HİTİT MEDICAL JOURNAL
HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

e-ISSN: 2687-4717 Cilt|Volume: 7 • Sayı|Issue: 2 - Haziran|June 2025

Relationship Between Atherogenic Indices and Cardiovascular Thromboembolic Events in Patients with Covid-19 Pneumonia

COVID-19 Pnömonili Hastalarda Aterojenik İndeksler ile Kardiyovasküler Tromboembolik Olaylar Arasındaki İlişki

Hakan Kilci [1] | Adem Melekoğlu[2] | Güneş Melike Doğan[1] | Mutlu Çağan Sümerkan[1] Özgür Selim Ser[1] | Ertuğrul Altınbilek[2]

[1]University Of Health Sciences, İstanbul Şişli Hamidiye Etfal Health Research Center, Department of Cardiology, Istanbul, Türkiye
[2]University Of Health Sciences, İstanbul Şişli Hamidiye Etfal Health Research Center, Department of Emergency, Istanbul, Türkiye

Sorumlu Yazar | Correspondence Author
Hakan Kilci
drkilci@gmail.com
Address for Correspondence: University of Health Sciences, İstanbul Şişli Hamidiye Etfal Health Research Center, Department of Cardiology, 34396 Istanbul, Türkiye.

Makale Bilgisi | Article Information
Makale Türü | Article Type: Araştırma Makalesi | Research Article
Doi: https://doi.org/10.52827/hititmedj.1594744
Geliş Tarihi | Received: 17.12.2024
Kabul Tarihi | Accepted: 21.05.2025
Yayım Tarihi | Published: 23.06.2025

Atıf | Cite As
Kilci H, Melekoğlu A, Doğan GM, Sümerkan MÇ, Ser ÖS, Altınbilek E. Relationship Between Atherogenic Indices and Cardiovascular Thromboembolic Events in Patients with Covid-19 Pneumonia. Hitit Medical Journal 2025;7(2):227-234. https://doi.org/10.52827/hititmedj.1594744

Hakem Değerlendirmesi: Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
Etik Beyanı: Bu çalışma Şişli Hamidiye Etfal Eğitim ve Araştırma Hastanesi yerel etik kurulu tarafından 3227 numaralı protokolle onaylandı.
İntihal Kontrolleri: Evet (iThenticate)
Çıkar Çatışması: Yazarlar çalışma ile ilgili çıkar çatışması beyan etmemiştir.
Şikayetler: hmj@hitit.edu.tr
Katkı Beyanı: Fikir/Hipotez: HK, AM Tasarım: HK, AM Data Collection/Data Processing: HK, GMD, ÖSS Veri Analizi: HK, AM, MÇS Makalenin Hazırlanması: HK, EA
Hasta Onamı: Gerek yoktur.
Finansal Destek: Bu çalışma ile ilgili herhangi bir finansal kaynaktan yararlanılmamıştır.
Telif Hakı & Lisans: Dergi ile yayın yapan yazarlar, CC BY-NC 4.0 kapsamında lisanslanan çalışmalarının telif hakkını elinde tutar.
Bilgi: Bu çalışma 2021 Kardiyovasküler Akademi Kongresi'nde sözlü bildiri olarak sunulmuştur.

Peer Review: Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
Ethical Statement: This study was approved by the local ethics committee of Sisli Hamidiye Etfal Training and Research Hospital with protocol No. 3227.
Plagiarism Check: Yes (iThenticate)
Conflict of Interest: The authors declared that, there are no conflicts of interest.
Complaints: hmj@hitit.edu.tr
Authorship Contribution: Idea/Hypothesis: HK, AM Design: HK, AM Data Collection/Data Processing: HK, GMD, ÖSS Data Analysis: HK, AM, MÇS Manuscript Preparation: HK, EA
Informed Consent: Not applicable.
Financial Disclosure: There are no financial funds for this article.

İnformation: This study was presented as an oral presentation in Cardiovascular Academy Congress 2021.

Relationship Between Atherogenic Indices and Cardiovascular Thromboembolic Events in Patients with COVID-19 Pneumonia

ABSTRACT

Objective: COVID-19, caused by coronavirus SARS-CoV-2, is a pandemic viral respiratory infection in which venous and arterial thromboembolic events are often observed. This study aimed to investigate the relationship between atherogenic indices and cardiovascular thromboembolic events in patients with COVID-19 pneumonia.

Material and Method: In this retrospective study, a total of 805 inpatients (median age 63 [IQR: 52-74] years; 45.1% female) who were diagnosed with COVID-19 pneumonia between March 2020 and December 2020 were evaluated. Patients were divided into two groups based on cardiovascular thromboembolic events with cardiovascular thromboembolic events (n=96) and without-cardiovascular thromboembolic events (n=709). All clinical and demographic data and laboratory results were analyzed. Atherogenic Index of Plasma (AIP (log10 (triglyceride/ HDL)), Atherogenic Coefficient (AC (HDL/ non-HDL)), Risk Index of Castelli-I (CRI-I (Total cholesterol/ HDL)), and Risk Index of Castelli-II (CRI-II (LDL/ HDL)) were calculated.

