

Hospitalisations with myocarditis before and during the COVID-19 pandemic – a nationwide cohort study

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Summary

AIMS OF THE STUDY: Over the past decade, there has been a steady increase in myocarditis cases, paralleling the expanded availability and use of cardiac magnetic resonance imaging. Although some have speculated that COVID-19 or its vaccines may be contributing to this increase, recent studies have not provided conclusive proof. Therefore, this study aims to analyse the association between COVID-19 and myocarditis in hospitalised patients.

METHODS: In this nationwide cohort study, the primary outcome was trends in hospitalisations with myocarditis before (years 2012–2019) and during (years 2020–2022) the COVID-19 pandemic. Trends were calculated using linear mixed-effects segmented regression models. Secondary outcomes included in-hospital mortality, intensive care unit admission, length of stay, and 30-day hospital readmission. Results were stratified by sex and age for subgroup analyses.

RESULTS: During the pre-pandemic period, 4,304 hospitalisations with myocarditis were recorded, compared with 2,749 during the pandemic. The incidence rate of myocarditis increased from 26.7 cases per 100,000 hospitalisations in 2012 to 73.8 per 100,000 in 2022 (p for trend <0.001). The quarterly slope of incidence rose significantly during the pandemic (slope, 2.008 [95% CI: 2.006 to 2.011]) compared with that during the pre-pandemic period (slope, 1.141 [95% CI: 1.140 to 1.141]). Subgroup analyses showed the steepest increases in young and middle-aged males. Sensitivity analyses based on the Swiss population confirmed this pattern, with a population-adjusted quarterly increase in myocarditis hospitalisations from 1.0 to 2.6 per 100,000 inhabitants between 2012 and 2022 (p for trend <0.001).

CONCLUSION: This nationwide cohort study found a marked increase in the incidence of hospitalisations with myocarditis during the COVID-19 pandemic, suggesting a causal relationship between COVID-19 infection and/or its vaccination and the increased incidence of myocarditis.

Introduction

Myocarditis is an inflammatory disease of the myocardium that has traditionally been diagnosed based on histologic, immunologic, and immunohistochemical criteria [1]. However, in recent clinical practice, the diagnosis is commonly established through a combination of clinical signs, laboratory testing, and cardiac imaging [2–4]. The incidence of myocarditis gradually increased from 2005 to 2014, a trend that coincides with the expanded use of cardiac magnetic resonance imaging (MRI) [5]. According to the most recent Global Burden of Disease statistics prior to the COVID-19 pandemic, the worldwide prevalence of myocarditis and cardiomyopathy was between 10.2 and 105.6 cases per 100,000 individuals [6, 7]. A recent German study reported an incidence of myocarditis of 6.2 to 7.8 per 100,000 inhabitants between 2007 and 2022 [8], and in the United States, a similar incidence rate of 1 to 10 cases per 100,000 individuals was found before the pandemic [9].

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Myocarditis presents a significant clinical challenge due to its diverse aetiologies and wide spectrum of clinical manifestations [10]. Viral infections, particularly those caused by enteroviruses and adenoviruses, are well-established causes, leading to both direct myocardial injury and T-cell-mediated cytotoxicity [11, 12]. During the COVID-19 pandemic, cardiovascular involvement was observed in up to 30% of patients with SARS-CoV-2 infection, correlating with increased disease severity [13, 14]. Myocarditis, thrombotic events, ischaemic stroke, and myocardial infarction emerged as the most frequently reported cardiovascular complications associated with COVID-19 [15-17].

Early in the pandemic, evidence for COVID-19-associated myocarditis was primarily derived from case reports, highlighting an elevated risk of myocarditis among patients with COVID-19. Subsequent studies established a link between myocarditis and both SARS-CoV-2 infection and vaccination, although the incidence remained low [17-20]. The Centers for Disease Control and Prevention estimated that the incidence of myocarditis in the United States was approximately 150 cases per 100,000 individuals among those infected with SARS-CoV-2, compared with 9 cases per 100,000 in the general population during the same period [20, 21]. However, these findings require careful interpretation, as they do not conclusively establish a causal relationship between SARS-CoV-2 infection and myocarditis.

Contrary to expectations of a pandemic-driven rise in myocarditis and pericarditis cases, a recent study from Italy reported a decrease in acute myocarditis and stable rates of pericarditis and myopericarditis/perimyocarditis during the pandemic compared with the pre-pandemic period [22].

In light of the existing uncertainty and inconclusive data, we conducted a nationwide population-based study to compare myocarditis and pericarditis hospitalisation rates before and during the COVID-19 pandemic.

Methods

Research design and study population

For this retrospective cohort study, we used a nationwide database provided by the Swiss Federal Statistical Office (Schweizerisches Bundesamt für Statistik) based on the mandatory full disclosure of all hospitalisations in Swiss acute care, general, and speciality hospitals. The dataset included individual patient demographics, diagnoses, clinical interventions, diagnostics, hospital typology, healthcare utilisation, type of insurance, and in-hospital outcomes between 2012 and 2022. The control population was defined as all acute care hospitalisations without myocarditis during the study period, excluding non-acute and psychiatric admissions. All diagnoses were coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, German Modification (ICD-10-GM), while interventions were coded according to the Swiss operational procedure codes (CHOP). The selection of ICD-10 codes was in line with previous studies [23-25]; the list of all ICD-10 and CHOP codes used in this study is shown in table S1 in the appendix. This study does not fall under the scope of the Human Research Act because the data were solely provided in anonymised form (as declared by the ethical review board of Northwestern and Central Switzerland, EKNZ Project-ID: Req-2021-01397). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines [26].

Outcomes

The primary outcome of this study was the difference in incidence rates of hospitalisation with myocarditis between the pre-pandemic period (2012–2019) and the pandemic period (2020–2022). Secondary outcomes included in-hospital mortality, intensive care unit (ICU) admission, length of ICU stay, length of hospital stay (LOS), and 30-day hospital readmission. As prespecified, subgroup analyses stratified by sex and age were also performed. To ensure the robustness of the findings, a sensitivity analysis was conducted accounting for the yearly population of Switzerland. As a marker of internal validity and for comparison with previous findings from other studies, incidence rates of hospitalisation with pericarditis across the same time period were also assessed.

Statistical analysis

Descriptive statistics were used to display baseline characteristics as median (interquartile range [IQR]) or numbers (%), as appropriate. Quarterly hospitalisation rates for myocarditis were calculated per 100,000 hospitalisations and adjusted for the annual population of Switzerland. Trends in quarterly hospitalisation rates were assessed with an interrupted time-series approach using segmented mixed-effects regression models, comparing the pre-pandemic phase with the pandemic phase. Specifically, a linear spline with a knot at the onset of the pandemic (Quarter 1 of 2020) was used. The model was adjusted for age, sex, admission from home, the Elixhauser comorbidity index, and frailty at the individual level, and the resulting coefficients can be interpreted as the quarterly mean change in incidence. Differences in in-hospital outcomes were analysed using generalised estimating equations (GEEs) adjusted for the same factors. This analysis was performed using all other acute care hospitalisations as controls. All analyses were performed using STATA version 17.0 (StataCorp LLC) with two-sided p-values, with $p < 0.05$ considered statistically significant.

