



## Investigation of the Relationship Between Stroke and STEMI in Young and Middle-Aged Patients and COVID-19

Stroke ve STEMI Tanılı Genç ve Orta Yaşlı Hastaların COVID-19 ile İlişkisinin Araştırılması

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### ABSTRACT

**Aim:** In this study, we aimed to elucidate the potential relationship between the COVID-19 pandemic and the increasing occurrence of stroke and ST-segment elevation myocardial infarction (STEMI) in younger individuals, as we have been encountering a growing number of such cases in routine clinical practice.

**Materials and Methods:** This study was conducted on patients aged 50 years or younger who presented to our clinic between January 1, 2024, and December 31, 2024, and were diagnosed with STEMI or stroke. The history of prior COVID-19 infection was evaluated retrospectively. Patients who had a positive Polymerase Chain Reaction (PCR) test or had been clinically and radiologically diagnosed with COVID-19 and received treatment were classified as having a history of COVID-19 positivity (Group I). Patients who did not meet either of these two criteria were classified as having no history of COVID-19 (Group II).

**Results:** A total of 196 patients aged 50 years or younger who were diagnosed with either infarction STEMI or ischemic stroke were included in the study. Patients were classified into two groups based on their history of COVID-19 infection: Group I (COVID-19 positive) and Group II (COVID-19 negative). The distribution of diagnoses between the two groups revealed a statistically significant difference between the rates of ischemic stroke and STEMI ( $p=0.026$ ). Specifically, a higher proportion of patients diagnosed with ischemic stroke were found to have a history of PCR-confirmed COVID-19 infection.

**Conclusion:** This study highlights the importance of considering not only the acute effects of the COVID-19 pandemic but also its potential to increase the risk of stroke in the long term, emphasizing the need for attention to its prolonged impact.

**Keywords:** COVID-19, STEMI, stroke

### ÖZET

**Amaç:** Bu çalışmada, rutin klinik pratikte giderek artan sayıda inme ve ST-segment yükselmeli miyokard enfarktüsü (STEMI) vakasıyla karşılaştığımız genç bireylerde COVID-19 pandemisi ile inme ve ST-segment yükselmeli miyokard enfarktüsü görülme sıklığındaki artış arasındaki olası ilişkiyi aydınlatmayı amaçladık.

**Gereç ve Yöntemler:** Bu çalışma, 01.01.2024 ile 31.12.2024 tarihleri arasında kliniğimize başvuran ve 50 yaş ve altında olan, ST segment elevasyonlu miyokard enfarktüsü veya inme tanısı almış hastalar üzerinde gerçekleştirilmiştir. Hastaların özgeçmişlerinde COVID-19 geçirmiş olma durumları retrospektif olarak değerlendirilmiştir. Dahil edilen hastalardan, Polimeraz Zincir Reaksiyon (PCR) testi pozitif olanlar ya da klinik ve radyolojik bulgularla COVID-19 tanısı alarak tedavi görmüş olanlar “özgeçmişinde COVID-19 pozitif” (Grup I) olarak kabul edilmiştir. Bu iki kriterden herhangi birini karşılamayan hastalar ise “özgeçmişinde COVID-19 negatif” (Grup II) olarak sınıflandırılmıştır.

**Bulgular:** Çalışmaya, 50 yaş ve altı olup iskemik inme veya ST segment elevasyonlu miyokard enfarktüsü (STEMI) tanısı alan toplam 196 hasta dahil edildi. Hastalar, COVID-19 geçirme öyküsüne göre iki gruba ayrıldı: Grup I (COVID-19 pozitif) ve Grup II (COVID-19 negatif). Tanı dağılımı değerlendirildiğinde, gruplar arasında iskemik inme ve STEMI sıklığı açısından istatistiksel olarak anlamlı bir fark saptandı ( $p=0,026$ ). Özellikle, iskemik inme tanısı alan hastalarda PCR ile doğrulanmış COVID-19 öyküsünün daha yüksek oranda bulunduğu gözlemlendi.

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**Cite this article as:** Dursun Yılmaz G, Baykan N, Yıldırım H, Akdağ AYTEKİN R, Toket İ.

Investigation of the Relationship Between Stroke and STEMI in Young and Middle-Aged Patients and COVID-19 JAMER 2025;10(2):28-32.

**Received:** 26.03.2025

**Accepted:** 06.08.2025

**Online Published:** 31.08.2025

**Sonuç:** Bu çalışmayla COVID-19 pandemisinin sadece akut zararlarına değil sonrasında inme olasılığını artırma durumu da göz önüne alınarak uzun dönemdeki etkilerine dikkat edilmesi gerektiği sonucuna varıldı.