Results: Atherogenic Coefficient, CRI-I, and CRI-II values were significantly higher in the cardiovascular thromboembolic event group (*p=0.001*, *p=0.001*, *p=0.007*, respectively). AIP values were higher in the cardiovascular thromboembolic events group but were not statistically significant (*p=0.051*). In the cardiovascular thromboembolic events group, HDL values were found to be significantly lower (*p=0.001*), but CRP and D-dimer values were found to be significantly higher (*p<0.001*, *p=0.006*, respectively). In the multivariable analysis, Atherogenic Coefficient (OR: 1.294, 95% CI: 1.089-1.1537, *p=0.003*), D-dimer, Hypertension, and current smoking were found to be independent predictors of cardiovascular thromboembolic events in patients with COVID-19 pneumonia.

Conclusion: Atherogenic indices could be used to predict cardiovascular thromboembolic events in patients with COVID-19 pneumonia.

Keywords: Atherogenic indices, cardiovascular events, COVID-19 pneumonia.

ÖZET

Amaç: Koronavirüs SARS-CoV 2'nin neden olduğu COVID-19, venöz ve arteriyel tromboembolik olayların sıklıkla görüldüğü pandemik bir viral solunum yolu enfeksiyonudur. Bu çalışma COVID-19 pnömonili hastalarda aterojenik indeksler ile kardiyovasküler tromboembolik olaylar arasındaki ilişkiyi araştırmayı amaçlamıştır.

Gereç ve Yöntem: Bu retrospektif çalışmaya Mart 2020 ile Aralık 2020 arasında COVID-19 pnömonisi tanısı alan toplam 805 yatan hasta (ortanca yaş 63 [IQR: 52-74] yıl; %45,1 kadın) dahil edildi. Hastalar kardiyovasküler tromboembolik olaylara göre kardiyovasküler tromboembolik olay olanlar (n=96) ve kardiyovasküler tromboembolik olay olmayanlar (n=709) olarak iki gruba ayrıldı. Tüm klinik ve demografik veriler ve laboratuvar sonuçları analiz edildi. Çalışmaya dahil edilen hastalarda Plazmanın Aterojenik İndeksi (AIP (Log10 (trigliserit / HDL)), Aterojenik Coefficient (AC (HDL / HDL olmayan)) Castelli-I Risk İndeksi (CRI-I (Total kolesterol / HDL)), Castelli-II Risk İndeksi (CRI-II (LDL / HDL)) hesaplanmıştır.

Bulgular: Aterojenik Coefficient, CRI-I ve CRI-II değerleri kardiyovasküler tromboembolik olay grubunda istatistiksel anlamlı derecede yüksek saptandı (sırasıyla *p=0,001*, *p=0,001*, *p=0,007*). Kardiyovasküler tromboembolik olaylar grubunda AIP değerleri daha yüksekti ancak istatistiksel olarak anlamlı değildi (*p=0,051*). Kardiyovasküler tromboembolik olaylar grubunda HDL değerleri istatiksel olarak anlamlı derecede düşük bulundu (*p=0,001*), CRP ve D-dimer değerleri ise istatiksel olarak anlamlı olarak yüksek bulundu (sırasıyla *p<0,001*, *p=0,006*). Çok değişkenli analizde COVID-19 pnömonili hastalarda Aterojenik Coefficient (OR: 1,294, %95 CI: 1,089-1,1537, *p= 0,003*), D-dimer, Hipertansiyon ve mevcut sigara içiminin kardiyovasküler tromboembolik olayların bağımsız öngördürücüleri olduğu saptandı.

Sonuç: Bu çalışmanın sonuçları COVID-19 pnömonili hastalarda kardiyovasküler tromboembolik olayları tahmin etmek için aterojenik indeksler kullanılabileceğini göstermektedir.

Anahtar Sözcükler: Aterojenik indeksler, COVID-19 pnömonisi, kardiyovasküler olaylar

Introduction

In recent years, a new coronavirus infection called COVID-19, caused by the coronavirus SARS-CoV-2, has created a pandemic and caused severe morbidity and mortality all over the world. Clinical findings of the infection may be asymptomatic, mild upper respiratory disease, mild pneumonia, or severe pneumonia, which causes respiratory insufficiency syndrome. Coagulation disorders and related complications are also frequently observed both in the autopsy studies performed and in the patients who were hospitalized and followed up due to COVID-19 (1–3). It has been reported that D-dimer values, a marker of hypercoagulation, are often increased in this infection and are associated with poor outcomes, especially in those with severe disease (4,5).