Results

Baseline characteristics

Among 7,053 hospitalisations with myocarditis, 4,304 (61.0%) occurred during the pre-pandemic period and 2,749 (39.0%) during the pandemic. In the pre-pandemic phase, 30.5% of patients were female, compared with 29.9% during the pandemic. Age distribution also changed, with patients under 30 comprising 24.2% of pre-pandemic hospitalisations and 25.6% of hospitalisations during the pandemic; those aged 30–60 decreased from 43.1% to 38.6%, and those over 60 increased from 32.8% to 35.8%. Patients hospitalised with myocarditis during the pandemic exhibited a slightly higher burden of comorbidities compared with those hospitalised during the pre-pandemic period. Notably, the proportion of patients diagnosed using cardiac MRI was higher during the pandemic phase (table 1).

Table 1: Baseline characteristics of patients hospitalised with myocarditis before and during the pandemic.

Variables		All patients	Pre-pandemic, n (%)	Pandemic, n (%)	p-value
Total hospitalisations with myocarditis		n = 7,053	n = 4,304	n = 2,749	
Sociodemographic	Female Patients	2,136 (30.3%)	1,313 (30.5%)	823 (29.9%)	0.61
	Swiss citizen	5,262 (74.6%)	3,224 (74.9%)	2,038 (74.1%)	0.47
	Year of admission				<0.001
	... 2012	307 (4.4%)	307 (7.1%)	0 (0.0%)	
	... 2013	378 (5.4%)	378 (8.8%)	0 (0.0%)	
	... 2014	428 (6.1%)	428 (9.9%)	0 (0.0%)	
	... 2015	545 (7.7%)	545 (12.7%)	0 (0.0%)	
	... 2016	608 (8.6%)	608 (14.1%)	0 (0.0%)	
	... 2017	669 (9.5%)	669 (15.5%)	0 (0.0%)	
	... 2018	626 (8.9%)	626 (14.5%)	0 (0.0%)	
	... 2019	743 (10.5%)	743 (17.3%)	0 (0.0%)	
	... 2020	792 (11.2%)	0 (0.0%)	792 (28.8%)	
	... 2021	982 (13.9%)	0 (0.0%)	982 (35.7%)	
	... 2022	975 (13.8%)	0 (0.0%)	975 (35.5%)	
	Age				
	... <30 years	1,744 (24.7%)	1,040 (24.2%)	704 (25.6%)	0.17
	... 30–59 years	2,914 (41.3%)	1,853 (43.1%)	1,061 (38.6%)	<0.001
	... ≥60 years	2,395 (34.0%)	1,411 (32.8%)	984 (35.8%)	0.009
Comorbidities	Diabetes type 1	29 (0.4%)	16 (0.4%)	13 (0.5%)	0.52
	Diabetes type 2	516 (7.3%)	260 (6.0%)	256 (9.3%)	<0.001
	Obesity	139 (2.0%)	60 (1.4%)	79 (2.9%)	<0.001
	Hypertension	1,827 (25.9%)	1,045 (24.3%)	782 (28.4%)	<0.001
	Heart failure	1,236 (17.5%)	682 (15.8%)	554 (20.2%)	<0.001
	Coronary heart disease	1,330 (18.9%)	805 (18.7%)	525 (19.1%)	0.68
	Atrial fibrillation	956 (13.6%)	660 (15.3%)	296 (10.8%)	<0.001
	Cerebrovascular disease	197 (2.8%)	103 (2.4%)	94 (3.4%)	0.011
	Peripheral artery disease	101 (1.4%)	50 (1.2%)	51 (1.9%)	0.017
	Chronic kidney disease	602 (8.5%)	312 (7.2%)	290 (10.5%)	<0.001
	Hepatopathy	335 (4.7%)	162 (3.8%)	173 (6.3%)	<0.001
	COPD	226 (3.2%)	120 (2.8%)	106 (3.9%)	0.013
	OSAS	176 (2.5%)	80 (1.9%)	96 (3.5%)	<0.001
	Dyslipidaemia	979 (13.9%)	540 (12.5%)	439 (16.0%)	<0.001
	Cancer	414 (5.9%)	156 (3.6%)	258 (9.4%)	<0.001
	Elixhauser comorbidity index, mean (SD)	1.7 (2.0)	1.5 (1.8)	2.0 (2.2)	<0.001
Specific diagnostics	Endomyocardial biopsy	213 (3.0%)	152 (3.5%)	61 (2.2%)	0.002
	Coronary angiography	2,053 (29.1%)	1,399 (32.5%)	654 (23.8%)	<0.001
	cardiac MRI	1,653 (23.4%)	882 (20.5%)	771 (28.0%)	<0.001
	Cardiac CT	308 (4.4%)	182 (4.2%)	126 (4.6%)	0.48
	Myocardial scintigraphy	27 (0.4%)	19 (0.4%)	8 (0.3%)	0.32
	cardiac PET	82 (1.2%)	53 (1.2%)	29 (1.1%)	0.50
	Transthoracic echocardiogram (TTE)	1,468 (20.8%)	906 (21.1%)	562 (20.4%)	0.54
	Transoesophageal echocardiogram (TEE)	277 (3.9%)	195 (4.5%)	82 (3.0%)	0.001

Incidence rate of myocarditis

The incidence rate of myocarditis increased from 26.7 per 100,000 hospitalisations in Q1 of 2012 to 73.8 per 100,000 hospitalisations in Q4 of 2022 (p for trend <0.001) (table S2 in the appendix). During the pandemic period, the incidence of myocarditis hospitalisations increased more rapidly (slope: 2.008; 95% confidence interval [CI], 2.006 to 2.011) than during the pre-pandemic period (slope: 1.141; 95% CI, 1.140 to 1.141) (table 2, figure 1a).

Table 2: Random-slope mixed-effects model of changes in myocarditis hospitalisation incidence between 2012 and 2022.

