RESEARCH ARTICLE

Evaluation of patients diagnosed with thromboembolism in the emergency department before and during the Covid-19 pandemic

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ABSTRACT

Background: A new coronavirus known as severe acute respiratory syndrome coronavirus 2 spread rapidly in late 2019 and caused a worldwide pandemic. Due to the pandemic, people are hesitant to go to the hospital and they move much less compared to normal life, which has caused new health problems to emerge.

Aims: This study aimed to examine the demographic characteristics of patients who admitted to the emergency department due to thromboembolic events before and during the COVID-19 pandemic in our country, and to investigate the effect of the pandemic on thromboembolic events. As a result, it was aimed to determine the effects of the COVID-19 pandemic on thromboembolic events and hospital admissions.

Methods: Patients with a thromboembolic event detected between July 01,2019-December 31, 2019 were classified as Group I, and patients with a thromboembolic event detected between July 01,2019- December 31, 2020 were classified as Group II. A total of 859 patients over the age of 18, who had no previous comorbidities, not pregnant, and were hospitalized and treated due to thromboembolic events were included in the study. 447 of these patients were in group I and 412 were in group II. Only 20 (4.9%) of the patients in Group II had a history of previous Covid 19 infection.

Results: It was observed that there was no significant difference in the comparison of the number of cases of thromboembolic events seen in Group I and Group II (p = 0.536). When looking at the distribution of diseases by month, a significant difference was detected in 2019 (mostly in October)(p=0.006,Chi Square: 59.844), while there was no significant difference in Group II (p=0.503,Chi square:34.263).

Conclusion: From the period after the beginning of the pandemic, we saw that the rate of hospitalization due to thromboembolic event was 4% less than in the same period of the previous year. We think that this may be due to fewer hospital admissions due to the risk of disease transmission during the pandemic period, or the fact that Covid 19 infection does not significantly increase the susceptibility to thrombosis.

Keywords: Covid-19, emergency medicine, pandemic, thromboembolism.

Introduction

A new coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spread rapidly in late 2019 and caused a worldwide pandemic. This new respiratory infectious disease was first diagnosed in Wuhan, Hubei Province, China, in December 2019[1]. This disease spread from Asia to Europe and America in a short time period and was declared as a "Pandemic" by the World Health Organization (WHO) on March 11, 2020[2]. In Turkey, the first case was announced by the Ministry of Health of the Republic of Turkey on March 10, 2020[3].

It is believed that there is a high risk of thrombosis in both the arterial and venous systems associated with COVID-19 infection. It has been reported that especially patients who are followed up in intensive care units have a higher risk of thrombotic complications and death.. It has also been stated that COVID-19 infection has an impact on the development of pulmonary embolism (PE) and deep vein thrombosis (DVT)[4,5].

Atherosclerosis and ischemic stroke are known as diseases that were caused by multiple pathophysiological factors, including cardiac and vascular pathologies. It is thought that COVID-19 infection also affects this pathophysiological condition and increases the tendency to thrombosis[6]. In a study, it was stated that COVID-19 infection increases the risk of myocardial ischemia and ischemic stroke[7]. Although it is more common in ischemic stroke, it has been observed that it affects especially elderly individuals and individuals with serious infections and comorbid diseases (hypertension (HT), diabetes mellitus (DM) and coronary artery disease (CAD))[8].

The mechanism of thromboembolism, ischemia and stroke development in individuals with COVID-19 infection is not yet fully understood. Hypercoagulability developing due to systemic inflammatory response, cytokine storm, and endothelial inflammation secondary to coronavirus infection seems to be responsible in the etiology[9,10]. In a prospective cohort study[11], it was found that

1.1% of patients with positive COVID-19 infection experienced a thromboembolic event within one year.

Due to the pandemic, people are hesitant to go to the hospital and they move much less compared to normal life, which has caused new health problems to emerge. While one of the risk factors for thromboembolism is a sedentary lifestyle, it is thought that people not leaving their homes during the Covid-19 pandemic may cause an increase in such pathologies. Another risk factor is the covid 19 infection itself. It is also known that people who have had the infection are more prone to thromboembolic events than other people.

