Original article

Incidence of acute myocarditis and pericarditis during the coronavirus disease 2019 pandemic: comparison with the prepandemic period

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Background **Myocarditis and pericarditis have been proposed to account for a proportion of cardiac injury during SARS-CoV-2 infection. The impact of COVID-19 the pandemic on the incidence of this acute inflammatory cardiac disease was not systematically evaluated.**

Aim **To examine the incidence and prevalence of inflammatory heart disorders prior to and during the COVID-19 pandemic.**

Methods **We compared the incidence and prevalence of acute inflammatory heart diseases (myocarditis, pericarditis) in the provinces of Pisa, Lucca and Livorno in two time intervals: prior to (PRECOVID, from 1 June 2018 to 31 May 2019) and during the COVID-19 pandemic (COVID, from 1 June 2020 to May 2021).**

Results **Overall 259 cases of inflammatory heart disease (myocarditis and/or pericarditis) occurred in the areas of interest. The annual incidence was of 11.3 cases per 100 000 inhabitants. Particularly, 138 cases occurred in the pre-COVID, and 121 in the COVID period. The annual incidence of inflammatory heart disease was not significantly different (12.1/100 000 in PRECOVID vs 10.3/100 000 in COVID, $P = 0.22$). The annual incidence of myocarditis was significantly higher in PRECOVID than in COVID, respectively 8.1/100 000/year vs. 5.9/100 000/year ($P = 0.047$) consisting of a net reduction of 27% of cases. Particularly the incidence of myocarditis was significantly lower in COVID than in PRECOVID in the class of age 18–24<th> years. Despite this, myocarditis of the COVID period had more wall motion abnormalities and greater LGE extent. The annual incidence of pericarditis was, instead, not significantly different (4.03/100 000 vs, 4.47/100 000, $P = 0.61$).**

Conclusion **Despite a possible etiologic role of SARS-CoV-2 and an expectable increased incidence of myocarditis and pericarditis, data of this preliminary study, with a geographically limited sample size, suggest a decrease in acute myocarditis and a stable incidence of pericarditis and of myopericarditis/perimyocarditis.**

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Introduction

Cardiovascular damage occurred in up to 30% of patients during the coronavirus disease 2019 (COVID-19) pandemic caused by SARS-CoV-2 infection, and was related to higher disease severity.[1] Myocarditis, stroke, various thrombotic events, and myocardial infarction were the most frequently reported cardiovascular consequences of SARS-CoV-2.[2] Myocarditis has been proposed to account for a proportion of cardiac injury. Viral infections, such as enteroviruses and adenoviruses, are common causes of myocarditis, which can cause a combination of direct cellular injury and T-cell cytotoxic response. The suggested mechanisms of myocardial injury in patients with COVID-19 include myocardial damage by a cytokine storm triggered by an imbalanced response of T helper 1 cells (TH1 cells) and T helper 2 cells (TH2 cells) and respiratory dysfunction and hypoxaemia caused by SARS-CoV-2 infection.[3]

In the initial phase of the COVID 19 pandemic, the evidence for COVID-19 myocarditis has been limited to case reports and case series.[4] More recently, a 16 times increased risk for myocarditis among patients with COVID-19 was reported, in particular among children and older adults.[5] Attention has to be put in interpreting these reports as suggestive of a causality link between SARS-CoV-2 infection and myocarditis occurrence.

The aim of this study is to explore the incidence and prevalence of acute inflammatory heart diseases

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analyzing the occurrence of these diseases prior to and during the COVID-19 pandemic.

Methods

This is a retrospective cohort study examining the incidence and prevalence of acute inflammatory heart diseases (myocarditis, pericarditis, myopericarditis, and perimyocarditis) in the Tuscany area including the provinces of Pisa, Lucca, and Livorno (total population of 1 141 285 inhabitants) by comparison of two time intervals of 1 year each: prior to the COVID-19 (PRECOVID, from 1 June 2018 to 31 May 2019) and during the pandemic period (COVID, from 1 June 2020 to 31 May 2021). We excluded the time between June and December 2019 as we could not rule out the presence of SARS-COV2 in Italy during this period. Yet, we excluded the time between January and May 2020 because of of the strict lockdown in Italy. Clinically suspected myocarditis occurring within 10 days from a SARS-COV2 dose of vaccination were excluded because it was iatrogenic myocarditis.

A diagnostic algorithm adapted from the European Society of Cardiology guidelines was used to diagnose acute myocarditis.[6] Coronary artery angiography was performed on all patients to rule out obstructive coronary artery disease, excluding those younger than 30 years of age with a low risk of coronary artery disease. Clinically suspected acute myocarditis was diagnosed when symptomatic patients with chest pain (pericardial or pseudoischemic pain) met one or more diagnostic criteria (increased high-ssensitivity troponin, new ECG modification, wall motion abnormalities with preserved LVEF on echocardiography) or when asymptomatic patients met two or more diagnostic criteria. In case of suspected myocarditis with chest-pain presentation in hemodynamic stable patients, cardiac magnetic resonance (CMR) was used for complete diagnosis. Using the CMR revised Lake Louise criteria, a diagnosis was fullfilled by the presence of a T2-based criterion (myocardial edema, increased native T2 at mapping) and of a T1-based criterion (late gadolinium enhancement, increased native T1 at mapping, increased extracellular volume).[7]

In case of life-threatening clinical presentation of myocarditis caused by ventricular arrhythmias or acute heart failure, endomyocardial biopsy (EMB) was performed and eventually CMR was used to evaluate the signs of myocardial damage after patient hemodynamic stabilization[6].