Outcome and study phase*			Coef. (95% CI)	Slope (95% CI)	Slope differs from zero	Change in slope from prior slope	Difference in slopes (male vs female)
All patients	Overall	Pre-pandemic	1.141 (1.140 to 1.141)	1.141 (1.140 to 1.141)	<0.001		
		Pandemic	0.868 (0.865 to 0.871)	2.008 (2.006 to 2.011)	<0.001	<0.001	
	Female	Pre-pandemic	0.747 (0.747 to 0.748)	0.747 (0.747 to 0.748)	<0.001		
		Pandemic	0.119 (0.115 to 0.124)	0.867 (0.862 to 0.871)	<0.001	<0.001	
	Male	Pre-pandemic	0.806 (0.805 to 0.807)	1.554 (1.553 to 1.554)	<0.001		<0.001
		Pandemic	1.549 (1.542 to 1.555)	3.221 (3.217 to 3.226)	<0.001	<0.001	<0.001
Inhabitants	Overall	Pre-pandemic	0.041 (0.041 to 0.041)	0.041 (0.041 to 0.041)	<0.001		
		Pandemic	0.020 (0.020 to 0.020)	0.060 (0.060 to 0.060)	<0.001	<0.001	
	Female	Pre-pandemic	0.028 (0.028 to 0.028)	0.028 (0.028 to 0.028)	<0.001		
		Pandemic	-0.005 (-0.005 to -0.004)	0.023 (0.023 to 0.023)	<0.001	<0.001	
	Male	Pre-pandemic	0.026 (0.026 to 0.026)	0.053 (0.053 to 0.054)	<0.001		<0.001
		Pandemic	0.047 (0.047 to 0.048)	0.096 (0.096 to 0.096)	<0.001	<0.001	<0.001
Age <30 years	Overall	Pre-pandemic	0.820 (0.818 to 0.821)	0.820 (0.818 to 0.821)	<0.001		
		Pandemic	3.564 (3.548 to 3.580)	4.383 (4.368 to 4.399)	<0.001	<0.001	
	Female	Pre-pandemic	0.529 (0.526 to 0.532)	0.529 (0.526 to 0.532)	<0.001		
		Pandemic	-0.299 (-0.328 to -0.271)	0.230 (0.203 to 0.258)	<0.001	<0.001	
	Male	Pre-pandemic	0.596 (0.591 to 0.600)	1.125 (1.122 to 1.128)	<0.001		<0.001
		Pandemic	8.584 (8.542 to 8.626)	9.410 (9.380 to 9.439)	<0.001	<0.001	<0.001
Age 30-59 years	Overall	Pre-pandemic	1.545 (1.544 to 1.547)	1.545 (1.544 to 1.547)	<0.001		
		Pandemic	0.268 (0.263 to 0.273)	1.814 (1.809 to 1.818)	<0.001	<0.001	
	Female	Pre-pandemic	0.881 (0.879 to 0.883)	0.881 (0.879 to 0.883)	<0.001		
		Pandemic	0.100 (0.090 to 0.111)	0.982 (0.972 to 0.991)	<0.001	<0.001	
	Male	Pre-pandemic	1.612 (1.609 to 1.615)	2.493 (2.491 to 2.496)	<0.001		<0.001
		Pandemic	0.312 (0.296 to 0.328)	2.905 (2.894 to 2.917)	<0.001	<0.001	<0.001
Age ≥60 years	Overall	Pre-pandemic	1.092 (1.091 to 1.092)	1.092 (1.091 to 1.092)	<0.001		
		Pandemic	-0.487 (-0.490 to -0.484)	0.605 (0.602 to 0.608)	<0.001	<0.001	
	Female	Pre-pandemic	0.773 (0.771 to 0.774)	0.773 (0.771 to 0.774)	<0.001		
		Pandemic	-0.058 (-0.063 to -0.053)	0.715 (0.710 to 0.719)	<0.001	<0.001	
	Male	Pre-pandemic	0.628 (0.626 to 0.630)	1.401 (1.399 to 1.402)	<0.001		<0.001
		Pandemic	-0.912 (-0.919 to -0.905)	0.430 (0.426 to 0.434)	<0.001	<0.001	<0.001

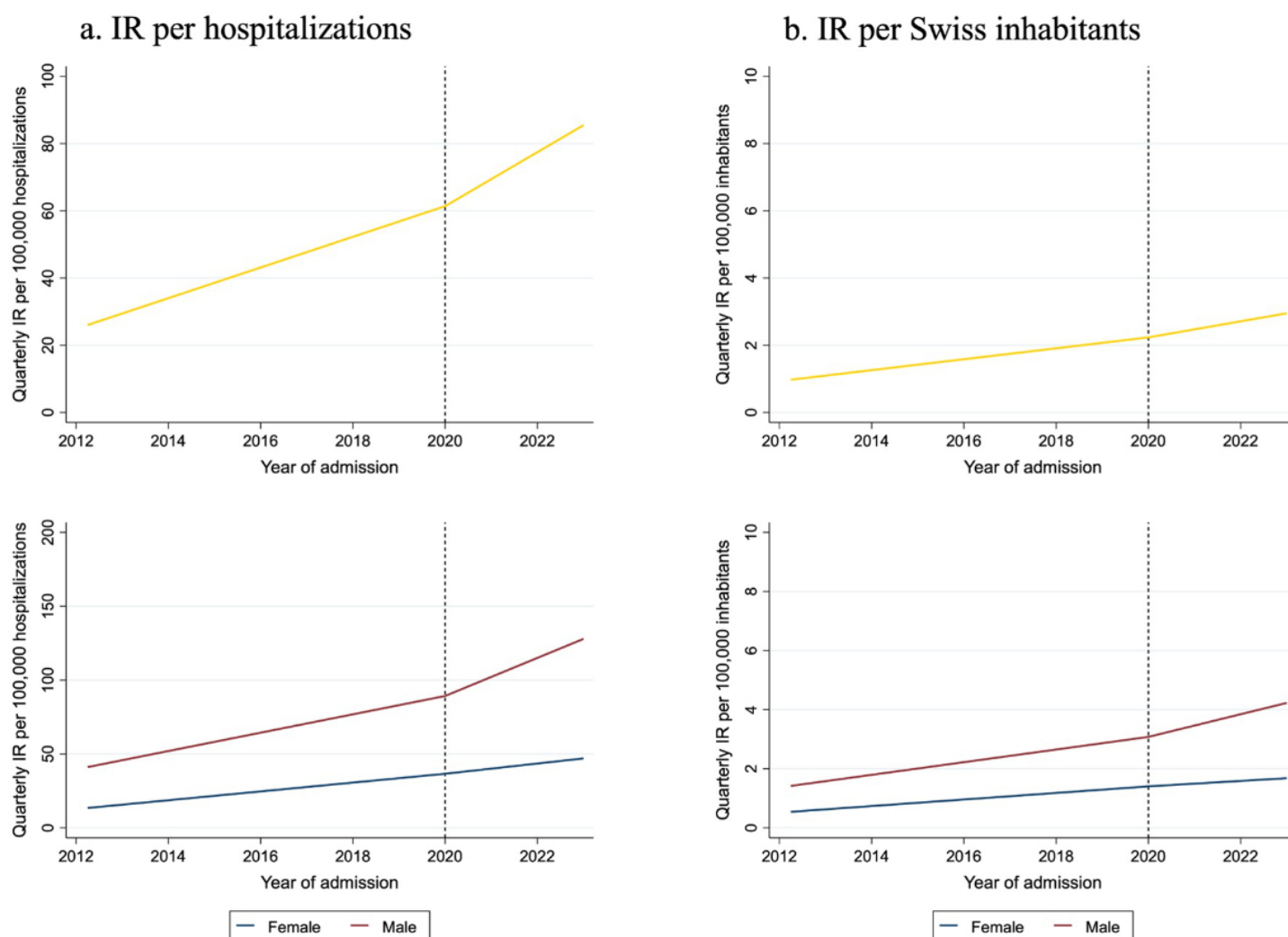


Figure 1: Primary outcome: myocarditis hospitalisation incidence over time for a) all patients and b) Swiss inhabitants.

