandemic was the need to continue to provide services to non-COVID-19 patients who needed intensive care unit admission, although non-COVID-19 emergency department visits due to urgent medical conditions decreased both in our country and in the world (1-4). Soon after intensive care beds were organized for COVID-19 patients, non-COVID-19 intensive care units were faced with high and complicated patient numbers. Another point emphasized in the current literature is the increased critically ill patient mortality (5-9); whereas it was also reported that mortality did not change compared to pre-pandemic in different studies (10,11). It is also noteworthy that lockdown periods increased in-hospital mortality (12). In addition to increased mortality, other points investigated were interventions such as intensive care unit (ICU) length of stay, renal replacement therapy (RRT), mechanical ventilation (MV), extracorporeal membrane oxygenation (ECMO) (9,11). Among studies conducted in our country, it was determined that

the duration of ICU hospitalization had prolonged during the pandemic (13), and mortality had increased (14). When non-COVID-19 patients were evaluated according to the course of the waves, hospitalization during the first pandemic wave in 2020 was determined as an independent risk factor for non-COVID mortality with longer hospital stays (15). Also in another study, higher mortality was observed during the first lockdown compared with the second and third lockdowns (16).

In this retrospective cohort study, we aimed to compare the characteristics and outcomes of patients admitted to internal medicine ICU from emergency department without COVID-19 infection in Ege University Hospital between two time points: the first 2 years of the COVID-19 pandemic (March 2020-March 2022) and the same 2-year period before the pandemic (March 2018-March 2020).

## MATERIALS and METHODS

We performed a retrospective study on patients followed up in the Ege University Faculty of Medicine Department of Internal Medicine ICU between 2018–2022. The study was approved by the Ege University Ethics Committee, number 23-5.1T/15 and adhered to the principles of the

Declaration of Helsinki. The first case of COVID-19 in Turkey was diagnosed on March 11<sup>th</sup>, 2020 (17). As a matter of hospital policy, our intensive care unit was designated to be COVID-19 free critical care admissions. We included adult patients  $\geq 18$  years old without a COVID-19 diagnosis who were admitted to internal medicine ICU from emergency department. We excluded patients admitted to ICU from inpatient services, other ICUs, outpatient clinics, COVID-19 ICU and died shorter than 24 hours. Flowchart of the inclusion is shown in Figure-1.

The primary outcome was number of patient hospitalizations. Secondary outcomes included ICU length of stay and ICU mortality.

To assess the possible effect of the pandemic on ICU mortality and patient hospitalizations, the period under examination was divided into four periods, according to the increase in the number of cases per day reported by the Ministry of Health of Turkey<sup>17</sup>.

1. Wave 1, from 11 March 2020 to 1 June 2020
2. Wave 2, from 5 August 2020 to 11 January 2021
3. Wave 3, from 23 March 2021 to 16 May 2021
4. Wave 4, from 28 December 2021 to 10 March 2022.

Demographic characteristics, comorbidities, ICU admission diagnosis, and laboratory results were recorded from the electronic medical records. Comorbidities were confirmed with clinical records and recorded including hypertension (HT), diabetes mellitus (DM), cardiovascular disease (CVD), chronic kidney disease (CKD), and heart failure (HF), cerebrovascular disease (CVD), dementia, malignancy and chronic liver disease were sufficient. The Sepsis-3 criterion was used to define sepsis (18). Comorbidity was assessed using the Charlson Comorbidity Index (CCI) (19). For detecting acute kidney injury (AKI) at any stage, the international definition of AKI according to the KDIGO criteria was used (20). Time-to-treatment initiation was defined as the number of days from symptom onset to initiation of first treatment. If there was any infection suspected, clinically documented, and supported by diagnostic imaging findings without microbiological documentation or with microbiological documentation, the related organ or system to the infection was considered to be the source of sepsis.

