

Hospitalization Due to Acute Coronary Syndrome and Myocarditis in Patients Under 45 Years Old: A Single-Center Coronary Care Unit Retrospective Analysis of Hospitalizations Before, During, and After the Coronavirus Disease 2019 Pandemic

45 Yaş Altı Hastalarda Akut Koroner Sendrom ve Miyokardit Nedeniyle Hastaneye Yatış: COVID-19 Pandemisi Öncesi, Sırası ve Sonrasına Ait Tek Merkezli Koroner Yoğun Bakım Ünitesi Retrospektif Yatış Kayıtları

ABSTRACT

Objective: Whether Coronavirus Disease 2019 (COVID-19) infection and vaccination contribute to the development of acute coronary syndrome (ACS) or myocarditis, particularly in young adults, remains controversial. This study aimed to evaluate the hospitalization rates for ACS and myocarditis in patients under 45 years of age during the pre-pandemic, pandemic, and post-pandemic periods.

Method: This retrospective, single-center study included 944 patients under the age of 45 who were admitted to the coronary care unit with a diagnosis of ACS or myocarditis. Patients were categorized into three groups based on admission periods: pre-pandemic (January 2019 to March 31, 2020), pandemic (April 1, 2020 to September 30, 2022), and post-pandemic (October 1, 2022 to December 31, 2023).

Results: There were no significant differences in the proportion of patients under 45 years old among total coronary care unit admissions across the three periods (12.9% vs 11.0% vs. 11.8%, respectively; $P = 0.134$). Similarly, although a slight increase was observed in the proportion of myocarditis cases relative to ACS over time, the difference was not statistically significant (29.9% vs. 70.1%, 32.0% vs. 68.0%, and 34.2% vs. 65.8%, respectively; $P = 0.600$). The rate of myocarditis was comparable between vaccinated and unvaccinated patients, with no significant differences based on vaccine types.

Conclusion: Hospitalization rates for ACS and myocarditis among patients under 45 years of age at our center were similar across the pre-pandemic, pandemic, and post-pandemic periods. These findings support previous studies suggesting no association between COVID-19 infection or vaccination and the occurrence of ACS or myocarditis. However, as a single-center retrospective study, our findings are limited to hospitalized cases and do not provide data on the overall incidence, prevalence, or causal relationships between these conditions and the pandemic.

Keywords: Acute coronary syndrome, Coronavirus Disease 2019 pandemic, COVID-19 vaccine, myocarditis

ÖZET

Amaç: COVID-19 enfeksiyonu ve aşılmasının, özellikle genç yetişkinlerde akut koroner sendrom (AKS) ve miyokardite neden olup olmadığı hala tartışmalıdır. Bu çalışmanın amacı, pandemi öncesi, pandemi dönemi ve pandemi sonrası dönemlerde 45 yaş altı hastalarda AKS ve miyokardit nedeni ile hastaneye yatış oranlarını incelemektir.

Yöntem: Bu retrospektif, tek merkezli çalışmaya, AKS veya miyokardit tanısıyla koroner yoğun bakım ünitesine başvuran 45 yaş altı 944 hasta dahil edilmiştir. Hastalar başvuru tarihine göre üç gruba ayrılmıştır: pandemi öncesi grup (Ocak 2019 - 31 Mart 2020), pandemi grubu (1 Nisan 2020 - 30 Eylül 2022) ve pandemi sonrası grup (1 Ekim 2022 - 31 Aralık 2023).

Bulgular: 45 yaş altı hastaların toplam koroner yoğun bakım başvuruları içindeki oranları gruplar arasında anlamlı bir fark göstermemiştir (%12,9 vs %11,0 vs %11,8, $p=0,134$). Benzer şekilde, gruplar arasında miyokardit oranında AKS'ye göre hafif bir artış görülmesine rağmen bu fark anlamlı değildi (%29,9 vs %70,1, %32,0 vs %68,0 ve %34,2 vs %65,8, $p=0,600$). Miyokardit oranı, aşı ve aşısız hastalar arasında benzerdi ve aşı türlerine göre anlamlı bir fark gözlenmedi.

ORIGINAL ARTICLE KLİNİK ÇALIŞMA

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Received: December 17, 2024

Accepted: March 27, 2025

Cite this article as: Demirci M, Özben B, Yurdabakan S, et al. Hospitalization Due to Acute Coronary Syndrome and Myocarditis in Patients Under 45 Years Old: A Single-Center Coronary Care Unit Retrospective Analysis of Hospitalizations Before, During, and After the Coronavirus Disease 2019 Pandemic. *Türk Kardiyol Dern Ars.* 2025;53(4):254-262.