Subgroup analyses

While the change in slopes between the pre-pandemic and pandemic periods among female patients did not translate into a clinically meaningful difference, the incidence of myocarditis hospitalisations in male patients was consistently higher throughout both periods, with a marked increase during the pandemic (table 2, figure 1a). Age stratification revealed a pronounced increase in myocarditis incidence among the young and middle-aged groups during the pandemic, whereas a smaller increase was noted in the incidence of myocarditis hospitalisations among the older population (table 2, figure 2).

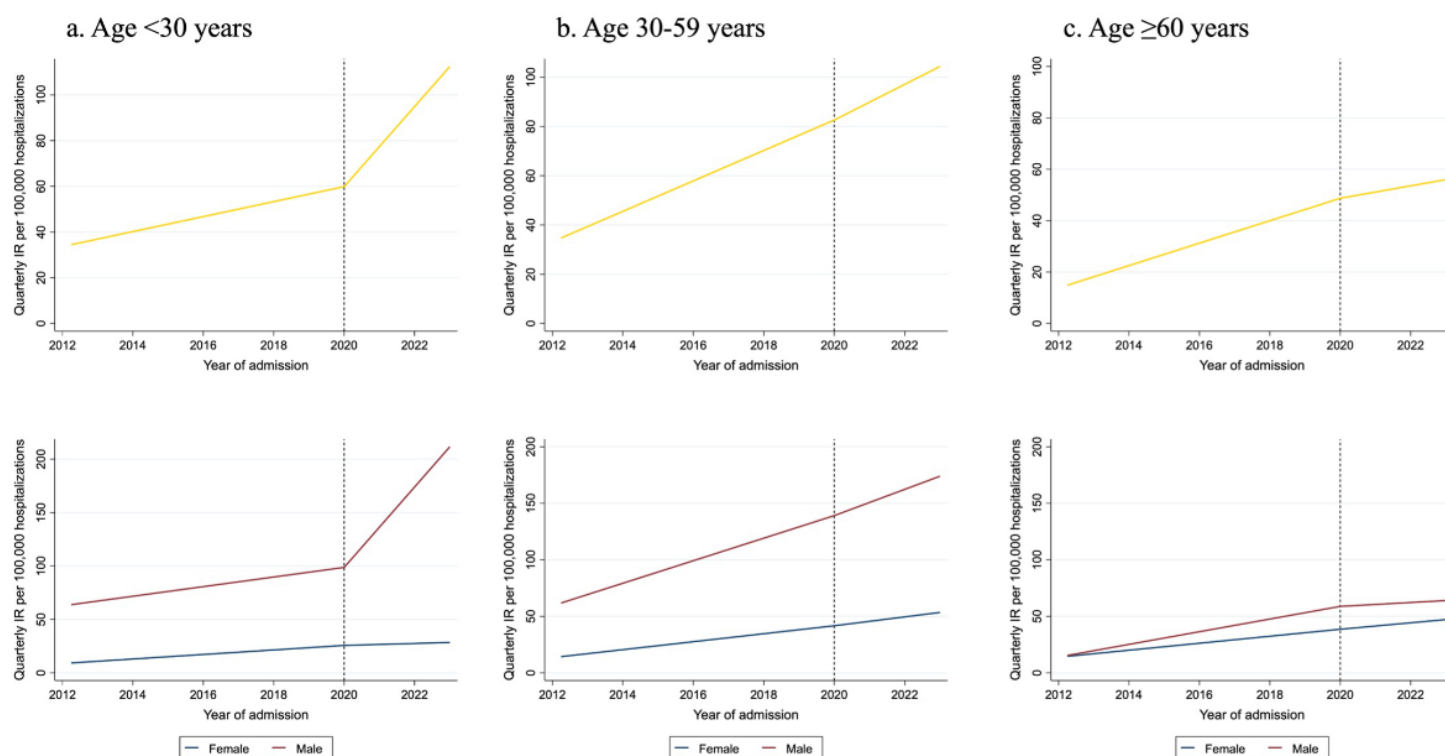


Figure 2: Myocarditis hospitalisation incidence over time by age group.

Sensitivity analysis

To assess the robustness of our findings, we conducted sensitivity analyses using the annual population of Switzerland. For every 100,000 inhabitants, the quarterly incidence of myocarditis hospitalisations increased from 1.0 in 2012 to 2.6 in 2022 (p for trend <0.001). Notably, the increase in myocarditis hospitalisations was more pronounced during the pandemic period, with a slope of 0.060 (95% CI: 0.060 to 0.060; $p <0.001$) compared with the pre-pandemic period slope of 0.041 (95% CI: 0.041 to 0.041; $p <0.001$) (table 2, figure 1b).

Trend in incidence of pericarditis hospitalisations

Baseline characteristics of patients hospitalised with pericarditis are presented in table S3 in the appendix. The quarterly incidence of pericarditis hospitalisations increased from 222.4 to 325.8 cases per 100,000 hospitalisations over the study period (table S4 in the appendix). However, when adjusted for population growth in Switzerland, this rise did not translate into a clinically meaningful increase in the incidence of pericarditis hospitalisations during the pandemic period (table S5, figure S1 in the appendix). Between subgroups, the incidence of pericarditis hospitalisation was higher in the older and male population, with the largest gap between sexes in the middle-aged group (table S5, figure S2 in the appendix).

In-hospital outcomes

Patients with myocarditis had an increased risk of in-hospital outcomes compared to controls in both the pre-pandemic and pandemic periods. The relative risk differed significantly between the two phases. ICU admission rates declined (31.3% before the pandemic to 24.8% during the pandemic), along with a less pronounced association between myocarditis and ICU admission (OR 5.94 vs 4.17; $p <0.001$ for interaction). By contrast, in-hospital mortality increased among patients with myocarditis during the pandemic (2.0% to 3.8%), with a corresponding increase in effect size (OR 1.12 to 1.66; $p = 0.010$) compared with controls. Similarly, myocarditis was associated with a greater increase in intubations (OR 2.93 vs 2.30; $p = 0.010$) and in hospital length of stay during

the pandemic (coef. 1.34 vs 0.64; $p = 0.007$). Although 30-day readmission rates remained relatively stable, the protective association of myocarditis before the pandemic decreased ($p = 0.008$). No significant interaction was observed for ICU length of stay (table 3).

Table 3: In-hospital outcomes for patients hospitalised with myocarditis before and during the pandemic.