The association of adverse complications with the severity of the disease was also found at a high rate. Inflammation also plays a vital role in the pathogenesis of atherosclerosis and thrombosis. Due to severe inflammation of COVID-19 infection, endovascular damage might play a crucial role in the occurrence of acute myocardial infarction, stroke, pulmonary embolism, and venous thrombosis. It has been reported that pulmonary embolism, myocardial infarction, and stroke, which are fatal thromboembolic events, are frequently observed during the disease and are associated with a large majority of deaths due to COVID-19 in inpatient and outpatient patients (6–9). So, many societies have made notifications recommending antithrombotic agents in appropriate patient groups (10,11).

Some studies suggested that cardiovascular disease, hypertension, diabetes mellitus, and other cardiovascular risk factors are associated with the severity of the COVID-19 infection and related mortality and morbidities (9,12). Dyslipidemia is one of the significant risk factors for cardiovascular diseases such as myocardial infarction, stroke, peripheral vascular disease, etc. Increasing serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-c), triglycerides (TG) values, and a decrease in high-density level (HDL-c) cholesterol values are well-known associated with cardiovascular disease (13,14). Recent studies suggested that some atherogenic indices, such as the atherogenic index of plasma (AIP), atherogenic coefficient (AC), and risk index of Castelli-I and II (CRI-I and II), could be used for identifying cardiovascular disease and thromboembolic events (15,16).

In this study, we aimed to investigate the link between atherogenic indices and cardiovascular thromboembolic events in patients with COVID-19 pneumonia.

Material and Method

In this retrospective study, hospitalized patients diagnosed with COVID-19 pneumonia by laboratory and thoracic computed tomography in the emergency department between March 2020 and December 2020 were included. Patients older than 18 years who did not receive lipid-lowering therapy and whose lipid profile was studied at hospitalization were determined as the inclusion criteria.

After the criteria for inclusion in the study, the data of a total of 805 patients were analyzed. Patients were divided into two groups: those who had cardiovascular thromboembolic events during in-hospital follow-up and those who did not have cardiovascular thromboembolic events. Cardiovascular thromboembolic events were defined as acute coronary syndrome, stroke, pulmonary embolism, and/or deep vein thrombosis.

All biochemical and hematological parameters and demographic characteristics of the patients during hospitalization were recorded from the hospital database. Demographic characteristics of the patients, comorbid diseases, and biochemical tests, which were the measurements of C-reactive protein (CRP), D-dimer, and standard lipid profile, were also recorded. The lipid profiles included triglyceride (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), and low-density lipoprotein cholesterol (LDL-c). The atherogenic coefficient (AC; non-HDL-c/HDL-c), risk index of Castelli-I (CRI-I; TG/HDL-c), risk index of Castelli-II (CRI-II; LDL-c/HDL-c), and atherogenic index of plasma (AIP; logarithm TG/HDL-c) were calculated by utilizing lipid parameters.

This study was approved by the local ethics committee on 27/04/2021 with protocol No. 3227.

Statistical Analysis

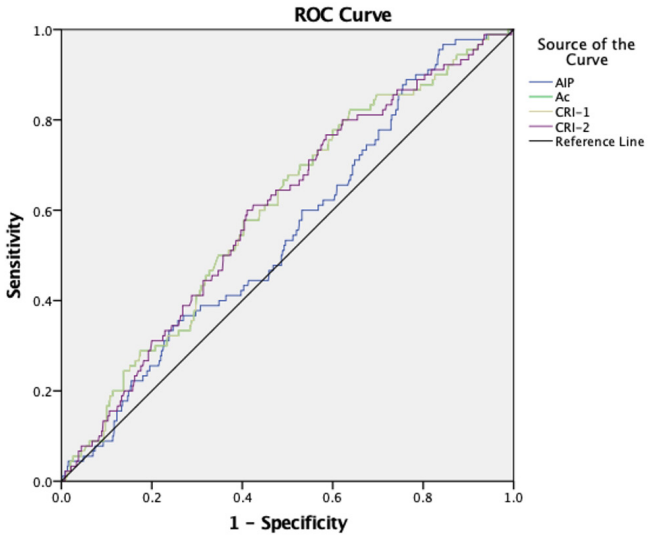
Statistical analysis of the data was performed in

SPSS program, version 22.0 (IBM, Armonk, NY, USA). The Kolmogorov-Smirnov test was used to check the normal distribution of continuous variables. Mean (±SD) and median (IQR) were used for quantitative variables, and the number of patients (percentage) was used for qualitative variables. Continuous variables were compared between groups using an independent-sample T-test or the Mann–Whitney U test, as appropriate. Categorical data were compared using the Chi-square or Fisher's Exact test. The univariable and multivariable logistic regression analyses were used to determine the risk factors affecting cardiovascular thromboembolic events. The evaluation of atherogenic indices as a predictive factor for cardiovascular thromboembolic events was performed using predicted probability curves and diagnostic accuracy assessments based on receiver operating characteristic (ROC) analysis. A value of *p<0.05* was considered statistically significant.