This study aimed to examine the demographic characteristics of patients who admitted to the emergency department due to thromboembolic events before and during the COVID-19 pandemic in our country, and to investigate the effect of the pandemic on thromboembolic events. As a result, it was aimed to determine the effects of the COVID-19 pandemic on thromboembolic events and hospital admissions.

Methods

This study was conducted among patients with thromboembolic events who admitted to the second level adult emergency department, between July 01, 2019- December 31, 2019 (when the COVID-19 pandemic had not yet started), and July 01, 2020- December 31, 2020, (when the COVID-19 pandemic was at its most severe). Ethics committee approval was received for the study from Nevşehir Hacı Bektaş Veli University Rectorate Scientific Clinical Research Ethics Committee (decision number 2021.09.320 on 25/08/2021).

Patients with a thromboembolic event detected between July 01, 2019- December 31, 2019 were classified as Group I, and patients with a thromboembolic event detected between July 01, 2020- December 31, 2020 were classified as Group II. Therefore, patients who were admitted to the emergency department with a thromboembolic event before the COVID-19 pandemic were

included in Group I, while patients who had a thromboembolic event during the COVID-19 pandemic were included in Group II. Percutaneous transcoronary angiography was used for the diagnosis of acute coronary syndrome, while computed tomography and magnetic resonance imaging were used for the diagnosis of ischemic stroke, color Doppler ultrasonography for the diagnosis of deep vein thrombosis, and color Doppler ultrasonography as well as computed tomography angiography were used for the diagnosis of acute arterial occlusion.

A total of 1748 patients diagnosed with thromboembolic events were identified within the specified date ranges of 2019 and 2020. However, 889 patients who had a history of previous thromboembolic events, were pregnant, had underlying diseases that increase the risk of thromboembolism, such as cancer, etc., were excluded from the study.A total of 859 patients over the age of 18, who had no previous comorbidities, not pregnant, and were hospitalized and treated due to thromboembolic events were included in the study. 447 of these patients were in group I and 412 were in group II. Only 20 (4.9%) of the patients in Group II had a history of previous or current Covid 19 infection. Since the largest number of patients in both groups were those presenting with acute coronary syndrome, these patients were also classified separately for each group. Patients presenting with ischemic stroke, pulmonary thromboembolism, deep vein thrombosis and acute arterial occlusion were also evaluated separately in both groups. In order to investigate the seasonal effect on thromboembolic events, subgroups were also evaluated in terms of admission month.Patients hospitalized with a diagnosis of myocardial infarction (MI) were divided into two groups as non-ST segment elevation (NSTEMI) and acute ST segment elevation (STEMI) (inferior, anterior, lateral and posterior wall MI) according to electrocardiogram (ECG) and percutaneous transcoronary intervention (PCI) results. All patients diagnosed with acute coronary syndrome underwent percutaneous transcoronary angiography.All patients in Group I had positive COVID-19 polymerase chain reaction (PCR) tests. The time period between the COVID-19 diagnosis date and the thromboembolic event date of these patients was determined and recorded in the study form.

Data collection and statistical analysis

Data scanned retrospectively using hospital information management system records were recorded in the previously created study form. Statistical Package for Social Sciences for Windows 21.0 (SPSS 21.0 IBM Corp., Armonk, NY, USA) program was used in the statistical analysis of the data obtained. Chi-square test were used to compare categorical variables and descriptive statistics (frequency, percentage distribution) between two groups. 'T test' analysis was performed to compare two independent groups. Results are presented as mean ± SD or frequency (percentage), and $p < 0.05$ at the 95 percent confidence interval was considered statistically significant.