Origin of infection was recorded as hospital or community acquired. Culture positive samples

were classified as Gram-negative bacteria, Gram-positive bacteria and fungal infections. More than one bacteria in the same sample was recorded as polymicrobial. Antimicrobial resistances were recorded according to multiple drug resistant (MDR) (resistant to at least one agent in three or more antimicrobial categories) and extensively drug resistant (XDR) (resistant to all antimicrobial agents except in two or less antimicrobial categories) definitions (21). The sequential organ failure assessment (SOFA) score was calculated.

We compared outcomes of the "pandemic cohort" to a "pre-pandemic cohort" in adult patients admitted to ICU from emergency department.

### Statistics

Data were analyzed using the statistical package program IBM SPSS Statistics 25.0 (IBM Corp., Armonk, New York, USA). Descriptive statistics were presented as number of units (n), percentage (%), median (M), interquartile range (IQR) values. The Shapiro–Wilk test and Q-Q graphics were used to check the normality of the continuous variables. Mann-Whitney U test and Kruskal-Wallis test were used to compare continuous variables between groups. Pearson chi-square test was used to compare categorical variables. Survival time was calculated by Kaplan-Meier analysis and logrank test. Factors affecting survival time were investigated by Cox proportional hazard regression. In Cox regression analysis, variables were included in the model by Backward Wald method.  $p$ -value  $< 0.05$  was determined statistically significant.

### RESULTS

Overall, 579.657 non-surgical patients were admitted to emergency department during study period. Of these patients, 63.33% (n=367.154) were pre-pandemic period and 36.67% (n=212.503) were in the pandemic period. During the pre-pandemic period, number of patients hospitalized in the ICU was 630 and it was 581 during the pandemic period. Among these patients we included 493 in the pre-pandemic cohort and 460 patients in the pandemic cohort. Flowchart for patient inclusion is shown in Figure-1.

Table-1 summarizes patient characteristics and baseline comorbidities in the pre-pandemic and pandemic cohorts. Median age was 64 in the pandemic cohort and 61 in the pre-pandemic

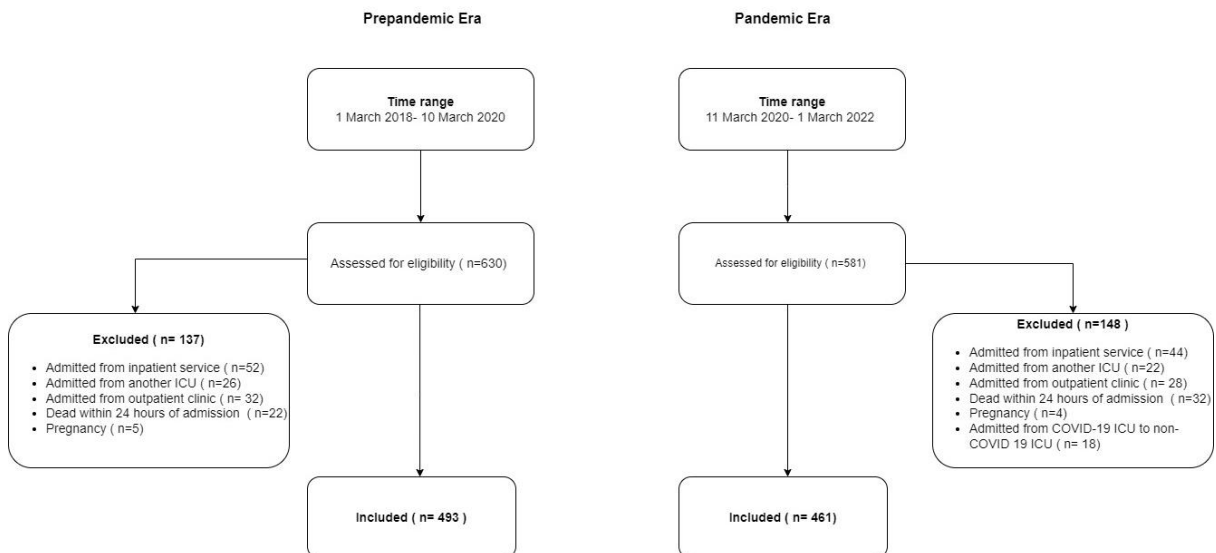
cohort;  $p=0.022$ . Gender distribution was similar between both cohorts. Previous history of DM, HT, HF, CKD, patients on dialysis, CVD, dementia, malignancy, and chronic liver diseases were similar between the groups. A higher proportion of patients in the pandemic cohort had COPD compared with the pre-pandemic cohort (10% vs 5.9%;  $p=0.018$ ). Fewer patients had a previous history of CAD in the pandemic cohort (15.7% vs 22.1%;  $p=0.011$ ). Despite these differences among comorbidities, median CCI was higher in the pre-pandemic cohort.