Results

A total of 805 patients (363 female, 45.1%) diagnosed with COVID-19 pneumonia were analyzed. The baseline demographic, clinical, and laboratory characteristics of the study population are listed in Table I. The median age of the patients was 63 [IQR: 52-74 years]. A total of 76 patients were identified with cardiovascular thromboembolic events (acute coronary syndrome, stroke, pulmonary emboli, and/or VTE) in-hospital follow-up. The distribution of patients who experienced a cardiovascular thromboembolic event is as follows: 23 patients had acute coronary syndrome, two patients had both acute coronary syndrome and stroke, three patients had deep vein thrombosis, four patients had both deep vein thrombosis and pulmonary embolism, six patients had pulmonary embolism, two patients had both stroke and pulmonary embolism, 36 patients had strokes. No significant difference was observed among patients with and without cardiovascular thromboembolic events group in terms of diabetes mellitus, sex, eGFR, previous history of coronary artery disease, chronic renal failure, and malignancy. Patients in the cardiovascular thromboembolic events group were older than the without-cardiovascular thromboembolic events group (63 (51-74) vs. 68 (57-80), *p=0.012*). Hypertension, atrial fibrillation, current smoking, chronic obstructive pulmonary disease (COPD), and previous history of stroke were significantly higher in the cardiovascular thromboembolic events group. In lipid parameters, HDL-c values were significantly low in the cardiovascular thromboembolic events group (*p=0.001*), but total cholesterol, LDL-c, and TG values were similar between the two groups. AC, CRI-I and CRI-II were found statistically significant when comparing cardiovascular thromboembolic events and without-cardiovascular thromboembolic events groups (4.00 (3.18-4.88) vs.3.47 (2.62-4.43), *p=0.001*; 5.00 (4.18-5.88) vs. 4.48 (3.62-5.43), *p=0.001*; 3.09± 0.96 vs. 2.78 ±1.03, *p=0.007*, respectively). However, AIP was higher in the cardiovascular thromboembolic events group than in the non-cardiovascular thromboembolic events group (0.23±0.24 vs. 0.17±0.25), but the p-value was found to be *0.051*. In addition, the CRP and D-dimer were also found to be statistically significant in patients who developed cardiovascular thromboembolic events (102 (28-183) vs. 150 (64-229), *p=0.002*; 869 (494-1627) vs. 1290 (585-2803), *p=0.006*, respectively).

Figure I. Receiver operating characteristic graphic to detect the best cut-off values of AC, CRI-I, CRI-II, and AIP for cardiovascular thromboembolic events development.



In the univariable logistic regression analysis (Table II), AC, age, D-dimer, current smoking, hypertension, CRP, CRI-I, and CRI-II were associated with cardiovascular thromboembolic events (*p=0.001; p=0.03; p=0.018; p<0.001; p=0.007; p=0.005; p=0.002; p=0.008,* respectively). Multivariable logistic regression analysis (Table 2) showed that AC was an independent predictor of cardiovascular

thromboembolic events (OR: 1.294, 95% CI: 1.089-1.1537, *p=0.003*). Current smoking, hypertension, and D-Dimer were also independent predictors of cardiovascular thromboembolic events (OR:6.113, 95% CI: 3.510-10.649, *p< 0.001;* OR:1.852, 95% CI: 1.078-3.179, *p=0.026*, and OR: 1.000077, 95% CI: 1.000013-1.000140, *p=0.018*, respectively).

Table I. Clinical, Demographic, and Laboratory Characteristics of the Study Group According to Cardiovascular Thromboembolic Events in Patients with COVID-19 Pneumonia