Results

A total of 859 patients, 447 from Group I and 412 from Group II, were evaluated in the study. 577 (67.2%) of the patients were male, and the average age of all patients was 67.82±13.14 years. In cases with STEMI, inferior MI (42.7%) and anterior MI (13.9%) were most frequently diagnosed according to ECG findings. Demographic characteristics and diagnoses of the patients according to groups are shown in Table 1. When the patients in Group I and Group II were compared among themselves in terms of gender, thromboembolic events were significantly higher in male patients in both groups (Group I; $p < 0.05$, Chi square: 25.632, Group II; $p < 0.05$, Chi square : 31.999). In the comparative analysis made according to age ranges, it was determined that the diseases were significantly more common in the 61-80 age group in Group I ($p < 0.05$, Chi Square: 53.863) and Group II ($p < 0.05$, Chi Square: 54.479) (Table 2).

Table 1. Demographic data

Year	Mean±SD	Group I Mean±SD	Group II Mean±SD	p**
Age	67,82±13,14	67,87± 13,70	67,76±12,52	0,904
Gender	n / (%)		n / (%)	
Male	577 (67,2)	290 (64,9)	287 (69,7)	0,136
Female	282 (32,8)	157 (35,1)	125 (30,3)	
Diagnosis*				
NSTEMI	367 (42,7)	207 (46,3)	160 (38,8)	
Inferior MI	119 (13,9)	58 (13)	61 (14,8)	
Anterior MI	106 (12,3)	51 (11,4)	55 (13,3)	
Lateral MI	13 (1,5)	6 (1,3)	7 (1,7)	
Posterior MI	12 (1,4)	7 (1,6)	5 (1,2)	0,097
Pulmonary Thromboembolism	10 (1,2)	6 (1,3)	4 (1)	
Ischemic stroke	226 (26,3)	109 (24,4)	117 (28,4)	
Deep Vein Thrombosis	3 (0,3)	3 (0,7)	0 (0)	
Peripheral Artery Embolism	3 (0,3)	0 (0)	3 (0,7)	
Total	859 (100)	447 (100)	412 (100)	0,536

*MI: Myocardial infarction, NSTEMI: Non-ST elevation myocardial infarction

** T test was used to compare independent variables and p<0.05 was considered significant.

Table 2. Comparative analysis of demographic data

Data* / Diagnosis	Group I Male n (%)	Female n (%)	Statistical Analysis**	21-40 n (%)	41-60 n (%)	61-80 n (%)	81-100 n (%)	Statistical Analysis**	Group II Male n (%)	Female n (%)	Statistical Analysis**	21-40 n (%)	41-60 n (%)	61-80 n (%)	81-100 n (%)	Statistical Analysis**
NSTEMI	132 (63,8)	75 (36,2)		6 (2,9)	64 (30,9)	99 (47,8)	38 (18,4)		120 (75)	40 (25)		2 (1,2)	51 (31,8)	87 (54,5)	20 (12,5)	
İnferior MI	49 (84,5)	9 (15,5)		2 (3,4)	19 (32,8)	30 (51,7)	7 (12,8)		47 (77)	14 (33)		1 (1,7)	19 (31,1)	36 (59)	5 (8,2)	
Anterior MI	39 (76,5)	12 (23,5)		1 (2)	17 (33,3)	30 (58,8)	3 (5,9)		45 (81,8)	10 (18,2)		0 (0)	26 (47,2)	21 (38,1)	8 (14,7)	
Lateral MI	4 (66,7)	2 (33,3)	p<0,05 Chi square:25.632	0 (0)	1 (16,7)	5 (83,3)	0 (0)	p<0,05 Chi square: 53.863	6 (15,7)	1 (14,3)	p<0,05 Chi square: 31.999	0 (0)	3 (42,8)	4 (57,2)	0 (0)	P<0,05 Chi square:54.479
Posterior MI	3 (42,9)	4 (57,1)		0 (0)	2 (18,6)	4 (57,1)	1 (14,3)		5 (100)	0 (0)		0 (0)	4 (80)	1 (20)	0 (0)	
PTE	1 (16,7)	3 (83,3)		1 (16,7)	1 (16,7)	3 (50)	1 (16,7)		1 (25)	3 (75)		0 (0)	0 (0)	4 (100)	0 (0)	
Ischemic stroke	61 (56)	48 (44)		2 (1,8)	19 (17,4)	45 (41,3)	43 (39,4)		61 (52,1)	56 (47,9)		2 (1,7)	13 (11,1)	68 (58,1)	34 (29,1)	
DVT	1 (33,3)	2 (66,7)		1 (33,3)	0 (0)	1 (33,3)	1 (33,3)		0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)	
PAE	0 (0)	0 (0)		0 (0)	0 (0)	0 (0)	0 (0)		2 (66,7)	1 (33,3)		0 (0)	0 (0)	3 (100)	0 (0)	
TOPLAM	290 (64,9)	157 (35,1)		13 (2,9)	123 (27,5)	217 (48,5)	94 (21,1)		287 (69,7)	125 (30,3)		5 (1,2)	116 (28,2)	224 (54,4)	67 (16,2)	