Table-2 summarizes patient outcomes. The leading major diagnosis was sepsis on ICU admission in both cohorts. Although it is not statistically significant; malignancies, hematological and rheumatologic emergencies, ESRD admissions were less in the pandemic cohort compared with the pre-pandemic cohort. Patients hospitalized in ICU due to AKI in the pandemic cohort was higher than the pre-pandemic cohort (19.8% vs 12.6%); however, it was not statistically significant. ESRD admissions significantly decreased in the pandemic cohort (2.4% vs 3.4%;  $p=0.002$ ). There was not a significant increase in mortality among patients in the pandemic cohort compared with the pre-pandemic cohort (24.3% vs 25.2%;  $p=0.760$ ). Length of ICU stay and time from first symptom onset to initiation of treatment was similar between two cohorts. There was a significant increase in AKI frequency in the pandemic cohort (41.3% vs 33.3%;  $p=0.01$ ). Frequencies of acute

hemodialysis was similar but significantly higher proportion of patients were discharged on routine hemodialysis program in the pandemic cohort (50% vs 30%;  $p=0.032$ ). Median SOFA scores were similar in both cohorts. Origin of infections were community-acquired and Gram-negative bacteria were the most frequent microorganism in both cohorts; there was a significant decrease in the Gram-positive bacterial growth in the pandemic cohort (25.9% vs 19%;  $p=0.001$ ). The leading source of infections was urinary tract followed by bloodstream infections in both cohorts. MDR and XDR bacterial growth frequencies were similar in both cohorts and there was not a significant difference in vasopressor requirements.

Figure-2 shows survival curve of pre-pandemic and pandemic cohorts in ICU. The overall survival time of the 953 patients included in the study was  $29.90 \pm 2.57$  days. In addition, the groups had no effect on survival time ( $p=0.910$ ). The survival time of pre-pandemic cohort was  $31.39 \pm 3.32$  days, while that of pandemic cohort was  $24.18 \pm 1.49$  days. Factors affecting survival time were determined as need for vasopressors and SOFA score;  $p<0.001$  and  $p=0.003$ , respectively. Table-3 shows the results.

Table-4 summarizes number of weekly patient hospitalizations and mortality during the COVID-19 wave dates in the pandemic cohort. There was not a significant difference in the ICU admissions and mortality among the four waves;  $p=0.347$  and  $p=0.297$ , respectively.