Control	Pericarditis	Pre-pandemic		Pandemic		P of interaction
		Control	Pericarditis			
Outcome	Hospitalisations, n	9,808,097	27,243	3,662,763	12,940	
ICU admission	Events, n (%)	657156 (6.7)	10873 (39.9)	219503 (6.0)	4449 (34.4)	
	OR (95% CI)	5.92 (5.75 to 6.10)		4.73 (4.52 to 4.95)		<0.001
30-day readmission	Events, n (%)	664807 (6.8)	2731 (10.0)	258377 (7.1)	1334 (10.3)	
	OR (95% CI)	1.10 (1.05 to 1.15)		1.02 (0.95 to 1.08)		0.06
Intubation	Events, n (%)	219481 (2.2)	5883 (21.6)	80369 (2.2)	2449 (18.9)	
	OR (95% CI)	6.81 (6.57 to 7.06)		5.22 (4.94 to 5.53)		<0.001
In-hospital mortality	Events, n (%)	192690 (2.0)	2025 (7.4)	77573 (2.1)	997 (7.7)	
	OR (95% CI)	2.15 (2.04 to 2.26)		1.92 (1.78 to 2.07)		0.013
Length of hospital stay	Mean (SD)	5.79 (8.55)	11.9 (16.93)	5.22 (6.94)	11.23 (14.28)	
	Coef. (95% CI)	3.51 (3.32 to 3.70)		2.91 (2.68 to 3.13)		<0.001
Length of ICU stay	Mean (SD)	3.1 (7.13)	5.60 (12.83)	3.55 (7.89)	5.4 (10.73)	
	Coef. (95% CI)	2.08 (1.85 to 2.30)		1.39 (1.09 to 1.69)		<0.001

Pericarditis was associated with a higher risk of adverse outcomes both before and during the pandemic compared with controls. Although the strength of association with ICU admission, hospital stay, and intubation declined during the pandemic (all $p < 0.001$), the risk remained elevated, whereas the association with in-hospital mortality decreased modestly ($p = 0.013$). No significant change was observed in 30-day readmission ($p = 0.06$) (table S6 in the appendix).

Discussion

In this study investigating 7,053 myocarditis hospitalisations in Switzerland, we detected a significant increase in incidence rates from 26.7 to 73.8 per 100,000 hospitalisations from Q1 of 2012 to Q4 of 2022, with a more pronounced increase during the COVID-19 pandemic. This increase was particularly notable among young and middle-aged male patients, whereas a decline was observed in the older population. Furthermore, the pandemic was linked to worse in-hospital outcomes for patients with myocarditis, including higher mortality, more intubations, and higher readmission rates, along with longer stays in hospitals and ICUs.

During the first weeks and months of the pandemic, total hospitalisations and presentations at the emergency ward in Switzerland decreased [27, 28]. For this reason, we performed a sensitivity analysis based on the yearly population of Switzerland to minimise potential confounding. This enabled us to analyse the association between the COVID-19 pandemic and the incidence of inflammatory heart disease hospitalisations, despite the possible reduction of other pathogens with myocardial tropism (i.e. adenoviruses and enteroviruses) [11].

Our study findings underscore a substantial rise in myocarditis hospitalisations during the COVID-19 pandemic, aligning with the pre-pandemic incidence estimates in the United States, ranging from 1 to 10 cases per 100,000 individuals, as reported by Raffaniello et al. [9]. This increase likely reflects the elevated risk of myocarditis associated with SARS-CoV-2 infection and subsequent vaccination efforts [6, 29–31], highlighting a significant public health concern. Mechanistically, SARS-CoV-2 utilises angiotensin-converting enzyme 2 (ACE2) as a cellular entry receptor, which is highly expressed in cardiac tissue and serves a critical counter-regulatory role within the renin-angiotensin-aldosterone system (RAAS) [32, 33]. Viral binding to ACE2 may impair its protective effects, thereby promoting inflammation and myocardial injury [33]. Supporting this hypothesis, in another study, we demonstrated evidence of RAAS downregulation in patients admitted with COVID-19 compared with SARS-CoV-2-negative matched controls presenting with comparable clinical features, suggesting a potential pathway linking infection to myocardial inflammation [34].

In contrast to our findings, a recent study noted a decline in myocarditis hospitalisations in 2020 compared with the pre-pandemic period [35]. However, it is critical to note that this study did not extend into the period of widespread SARS-CoV-2 vaccinations, which have been associated with an increase in myocarditis cases, particularly among younger males, as reported by the CDC [9]. While the exact pathomechanism for vaccine-associated myocarditis remains unclear, the most promising explanations involve molecular mimicry and excessive innate immune activation [36]. Consistent with historical data, myocarditis predominantly affected younger males under 50 years during both the pre-pandemic and pandemic periods, maintaining a sex ratio of approximately 2 to 4 males for every female [37, 38]. Similarly, other studies showed myocarditis due to COVID-19 to be more common in men than in women [39].

Furthermore, studies have shown autoimmune inflammatory rheumatic disease flares after mRNA COVID-19 vaccination in approximately 10–15% of patients. This highlights the potential role of underlying immune dysregulation in shaping post-vaccination inflammatory responses. Such variability in immune regulation may further explain why only a subset of exposed individuals develops clinically manifest myocarditis requiring hospitalisation [45, 46].

Our findings indicate an increased in-hospital mortality rate among patients hospitalised with myocarditis during the pandemic period. This patient group was generally older and exhibited more comorbidities than those hospitalised during the pre-pandemic period. One potential explanation for these differences could be the underreporting of ICD-10 and CHOP codes in our nationwide database during the pre-pandemic period. Supporting our observations, other studies have also documented a rise in mortality rates during the pandemic period [35, 39, 47]. This increase may be further compounded by a reduction in hospitalisations for less severe diseases during the pandemic, as myocarditis can often present subclinically, with atypical or minor symptoms [48]. Furthermore, fewer patients with myocarditis required ICU stays during the pandemic, likely due to the scarcity of resources for intensive care, exacerbated by the high demand from patients with COVID-19 and a shortage of ICU nursing staff [49, 50].

Current studies showed similar incidences of pericarditis in the last decade [51]. In contrast to myocarditis, the incidence of pericarditis did not increase significantly more during the pandemic period compared with the pre-pandemic period. One reason for this finding could be that beyond viral infections, the etiological spectrum of pericarditis contains a wide spectrum of non-infective conditions, including rheumatological diseases, which were not influenced by the pandemic [52, 53]. Our findings align with other studies that also found no evidence of an increased incidence of pericarditis following SARS-CoV-2 vaccination or COVID-19 [18, 54].

This study is limited by its use of administrative data from the Swiss Federal Statistical Office, which does not allow for the confirmation of diagnostic methods or the determination of myocarditis and pericarditis aetiology. Therefore, we could not assess whether cases were related to SARS-CoV-2 infection, vaccination, or other causes. In addition, because the database includes only hospitalisation diagnoses and no outpatient history or medication data, underlying autoimmune disease and immunosuppressive therapy could not be adequately assessed. Furthermore, this study relied on Swiss nationwide data and may not be fully generalisable to countries with different demographics, healthcare access, or pandemic and vaccination dynamics. However, given the similarities between the Swiss healthcare system and other high-income settings, our findings are likely applicable to comparable populations, though confirmation in diverse settings is warranted. Moreover, greater use of cardiac MRI over time may have increased the detection of myocarditis, so part of the observed increase in incidence could reflect improved ascertainment rather than a true increase in disease burden. However, we lacked data to distinguish between these effects. Finally, although no clear evidence of misclassification was observed, given the nature of the data, potential misclassification and underreporting of diagnoses and diagnostic procedures cannot be ruled out.