Variables	Total n=805	Without-cardiovascular thromboembolic events n=709	Cardiovascular thromboembolic events n=96	*p value*
Age, years	63 (52-74)	63 (51-74)	68 (57-80)	*0.012*
Female, n (%)	363 (45.1)	325 (45.8)	38 (39.6)	*0.248*
Diabetes Mellitus, n (%)	300 (37.3)	260 (36.7)	40 (41.7)	*0.342*
Hypertension, n (%)	406 (50.4)	345 (48.7)	61 (63.5)	*0.006*
Current smoking, n (%)	102 (12.7)	70 (9.9)	32 (33.3)	*<0.001*
Coranary artery diseases, n (%)	173 (21.5)	149 (21)	24 (25)	*0.372*
COPD/Asthma, n (%)	82 (10.2)	62 (8.7)	20 (20.8)	*<0.001*
Chronic renal failure, n (%)	120 (14.9)	112 (15.8)	8 (8.3)	*0.054*
Cerebrovascular diseases, n (%)	62 (7.7)	45 (6.3)	17 (17.7)	*<0.001*
Atrial fibrillation, n (%)	65 (8.1)	52 (7.3)	13 (13.5)	*0.036*
Malignancy, n (%)	104 (12.9)	93 (13.1)	11 (11.5)	*0.649*
eGFR ml/ min/1.73 m^2	77.6± 40.3	76.8 ±40.1	83.9 ±40.9	*0.106*
Total cholesterol, mg/dL	169 (137-204)	169 (137-204)	165 (139-205)	*0.883*
LDL cholesterol, mg/dL	101 (77-131)	102 (77-131)	100 (76-136)	*0.878*
HDL cholesterol, mg/dL	37 (30-46)	38 (31-47)	35 (28-40)	*0.001*
Triglyceride, mg/dL	129 (95-174)	129 (94-174)	125 (95-174)	*0.869*
C-Reactive Protein, mg/L	106 (31-190)	102 (28-183)	150 (64-229)	*0.002*
D-dimer, ng/ml	893 (500-1803)	869 (494-1627)	1290 (585-2803)	*0.006*
Creatinine, mg/dl	0.93 (0.73-1.29)	0.94 (0.74-1.29)	0.86 (0.67-1.30)	*0.156*
Atherogenic index of plasma (AIP)	0.18 ±0.26	0.17 ±0.25	0.23±0.24	*0.051*
Atherogenic coefficient (AC)	3.54 (2.66-4.46)	3.47 (2.62-4.43)	4.00 (3.18-4.88)	*0.001*
Risk Index of Castelli-I	4.55 (3.67-5.46)	4.48 (3.62-5.43)	5.00 (4.18-5.88)	*0.001*
Risk Index of Castelli-II	2.82 ±1.03	2.78 ±1.03	3.09± 0.96	*0.007*

COPD; Chronic obstructive pulmonary disease, eGFR; estimated glomerular filtration rate. HDL-C; High-density lipoprotein-cholesterol, LDL-C; Low-density lipoprotein-cholesterol,

a Data are presented as mean + SD, median (inter-quarter range) or n (%).

ROC analysis showed that the AC value for predicting the development of cardiovascular thromboembolic events was 3.78, with 59.4 % sensitivity and 41 % specificity (area under the ROC curve [AUC] =0.604; 95 % CI: 0.546-0.661; *p=0.001*, figure 1). Regarding ROC assessment, the AUC of the CR-I values was 0.603 (95 % CI: 0.545-0.660; *p=0.001*), and the AUC of the CR-II values was 0.597 (95 % CI: 0.537-0.657; *p=0.003*) (Figure I).

Table II. Univariable and Multivariable Logistic Regression Analysis to Detect The İndependent Predictors Of Cardiovascular Thromboembolic Events in Patients with COVID-19 Pneumonia

Variables	Univariable Analysis			Multivariable Analysis		
	OR	**(95% CI)**	***p value***	**OR**	**(95% CI)**	***p value***
Atherogenic coefficient (AC)	1.286	1.103-1.499	***0.001***	1.294	1.089-1.1537	*0.003*
Age	1.015	1.001-1.029	***0.030***	1.010	0.993-1.027	*0.262*
Gender	0.774	0.501-1.196	*0.249*	1.042	0.635-1.709	*0.872*
D-Dimer	1.000076	1.000013-1.000138	***0.018***	1.000077	1.000013-1.000140	***0.018***
Diabetes Mellitus	1.234	0.800-1.903	*0.343*	0.977	0.595-1.602	*0.925*
Current Smoking	4.564	2.794-7.457	***<0.001***	6.113	3.510-10.649	***<0.001***
Hypertension	1.839	1.183-2.858	***0.007***	1.852	1.078-3.179	***0.026***
C-Reactive protein	1.003	1.001-1.004	***0.005***	1.001	0.999-1.003	*0.189*
Atherogenic index of plasma (AIP)	2.270	0.994-5.186	*0.052*			
Castelli Risk Index I (CRI-I)	1.283	1.100-1497	***0.002***			
Castelli Risk Index II (CRI-II)	1.319	1.075-1617	***0.008***			

Discussion

In this study, we evaluated the association between lipid parameters and cardiovascular thromboembolic events in patients with COVID-19 pneumonia. AC, CRI-I, and CRI-II were independent predictors of the development of cardiovascular thromboembolic events in these patients. We also found that current smoking, hypertension, and D-dimer are independent risk factors for developing cardiovascular thromboembolic events in patients with COVID-19 pneumonia.