*NSTEMI: Non-ST elevation myocardial infarction, MI: Myocardial Infarction, PTE: Pulmonary Thromboembolism, DVT: Deep Vein Thrombosis, PAE: Peripheral Artery Embolism

** Pearson chi-square test was used to compare the data. p<0.05 was considered significant within the 95% confidence interval.

It was observed that there was no significant difference in the comparison of the number of cases of thromboembolic events seen in Group I and Group II (p = 0.536). When looking at the distribution of diseases by month, a significant difference was detected in 2019 (mostly in October) (p=0.006 Chi Square: 59.844), while there was no significant difference in Group II (p=0.503, Chi square: 34.263). Figure 1 and 2 show case distributions in terms of months in both years.
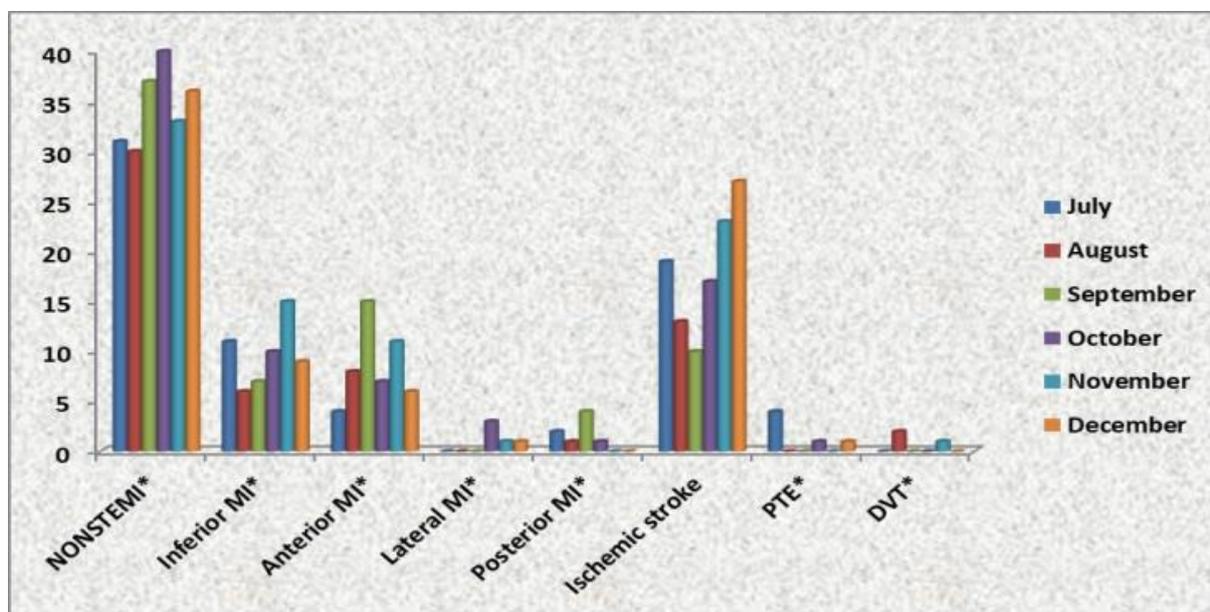