**Anahtar Kelimeler:** COVID-19, inme, STEMI

## INTRODUCTION

ST-segment elevation myocardial infarction (STEMI) and stroke are time-sensitive, life-threatening emergencies where treatment timing impacts mortality and recovery (1). ST-segment elevation myocardial infarction results from a ruptured atherosclerotic plaque, triggering thrombus formation and coronary artery occlusion, leading to myocardial necrosis (2). It is defined by ischemic symptoms, electrocardiogram (ECG) ST-segment elevation or new left bundle branch block, and biomarkers of myocardial injury (3). ST-segment elevation myocardial infarction is especially devastating in young patients, highlighting the need for further investigation of its presentation and treatment in this group (4). Stroke in young adults (ages 18–50) accounts for 10-15% of all strokes. A comprehensive evaluation of stroke etiology, including vascular, cardiac, and blood factors, is necessary, along with investigation of less common risk factors (5). Revascularization procedures, such as intravenous thrombolysis and endovascular procedures, are time-dependent, making reduced door-to-needle time critical (6). As of 2 March 2025, there have been 777.594.331 confirmed cases of coronavirus disease 2019 (COVID-19) worldwide, including 7.089.989 deaths reported to the World Health Organization (7). The body's inflammatory response to COVID-19 has many pathways through which it promotes a state of hypercoagulability. Activation of the fibrinolytic system, which inhibits hemostasis, can occur after COVID-19 and can lead to paralysis. The virus has an affinity for angiotensin-converting enzyme 2 (ACE2) receptors, which affect the renin-angiotensin system and increase the likelihood of stroke in COVID-19 patients (8).

With this study, we aimed to reveal the relationship between COVID-19, which has affected millions of people worldwide, and strokes and STEMIs at a young age, which we now encounter more frequently in clinical practice.

## MATERIALS and METHODS

The study was conducted in the Emergency Medicine Clinic of Kayseri City Hospital. The retrospective study was conducted with patients diagnosed with stroke and STEMI aged 50 years and younger between 01/01/2024 and 31/12/2024. Patients diagnosed with STEMI were categorized into subgroups based on electrocardiographic findings and the presumed location of myocardial infarction as anterior, inferior, and other. The 'other' subgroup included patients with lateral, anteroseptal, anterolateral, inferolateral and posterior myocardial infarctions. Patients

under 18 years of age, pregnant women, traumatic patients, patients with missing data during the study period, and patients with other acute coronary syndrome diagnoses and stroke-like diagnoses such as hemorrhagic stroke and transient ischemic attack were excluded. The demographic data of the patients included in the study were analyzed, including the type of outcome in the emergency department, in-hospital mortality status, and history of COVID-19. Patients who were diagnosed and treated for COVID-19 as a result of the presence of PCR test positivity and clinical and radiologic evaluation of the included patients were considered as COVID-19 (+) (Group I) in the study. Patients who did not meet either of these two criteria were considered as COVID-19 (-) (Group II).

A total of 354 patients aged 50 years and younger who were diagnosed with STEMI and stroke in our clinic during our study period were included in the study. 2 patients were excluded from the study because they had an arrest and exitus before they could be taken to angiography after being diagnosed with STEMI. 156 patients were excluded because of missing PCR and imaging data in the system screening. The study was performed with a total of 196 patients.

### Statistical Analysis

Statistical analyses were performed with Statistical Package for Social Sciences (SPSS) version 22 (IBM Corp.Armonk, NY, USA). The normality assessment of the numerical data recorded in the study was checked by Kolmogorov-Smirnov and Shapiro-Wilk tests. In descriptive statistics, mean  $\pm$  standard deviation was used for parametric data if they fit the normal distribution or median (minimum-maximum) if they do not fit the normal distribution, and frequency and percentage values were used for categorical data. In the comparison of parametric measurements between groups, independent group T test was used if the groups were normally distributed, and Mann Whitney-U test was used if the groups were not normally distributed. Chi-square test was used for comparison of categorical variables. For the expression of significant value,  $p < 0.05$  was accepted.

## RESULTS

The median age of a total of 196 patients included in the study was 46 (IQRs: 41- 48, min: 20 max: 50) years. Of the study population, 153 patients (78.1%) were male and 43 patients (21.9%) were female. 138 (70.4%) patients

had a diagnosis of STEMI and 58 (29.6%) patients had a diagnosis of ischemic stroke.

Among patients with STEMI, 69 cases (50.0%) were classified as inferior STEMI, 56 cases (40.6%) as anterior STEMI, and 13 cases (9.4%) as other types, including anterolateral, anteroseptal, inferolateral, lateral, and posterior localizations. With respect to COVID-19 status, 22 patients (11.2%) were categorized as Group I (COVID-19 positive), and 174 patients (88.8%) as Group II (COVID-19 negative) (Table 1).