DOI: 10.5543/tkda.2025.93630



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Sonuç: Merkezimizde AKS ve miyokardit nedeniyle hastaneye yatış oranları, pandemi öncesi, pandemi ve pandemi sonrası dönemlerde 45 yaş altı hastalar için benzer bulunmuş olup, bu durum COVID-19 enfeksiyonu ve aşılmasının AKS ve miyokarditle ilişkili olmadığını gösteren çalışmalarını desteklemektedir. Bununla birlikte, bu çalışma akut koroner sendrom ve miyokardit nedeniyle hastaneye yatırılan vakalara ilişkin tek merkez kayıtlarını yansıtmakta olup, bu hastalıkların pandemi ile olan nedensel ilişkisini, genel insidansını veya prevalansını ortaya koymamaktadır.

Anahtar Kelimeler: Akut koroner sendrom, COVID-19 pandemisi, COVID-19 aşısı, miyokardit

Acute coronary syndrome (ACS) and myocarditis are serious cardiovascular conditions associated with significant morbidity and mortality.^{1,2} The risk of ACS generally increases with advancing age, smoking, and comorbidities such as hypertension, diabetes, and hyperlipidemia.³ Since the onset of the Coronavirus Disease 2019 (COVID-19) pandemic in 2020, numerous cases of ACS and myocarditis have been reported in association with the virus itself.⁴ Additionally, following the rollout of widespread vaccination campaigns, instances of vaccine-associated myocarditis have also been documented.⁵

Research indicates that Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus can directly damage heart muscle, exacerbating pre-existing cardiovascular conditions.^{6,7} COVID-19 patients frequently present with elevated cardiac troponin levels, increased interleukin concentrations, and prolonged procoagulant activity, all of which suggest a strong link between the infection and myocardial injury.⁸ Furthermore, observational data have highlighted an increase in cases of ACS and myocarditis during the pandemic, particularly among younger individuals.⁹ Studies have also investigated the cardiovascular side effects of COVID-19 vaccines, with population-based data indicating a higher incidence of myocarditis, especially in young men, following the second dose of mRNA vaccines.^{10,11}

The aim of this study was to examine hospitalization rates for ACS and myocarditis in patients under 45 years of age across the pre-pandemic, pandemic, and post-pandemic periods.

Materials and Methods

Study Design and Participants

This single-center retrospective study included consecutive patients under the age of 45 who were admitted to the coronary intensive care unit at Marmara University Hospital with a confirmed diagnosis of ACS or myocarditis between January 1, 2019 and December 31, 2023. The age cut-off for premature coronary artery disease was considered to be 45 years.¹² All discharge summaries and coronary angiography reports for patients under 45 were thoroughly reviewed. ACS was defined based on clinical presentation, electrocardiogram (ECG) abnormalities, and elevated cardiac troponin levels. Patients with ACS included those diagnosed with ST-segment elevation myocardial infarction (STEMI) or non-ST-segment elevation myocardial infarction (NSTEMI).¹³ All patients underwent invasive coronary angiography, and the presence of a thrombotic culprit lesion was a mandatory criterion for the diagnosis of ACS. The diagnosis of myocarditis was based on a comprehensive

ABBREVIATIONS

ACS	Acute coronary syndrome
COVID-19	Coronavirus Disease 2019
ECG	Electrocardiogram
NSTEMI	Non-ST-segment elevation myocardial infarction
PCR	Polymerase chain reaction
SARS-CoV-2	Severe Acute Respiratory Syndrome Coronavirus 2
STEMI	ST-segment elevation myocardial infarction
VAERS	Vaccine Adverse Event Reporting System

review of patient records, including clinical presentation, physical examination findings, laboratory results (elevated troponin levels), and coronary angiography showing no culprit lesion. Patient records were also reviewed to collect demographic data, including age, sex, and comorbidities. Patients with unexplained cardiac arrest were excluded if coronary angiography could not be performed. Similarly, patients with elevated troponin levels due to secondary causes, for whom coronary angiography was not performed, were also excluded.

Patients were divided into three groups based on their admission dates: the pre-pandemic group, the pandemic group, and the post-pandemic group. Since the first COVID-19 case in Türkiye was reported on March 11, 2020, patients hospitalized between January 1, 2019 and March 31, 2020 were classified as the pre-pandemic group. The pandemic period was defined as April 1, 2020 to September 30, 2022, representing the peak incidence of COVID-19 cases according to data from the Turkish Ministry of Health (Figure 1A). Patients hospitalized between October 1, 2022 and December 31, 2023 were classified as the post-pandemic group. Case numbers for the pandemic and post-pandemic periods were obtained from official data published by the Ministry of Health.¹⁴

Information on positive COVID-19 polymerase chain reaction (PCR) test results prior to hospitalization were documented. Due to restrictions, no active COVID-19 patients were admitted to the coronary care unit. Data regarding the types of vaccines administered to the patients were also recorded. The vaccination program in Türkiye began with healthcare workers on January 11, 2021, followed by individuals over the age of 65 and those with chronic illnesses. Vaccination for individuals younger than 45 years started after June 2021. The types of vaccines administered were either mRNA vaccines or inactivated vaccines. Patients were grouped into three categories: those who received only mRNA vaccines, those who received only

