

## Do thromboembolic events increase in the emergency department during COVID-19 era?

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### ABSTRACT

**Objectives:** In this study, we aimed to investigate whether thromboembolic events increased in the emergency department (ED) setting due to asymptomatic carriers.

**Patients and methods:** This single-center, retrospective study included a total of 40,633 patients who were admitted to ED after the first case of COVID-19 in Turkey, between 11 March 2020 and 26 May 2020 and the corresponding dates in 2019. The number of patients and demographic and clinical characteristics were compared between the two years for cardiovascular surgery (CVS)-related venous and arterial thromboembolism events.

**Results:** Emergency department admissions requiring CVS consultations decreased by 41.6% from 77 patients in 2019 to 45 patients in 2020. Total CVS consultations over the 11-week period per 1,000 ED admissions increased from 2.9 to 3.2. The number of deep vein thrombosis decreased from 14 to 9 during pandemic, while there was no significant difference in weekly cases of venous thrombosis. The number of arterial thromboembolism cases was 11 in 2019 and six in 2020. Weekly arterial thromboembolism admissions were not significantly different between the two years.

**Conclusion:** Our study results showed that the rate of thromboembolic events did not increase in the general population admitted to the ED during the first 11 weeks of the COVID-19 pandemic in Rize province of Turkey.

**Keywords:** Arterial thromboembolism, COVID-19, deep vein thrombosis, SARS-CoV2, thrombosis, venous thromboembolism.

Since its emergence in December 2019 in Wuhan, China, the novel coronavirus 2019 (severe acute respiratory syndrome coronavirus-2 [SARS-CoV-2]) has spread worldwide causing a pandemic. As of June 1<sup>st</sup>, more than six million cases were diagnosed across the world.<sup>[1]</sup> Mainly presenting with pneumonia of varying severity, clinicians were challenged with the wide range of clinical spectrum with which the COVID-19 is associated, pursuing to battle the public health emergency and understand it at the same time. Typical symptomatology of COVID-19 includes fever, cough, and shortness of breath.<sup>[2,3]</sup> Limiting diagnosis and screening to these symptoms overlooks many cases with COVID-19 as an estimated 30 to 50% of all infected individuals transmitted the disease with no or atypical symptoms, including but not limited to gastrointestinal, neurological, and cardiovascular complaints.<sup>[4]</sup>

Recent observations have revealed that, in hospitalized patients with COVID-19 infection, venous and arterial thrombotic events are frequent,

even in low-risk and anticoagulated patients.<sup>[5-7]</sup> Deep vein thrombosis and pulmonary embolism, coronary and limb ischemia complicate the course of the disease. Both COVID-19 infection itself, the inflammatory response in severe cases, and the drug-drug interactions in the admitted patients with underlying risk factors can predispose to thrombosis.<sup>[8]</sup> Due to this predisposition and the risk of drug-drug interactions, low-molecular-weight heparin or unfractionated heparin is recommended for prophylaxis in all patients without a contraindication for COVID-19.<sup>[9]</sup> However, it is still unclear whether COVID-19 itself directly plays a role in thromboembolism or the immune system response to the infection with varying

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scale has thrombotic effects, and patients with no evident respiratory symptoms may be affected by the prothrombotic changes.

In the present study, we aimed to investigate whether thromboembolic events increased in the emergency department (ED) setting due to asymptomatic carriers in the COVID-19 era.

## PATIENTS AND METHODS

This single-center, retrospective study included a total of 40,633 patients who were admitted to ED after the first case of COVID-19 in Turkey, between 11 March 2020 and 26 May 2020 and the corresponding dates in 2019 in Rize province. All patients with ED admissions throughout the study were included. Pediatric patients with <18 years of age were excluded. Patients consulted to the cardiovascular surgery (CVS) department for any cause were classified as CVS-related admissions. Data including demographic and clinical characteristics of the patients, diagnoses and comorbidities were recorded. A written informed consent was obtained from each patient. The study protocol was approved by the Recep Tayyip Erdoğan University Training and Research Hospital Ethics Committee and the Republic of Turkey, Ministry of Health. The study was conducted in accordance with the principles of the Declaration of Helsinki.

All lower and upper extremity deep vein thrombosis, and central venous thrombosis were classified as venous thrombosis. Upper and lower limb arterial thromboembolisms (ATEs) were classified as arterial thrombosis. Cerebral venous thrombosis, stroke, or acute coronary syndrome cases were excluded, as they were not consulted to the CVS department. Aortic dissections included all types of acute aortic dissections, and aortic aneurysms included all aortic aneurysms of any location with or without rupture. Vascular traumas included isolated vascular injuries or multi-trauma with vascular injuries.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS version 25.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were expressed in mean  $\pm$  standard deviation (SD) or median (min-max), while categorical variables were presented in number and percentage. The chi-square test was used to analyze categorical variables, while the Student's t-test was used to analyze normally distributed continuous