COVID-19 pneumonia is a severe viral infection that progresses to acute respiratory failure syndrome and is accompanied by severe inflammation (17,18). It is also well known that severe inflammation

triggers plaque rupture and erosion, especially in atherosclerotic patients with sensitive plaque, triggering fatal diseases such as acute myocardial infarction. It has been reported that early and late follow-up of patients suffering from COVID-19 infection develops conditions that cause severe mortality and morbidity, such as acute myocardial infection, stroke, and arterial and venous thromboembolism (6,9,19,20)the most significant medical challenge in the last century. COVID-19 is associated with notable increases in morbidity and death worldwide. Preexisting conditions, like cardiovascular disease (CVD. Our study found that thromboembolic events developed in about 12% of the patients we followed up with COVID-19 pneumonia. CRP values were statistically significantly higher in patients with an event. Similarly, we found that events occurred at a statistically high rate in those with underlying COPD. These findings suggest that the severity of COVID-19 infection plays a crucial role in the development of cardiovascular thromboembolic events.

In some studies conducted with COVID-19, it has been found that atherosclerotic risk factors are associated with poor outcomes (21,22). Although there was no difference between the groups regarding coronary artery disease in our study, it was found that the patients who had an event were older, hypertensive, and smokers, similar to the recent studies. It has been shown that hypertension and smoking are powerful predictors that independently predict the development of events. This supports the hypothesis of underlying silent atherosclerosis and the development of arterial and venous thromboembolism after the rupture and erosion of existing vulnerable plaques in patients with COVID-19 pneumonia.

COVID-19 infection is usually associated with thrombotic complications in both arterial and venous circulations. Thromboembolism is a common complication in hospitalized patients due to COVID-19 disease and is monitored in about 25-40% (23,24). Abnormal clotting parameters, such as high D-dimer levels, are often encountered in COVID-19 infection, even in patients who do not have apparent signs of thrombus (25). Some studies have also suggested a dynamic relationship between the level of D-dimer and the prognosis of COVID-19 patients and the need for anticoagulation (4,5,26). Potential mechanisms for increased D-Dimer levels in patients with COVID-19 include pulmonary endothelial damage with inflammation-induced intra-alveolar fibrin deposits, systemic endothelial damage with diffuse thrombosis of smaller vessels or larger vessels, and coagulopathy (27).

Some studies have shown that interleukin (IL), CRP, and D-dimer are associated with the severity of COVID-19 disease, and high CRP and D-dimer values are associated with mortality (26,28,29). Again, similarly, high D-dimer and CRP values have been shown to be associated with severe complications in the course of this disease, and it is thought that they can be used as biomarkers to detect hostile terminations in these patient groups (18). In our study, it was also found that CRP and D-dimer levels were significantly higher in the thromboembolic event group that occurred in the patient groups that had COVID-19 pneumonia, which supports the hypothesis.

The endothelium, which plays a fundamental role in ensuring hemostasis, regulating vascular permeability, and regulating the response of blood cells and immunomodulators, might become the target of viral infections that cause severe infection, such as the coronavirus (30). Histopathological studies have shown direct infection of the endothelium with the virus in both arterial and venous circulation, diffuse endothelial infection, and micro- and macrovascular thrombosis. Cytokine storms (IL-6, IL-2, TNF-α), also shown in COVID-19 infections, can also contribute to endothelial dysfunction and leukocyte uptake into the microvascular system. It is also known that endothelial dysfunction plays a significant role in organ dysfunction during viral infections, as it causes an anticoagulant state, microvascular leakage, and organ ischemia (31,32). The leading cause of thrombus formation in the vascular lumen in acute coronary syndrome and stroke is erosion or rupture of vulnerable plaque. The histopathological description of vulnerable plaque includes a lesion rich in lipid content, with a necrotic nucleus with signs of inflammation, including infiltration by macrophages and lymphocytes, with features such as a thin fibrous cap and neovascularization. Endothelial dysfunction is not only the first step of the atherosclerotic process that causes plaque

formation, but it also causes the plaque to grow, crack, and trigger thrombogenic events. As a result of the rupture of the thin fibrous cap on vulnerable plaques, direct contact of circulating blood with the thrombogenic content of the lipid-rich nucleus can lead to rapid activation of the coagulation cascade and acute thrombosis.

Although endothelial dysfunction is one of the most basic mechanisms in the atherosclerotic process, all known atherosclerotic risk factors, such as Dyslipidemia, cause chronic damage to the endothelium, leading to a decrease in vasodilatory response. Dyslipidemia is one of the most critical factors involved in the pathogenesis of atherosclerosis. Epidemiology studies show that increased serum cholesterol levels alone are sufficient for the development of atherosclerosis, even in the absence of other known risk factors.