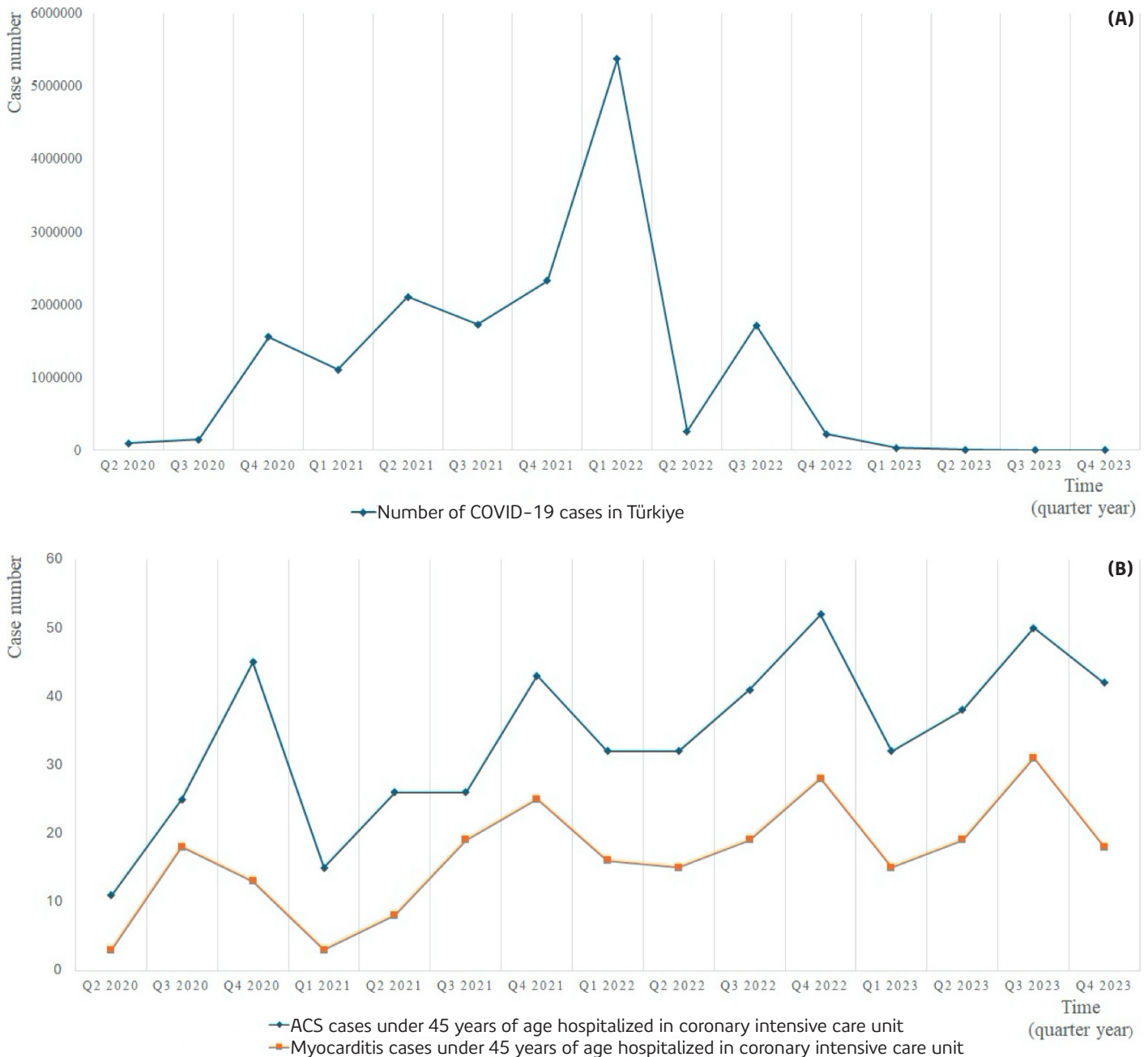


Figure 1. (A) Quarterly distribution of confirmed Coronavirus Disease 2019 (COVID-19) cases in Türkiye from Q2 2020 to Q4 2023, illustrating the major peaks and declines observed during the study period (April 2020 to December 2023). (B) Quarterly distribution of acute coronary syndrome (ACS) and myocarditis cases in patients under 45 years of age hospitalized in the coronary intensive care unit from Q2 2020 to Q4 2023, highlighting temporal trends throughout the study period.

inactivated vaccines, and those who received a mixed regimen. The dates of vaccination were also recorded to determine whether hospitalization for ACS or myocarditis occurred before or after vaccination.

