








RESEARCH
ARTICLE

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Evaluation of Lower Extremity Venous Doppler Ultrasonography Outcomes Before and After The COVID-19 Pandemic; A Retrospective Study**ABSTRACT**

Objective: COVID-19 test positivity has been reported among asymptomatic individuals and asymptomatic people are also considered to be at risk for thromboembolic events. The aim of this study was to compare the results of patients who underwent lower extremity Doppler ultrasonography (DUS) with a preliminary diagnosis of deep vein thrombosis (DVT) before and after the pandemic, regardless of COVID-19 testing.

Method: Patients who underwent RDUS in the Department of Radiology during a total period of 35 months (01/08/2018 - 01/07/2021) were analyzed. A total of 599 patients underwent RDUS during the study period.

Results: More positive DVT findings were observed after the pandemic (n=43, 18.3%, p=0.005) (only two of these patients had a positive COVID-19 result). History of hospitalization in the last three months, D-dimer, Platelet (PLT) count, Mean platelet volume (MPV), White blood cell (WBC) count, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR) values, comorbidity and antiaggregant use were not different (p>0.05).

Conclusion: Even individuals (especially elderly individuals) who have been exposed to the virus during the pandemic but who do not show symptoms are at risk of DVT.

Keywords: COVID-19, Deep Vein Thrombosis, Doppler Ultrasonography.

COVID-19 Pandemisi Öncesi ve Sonrası Alt Ekstremitte Venöz Doppler Ultrasonografi Sonuçlarının Değerlendirilmesi; Retrospektif Bir Çalışma**ÖZET**

Amaç: COVID-19 testi pozitifliği asemptomatik bireyler arasında bildirilmiştir ve asemptomatik kişilerin de tromboembolik olaylar için risk altında olduğu düşünülmektedir. Bu çalışmanın amacı, COVID-19 testinden bağımsız olarak, pandemi öncesi ve sonrasında derin ven trombozu (DVT) ön tanısıyla alt ekstremitte Doppler ultrasonografisi (DUS) yapılan hastaların sonuçlarını karşılaştırmaktır.

Yöntem: Toplam 35 aylık süre boyunca (01/08/2018 - 01/07/2021) Radyoloji Bölümünde RDUS yapılan hastalar analiz edildi. Çalışma dönemi boyunca toplam 599 hastaya RDUS yapılmıştır.

Bulgular: Pandemi sonrasında daha fazla pozitif DVT bulgusu gözlenmiştir (n=43, %18,3, p=0,005) (bu hastaların yalnızca ikisinde pozitif COVID-19 sonucu vardı). Son üç ay içinde hastaneye yatış öyküsü, D-dimer, platelet (PLT), ortalama platelet hacmi (MPV), (lökosit sayısı) WBC, nötrofil sayısı, lenfosit sayısı, nötrofil/ lenfosit oranı (NLR) değerleri, komorbidite ve antiagregan kullanımı farklı değildi (p>0.05).

Sonuç: Pandemi sırasında virüse maruz kalan ancak semptom göstermeyen bireyler (özellikle yaşlı bireyler) bile DVT riski altındadır.

Anahtar Kelimeler: COVID-19, Derin Ven Trombozu, Doppler Ultrasonografi.

INTRODUCTION

The COVID-19 pandemic caused by a new type of coronavirus called SARS-CoV-2 has been effective all over the world since the first months of 2020 (1,2). The first case was seen in our country on 11/03/2020. Infected individuals may be asymptomatic or may have clinical presentations ranging in severity from upper respiratory tract disease such as fever, dry cough, fatigue, sore throat to lower respiratory tract infection that can progress to ARDS (3,4).

It is known that COVID-19 infection causes coagulation abnormalities and leads to thromboembolic events and this contributes to morbidity and mortality related to the disease (5). Polymerase chain reaction (PCR), which is the gold standard diagnostic method during the pandemic period, cannot be performed in every center and some patients may not apply to health institutions because they are asymptomatic (3). As up to 30% PCR positivity has been reported among asymptomatic individuals (6,7), asymptomatic patients are also considered to be at risk for thromboembolic events (8).

Based on this information, in this study, analyses were performed independently of the COVID-19 PCR test. The aim of this study was to compare the results of patients who underwent lower extremity Doppler ultrasound (DUS) with a prediagnosis of deep vein thrombosis (DVT) in our hospital before and after the pandemic.

MATERIALS AND METHODS

The study was planned retrospectively in the emergency department of a tertiary hospital. Ethics committee approval was obtained from local ethic committee (Decision no: 2022/147 Date: 03/20/2022).