**Table 1.** Demographic data of patients

Variable	n (%)
Age (median, IQR <sup>#</sup> , years)	46 (41-48)
Gender	
Male	153 (78.1)
Female	43 (21.9)
Diagnosis	
STEMI <sup>x</sup>	138 (70.4)
Stroke	58 (29.6)
STEMI subgroup	
Inferior	69 (50)
Anterior	56 (40.6)
Other*	13 (9.4)
COVID-19	
Group I	22 (11.2)
Group II	174 (88.8)

#**IQR**: Interquartile range; **STEMI**: xST segment elevation myocardial infarction; \***Other**: Anterolateral, Anteroseptal, Inferolateral, Lateral, Posterior

The median age was 43.5 years (IQR: 41.75–48) in Group I and 46 years (IQR: 41–48) in Group II. The difference in age between the groups was not statistically significant (p=0.631). In terms of gender distribution, Group I included 19 male patients (86.4%) and 3 female patients (13.6%), while Group II included 134 male patients (77.0%) and 40 female patients (23.0%). The difference in gender distribution between the groups was not statistically significant (p = 0.318).

The prevalence of stroke was significantly higher in Group I compared to Group II, with 50.0% (n=11) of patients in Group I diagnosed with stroke versus 27.0% (n=47) in Group II (p=0.026). This difference indicates a statistically significant association between COVID-19 positivity and stroke occurrence within the study population. Among patients with STEMI, anterior localization was found in 5 patients (45.5%) in Group I and 51 patients (40.2%) in Group II (p= 0.537). Inferior STEMI was seen in 6 patients (54.5%) in Group I and 63 patients (49.6%) in Group II. Other STEMI subtypes (anterolateral, anteroseptal, inferolateral, lateral, posterior) were not observed in Group I, while 13 patients (10.2%) in Group II were categorized

under this group. There was no statistically significant difference between the groups in terms of STEMI subtype distribution (p= 0.537).

STEMI was present in 11 patients (50.0%) in Group I and 127 patients (73.0%) in Group II. This difference was complementary to the stroke distribution and reached statistical significance (p=0.026) (Table 2).

**Table 2.** Comparison of age, gender, and diagnosis between groups.

Variable	Group I	Group II	p-value*
Age, median, IQR, years	43.5 (41.75- 48)	46 (41- 48)	0.631
Gender, n (%)			
Male	19 (86.4%)	134 (77.0%)	0.318
Female	3 (13.6%)	40 (23.0%)	
Diagnosis, n (%)			
Stroke	11 (50.0%)	47 (27.0%)	0.026
STEMI	11 (50.0%)	127 (73.0%)	
Subgroups, n (%)			
Anterior STEMI	5 (45.5%)	51 (40.2%)	0.537
Inferior STEMI	6 (54.5%)	63 (49.6%)	
Other	0 (0.0%)	13 (10.2%)	

**STEMI**: ST-segment elevation myocardial infarction **IQR**: Interquartile range; \*Mann-Whitney U test. Other statistical evaluations were calculated by Chi-square test

Among patients diagnosed with STEMI, further subgroup analysis was performed to compare anterior, inferior, and other localizations between COVID-19 positive (Group I) and negative (Group II) patients. The frequency of anterior STEMI was 45.5% (n=5) in Group I and 40.2% (n=51) in Group II. The distribution of anterior versus non-anterior STEMI did not differ significantly between the groups (p=0.667). Inferior STEMI was observed in 54.5% (n=6) of Group I and 49.6% (n=63) of Group II. There was no statistically significant difference in the distribution of inferior versus non-inferior STEMI between the two groups (p=0.676). Other STEMI subtypes were not observed in Group I (0.0%, n=0), while 10.2% (n=13) of Group II patients had other STEMI localizations. The difference in other versus non-other STEMI distribution was not statistically significant (p=0.226) (Table 3).

**Table 3.** STEMI distribution

STEMI Subgroup	Group I (n= 11)	Group II (n = 127)	p-value
Anterior	5 (45.5%)	51 (40.2%)	0.667
Inferior	6 (54.5%)	63 (49.6%)	0.676
Other*	0 (0.0%)	13 (10.2%)	0.226

\***Other**: Includes anterolateral, anteroseptal, inferolateral, lateral, and posterior STEMI localizations.

## DISCUSSION

The coronavirus pandemic has led to a significant increase in morbidity and mortality worldwide. Patients with COVID-19 are at increased risk of developing cardiovascular conditions such as acute coronary syndromes and cerebrovascular events, including stroke (9). The association between stroke incidence and COVID-19 has been reported since the early days of the pandemic.