Additionally, the total number of patients hospitalized in the coronary intensive care unit of Marmara University Hospital between January 1, 2019 and December 31, 2023, was documented. We compared the proportion of patients under 45 years of age among all coronary care admissions across the three time periods.

Ethics

This study was conducted in accordance with ethical standards and the principles of the Declaration of Helsinki, revised in 2013. Ethical approval was obtained from the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Approval Number: 09.2023.1491, Date: 03.11.2023).

Statistical Analysis

Statistical analyses were performed using a commercially available software program (Statistical Package for the Social Sciences (SPSS) version 20.0 for Windows, Chicago, IL, USA).

Table 1. Characteristics of Patients According to Hospitalization Period

	Pre-Pandemic Group (n = 184)	Pandemic Group (n = 435)	Post-Pandemic Group (n = 325)	P
Age (years)	37 ± 8	37 ± 8	38 ± 7	0.721
Male sex (n, %)	156 (84.8%)	373 (85.7%)	273 (84%)	0.799
Myocarditis (n, %)	55 (29.9%)	139 (32.0%)	111 (34.2%)	0.600
ACS (n, %)	129 (70.1%)	296 (68.0%)	214 (65.8%)	
STEMI	88 (68.2%)	187 (63.2%)	133 (62.1%)	0.600
NSTEMI	41 (31.8%)	109 (36.8%)	81 (37.9%)	0.499
Hypertension (n, %)	29 (15.8%)	65 (14.9%)	55 (16.9%)	0.760
Diabetes mellitus (n, %)	30 (16.3%)	49 (11.3%)	34 (10.5%)	0.123
Hyperlipidemia (n, %)	45 (24.5%)	125 (28.7%)	98 (30.2%)	0.382
Family history (n, %)	23 (12.5%)	43 (9.9%)	34 (10.5%)	0.624
Smoking (n, %)	69 (37.5%)	108 (24.8%)	73 (22.5%)	<0.001
COVID-19 PCR positivity (prior to hospitalization) (n, %)	0	71 (16.3%)	71 (21.8%)	0.053
Vaccination (any time) (n, %)	149 (81.0%)	370 (85.1%)	280 (86.2%)	0.282
Vaccination prior to hospitalization (n, %)	0	224 (51.5%)	280 (86.2%)	<0.001
mRNA vaccine (n, %)	189 (84.4%)	251 (89.6%)		
Inactivated vaccine (n, %)	26 (11.6%)	21 (7.5%)		0.208
Mixed regimen (n, %)	9 (4.0%)	8 (2.9%)		
One dose (n, %)	23 (10.3%)	36 (12.9%)		
Two doses (n, %)	128 (57.1%)	140 (50.0%)		0.267
≥ Three doses (n, %)	73 (32.6%)	104 (37.1%)		
In-hospital mortality (n, %)	6 (3.3%)	8 (1.8%)	7 (2.2%)	0.545
LVEF (%)	54 ± 10	56 ± 10	56 ± 10	0.080
Creatinine (mg/dL)	0.81 ± 0.16	0.83 ± 0.16	0.84 ± 0.17	0.125
WBC (×10 ⁹ /L)	11.75 ± 4.29	11.79 ± 4.09	11.98 ± 4.55	0.784
Hemoglobin (g/dL)	13.88 ± 1.26	14.02 ± 1.51	14.12 ± 1.59	0.219
Platelet count (×10 ³ /μL)	264.26 ± 82.04	264.65 ± 72.43	272.67 ± 77.76	0.297
TC (mg/dL)	192.64 ± 59.07	188.78 ± 53.42	188.68 ± 48.32	0.834
LDL-C (mg/dL)	116.67 ± 43.53	118.12 ± 45.06	116.32 ± 39.14	0.919
Prior ASA use (n, %)	11 (6.0%)	15 (3.4%)	20 (6.2%)	0.170
Prior ACEI/ARB use (n, %)	15 (8.2%)	32 (7.4%)	26 (8.0%)	0.921
Prior BB use (n, %)	6 (3.3%)	9 (2.1%)	8 (2.5%)	0.679
Prior CCB use (n, %)	6 (3.3%)	12 (2.8%)	7 (2.2%)	0.742
Prior statin use (n, %)	25 (13.6%)	48 (11.0%)	36 (11.1%)	0.628
Prior antidiabetic use (n, %)	19 (10.3%)	31 (7.1%)	20 (6.2%)	0.215

Data represent only patients hospitalized in a single coronary care unit. Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are presented as n (%). ACEI, Angiotensin-Converting Enzyme Inhibitor; ACS, Acute Coronary Syndrome; ARB, Angiotensin II Receptor Blocker; ASA, Acetylsalicylic Acid; BB, Beta-Blocker; CCB, Calcium Channel Blocker; DM, Diabetes Mellitus; HT, Hypertension; LDL-C, Low-Density Lipoprotein Cholesterol; LVEF, Left Ventricular Ejection Fraction; mRNA, Messenger Ribonucleic Acid; NSTEMI, Non-ST-Elevation Myocardial Infarction; PCR, Polymerase Chain Reaction; STEMI, ST-Elevation Myocardial Infarction; TC, Total Cholesterol; WBC, White Blood Cell Count.