Various lipoprotein ratios, which are also called atherogenic indices, have been defined in order to optimize the role of the lipid profile on atherosclerosis. Some studies have suggested that atherogenic indicators calculated from the lipid profile predict cardiovascular risk better than lipid parameters alone (33). The atherogenic indices consist of non-HDL cholesterol (NHC), AIP, CRI-I, CRI-II, and AC, which have been shown to be known independent risk factors for cardiovascular risk. Günay et al. suggested that atherogenic indices (AC, AIP, CRI-I, CRI-II) may be helpful in predicting the risk of atherosclerosis and cardiovascular diseases in stable patients with COPD (34). Another study suggested that atherogenic lipid indices were significantly higher in stroke patients compared to controls. NHC, AC, and CRI-I have been shown to contribute considerably to stroke risk (35). Turgay et al. showed that high AIP levels can predict in-hospital mortality for COVID-19 patients. It has also been suggested that AIP can be used as an early biomarker to predict pneumonia, intubation, and intensive care needs (36). Given the results of the above studies, it is not surprising that atherogenic indicators were found to be significantly higher in patients with COVID-19 pneumonia and cardiovascular thromboembolic events in our study.

In conclusion, COVID-19 pneumonia is a type of viral pneumonia that is accompanied by severe inflammation. It is highly likely that severe inflammation triggers thromboembolic events, especially in cardiovascular risk conditions that trigger endothelial dysfunction, such as Dyslipidemia. Early recognition and close monitoring of COVID-19 pneumonia patients with high cardiovascular is essential for preventing thromboembolic events and timely intervention. In our study, it was found that there is a significant association between atherogenic indices and cardiovascular thromboembolic events in patients with COVID-19 pneumonia. According to the results of this study, atherogenic indices such as AC, CRI-I, CRI-II, and AIP can be used for risk assessment in patients with COVID-19 pneumonia. Further studies may be useful both in terms of this relationship between atherogenic indices with cardiovascular thromboembolic events and treatment planning.

References

1. Al-Ani F, Chehade S, Lazo-Langner A. Thrombosis risk associated with COVID-19 infection. A scoping review. Thrombosis Research 2020 Aug;192:152–160.

2. Wichmann D, Sperhake JP, Lütgehetmann M, et al. Autopsy Findings and Venous Thromboembolism in Patients With COVID-19: A Prospective Cohort Study. Annals of Internal Medicine 2020 Aug 18;173(4):268–277.

3. Ribes A, Vardon-Bounes F, Mémier V, et al. Thromboembolic events and Covid-19. Advances in Biological Regulation 2020 Aug;77:100735.

4. Li Y, Zhao K, Wei H et al. Dynamic relationship between D-dimer and COVID-19 severity. Br J Haematol 2020 Jul;190(1):e25-27.

5. Wagner J, Garcia-Rodriguez V, Yu A, et al. Elevated D-Dimer Is Associated with Multiple Clinical Outcomes in Hospitalized Covid-19 Patients: a Retrospective Cohort Study. SN Compr Clin Med 2020 Dec;2(12):2561–2567.

6. Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. The American Journal of Emergency Medicine 2020 Jul;38(7):1504–1507.

7. Chen J, Wu Y, Chen Z et al. High incidence of stroke in COVID-19 patients. Aging 2020 Nov 20; 12(22):22390-22398.

8. Del Prete A, Conway F, Della Rocca DG, et al. COVID-19, Acute Myocardial Injury, and Infarction. Cardiac Electrophysiology Clinics 2022 Mar;14(1):29–39.

9. Magadum A, Kishore R. Cardiovascular Manifestations of COVID-19 Infection. Cells 2020 Nov 19;9(11):2508.

10. Thachil J, Tang N, Gando S, et al. ISTH interim guidance on recognition and management of coagulopathy in COVID-19. Journal of Thrombosis and Haemostasis 2020 May;18(5):1023–