Conclusion

This nationwide cohort study suggests a more pronounced increase in the incidence of hospitalisations with myocarditis during the COVID-19 pandemic. Further exploration is needed to determine whether this finding is directly linked to COVID-19 and its vaccinations, or whether it is driven by increased clinical awareness.

Data sharing statement

Restrictions apply to the availability of data generated or analysed during this study to preserve patient confidentiality or because the data were used under license. Upon request, the corresponding author will detail the restrictions and any conditions under which access to some data may be provided.

Notes

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Author contributions: Data access: Héritier, Laager, and Kutz had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: Héritier, Laager, Schellendorfer, and Kutz. Acquisition, analysis, or interpretation of data: Héritier, Laager, and Kutz. Drafting of the manuscript: Héritier, Laager, and Kutz. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: Héritier, Laager, and Kutz.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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Table S1: ICD-10-GM codes and CHOP codes (at any position)

Myocarditis	I40, I41, I51.4, B33.2, I01.2
Pericarditis	I30, I31.0, I31.1, I31.9, I32, I01.0, I09.2
Comorbidities	
Diabetes	E10, E11
Adipositas	E65, E66
Hypertonia	I10, I11, I12, I13, I15
Congestive heart failure	I50, I11.0, I13.0, I13.2
Coronary artery disease	I20, I21, I22, I23, I24, I25
Atrial fibrillation	I48
Cerebrovascular disease	I60, I61, I62, I63, I64, I65, I66, I67, I69
Peripheral arterial vascular disease	I70.2
Chronic kidney disease	N18, N19
Hepatopathia	K7
COPD	J44
Sleep apnoea	G47.3
Dyslipidemia	E78
Cancer	C0, C1, C2, C3, C4, C5, C6, C7, C8, C9
Diagnostics	
Endomyocardial biopsy	37.25.20
Coronary Angiography	37.22, 88.5, 37.2A
Cardiac MRI	88.92.2
Cardiac CT	87.41.1
Myocardial Scintigraphy	92.05.1
Cardiac PET	92.19.00
Transthoracic echocardiogram (TTE)	88.72.1
Transesophageal echocardiogram (TEE)	88.72.2

Abbreviations: Abbreviations: CHOP, Swiss operational procedure codes, COPD, chronic obstructive lung disease; CT, computed tomography; ICD-10-GM, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, German Modification (ICD-10, GM); MRI, magnetic resonance imaging; PET, positron emission tomography;

Table S2: Myocarditis incidence rates per 100'000 hospitalizations

	Q1/2012	Q4/2019	Q4/2022	P for Trend
All Patients				
Overall	26.7	62.4	73.8	<0.001
Female	13.9	33.4	41.3	<0.001
Male	41.6	94.9	109.3	<0.001
Inhabitants				
Overall	1.0	2.3	2.6	<0.001
Female	0.6	1.3	1.5	<0.001
Male	1.5	3.3	3.7	<0.001
Age <30 years				
Overall	34.9	60.0	86.5	<0.001
Female	5.4	37.5	18.5	<0.001
Male	68.9	85.5	160.3	<0.001
Age 30-59 years				
Overall	39.0	92.4	107.3	<0.001
Female	17.5	38.7	58.0	<0.001
Male	67.8	165.9	175.0	<0.001
Age ≥60 years				
Overall	13.7	44.2	48.8	<0.001
Female	15.4	27.6	39.4	<0.001
Male	11.9	60.5	57.9	<0.001

Table S3: Baseline characteristics of patients hospitalized with pericarditis before and during the pandemic

Variables	All Patients	Prepandemic, n(%)	Pandemic, n (%)	p-value
Total hospitalisations with pericarditis	N=40,183	N=27,243	N=12,940	
Sociodemographic				
Female Patients	15,972 (39.7%)	10,626 (39.0%)	5,346 (41.3%)	<0.001
Swiss citizen	31,370 (78.1%)	21,291 (78.2%)	10,079 (77.9%)	0.55
Year of admission				<0.001
2012	2,839 (7.1%)	2,839 (10.4%)	0 (0.0%)	
2013	3,083 (7.7%)	3,083 (11.3%)	0 (0.0%)	
2014	3,072 (7.6%)	3,072 (11.3%)	0 (0.0%)	
2015	3,226 (8.0%)	3,226 (11.8%)	0 (0.0%)	
2016	3,520 (8.8%)	3,520 (12.9%)	0 (0.0%)	
2017	3,638 (9.1%)	3,638 (13.4%)	0 (0.0%)	
2018	3,795 (9.4%)	3,795 (13.9%)	0 (0.0%)	
2019	4,070 (10.1%)	4,070 (14.9%)	0 (0.0%)	
2020	3,963 (9.9%)	0 (0.0%)	3,963 (30.6%)	
2021	4,450 (11.1%)	0 (0.0%)	4,450 (34.4%)	
2022	4,527 (11.3%)	0 (0.0%)	4,527 (35.0%)	
Age				
Age <30 years	4,330 (10.8%)	3,086 (11.3%)	1,244 (9.6%)	<0.001
Age 30-59 years	12,112 (30.1%)	8,487 (31.2%)	3,625 (28.0%)	<0.001
Age ≥60 years	23,741 (59.1%)	15,670 (57.5%)	8,071 (62.4%)	<0.001
Comorbidities				
Diabetes type 1	173 (0.4%)	116 (0.4%)	57 (0.4%)	0.83
Diabetes type 2	5,091 (12.7%)	3,241 (11.9%)	1,850 (14.3%)	<0.001
Obesity	1,117 (2.8%)	684 (2.5%)	433 (3.3%)	<0.001
Hypertension	16,394 (40.8%)	10,764 (39.5%)	5,630 (43.5%)	<0.001
Heart failure	10,020 (24.9%)	6,250 (22.9%)	3,770 (29.1%)	<0.001
Coronary heart disease	11,078 (27.6%)	7,375 (27.1%)	3,703 (28.6%)	0.001
Atrial fibrillation	11,483 (28.6%)	7,505 (27.5%)	3,978 (30.7%)	<0.001
Cerebrovascular disease	2,027 (5.0%)	1,223 (4.5%)	804 (6.2%)	<0.001
Peripheral artery disease	1,315 (3.3%)	797 (2.9%)	518 (4.0%)	<0.001
Chronic kidney disease	7,425 (18.5%)	4,925 (18.1%)	2,500 (19.3%)	0.003
Hepatopathy	2,264 (5.6%)	1,417 (5.2%)	847 (6.5%)	<0.001
COPD	2,649 (6.6%)	1,711 (6.3%)	938 (7.2%)	<0.001
OSAS	1,278 (3.2%)	771 (2.8%)	507 (3.9%)	<0.001
Dyslipidemia	7,485 (18.6%)	4,828 (17.7%)	2,657 (20.5%)	<0.001
Cancer	6,214 (15.5%)	4,041 (14.8%)	2,173 (16.8%)	<0.001
Elixhauser comorbidity index, mean (SD)	3.0 (2.4)	2.8 (2.4)	3.4 (2.5)	<0.001
Specific diagnostics				
Endomyocardial Biopsi	219 (0.5%)	151 (0.6%)	68 (0.5%)	0.71
Coronary Angiography	5,745 (14.3%)	4,185 (15.4%)	1,560 (12.1%)	<0.001
cardiac MRI	1,658 (4.1%)	1,019 (3.7%)	639 (4.9%)	<0.001
Cardiac CT	607 (1.5%)	289 (1.1%)	318 (2.5%)	<0.001
Myocardial Scintigraphy	123 (0.3%)	96 (0.4%)	27 (0.2%)	0.015
cardiac PET	57 (0.1%)	26 (0.1%)	31 (0.2%)	<0.001
Transthoracic Echokardiogram (TTE)	8,484 (21.1%)	5,886 (21.6%)	2,598 (20.1%)	<0.001
Transesophageal Echocardiogram (TEE)	4,442 (11.1%)	2,944 (10.8%)	1,498 (11.6%)	0.021