Continuous data were expressed as mean ± standard deviation, while categorical data were presented as numbers and percentages. Normality was assessed using the Kolmogorov-Smirnov test. Comparisons of continuous variables among three groups were performed using analysis of variance (ANOVA) or the Kruskal-Wallis test, while the Student's t-test or the Mann-Whitney U test was used for comparisons between two groups.

Categorical variables were compared using the chi-square test. A P-value of < 0.05 was considered statistically significant.

Results

This retrospective study included 944 consecutive patients (mean age: 37 ± 7 years; 802 male) with a confirmed diagnosis of ACS (639 patients) or myocarditis (305 patients).

Table 2. Characteristics of Patients According to Positive Polymerase Chain Reaction (PCR) Results and Vaccination Prior to Hospitalization

	Positive PCR Prior to Hospitalization (n = 142)	No Documented Positive PCR Prior to Hospitalization (n = 802)	P
Age (years)	36 ± 8	37 ± 7	0.072
Male sex (n, %)	112 (78.9%)	690 (86.0%)	0.028
Myocarditis (n, %)	55 (38.7%)	250 (31.2%)	0.076
ACS (n, %)	87 (61.3%)	552 (68.8%)	
STEMI	52 (59.8%)	356 (64.5%)	0.076
NSTEMI	35 (40.2%)	196 (35.5%)	0.394
	Vaccinated Prior to Hospitalization (n = 504)	Not Vaccinated Prior to Hospitalization (n = 440)	P
Age (years)	37 ± 8	37 ± 7	0.622
Male sex (n, %)	425 (84.3%)	377 (85.7%)	0.561
Myocarditis (n, %)	173 (34.3%)	132 (30.0%)	0.156
ACS (n, %)	331 (65.7%)	308 (70.0%)	
STEMI	206 (62.2%)	202 (65.6%)	0.156
NSTEMI	125 (37.8%)	106 (34.4%)	0.379

Data represent only patients hospitalized in a single coronary care unit. ACS, Acute Coronary Syndrome; NSTEMI, Non-ST-Elevation Myocardial Infarction; PCR, Polymerase Chain Reaction; STEMI, ST-Elevation Myocardial Infarction.

Among the ACS patients, 408 presented with STEMI, while 231 presented with NSTEMI. During the pre-pandemic period, 184 patients under the age of 45 were hospitalized, with a total of 1,426 coronary care admissions. In the pandemic period, 435 patients under 45 were hospitalized, out of 3,966 total admissions. During the post-pandemic period, 325 patients under 45 were hospitalized, with 2,754 total admissions. The proportions of patients under 45 years old among the total coronary care admissions across the three periods were not significantly different (12.9% vs. 11.0% vs. 11.8%, respectively; $P = 0.134$). Although there was a slight increase in the proportion of myocarditis cases, the ratio of myocarditis to ACS was similar across the pre-pandemic, pandemic, and post-pandemic groups (29.9% vs. 70.1%, 32.0% vs. 68.0%, and 34.2% vs. 65.8%, respectively; $P = 0.600$). An analysis of three-month intervals from April 2020 to December 2023 revealed no correlation between the peak periods of COVID-19 cases in Türkiye and the peak incidence of ACS or myocarditis among individuals under 45 years of age admitted to the coronary intensive care unit (Figure 1). Table 1 lists the characteristics of the patients according to the hospitalization period.

Table 2 summarizes the characteristics of patients based on their positive PCR results and vaccination status prior to hospitalization. The rate of myocarditis was higher among those vaccinated before hospitalization compared to those who were not, although the difference was not statistically significant.

Table 3 displays patient characteristics according to vaccination status across the pre-pandemic, pandemic, and post-pandemic periods. During the pandemic and post-pandemic periods, the

incidence of myocarditis was slightly higher among vaccinated patients; however, these differences were not statistically significant ($P = 0.186$ and $P = 0.831$, respectively). Furthermore, across the three periods, there was no significant difference in myocarditis rates between vaccinated and unvaccinated patients overall ($P = 0.591$).

Table 4 compares the characteristics of patients who were vaccinated prior to hospitalization, according to vaccine type. The incidence of myocarditis and ACS did not differ significantly among the vaccine types ($P = 0.241$). Among the patients who received at least one dose of a vaccine before hospitalization, 11 presented with ACS within the first week following vaccination (nine after mRNA and two after inactivated vaccines). Additionally, two patients presented with myocarditis within the first week after mRNA vaccination (one after the first dose of mRNA vaccine and one after the second dose).