An early retrospective study conducted in Wuhan, China, between January and February 2020 demonstrated that severe COVID-19 infection was associated with a higher prevalence of stroke compared to milder cases (8). Increasing evidence suggests that COVID-19-related coagulopathy leads to systemic arterial and venous thromboembolism, including but not limited to acute ischemic stroke.

Initial case reports describing stroke in COVID-19 patients were alarming, particularly in young patients without comorbidities; however, cases involving older patients with known stroke risk factors and worse outcomes have also been reported. The case fatality rate in COVID-19 and stroke patients was as high as 44.2% (10).

Similarly, recent data revealed a 52% increased risk of stroke among COVID-19 survivors (8). In the early stages of the pandemic, a case series from New York reported five young patients ( $\leq 50$  years) with SARS-CoV-2 infection who developed large-vessel occlusion ischemic stroke within a two-week period. In some of these cases, stroke occurred in the absence of known vascular risk factors. These observations suggest a significant increase in stroke incidence among young individuals and support the hypothesis that COVID-19 may contribute to ischemic stroke through thrombotic complications. This incidence was approximately seven times higher than in the previous year (11).

Consistent with these reports, our study found higher PCR positivity among patients diagnosed with ischemic stroke. COVID-19 patients who develop STEMI face higher morbidity and mortality compared to age and sex-matched STEMI patients without COVID-19 (9). In the recent past, hospitalizations with acute myocardial infarction (AMI) have increased in young individuals aged 35-54 years. This has been attributed to increased rates of tobacco consumption, smoking, obesity, lifestyle and dietary habits, diabetes and dyslipidemia during adolescence (12). A recent systematic review and meta-analysis by Shrestha et al. (2023) evaluated the long-term cardiovascular manifestations associated with COVID-19, with a particular focus on myocardial injury. Their findings

demonstrated that individuals in the post-COVID phase were at significantly increased risk of developing myocardial infarction and related complications, even in the absence of preexisting cardiovascular conditions. The analysis highlighted that myocardial injury in these patients commonly manifested as angina or STEMI, and was frequently accompanied by an increased risk of arrhythmias. These results emphasize the potential long-term prothrombotic and inflammatory consequences of SARS-CoV-2 infection, which may persist well beyond the acute phase of illness. The findings from this meta-analysis underscore the need for vigilant long-term cardiovascular follow-up in patients recovering from COVID-19, including young and middle-aged adults who may not have prior cardiac risk factors (13).

An association between COVID-19 and cardiovascular disease is well known. Studies have shown that patients infected with SARS-CoV-2 have an increased risk of serious illness and death in the presence of pre-existing cardiovascular disease. One study showed that the risk of acute cardiac disease in patients with COVID-19 was 8%, while this rate was 13 times higher in critically ill patients (14).

In our study, we observed a statistically significant association between SARS-CoV-2 PCR positivity and STEMI diagnosis, consistent with existing literature.

In a study by Zasada et al., it was explained that coronary artery stenosis was observed more frequently in the left anterior descending artery than in other arteries in young patients with STEMI (4). In our study, young patients in both PCR-positive and PCR-negative groups were diagnosed with inferior STEMI more frequently and coronary artery stenosis was found more frequently in the right coronary artery. These findings are different from the literature.

These findings differ from previous reports and may be attributable to the limited sample size. Including more patients with missing or unavailable data might have produced results more consistent with the literature.

## Conclusion

Our study supports the association between COVID-19 and increased risk of ischemic stroke, especially among young and middle-aged individuals, consistent with current literature. We also found a statistically significant link between SARS-CoV-2 PCR positivity and STEMI diagnosis, aligning with previous reports. However, some cardiac findings, such as the localization of coronary artery stenosis, differed from existing data, possibly

due to the limited sample size. These results highlight the importance of ongoing cardiovascular monitoring in COVID-19 survivors and emphasize the need for larger studies to further clarify the impact of SARS-CoV-2 on acute coronary syndromes and stroke.

**Ethics Committee Approval:** Approval was received from Kayseri City Hospital ethics committee dated 25.02.2025 and numbered 345.

**Conflict of Interest:** The authors declare no conflict of interest in this study.

**Financial Disclosure:** No financial support was received from any institution or organization for this study.

**Author Contributions:** Concept – G.,Y.,D.; NB; Design - R.,A.,A., H.,K.; Supervision – İ.,T.; Resources – N.,B.; Materials – G.,Y.,D.; Data Collection and/or Processing – H.,K.; Analysis and/or Interpretation – G.,Y.,D.; Literature Search – N.,B., İ.,T.; Writing Manuscript – G.,Y.,D., N.,B.; Critical Review – G.,Y.,D., R.,A.,A.

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