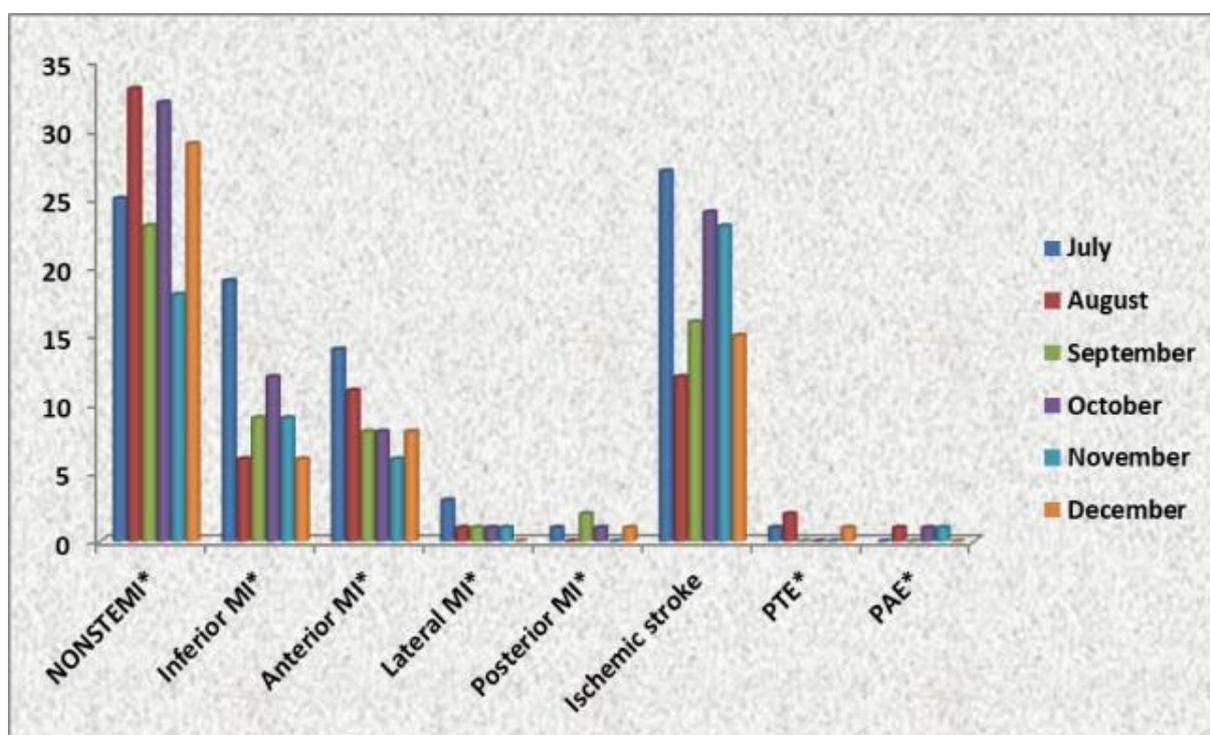**Figure 1.** Distribution of patients admitted in 2019 by months

Figure 2. Distribution of patients admitted in 2020 by months

Only 20 (4.8%) of the patients in Group II had a history of COVID-19 disease before thromboembolic event. It was determined that NSTEMI (35%) was the most common in these patients. The average age of the patients was 71.2±9.26, and 70% were male. The average duration of thromboembolic event after COVID-19 infection was found to be 27±26.94 (1-90) days. The most cases were seen in December (40%) (Table 3).