Table 5 compares the rates of myocarditis and ACS in male and female patients based on vaccination status prior to hospitalization. Among male patients, the frequency of myocarditis was slightly higher in those who were vaccinated compared to those who were not, although the difference was not statistically significant (32.7% vs. 27.3%, $P = 0.097$). In contrast, among female patients, the frequency of myocarditis was slightly lower in vaccinated individuals compared to non-vaccinated ones, also without statistical significance (43% vs. 46%, $P = 0.721$).

Table 6 compares the characteristics of myocarditis cases based on vaccination status prior to hospitalization and sex. Vaccination rates were similar between male and female patients with myocarditis.

Table 3. Characteristics of Patients According to Vaccination Status During Pre-Pandemic, Pandemic, and Post-Pandemic Periods

	Pre-Pandemic Group (n = 184)	Pandemic Group (n = 435)			Post-Pandemic Group (n = 325)			P
Vaccinated prior to hospitalization	0	Vaccinated (n = 224)	Not Vaccinated (n = 211)	P	Vaccinated (n = 280)	Not Vaccinated (n = 45)	P	
Age (years)	37 ± 8	37 ± 8	37 ± 7	0.468	37 ± 7	38 ± 7	0.379	0.750
Male sex (n, %)	156 (84.8%)	187 (83.5%)	186 (88.2%)	0.164	238 (85.0%)	35 (77.8%)	0.220	0.422
Myocarditis (n, %)	55 (29.9%)	78 (34.8%)	61 (28.9%)	0.186	95 (33.9%)	16 (35.6%)	0.831	0.591
ACS (n, %)	129 (70.1%)	146 (65.2%)	159 (71.1%)		185 (66.1%)	29 (64.4%)		
STEMI	88	90	97	0.186	116	17	0.831	0.591
NSTEMI	41	56	53	0.590	69	12	0.673	0.760

Data represent only patients hospitalized in a single coronary care unit. ACS, Acute Coronary Syndrome; NSTEMI, Non-ST-Elevation Myocardial Infarction; STEMI, ST-Elevation Myocardial Infarction.

Table 4. Characteristics of Patients Vaccinated Prior to Hospitalization According to Vaccine Type

	mRNA Vaccine (n = 440)	Inactivated Vaccine (n = 47)	Mixed vaccines (n = 17)	P
Age (years)	37 ± 8	38 ± 7	35 ± 11	0.287
Male sex (n, %)	374 (85.0%)	34 (72.3%)	17 (100%)	0.015
Myocarditis (n, %)	147 (33.4%)	17 (36.2%)	9 (52.9%)	0.241
ACS (n, %)	293 (66.6%)	30 (63.8%)	8 (47.1%)	
STEMI	111 (25.2%)	10 (21.2%)	4 (23.5%)	0.241
NSTEMI	182 (41.4%)	20 (42.6%)	4 (23.5%)	0.683

Data represent only patients hospitalized in a single coronary care unit. ACS, Acute Coronary Syndrome; mRNA, Messenger Ribonucleic Acid; NSTEMI, Non-ST-Elevation Myocardial Infarction; STEMI, ST-Elevation Myocardial Infarction.

Table 5. Myocarditis and Acute Coronary Syndrome (ACS) Rates According to Patients Sex

	Male (n = 802)			Female (n = 142)		
Vaccinated prior to hospitalization	Vaccinated (n = 425)	Not Vaccinated (n = 377)	P	Vaccinated (n = 79)	Not Vaccinated (n = 63)	P
Age (years)	37 ± 8	37 ± 7	0.400	38 ± 6	37 ± 8	0.420
Myocarditis (n, %)	139 (32.7%)	103 (27.3%)	0.097	34 (43.0%)	29 (46.0%)	0.721
ACS (n, %)	286 (67.3%)	274 (72.7%)		45 (57.0%)	34 (54.0%)	
STEMI	178	184	0.097	28	18	0.721
NSTEMI	108	90	0.224	17	16	0.408

Data represent only patients hospitalized in a single coronary care unit. ACS, Acute Coronary Syndrome; NSTEMI, Non-ST-Elevation Myocardial Infarction; STEMI, ST-Elevation Myocardial Infarction.

Discussion

This retrospective study demonstrated that hospitalization rates for ACS and myocarditis among patients under 45 years of age did not increase during the pandemic or post-pandemic periods compared to the pre-pandemic period at a single tertiary cardiology center's coronary care unit. While our study did not identify significant differences in myocarditis rates based on vaccination status or vaccine type, the retrospective design and single-center data limit the ability to draw definitive conclusions about the relationship between vaccination and myocarditis.