Table S4: Pericarditis incidence rates per 100'000 hospitalizations

	Q1/2012	Q4/2019	Q4/2022	P for Trend
All Patients				
Overall	222.4	338.7	325.8	<0.001
Female	161.0	241.0	269.0	<0.001
Male	294.2	448.2	387.9	<0.001
Inhabitants				
Overall	8.5	12.5	11.5	<0.001
Female	6.6	9.3	9.8	<0.001
Male	10.5	15.7	13.1	<0.001
Age <30 years				
Overall	117.7	179.9	158.6	<0.001
Female	46.0	106.9	77.0	<0.001
Male	200.5	263.0	247.1	0.004
Age 30-59 years				
Overall	239.0	293.5	290.4	<0.001
Female	139.8	165.2	217.1	<0.001
Male	371.9	468.9	391.1	0.001
Age ≥60 years				
Overall	262.4	434.9	413.9	<0.001
Female	237.3	358.5	387.2	<0.001
Male	289.2	509.7	439.4	<0.001

Table S5: Random slope mixed-effects model of changes in pericarditis hospitalization incidence between 2012 and 2022

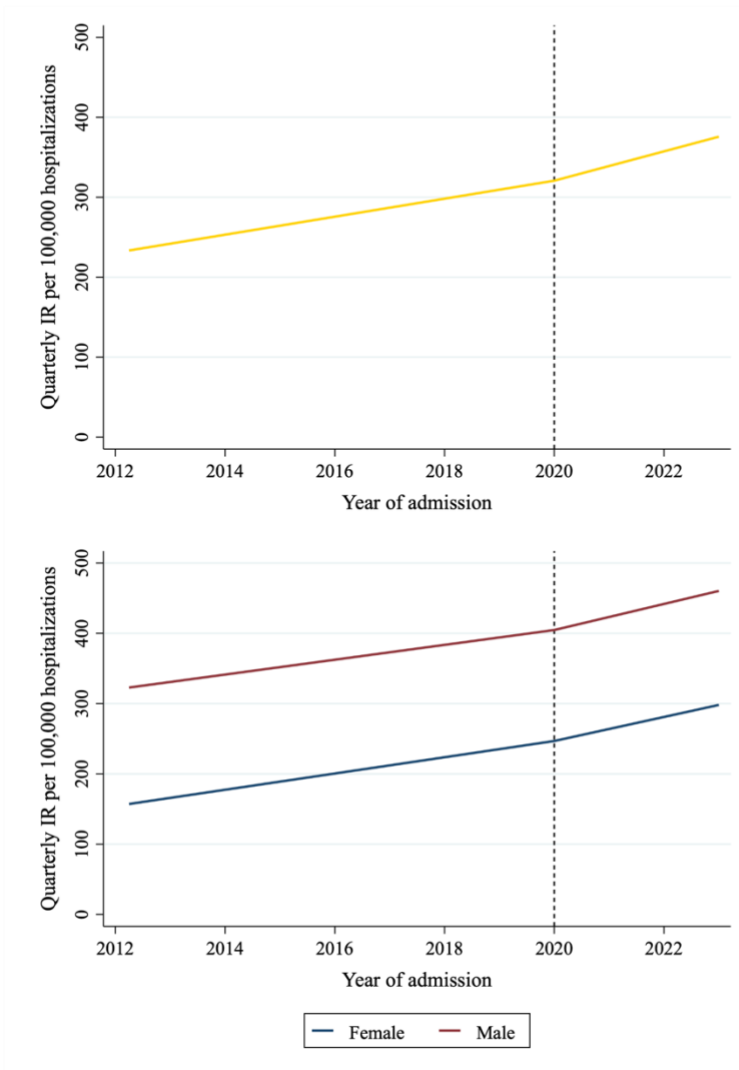
Outcome and study phase*	Coef. (95% CI)	Slope (95% CI)	Slope differs from zero	Change in slope from prior slope	Difference in slopes (male vs. female)
All Patients					
Overall					
Prepandemic	2.814 (2.813 to 2.815)	2.814 (2.813 to 2.815)	<0.001		
Pandemic	1.772 (1.768 to 1.776)	4.586 (4.582 to 4.589)	<0.001	<0.001	
Female					
Prepandemic	2.890 (2.889 to 2.892)	2.890 (2.889 to 2.892)	<0.001		
Pandemic	1.387 (1.379 to 1.394)	4.277 (4.270 to 4.283)	<0.001	<0.001	
Male					
Prepandemic	-0.250 (-0.252 to -0.248)	2.640 (2.638 to 2.642)	<0.001		<0.001
Pandemic	0.612 (0.601 to 0.622)	4.638 (4.632 to 4.645)	<0.001	<0.001	<0.001
Inhabitants					
Overall					
Prepandemic	0.097 (0.097 to 0.097)	0.097 (0.097 to 0.097)	<0.001		
Pandemic	0.017 (0.017 to 0.018)	0.114 (0.114 to 0.114)	<0.001	<0.001	
Female					
Prepandemic	0.102 (0.102 to 0.102)	0.102 (0.102 to 0.102)	<0.001		
Pandemic	0.014 (0.014 to 0.015)	0.116 (0.116 to 0.116)	<0.001	<0.001	
Male					
Prepandemic	-0.010 (-0.010 to -0.010)	0.092 (0.092 to 0.092)	<0.001		<0.001
Pandemic	0.005 (0.005 to 0.005)	0.111 (0.111 to 0.112)	<0.001	<0.001	<0.001
Age <30 years					
Overall					
Prepandemic	0.955 (0.953 to 0.957)	0.955 (0.953 to 0.957)	<0.001		
Pandemic	0.330 (0.317 to 0.343)	1.285 (1.273 to 1.297)	<0.001	<0.001	
Female					
Prepandemic	0.657 (0.653 to 0.661)	0.657 (0.653 to 0.661)	<0.001		
Pandemic	1.270 (1.248 to 1.292)	1.927 (1.907 to 1.947)	<0.001	<0.001	
Male					
Prepandemic	0.588 (0.582 to 0.594)	1.245 (1.241 to 1.249)	<0.001		<0.001
Pandemic	-1.838 (-1.871 to -1.806)	0.677 (0.655 to 0.698)	<0.001	<0.001	<0.001
Age 30-59 years					
Overall					
Prepandemic	1.849 (1.847 to 1.852)	1.849 (1.847 to 1.852)	<0.001		
Pandemic	1.553 (1.542 to 1.564)	3.402 (3.392 to 3.412)	<0.001	<0.001	
Female					
Prepandemic	2.069 (2.064 to 2.073)	2.069 (2.064 to 2.073)	<0.001		
Pandemic	1.449 (1.430 to 1.467)	3.517 (3.501 to 3.533)	<0.001	<0.001	
Male					
Prepandemic	-0.389 (-0.397 to -0.382)	1.679 (1.674 to 1.685)	<0.001		<0.001
Pandemic	0.014 (-0.016 to 0.043)	3.141 (3.122 to 3.160)	<0.001	<0.001	<0.001
Age ≥60 years					
Overall					
Prepandemic	4.078 (4.076 to 4.080)	4.078 (4.076 to 4.080)	<0.001		
Pandemic	1.662 (1.652 to 1.672)	5.741 (5.732 to 5.749)	<0.001	<0.001	
Female					
Prepandemic	4.401 (4.397 to 4.404)	4.401 (4.397 to 4.404)	<0.001		
Pandemic	0.522 (0.504 to 0.540)	4.922 (4.907 to 4.938)	<0.001	<0.001	
Male					
Prepandemic	-0.717 (-0.723 to -0.712)	3.683 (3.679 to 3.687)	<0.001		<0.001
Pandemic	1.798 (1.773 to 1.823)	6.003 (5.988 to 6.019)	<0.001	<0.001	<0.001