Table 3. Analysis of Patients with Thromboembolic event Following COVID-19 Infection

Number	Thromboembolic event	Age	Gender	Time period (Day)*	Month of sdmission
1	Ischemic stroke	91	Male	90	July
2	Inferior MI	76	Male	14	September
3	Anterior MI	71	Male	21	September
4	Anterior MI	76	Female	36	October
5	Inferior MI	61	Male	7	October
6	Anterior MI	55	Male	18	October
7	Inferior MI	81	Male	23	October
8	Ischemic stroke	77	Male	12	November
9	Ischemic stroke	70	Male	44	November
10	NSTEMI**	74	Male	15	November
11	NSTEMI**	63	Female	63	November
12	Anterior MI	69	Male	79	November
13	Ischemic stroke	70	Female	1	December
14	NSTEMI**	78	Male	4	December
15	NSTEMI**	57	Male	62	December
16	NSTEMI**	73	Male	16	December
17	Anterior MI	81	Female	1	December
18	NSTEMI**	70	Female	3	December
19	Ischemic stroke	71	Male	28	December
20	NSTEMI*	70	Male	3	December

*Time period between diagnosis of COVID-19 Infection and development of thromboembolic event

** Non-ST elevation myocardial infarction

Discussion

Thrombosis that develops due to COVID-19 disease can affect more than one system in the body and cause thromboembolic events, whether of arterial or venous origin[12]. Some studies conducted in Western countries have reported a decrease in hospitalizations due to acute cardiovascular diseases such as AMI and stroke during the COVID-19 pandemic[13,14]. In this study, we analyzed thromboembolic events before COVID-19 disease was seen in our country and after the disease appeared. However, we found that there was no significant difference in terms of thromboembolic events between the data of 2019 and 2020 (p = 0.536). While previous studies[6-8] have reported that the COVID-19 pandemic increases the susceptibility to thromboembolic events, the fact that no significant difference was found in our study suggests the need for a re-evaluation on this issue.

In a retrospective study conducted at Nihon Hospital in Japan[15], patients diagnosed with AMI in the same time period in 2017, 2019 and 2020 were analyzed and it was reported that there was a 5.7% decrease in the number of patients during the pandemic period. Within the same study, it was observed that there was an increase in the number of STEMI and a decrease in the number of NSTEMI during the pandemic period compared to previous years[15]. In a similar study conducted in Korea, a 13.5% decrease was observed in the number of patients hospitalized with AMI during the pandemic period compared to the pre-pandemic period, and it was reported that the reason for this decrease was the 18.8% decrease in patients with NSTEMI[16]. In our study, the NSTEMI patient rate was 46.3% in 2019 and 38.8% in 2020. While the rate of patients with STEMI was 27.3% before the pandemic, this rate increased to 31% in the same period of 2020 during the pandemic. We think that this situation may be related to the hesitation to admit to the hospital due to the pandemic. It is not yet clear whether a direct thrombosis effect of COVID-19 infection is effective in the development of acute MI[17]. In a study, it was reported that

complaints such as atypical chest pain and shortness of breath, which were among the symptoms of AMI in patients during the pandemic, were considered as symptoms of COVID-19 and the preference for recovery at home caused many patients with AMI to be diagnosed late[18]. This situation can be considered as the reason why NSTEMI cases are more common during the pandemic period. In our study, unlike the literature, the higher frequency of inferior myocardial infarctions among STEMI myocardial infections is another significant result. We believe that more comprehensive studies investigating the effects of Covid-19 infection on cardiac vessels may help explain this situation.

The second most common thromboembolic event in our study was ischemic stroke. When Group II data was examined, it was seen that 5(0.4%) of 117 patients diagnosed with ischemic stroke ha a history of COVID-19 infection in a period before the disease. In a study conducted during the pandemic, it was reported that the hospitalization rate due to acute ischemic stroke in patients with COVID-19 was estimated to be around 5%[19]. In other studies, it has been predicted that the probability of experiencing an ischemic stroke in patients receiving standard thromboprophylaxis may vary between 1-3%[20-22]. According to a meta-analysis evaluating the analysis results of 26 studies on the subject, the rate of ischemic stroke in those with COVID-19 infection is 1.5% and varies between 0.1% and 6.9% among hospitalized patients[6]. In a multicenter, observational study, it was determined that 0.5% of 26,175 patients hospitalized due to COVID-19 infection had a risk of ischemic stroke, and 79 (0.3%) of these patients were diagnosed with ischemic stroke[23].