Previous studies have reported an increased incidence of myocarditis following mRNA-based COVID-19 vaccines. Montgomery et al.¹¹ observed a higher incidence of myocarditis in young, healthy individuals after receiving mRNA vaccines. Similarly, Stowe et al.¹⁵ found that the mRNA-1273 (Moderna) vaccine was associated with the highest risk of myocarditis after the second dose, particularly among young men. Additionally, Patone et al.¹⁰ reported that men under 40 years of age are at greater risk of developing myocarditis after the second dose of the vaccine compared to women. Massari et al.¹⁶ also showed an increased risk of myocarditis following the second dose of

Table 6. Characteristics of Myocarditis Cases According to Vaccination Status Prior to Hospitalization and Patient Sex

Vaccinated prior to hospitalization	Myocarditis (n = 305)		P
	Vaccinated (n = 173)	Not Vaccinated (n = 132)	
Age (years)	31 ± 8	31 ± 9	0.827
Male sex (n, %)	139 (80.3%)	103 (78.0%)	0.621
Sex	Male (n = 242)	Female (n = 63)	
Age (years)	30 ± 8	35 ± 8	<0.001
Vaccinated prior to hospitalization	139 (57.4%)	34 (%54)	0.621

Data represent only patients hospitalized in a single coronary care unit.

Table 7. Summary of Large-Scale Myocarditis Studies Following mRNA Coronavirus Disease 2019 (COVID-19) Vaccination

Study	Study Population	Inclusion Criteria	Timing	Case Definition	Key Findings
Patone et al. ¹⁰ (2022)	Individuals aged ≥ 13 years (42.8 million vaccinated in England)	National health records	1-28 days post-vaccination	ICD-based case identification	Increased myocarditis risk in young males, especially after the second dose
Oster et al. ¹⁸ (2022)	192 million vaccinated individuals in the U.S.	VAERS database and hospital reports	Within 7 days post-vaccination	ICD-based case identification	Elevated risk of myocarditis in young males, particularly following the second dose
Massari et al. ¹⁶ (2022)	Individuals aged 12-39 years (3 million in Italy)	Emergency department and hospital records	Within 21 days post-vaccination	ICD-based case identification	Higher myocarditis risk in individuals aged 12-39 years, especially after the second dose
Stowe et al. ¹⁵ (2023)	50 million adults in the U.K.	Hospital admission data	Within 28 days post-vaccination	ICD-based case identification	Higher risk of myocarditis observed in individuals aged 16-39 after the second dose
Xu et al. ¹⁷ (2025)	8 million adults in Sweden	National health records	Within 14 days post-vaccination	ICD-based case identification	Myocarditis risk highest in males under 40, especially during the first week after the second dose

VAERS, Vaccine Adverse Event Reporting System.

the BNT162b2 (mRNA) vaccine in individuals under 40 years of age. Our study found no significant increase in myocarditis rates based on vaccination status or vaccine type. However, there was a slightly higher rate of myocarditis in vaccinated men compared to unvaccinated individuals, which is consistent with findings from previous studies. The absence of a significant association in our study may be attributed to its design, which included only hospitalized patients. This limitation could have led to an underestimation of the true incidence of myocarditis, as asymptomatic or mild cases are less likely to result in hospitalization. Xu et al.¹⁷ reported that the risk of myocarditis was highest in males aged 18-40, with the peak incidence occurring during the first week after the second dose of an mRNA vaccine. Table 7 highlights key studies investigating the risk of myocarditis following mRNA COVID-19 vaccination, emphasizing differences in study populations, inclusion criteria, timing, case definitions, and major findings. In addition, various pandemic-related factors, such as increased use of influenza vaccines, over-the-counter supplements, and changes in health behaviors, may have influenced cardiovascular outcomes and cannot be entirely separated from the effects of COVID-19 or COVID-19 vaccination.

Data from the Vaccine Adverse Event Reporting System (VAERS) indicate an association between mRNA-based vaccines and myocarditis, which typically occurs within seven days after the second dose.¹⁸ In our study, we observed two cases of myocarditis occurring within the first seven days after mRNA vaccination. However, due to the limited sample size, definitive conclusions cannot be drawn. We were unable to assess the risk profile of the mRNA-1273 (Moderna) vaccine, as it was not available in Türkiye. Furthermore, our analysis did not reveal any significant differences in the risk of myocarditis between mRNA-based vaccines and inactivated vaccines.