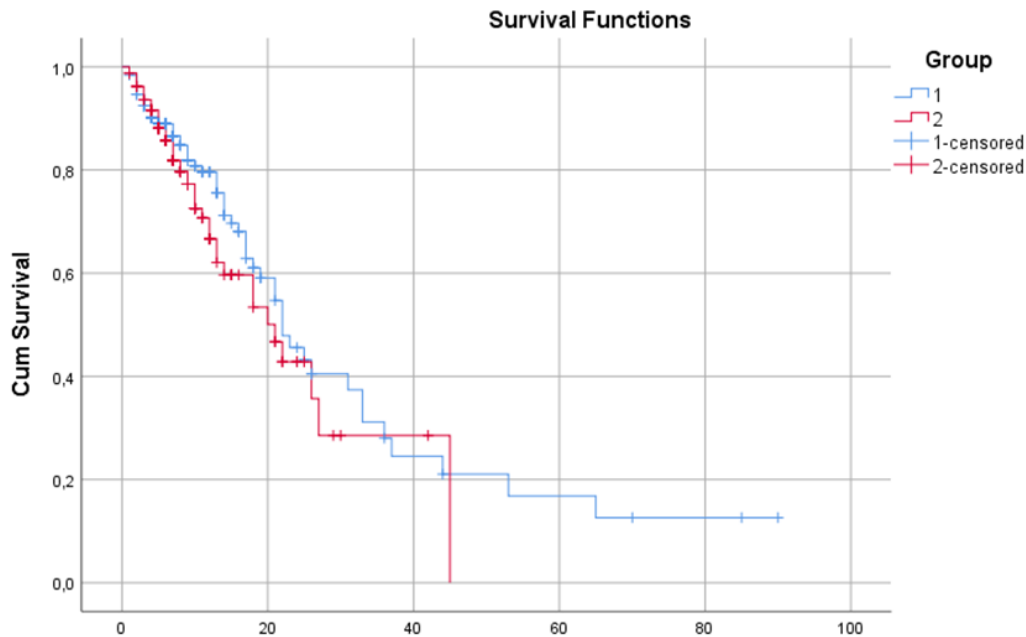


**Figure-1.** Flowchart of patient inclusion.

**Table-1.** Baseline characteristics of patients on ICU admission.

Characteristics	Pre-pandemic cohort (n=493)	Pandemic cohort (n=460)	p
Age, years	61 (30)	64 (26.8)	<b>0.022</b>
Gender, female n(%)	246 (49.9)	214 (46.5)	0.297
<b>Comorbidities, n (%)</b>			
Diabetes melitus	159 (32.3)	142 (30.9)	0.631
Hypertension	218 (44.2)	210 (45.7)	0.657
Heart failure	65 (13.2)	61 (13.3)	0.972
Coronary artery disease	109 (22.1)	72 (15.7)	<b>0.011</b>
COPD	29 (5.9)	46 (10.0)	<b>0.018</b>
Chronic kidney disease	105 (21.3)	87 (18.9)	0.359
On dialysis	43 (8.7)	29 (6.3)	0.158
Serebrovascular disease	27 (5.5)	20 (4.4)	0.426
Dementia	18 (3.7)	23 (5.0)	0.305
Malignancy	135 (27.4)	111 (24.1)	0.252
Cirrhosis	6 (1.2)	11 (2.4)	0.172
<b>Charlson comorbidity index</b>	4 (4)	3 (5)	<b>0.001</b>

ICU: intensive care unit, COPD: chronic obstructive pulmonary disease.



**Figure-2.** Survival curves of pre-pandemic (group 1) and pandemic (group 2) cohorts in non-COVID-19 intensive care unit.