**Table 1**  
Emergency Department Admissions between March 11-May 26 of 2019 and 2020

	2019			2020			<i>p</i>	
	n	Median	Mean $\pm$ SD	IQR	n	Median		Mean $\pm$ SD
Emergency department admissions								
All admissions	26,698				13,935			
Admissions per week	2,270			2167-2327.5	1,027			918.5-1332
Cardiovascular surgery consultations	77				45			
CVS consultations		2.9						
CVS consultations/1,000 ED admissions			7.1 $\pm$ 3.2			3.2		4.0 $\pm$ 1.9
Weekly CVS consultations			3.1 $\pm$ 1.3					3.5 $\pm$ 1.4
Weekly CVS consultations/1,000 ED admissions								
CVS related hospitalizations								
Emergent CVS hospitalizations	24				19			
Emergent CVS hospitalizations/1,000 ED admissions	2	0.90			1	1.36		
Weekly emergent CVS hospitalizations				2-3				1-2.5
Weekly emergent CVS hospitalizations/1,000 ED admissions			1.0 $\pm$ 0.5					1.5 $\pm$ 1.2

SD: Standard deviation; IQR: Interquartile range; CVS: Cardiovascular surgery; ED: Emergency department.

**Table 2**  
Presenting Diagnoses of Cardiovascular Surgery-related Emergency Department Admissions

	2019			2020			<i>p</i>
	n	Median	IQR	n	Median	IQR	
Emergency CVS diagnoses							
Venous thrombosis	14			9			
Venous thrombosis per week		1	0-2		1	0-1.5	0.519
Arterial thromboembolism	11			6			
Arterial thromboembolism per week		1	0.5-1.5		0	0-1	0.193
Acute aortic dissections	3			2			
Aortic aneurysm	5			8			
Vascular trauma	25			13			

IQR: Interquartile range; CVS: Cardiovascular surgery.

variables. Non-normally distributed variables were compared using the Mann-Whitney U test. A *p* value of <0.05 was considered statistically significant.

## RESULTS

Throughout the study period, there were 26,698 ED admissions in 2019 and 13,935 ED admissions in 2020. Details on ED admissions are presented in Table 1. Considering all ED admissions per week, there was a decrease in weekly ED admissions in 2020 (1,027 vs. 2,270,  $p < 0.001$ ). The ED admissions requiring CVS consultations decreased by 41.6% from 77 patients in 2019 to 45 patients in 2020. Total CVS consultations per 1,000 ED admissions increased from 2.9 to 3.2. Similarly, the mean total CVS consultations per week decreased (7.09 vs. 4.00,  $p = 0.013$ ), although this decrease was likely caused by the drop in total admissions as the mean total CVS-related admissions per 1,000 ED admissions increased (3.08 vs. 3.47,  $p = 0.496$ ), indicating no statistical significance.

In addition, CVS-related hospitalizations decreased from 24 patients in 2019 to 19 patients in 2020. In contrast, the ratio of CVS-related hospitalizations per 1,000 ED admissions increased from 0.90 in 2019 to 1.36 in 2020. Weekly CVS-related hospitalizations per 1,000 ED admissions increased from 1.00 to 1.46, indicating no statistical significance.

All CVS admissions were classified according to the presenting pathology (Table 2). Total cases of deep vein thrombosis decreased from 14 to 9 during the study, and there was no significant difference in weekly cases of venous thrombosis. Concerning

ATE, the number of cases was 11 in 2019, whereas six patients had ATE during the same period in 2020. Weekly arterial thrombosis admissions were not significantly different between 2019 and 2020.

All ED admissions in 2019 and 2020 were compared for comorbidities (Table 3). Among all patients consulted to CVS, there were fewer cases with chronic renal failure in 2020 (2.2% vs. 15.6%,  $p = 0.030$ ), while there were no significant differences in other comorbidities. Venous thrombosis patients and ATE patients in 2019 and 2020 showed no significant difference for documented comorbidities. In total, there were three cases of aortic dissection in 2019 and two cases in 2020. The number of patients consulted for aortic aneurysm with or without rupture was five in 2019 and eight in 2020. A major cause of CVS consultations was vascular trauma in 25 cases in 2019 and in 13 cases in 2020.

## DISCUSSION

In this single-center study, the rate of thrombotic diseases did not increase in the general population as evidenced by ED admissions during the COVID-19 era, compared to the same period in the previous year. In addition, there was no significant difference in the number of venous and arterial thrombotic cases between the two years.