1026.
11. Miesbach W, Makris M. COVID-19: Coagulopathy, Risk of Thrombosis, and the Rationale for Anticoagulation. Clin Appl Thromb Hemost 2020 Jan 1;26:1-7.
12. Medetalibeyoglu A, Emet S, Senkal N, Aydogan M, Kose M, Tukek T. Cardiovascular view of intermediate and high-riskCOVID-19 patients: single-centre experience with lowmortality and intensive care hospitalisation rates. CVJA 2021 Mar 1;32(2):25–32.
13. Di Angelantonio E, Gao P, Pennells L, et al. Lipid-Related Markers and Cardiovascular Disease Prediction. JAMA 2012 Jun 20;307(23):2499-2506.
14. Kim MK, Han K, Kim HS, et al. Cholesterol variability and the risk of mortality, myocardial infarction, and stroke: a nationwide population-based study. European Heart Journal 2017 Dec 21;38(48):3560–3566.
15. Fernández-Macías JC, Ochoa-Martínez AC, Varela-Silva JA, Pérez-Maldonado IN. Atherogenic Index of Plasma: Novel Predictive Biomarker for Cardiovascular Illnesses. Archives of Medical Research 2019 Jul;50(5):285–294.
16. Koca TT, Tugan CB, Seyithanoglu M, Kocyıgıt BF. The Clinical Importance of the Plasma Atherogenic Index, Other Lipid Indexes, and Urinary Sodium and Potassium Excretion in Patients with Stroke. Eurasian J Med 2019 Jun 14;51(2):171–175.
17. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. The Lancet 2020 May;395(10234):1417–1418.
18. Alzoughool F, Alanagreh L, Abumweis S, Atoum M. Cerebrovascular comorbidity, high blood levels of C-reactive protein and D-dimer are associated with disease outcomes in COVID-19 patients. CH 2021 Apr 24;77(3):311–322.
19. Modin D, Claggett B, Sindet-Pedersen C, et al. Acute COVID-19 and the Incidence of Ischemic Stroke and Acute Myocardial Infarction. Circulation 2020 Nov 24;142(21):2080–2082.
20. Kashi M, Jacquin A, Dakhil B, et al. Severe arterial thrombosis associated with Covid-19 infection. Thrombosis Research 2020 Aug;192:75–77.
21. Weiss P, Murdoch DR. Clinical course and mortality risk of severe COVID-19. The Lancet 2020 Mar;395(10229):1014–5.
22. Harrison SL, Buckley BJR, Rivera-Caravaca JM, Zhang J, Lip GYH. Cardiovascular risk factors, cardiovascular disease, and COVID-19: an umbrella review of systematic reviews. European Heart Journal - Quality of Care and Clinical Outcomes 2021 Jun 9;7:330-339.
23. Cui S, Chen S, Li X, Liu S, Wang F. Prevalence of venous thromboembolism in patients with severe novel coronavirus pneumonia. Journal of Thrombosis and Haemostasis 2020 Jun;18(6):1421–1424.
24. Brosnahan SB, Smilowitz NR, Amoroso NE, et al. Thrombosis at hospital presentation in patients with and without coronavirus disease 2019. Journal of Vascular Surgery: Venous and Lymphatic Disorders 2021 Jul;9(4):845–852.
25. Demelo-Rodríguez P, Cervilla-Muñoz E, Ordieres-Ortega L et al. Incidence of asymptomatic deep vein thrombosis in patients with COVID-19 pneumonia and elevated D-dimer levels. Thrombosis Research 2020 Aug;192:23–26.
26. Bosevski M, Krstevski G, Bosevska G, et al. The role of D-dimer in relation to the clinical course of patients with COVID-19. ABBS 2020 Nov 1;53(1):119–120.
27. Valerio L, Ferrazzi P, Sacco C et al. Course of D-Dimer and C-Reactive Protein Levels in Survivors and Nonsurvivors with COVID-19 Pneumonia: A Retrospective Analysis of 577 Patients. Thromb Haemost 2021 Jan;121(01):98–101.
28. Eljilany I, Elzouki AN. D-Dimer, Fibrinogen, and IL-6 in COVID-19 Patients with Suspected Venous Thromboembolism: A Narrative Review. VHRM 2020 Nov;16:455–462.
29. Bannaga AS, Tabuso M, Farrugia A, et al. C-reactive protein and albumin association with mortality of hospitalised SARS-CoV-2 patients: A tertiary hospital experience. Clin Med 2020 Sep;20(5):463–467.
30. Libby P, Lüscher T. COVID-19 is, in the end, an endothelial disease. European Heart Journal 2020 Aug 21;41(32):3038–3044.
31. Pons S, Fodil S, Azoulay E, Zafrani L. The vascular endothelium: the cornerstone of organ dysfunction in severe SARS-CoV-2 infection. Crit Care 2020 Dec;24(1):353.
32. Lin GL, McGinley JP, Drysdale SB, Pollard AJ. Epidemiology and Immune Pathogenesis of Viral Sepsis. Front Immunol 2018 Sep 27;9:2147.
33. Kinosian B. Cholesterol and Coronary Heart Disease: Predicting Risks by Levels and Ratios. Ann Intern Med 1994 Nov 1;121(9):641.
34. Gunay S, Sariaydin M, Acay A. New Predictor of Atherosclerosis in Subjects With COPD: Atherogenic Indices. Respir Care 2016 Nov;61(11):1481–1487.
35. Sujatha R, Kavitha S. Atherogenic indices in stroke patients: A retrospective study. Iran J Neurol 2017 Apr 4;16(2):78–82.
36. Turgay Yıldırım Ö, Kaya Ş. The atherogenic index of plasma as a predictor of mortality in patients with COVID-19. Heart & Lung 2021 Mar;50(2):329–333.