**Table-2.** Outcomes of ICU patients by admission period.

	Pre-pandemic cohort (n=493)	Pandemic cohort (n=460)	<i>p</i>
<b>Major diagnosis on ICU admission</b>			
Sepsis	100 (20.3)	99 (21.5)	
Malignancy	52 (10.5)	39 (8.5)	
AKI	62 (12.6)	91 (19.8)	
Hematological emergencies	51 (10.3)	21 (4.6)	
Rheumatologic emergencies	41 (8.3)	29 (6.3)	
Heart Failure	30 (6.1)	27 (5.9)	
ESRD	17 (3.4)	11 (2.4)	0.002
Others	140 (28.4)	143 (31.1)	
<b>Time-to-treatment, days</b>	4 (5)	4 (5)	0.782
<b>Length of ICU stay, days</b>	6 (6)	7 (5)	0.057
<b>Mortality in ICU, n (%)</b>	124 (25.2)	112 (24.3)	0.760
<b>AKI, n(%)</b>	164 (33.3)	190 (41.3)	<b>0.010</b>
<b>Acute Hemodialysis, n(%)</b>	88 (17.8)	86 (18.7)	0.736
<b>SOFA score</b>	4 (4)	4 (4)	0.428
<b>Method of discharge, on dialysis, n (%)</b>	18 (30.0)	25 (50.0)	<b>0.032</b>
<b>Origin of infection, n(%)</b>			0.333
Community-acquired	25 (67.6)	81 (75.7)	
Hospital-acquired	12 (32.4)	26 (24.3)	
<b>Source of infection, n(%)</b>			
Urinary tract	78 (41.7)	72 (45.2)	
Catheter and bloodstream	72 (38.5)	42 (26.4)	
Hepatobiliary tract	26 (13.9)	25 (15.7)	
Respiratory system	8 (4.3)	10 (6.2)	
Skin-soft tissue	2 (1.1)	6 (3.7)	
Endocarditis	1 (0.5)	4 (2.5)	
<b>Microorganism, n(%)</b>			
Gram negative bacteria	70 (49.0)	75 (71.4)	
Gram positive bacteria	37 (25.9)	20 (19.0)	<b>0.001</b>
Fungal infections	17 (11.9)	7 (6.7)	
Polymicrobial infections	19 (13.3)	3 (2.9)	
<b>MDR, present (%)</b>	61 (54.5)	38 (43.2)	0.113
<b>XDR, present (%)</b>	16 (23.9)	11 (18.0)	0.418
<b>Vasopressors, present (%)</b>	136 (27.6)	133 (28.9)	0.649

ICU: intensive care unit, ESRD: end stage renal disease, AKI: acute kidney injury, SOFA: sequential organ failure assesment, MDR: multidrug-resistant, XDR: extensively-drug resistant

**Table-3.** Factors affecting survival time in Pandemic Cohort.

	$\beta$	S.E.	Wald Statistics	$p$	HR	95% C.I. for HR	
						Lower	Upper
<b>Vasopressors</b>							
No (Ref)							
Present	-2,460	0,342	51,744	<b>&lt;0,001</b>	0,085	0,044	0,167
<b>SOFA score</b>	0,103	0,034	9,113	<b>0,003</b>	1,109	1,037	1,186

SOFA: sequential organ failure assesment

**Table-4.** Comparisons according to COVID-19 wave dates in the pandemic cohort.

Variables	Wave				$p$
	1	2	3	4	
<b>Number of hospitalizations, weekly</b>	6 (5)	3 (4)	3.5 (3.7)	4 (2)	0.347
<b>Mortality, n(%)</b>					0.297
Alive	52 (80)	68 (72.3)	19 (67.9)	36 (83.7)	
Deceased	13 (20)	26 (27.7)	9 (32.1)	7 (16.3)	

## DISCUSSION

In our retrospective single-center cohort study, in which non-COVID-19 patients hospitalized from the emergency department to the internal medicine ICU before and during the pandemic period were evaluated, we observed that the number of intensive care patient admissions remained similar despite the decrease in non-surgical emergency department admissions. Mortality and overall survival time during ICU admission was similar between the two cohorts. In addition, four waves of the pandemic period were evaluated and no difference in mortality rates was observed.

Many studies have reported a decrease in emergency department visits (1-4, 22, 23). However, with the similar number of ICU hospitalizations between the two cohorts despite the decrease in patient admissions in our country, our study has revealed the need for non-COVID-19 ICU during the COVID-19 pandemic.