The literature highlights that the risk of myocarditis following a COVID-19 infection is significantly higher than the risk associated with vaccination.¹⁹ Zuin et al.²⁰ demonstrated an increased risk of new-onset myocarditis within one year after the initial infection in recovered COVID-19 patients. Stowe et al.¹⁵ reported that the risk of myocarditis after infection was approximately 11 times higher, while Patone et al.¹⁰ found a 16-fold increase in risk following infection. In contrast, our study did not reveal a significant association between positive PCR results and myocarditis rates among hospitalized patients. This discrepancy

may be attributed to our study population, which primarily included younger individuals and excluded asymptomatic or mildly symptomatic cases that did not require hospitalization. Additionally, the relatively low proportion of patients with confirmed positive PCR results prior to hospitalization (16.5%) may have limited the statistical power to detect such a relationship. It is also important to note that actual myocarditis rates may be higher, as asymptomatic cases and those who were not tested were not captured in our analysis.

There was a notable decrease in NSTEMI cases during the early days of the pandemic, likely due to a reduction in hospital admissions.²¹ The TURKMI-2 study (Türkiye Acute Myocardial Infarction Registry), conducted during the initial phase of the COVID-19 pandemic, reported a 47.1% decrease in hospitalizations for acute myocardial infarction, specifically, a 56.4% decrease for NSTEMI and a 31.2% decrease for STEMI, compared to the pre-pandemic TURKMI study.²² These findings suggest that many patients experiencing myocardial infarction may have avoided seeking medical care during this time. Unlike the nationwide TURKMI study, which offers a population-based perspective on myocardial infarction trends, our study is limited to hospitalized patients at a single center. As such, it cannot provide conclusions regarding the overall incidence of ACS and myocarditis in the general population. Therefore, our findings primarily reflect hospitalization rates rather than the true incidence of ACS and myocarditis within the community.

Our study showed that STEMI and NSTEMI rates were similar across the different time periods. However, we lack detailed data on rates during periods of high COVID-19 case density and quarantine. Additionally, the study does not address the long-term effects of COVID-19 infection. An increase in ACS cases was observed in the post-pandemic period, and further research is needed to determine whether this rise is related to the long-term impact of COVID-19 or a rebound effect from reduced admissions during the pandemic.

Limitations

This study has several limitations. First, its retrospective design and the inclusion of only hospitalized patients with ACS or myocarditis may have introduced selection bias. Second, the relatively small sample size and the focus on patients under 45 years of age limit the generalizability of the findings to older populations. Patients with unexplained cardiac arrest were excluded if coronary angiography was not performed. Furthermore, the diagnosis of myocarditis was not confirmed using cardiac magnetic resonance imaging. Patients with myocardial infarction with non-obstructive coronary arteries may have been included in the myocarditis group if no culprit lesions were identified on coronary angiography, potentially influencing the study results. Similarly, due to pandemic-related restrictions, active COVID-19 patients were not admitted to our coronary care unit, which may have further impacted the findings. A multicenter study that includes referred patients would offer a more comprehensive perspective. The definition of the pandemic periods was based on data provided by the Turkish Ministry of Health. However, there may have been cases prior to the official announcement of the first COVID-19 case. Additionally, the time periods in our study were not of equal length, which may have affected the results. To account for

this, we used proportions rather than numbers when comparing groups. The reliability of positive PCR results in our dataset was also limited. The actual number of patients with prior COVID-19 infections may be higher due to false-negative test results, asymptomatic cases, or patients who were never tested. Finally, since our coronary intensive care unit functioned as a COVID-19 intensive care unit during the peak of the pandemic, this may have influenced hospitalization rates and patient selection.

Conclusion

In our study, hospitalization rates for ACS and myocarditis in patients under 45 years of age were similar across the pre-pandemic, pandemic, and post-pandemic periods. No significant increase in myocarditis rates was observed among patients with confirmed prior COVID-19 infections (PCR-positive cases). Myocarditis rates were slightly higher in vaccinated patients; however, no differences were observed in the incidence of myocarditis based on sex or vaccine type. As this is a single-center study based solely on hospitalized patients, it does not allow for definitive conclusions regarding the actual incidence or prevalence of ACS or myocarditis, nor their relationship with the pandemic or vaccination. Long-term follow-up of both vaccinated and unvaccinated individuals for myocarditis or ACS events is necessary to clarify the true relationship between COVID-19 vaccination and the occurrence of ACS and myocarditis.

Ethics Committee Approval: Ethical approval was obtained from the Marmara University Faculty of Medicine Clinical Research Ethics Committee (Approval Number: 09.2023.1491, Date: 03.11.2023).

Informed Consent: Written informed consent was not required.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: No artificial intelligence tools were used in the preparation of this study.

Author Contributions: Concept – M.K.T.; Design – M.K.T.; Supervision – M.K.T.; Resource – M.D.; Materials – A.E.G.; Data Collection and/or Processing – M.D., S.Y., İ.İ.A., A.E.Ç., Y.E.B., M.S., A.E.G.; Analysis and/or Interpretation – M.D., B.Ö.; Literature Review – M.D., B.Ö.; Writing – M.D., B.Ö.; Critical Review – M.D., B.Ö.

Peer-review: Both externally and internally peer-reviewed.

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