Table S6: In-hospital outcomes for patients hospitalized with pericarditis before and during the pandemic

Outcome	Pre-pandemic		Pandemic		P of interaction
	Control	Pericarditis	Control	Pericarditis	
Hospitalizations, n	9,808,097	27,243	3,662,763	12,940	
ICU admission					
events, n (%)	657,156 (6.7)	10,873 (39.9)	219,503 (6.0)	4,449 (34.4)	<0.001
OR (95% CI)	5.92 (5.75 to 6.10)		4.73 (4.52 to 4.95)		
30-day readmission					
events, n (%)	664,807 (6.8)	2,731 (10.0)	258,377 (7.1)	1,334 (10.3)	0.06
OR (95% CI)	1.10 (1.05 to 1.15)		1.02 (0.95 to 1.08)		
Intubation					
events, n (%)	219,481 (2.2)	5,883 (21.6)	80,369 (2.2)	2,449 (18.9)	<0.001
OR (95% CI)	6.81 (6.57 to 7.06)		5.22 (4.94 to 5.53)		
In-hospital mortality					
events, n (%)	192,690 (2.0)	2,025 (7.4)	77,573 (2.1)	997 (7.7)	0.013
OR (95% CI)	2.15 (2.04 to 2.26)		1.92 (1.78 to 2.07)		
Length of hospital stay					
mean (SD)	5.79 (8.55)	11.9 (16.93)	5.22 (6.94)	11.23 (14.28)	<0.001
Coef (95% CI)	3.51 (3.32 to 3.70)		2.91 (2.68 to 3.13)		
Length of ICU stay					
mean (SD)	3.1 (7.13)	5.60 (12.83)	3.55 (7.89)	5.4 (10.73)	<0.001
Coef (95% CI)	2.08 (1.85 to 2.30)		1.39 (1.09 to 1.69)		

Figure S1: Pericarditis hospitalization incidence over time

a. IR per hospitalizations



b. IR per Swiss inhabitants

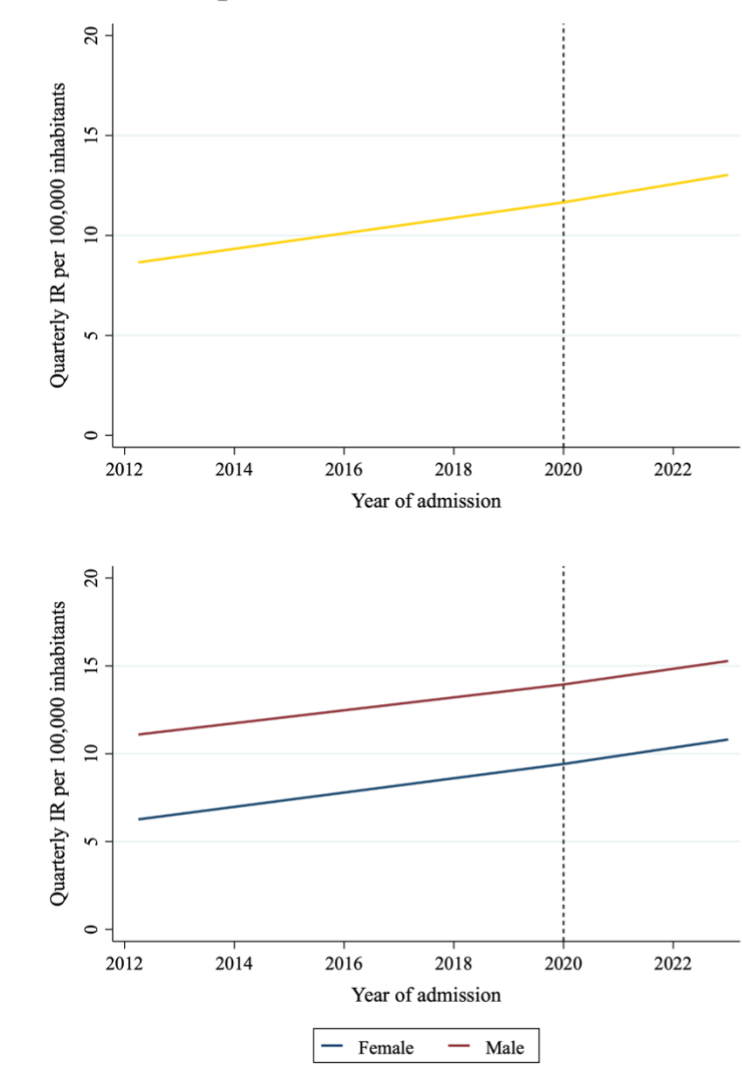


Figure S2: Pericarditis hospitalization incidence over time by age groups