In the current study median age was higher in the pandemic cohort, no significant difference was determined in gender. Among comorbidities; there was a significant increase in COPD frequency. This particularly is a result of the fact that Pulmonary ICU in our hospital was assigned for the critically ill Covid-19 patients. CAD frequency significantly reduced in the pandemic cohort, possibly as a result of the decrease in the

rate of admissions for acute medical conditions (24). Our results were compatible with the current literature in terms of comorbidities and demographic characteristics in our country (13, 14). However; in a population-based cohort study comparing the first 4 months of the pandemic cohort with the pre-pandemic cohort, preexisting cardiovascular comorbidities were fewer in the pandemic cohort (9). These different outcomes may be due to different inclusion periods in the studies.

ICU mortalities and length of ICU stay have been reported in many different studies. Among these, from Austria, ICU mortality and median length of stay was similar compared between pre-pandemic and pandemic cohort (11). Leafloor et al reported an increase in all-cause in-hospital mortality in ICU patients without COVID-19 infection but there was no different in ICU length of stay (9). Butt et al reported shorter length of stay but there was not a change in in-hospital mortality rate in COVID-19 vs. pre-COVID-19 era (25). Among studies reported from Turkey, the length of ICU stay (14) and the rate of mortality increased (13) during the pandemic period. The cause of increased mortality in reported studies are multifactorial; including different baseline characteristics, severity of illness, fewer admissions, fear of contracting COVID-19, lack of ICU beds for non-COVID-19 patients (9). In our study, ICU length of stay and mortality was

similar between the two cohorts. Although emergency department admissions decreased, there was not a decrease in ICU admissions due to rational use of ICU beds.

In our study, major diagnosis on ICU admission was similar with the leading cause sepsis in both cohorts. Admissions with ESRD decreased significantly in the pandemic cohort. AKI frequency during hospitalization significantly increased, while acute hemodialysis requirement was similar. On discharge, frequency of patients included in routine hemodialysis program increased significantly. The reason for the increase in the number of patients discharged from ICU on the dialysis program was thought to be delayed dialysis preparations due to failure of patients to attend routine outpatient clinic controls. Other countries have reported different clinical outcomes for various conditions. Bologheanu et al reported sepsis as the major medical diagnosis (11), while it was circulatory system in a research reported by Watanabe et al (10) and Butt et al reported increased admissions for respiratory tract infections (25). Among studies from Turkey, major diagnosis category in non-surgical conditions was respiratory system diseases (13). AKI among non-COVID-19 patients during pandemic were researched by Singh et al and in-hospital mortality was reported as 42% and the leading cause of AKI was sepsis (26). Dialysis requirement was 47.5% during ICU stay in the same study which is remarkably higher than our results. The reason may be related with patient characteristics; our ICU does not include post-surgery, multitrauma and acute cardiovascular diseases admissions. SOFA score and need for vasopressors were not different in pre-pandemic and pandemic period,

but when compared with survivors and non-survivors in the pandemic period, need for vasopressor and SOFA score were associated with worse survival.

Finally, we compared mortality according to wave dates and found no difference. Watanabe et al also reported that in-hospital mortality of non-COVID-19 ICU patients did not change during the waves (10). Bord et al reported high mortality during the first lockdown compared with the second and the third (16). When compared with pre-pandemic period, mortality was increased during the first wave in Spain; these patients were older, with longer hospital stay and increased disease severity (15). Our results particularly show that the in-hospital outcomes were not affected by the accessibility of ICU beds.

This study had some limitations. Firstly, it is retrospective and single study. Secondly, due to small number of subgroups we could not compare the mortality according to admission diagnosis. Finally, trauma and post-surgical patients are not hospitalized in our ICU, this study only involved medical ICU patients.

## CONCLUSION

In conclusion, due to decreased number of emergency department admissions, our ICU admissions did not decrease. We believe that adequate treatment in the ICU was readily available and the time to treatment was not longer than usual. It is necessary to provide routine health care delivery during pandemics.

**Conflict of interest:** The authors declare that they have no conflict of interests.

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