Patients who underwent RDUS in the Department of Radiology during a total period of 35 months (01/08/2018 - 01/07/2021) were analyzed. A total of 599 (annual average of 205.4) patients underwent RDUS during the study period. The data of 12 of these patients could not be accessed and were excluded from the study.

Patients; RDUS result (positive or negative for DVT), age, gender, history of hospitalization in the last three months, Covid PCR test result (checked for post-pandemic patients), laboratory tests [D-dimer, Platelet (PLT) count, Mean platelet volume (MPV), White blood cell (WBC) count, neutrophil count, lymphocyte count, neutrophil/lymphocyte ratio (NLR)], comorbid diseases, antiaggregant and anticoagulant use were questioned.

Patients' d-dimer values (<0.5, 0.5-1, >1), PLT counts (<50,000, 50,000-150,000, 150,000-450,000, >450,000), MPV values (<6, 6-9, 9-11 and >11), WBC values (<10, 000 and >10,000), lymphocyte counts (<1000, 1000-5000 and >5000),

neutrophil counts (<1000, 1000-8000 and >8000) and NLR values (<5 and >5).

Statistical Analysis: Descriptive statistics were presented as number and percentage. Demographic data were presented as Mean, Standard Deviation (SD), Median, IQR. Pearson chi-square test and Fisher's exact test (when the expected number was less than five) were used for independent categorical variables. Bonferroni correction was used for subgroup analyses and $p < 0.016$ was considered significant. Mc Nemar test was used for dependent categorical variables. Student-t test was used for numerical two-group variables with normal distribution. Mann Whitney U test was used for numerical two-group variables that did not show normal distribution. Statistical analyses were performed using SPSS software for Windows, version 23 (IBM, Chicago, IL, United States of America). $P < 0.05$ was considered significant.

RESULTS

A total of 587 patients were included in the study. Of these, 235 (40%) came after the pandemic, COVID-19 test results were obtained in a total of 70 (29.8%) patients, 9 (12.9%) of whom had positive COVID-19 test results. The majority of patients (52.9%) were male, the mean age was 61.19 ± 18.55 years, and right lower extremity venous doppler was requested the most (29.7%).

The mean age was higher after the pandemic (63.60 ± 17.222) ($p = 0.013$). Gender distribution was not different between the two periods ($p = 0.273$). More DVTs were observed after the pandemic ($n = 43$, 18.3%, $p = 0.005$) and only two of these patients had a positive COVID-19 PCR result. History of hospitalization in the last three months, D-dimer, PLT, MPV, WBC, neutrophil count, lymphocyte count, NLR values, comorbidity and antiaggregant use were not different ($p > 0.05$). After the pandemic, it was determined that DUS was requested more frequently in patients who did not use anticoagulants ($n = 40$, 17%, $p = 0.02$) (Table 1).

DISCUSSION

DVT describes unstable and excessive clotting that occurs most commonly in the popliteal vein, femoral vein and pelvic iliac veins and grows towards the heart, which is the direction of blood flow (9). Risk factors include; Reduced blood flow (conditions that cause prolonged immobilization such as bed rest, general anesthesia, surgeries, stroke, long journeys), increased venous pressure (neoplasm, pregnancy, stenosis), direct injury to the vein (trauma, surgery, peripherally placed venous catheters, intravenous drug use), increased blood viscosity (polycythemia, thrombocytosis, dehydration), genetic defects that create a tendency to coagulation (protein C and S deficiency,

Table 1. Descriptive and comparative data before and after the pandemic

		Period				p
		Pre-pandemic		Post-pandemic		
		n	%	n	%	
Gender	Male	180	51.14	131	55.74	0.273
	Female	172	48.86	104	44.26	
DVT	Yes	36	10.3	43	18.3	0.005
	No	315	89.7	192	81.7	
Hospitalization in the last three months	Yes	47	13.4	20	8.5	0.069
	No	304	86.6	215	91.5	
D-dimer	<0.5	12	18.46	7	8.24	0.162
	0.5-1.0	11	16.92	14	16.47	
	>1.0	42	64.62	64	75.29	
PLT	<50	4	1.47	3	1.37	0.988
	50-150	30	10.99	22	10.05	
	150-450	219	80.22	178	81.28	
	>450	20	7.33	16	7.31	
MPV	<6	0	0.00	2	0.91	0.363
	6-9	200	73.26	157	71.36	
	9-11	64	23.44	56	25.45	
	>11	9	3.30	5	2.27	
WBC	<10000	138	50.55	123	56.68	0.177
	>10000	135	49.45	94	43.32	
Lymphocyte	<1000	67	24.81	56	25.93	0.751
	1000-5000	200	74.07	156	72.22	
	>5000	3	1.11	4	1.85	
Neutrophil	<1000	3	1.11	5	2.31	0.104
	1000-8000	151	55.93	137	63.43	
	>8000	116	42.96	74	34.26	
NLR	<5	143	52.96	126	58.33	0.237
	>5	127	47.04	90	41.67	
Comorbidity	Yes	272	77.3	171	72.8	0.214
	No	80	22.7	64	27.2	
Antiaggregant using	Yes	127	36.7	75	31.9	0.234
	No	219	63.3	160	68.1	
Anticoagulant using	Yes	87	25.1	40	17.0	0.020
	No	259	74.9	195	83.0	