In the study conducted by Qureshi et al., 27,676 patients were analyzed and 103 (1.3%) of 8163 COVID-19 positive patients and 199 (1%) of 19513 COVID-19 negative patients were diagnosed with ischemic stroke[24]. In our study, the rate of ischemic stroke during the pandemic period was 4% higher than the previous year, but there was no significant difference in the number of cases between the two periods (p = 0.429). Therefore, it is not possible to say that there is a clear correlation between Covid 19 infection and the risk of developing ischemic stroke. It was observed that the ischemic stroke cases seen before and during the pandemic were more common in male gender and in the age range of 61-80. In the study conducted by Qureshi et al., it was stated that the majority of cases with ischemic stroke were over the age of 70[24]. In the same study, it was stated that among patients with ischemic stroke, 55.3% of those who were COVID-19 negative and 44.7% of those who were positive were male[24]. In our study, 80% of the patients who had ischemic stroke after COVID-19 were male. The fact that this rate is significantly high shows that infection significantly increases the susceptibility to ischemic stroke, especially in the male gender. We think that future large-scale studies on the reasons for this will provide more accurate results. Moreover, some studies in the literature have reported that COVID-19 infection is a predisposing factor for the risk of ischemic stroke[9,25,26].

Porfidia et al. stated that in their systematic review and meta-analysis; they found that the probability of venous thromboembolism (VTE) in patients with COVID-19 was between 6-26%[27]. In a study conducted with a retrospective analysis of 388 patients in Italy, the VTE rate was found to be 20% despite the routine use of low molecular weight heparin (LMWH) in patients diagnosed with COVID-19 over a two-month period[20]. According to the results of a single-center study, the PE rate in patients with this infection admitted to intensive care unit was 26.6[28]. In another study conducted in France, it was observed that 20.6% of patients with COVID-19 who were followed up in intensive care during a one-month period had PE, and a higher rate of PE cases was reported, with an increase of 7.5% compared to the previous year[29]. In our study, while the rate of cases hospitalized with a diagnosis of PE was 1.3% before the COVID-19 pandemic, only a 1% increase in this rate was detected during the pandemic period. We think that successful

thromboprophylaxis may be effective in this situation. Similarly, while the frequency of DVT was 0.7% before the pandemic, no patient was hospitalized with a diagnosis of DVT during the pandemic.

Studies have found that the incidence of arterial thromboembolism (ATE) is much lower than VTE. It has been reported that the rate of these cases in all embolic events, including acute coronary syndrome, ischemic stroke, mesenteric ischemia and extremity ischemia, varies between 0.7% and 3.7 %[20,21,29]. In a single-center study conducted in Madrid, 1419 COVID-19 patients were examined and the incidence of ATE was found to be 1%[30]. In our study, the frequency of ATE (98.5%) in patients hospitalized due to thromboembolic event was found to be quite high compared to VTE (1.5%). In a study, the incidence of acute extremity ischemia in COVID-19 patients was found to be 16.3% higher than in negative patients in cases seen in January, February and March in 2019 and 2020[31]. We think that this high rate may be due to the fact that COVID-19 infection damages the arterial system much more than the venous system through unknown mechanisms.

Conclusion

From the period after the beginning of the pandemic, we saw that the rate of hospitalization due to thromboembolic event was 4% less than in the same period of the previous year. We think that this may be due to fewer hospital admissions due to the risk of disease transmission during the pandemic period, or the fact that COVID-19 infection does not significantly increase the susceptibility to thrombosis.

Conflict of Interest:

The authors have no conflicts of interest to declare.

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