Our hospital serves a city of approximately 350,000 population. Within one week of the first COVID-19 case in Turkey, patients suspected of COVID-19 infections were diagnosed in the study hospital. The ED was arranged in accordance with the Republic of

**Table 3**  
Patient demographics in emergency department admissions during COVID-19 era

	2019 (n=77)			2020 (n=45)			p
	n	%	Mean±SD	n	%	Mean±SD	
<b>CVS related admissions (n=122)</b>							
Age (year)			59.2±18.1			64.6±19.8	0.127
Diabetes mellitus	2	2.6		1	2.2		1.000
Hypertension	35	45.5		23	51.1		0.546
Coronary artery disease	9	11.7		6	13.3		0.789
Congestive heart failure	3	3.9		6	13.3		0.054
Chronic renal failure	12	15.6		1	2.2		0.030
Malignancy	5	6.5		2	4.4		1.000
Atrial fibrillation	2	2.6		2	4.4		0.625
<b>Venous thrombosis (n=23)</b>							
			2019 (n=14)			2020 (n=9)	
Age (year)			62.9±20.7			72.0±18.1	0.243
Diabetes mellitus	0	0		0	0		
Hypertension	6	42.9		5	55.6		0.552
Coronary artery disease	2	14.3		0	0		0.502
Congestive heart failure	1	7.1		2	22.2		0.538
Chronic renal failure	2	14.3		0	0		0.502
Malignancy	4	28.6		1	11.1		0.611
Atrial fibrillation	0	0		0	0		
<b>Arterial thromboembolism (n=17)</b>							
			2019 (n=11)			2020 (n=6)	
Age (year)			73.7±19.6			76.3±8.1	0.756
Diabetes mellitus	1	9.1		0	0		1.000
Hypertension	6	54.5		4	66.7		0.627
Coronary artery disease	1	9.1		3	50.0		0.099
Congestive heart failure	1	9.1		1	16.7		1.000
Chronic renal failure	1	9.1		0	0		1.000
Malignancy	0	0		0	0		
Atrial fibrillation	0	0		0	0		

SD: Standard deviation; CVS: Cardiovascular surgery.

Turkey, Ministry of Health guidelines, with suspected COVID-19 patients examined in an area separate from the other ED admissions. If a patient carried the COVID-19, but did not show any infectious or respiratory symptoms, they would be unaware of their infection and might have presented with other atypical symptoms, and such cases would not be initially suspected of COVID-19. There are reported cases of COVID-19 presenting with venous thrombotic events or stroke and subsequently being diagnosed with COVID-19.<sup>[10,11]</sup> We believe that such cases would

result in more ED admissions for thrombotic events during the pandemic, but failed to show an increase in thrombotic events in the ED of the study center.

Most reports of venous or arterial thrombosis in COVID-19 patients are based on patients with a severe course of infection and in the intensive care unit (ICU) setting.<sup>[12-15]</sup> However, not all thrombotic events related to COVID-19 were associated with ICU requirement, and severe arterial or venous thromboembolism (VTE) were detected in patients with milder symptoms<sup>[5,6,16-18]</sup> or even as presenting

symptoms.<sup>[10,19]</sup> It is likely that the risk of thrombosis is high in severe cases and low in mild or asymptomatic cases. As the patients with CVS-related admissions did not present with typical symptoms of COVID-19 and they were not tested for the novel coronavirus, the number of COVID-19 infections among this patient group may be undetermined.

There was a drop in the absolute number of total ER admissions during the COVID-19 era. Self-isolation, stay-at-home orders by the government, or fear of contracting the virus at the hospital may have prevented patients from seeking emergency care. Despite the drop in total ED admissions, there was an insignificant increase in the number of CVS-related admissions. The demographic factors were overall not different between the two years, except for chronic renal failure which was less frequent in 2020; therefore, the lack of increase in thrombotic events cannot be attributed to the differences in comorbidities. It is possible that patients with more severe symptomatology opted to seek emergency care during the pandemic and patients with mild symptoms of any cause did not admit to the ED. Due to similar reasons, some minor VTE or ATE may not have reached the hospital due to fears of leaving the house or waiting in the hospital. Italy is one of the European countries with the largest impact of COVID-19 and the association with thrombosis notwithstanding, admissions for acute coronary syndrome reduced in all parts of the country.<sup>[20]</sup> Likewise, recorded cases of strokes diminished in a neurological center in Italy during the March.<sup>[21]</sup> The prominent explanation in both cases in Italy and our case is the fear of contact with the virus, while seeking medical attention for other causes. It is a point of concern that some patients with minor thrombotic disease, such as a distal deep vein thrombosis or a mild new-onset claudication may wait, until the pandemic recedes to seek medical attention and their disease may complicate the course of treatment.

The main limitation of this study is its retrospective design and insufficient data collection. Another limitation is that our study was conducted in a single state hospital serving a city of a relatively small population. Although the study hospital is the largest in the city, there could be patients admitted to smaller distant hospitals and, therefore, not included in the study. Thus, further studies from larger cities or multi-center studies are needed to confirm our results.

In conclusion, the rate of thromboembolic events did not increase in the general population admitted to the ED during the first 11 weeks of the COVID-19 pandemic in Rize province of Turkey. However, further studies from other centers are needed to determine whether thromboembolic events tend to increase due to mild or asymptomatic cases of COVID-19.

#### Declaration of conflicting interests

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