*Bonferroni correction was made for subgroup analyses and $p < 0.016$ was considered significant. DVT: deep vein thrombosis, PLT: Platelet, MPV: Mean platelet volume, WBC: White blood cell, NLR: neutrophil/lymphocyte ratio.

antithrombin III deficiency, factor V Leiden mutation), acquired causes predisposing to clotting (cancer, sepsis, myocardial infarction, heart failure, vasculitis, systemic lupus erythematosus and lupus anticoagulant, Inflammatory bowel disease, nephrotic syndrome, burns, oral estrogens, smoking, hypertension, diabetes, obesity, pregnancy, age over 60, surgery, intensive care hospitalization (9-11). Endothelial damage, hypercoagulability and venous blood stasis (Virchow's triad) play an important role in the pathophysiology of thrombosis (9,12). Damage to the vessel wall leads to pro-inflammatory (and prothrombotic) cytokine production, increase in available tissue factor, proliferation of adhesion molecules and increased platelet activation. These cytokines initiate interactions between leukocytes and endothelial cells that trigger inflammation. Activation of leukocytes and endothelial cells ultimately leads to the formation of adhesion

molecules, which triggers a process that initiates clot formation (9,11,12).

In COVID-19 patients, one of the factors aggravating the disease is the overproduction of inflammatory mediators, defined as a cytokine storm (13,14). In COVID-19 patients, factors such as platelet hyperactivation, increased mean platelet volume, and increased release of P-selectin and E-selectin adhesion molecules on the surface of endothelial cells are thought to be involved in vascular occlusive events that increase in the course of the disease (14-16). Occlusive vascular events are thought to be both complications and aggravating factors, including the measures taken.

PCR test positivity in patients admitted to hospital with COVID-19 symptoms ranges from 0.005% to 39.7% (6,17,18). COVID-19 PCR test positivity in asymptomatic patients varies according to the prevalence of the disease in the community (1-30%) (7,19). Asymptomatic and symptomatic

individuals are also thought to have a higher risk for vascular phenomena (8). This suggests that vascular events such as DVT may increase in the community, although it is almost impossible to know the number of asymptomatic individuals.

In a meta-analysis of 63 studies including 104920 COVID-19 positive patients, the rate of deep vein thrombosis was found to be 20%, pulmonary embolism 8% and arterial thrombosis 5% (10). In this study, the prevalence of deep vein thrombosis was found to be high especially in elderly patients ($P<0.05$) (10). In another review, 42 studies were evaluated, the prevalence of DVT was found to be 0.43-60.87% in COVID-19 positive cases and it was pointed out that DVT was a factor worsening the COVID-19 clinic (11). Based on the available data, this study was planned with the idea that there are infected but asymptomatic individuals who have encountered the virus during the COVID-19 pandemic and that these individuals are at risk for DVT and will increase the incidence of DVT. In our study, more positive findings (18.3%) were observed in DUS results obtained after the

pandemic. Only two of these patients (2/43) had positive COVID-19 PCR results. Exposure to the virus may have caused the increase in DVT positivity, which was 10.3% before the pandemic, as well as staying at home more and moving less as part of the precautions.

LIMITATIONS

The limitations of the study are that it was a single center, the number of patients was small, and there was insufficient information about the mobilization status of the patients. In addition, the fact that fewer patients underwent DUS in the post-pandemic period and the mean age was higher may suggest that patient selection was more sensitive.

CONCLUSION

After the COVID-19 pandemic, more DVT findings were observed in lower extremity DUS results evaluated independently of the PCR test. This result suggests that even individuals (especially elderly individuals) who have been exposed to the virus during the pandemic but who do not show symptoms are at risk of DVT.

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