For the diagnosis of acute pericarditis, clinically suspected acute pericarditis was diagnosed when at least two of the following criteria were present: typical chest pain, pericardial friction rub, suggestive ECG changes, new or worsening pericardial effusion.[8,9] A definite diagnosis of acute pericarditis was made, through CMR, in patients who presented signal hyperintensity of the pericardial layers in T2-STIR pulse sequence and/or enhancement of layers in LGE images with or without pericardial effusion.

In the presence of both signs of myocardial and pericardial inflammation, we defined as myopericarditis in case of pericarditis with minimal signs of myocardial involvement, and on the contrary, perimyocarditis when myocarditis was associated with mild signs of pericardial involvement (as pericardial effusion without signs of inflammation or signs of parcel pericardial inflammation).[10]

Cardiac magnetic resonance acquisition protocol

CMR imaging was performed in a single core-lab of Pisa, with a 1.5-T magnetic resonance scanner (Artist, GE Healthcare, Milwaukee, Wisconsin, USA) using dedicated cardiac software, a 16-channel phased-array surface receiver coil, and vectocardiogram triggering. We acquired cine balanced steady-state free precession (cine-bSSFP) images, T2-weighted images, T1 and T2 mapping, and LGE at 10 min after gadolinium injection in the short-axis (9–13 images covering the entire LV), two-chamber, and four-chamber planes. Short-axis cine-bSSFP images were acquired immediately after gadolinium injection for hyperemia assessment.

Cardiac magnetic resonance analysis

All CMR studies were analyzed off-line using a workstation with dedicated cardiac software (cvi42, Circle Software) with consensus among three experienced observers who were blinded to the clinical presentation results. To evaluate LV global and regional function and calculate LV mass, the endocardial and epicardial borders were manually drawn in the end-diastolic and end-systolic short-axis cine-SSFP images. Papillary muscles and trabeculae were not included in the myocardium. LV end-diastolic volume (EDV), LV end-systolic volume, LVEF, and LV mass were determined.

Edema was deemed present on T2-weighted images when the ratio of the signal intensity of the myocardium to the mean signal intensity of skeletal muscle was at least 2.[11,12] LGE was examined subjectively and was seen to have a nonischemic distribution pattern (i.e. subepicardial or midventricular enhancement).[13,14] As previously reported, myocardial hyperemia was assessed using the postcontrast SSFP cine sequences.[13] Each of the 17 LV segments was examined for the presence of edema, hyperemia, or LGE.[13,14]

Statistical analysis

For variables with normal or nonnormal distributions, values are expressed as the mean [standard deviation (SD)] or the median [interquartile range (IQR)], respectively. For parametric analysis, values with a nonnormal distribution as determined by the Kolmogorov–Smirnov test were logarithmically converted. Percentages are used

to express qualitative data. Whenever applicable, categorical variables were compared using the Chi-square or Fisher exact test. Continuous variables were compared by the Student's independent *t*-test and analysis of variance or by the Wilcoxon nonparametric test whenever appropriate. Comparison of rates tests and the measurement of the incidence rate ratio (IRT) was performed to compare the annual incidence of myocarditis and pericarditis during the PRECOVID and COVID time periods. Statistical significance was defined as a *P*-value less than 0.05. Statistical analysis was performed using MedCalc software (version 20.0.14, MedCalc Software Ltd, Ostend, Belgium).

Results

Overall, during the two time intervals evaluated, 259 cases of inflammatory heart disease (myocarditis and/or pericarditis) occurred in the areas of Pisa, Lucca and Livorno. Characteristics of the entire population are shown in Table 1. The annual incidence was of 11.3 cases per 100 000 inhabitants. Particularly, 138 cases occurred in the PRECOVID, and 121 in the COVID period. During the COVID period, three patients had clinically suspected myocarditis within 10 days of a dose of SARS-COV2 vaccination and were excluded from the analysis. Then the final cases of inflammatory heart disease numbered 118 during the COVID year. During the COVID period, a positive swab for COVID-19 was found in only nine (8%) cases. As shown in Supplemental Table 1, http://links.lww.com/JCM/A457, patients with a positive swab for COVID-19 had more frequent myocarditis than pericarditis and presented significantly lower LV and RV EDVi and ESVi.

The annual incidence of inflammatory heart disease was not significantly different: 12.1/100 000 in PRECOVID vs 10.3/100 000 in the COVID period [IRT 1.17, 95% confidence interval (CI) 0.91–1.5, $P = 0.22$].

During the PRECOVID period, we recorded 89 out of 138 (64.5%) myocarditis, 25 (18.1%) pericarditis and 21 (15.2%) cases of myopericarditis and 3 (2.2%) perimyocarditis.

In the COVID period, 64 out of 118 (54.2%) were recorded, with further 29 (24.6%) pericarditis and 22(18.6%) cases of myopericarditis and 3 (2.4%) perimyocarditis.

Overall, the cases of myocarditis (including also cases of perimyocarditis with minimal signs of pericardial involvement) were 92 in PRECOVID and 67 in the COVID period. The annual incidence of myocarditis was significantly higher in PRECOVID than in the COVID period, respectively 8.1/100 000/year vs. 5.9/100 000 year (IRT 1.37, 95% CI 0.99–1.99, $P = 0.047$), consisting of a net reduction of 27% of cases. The CMR characteristics of patients with myocarditis are reported in Table 2. Interestingly, LV mass index was significantly higher in the COVID group than in PRECOVID ($P = 0.01$). Myocarditis of COVID had more frequently wall motion abnormalities ($P = 0.047$) and more myocardial segments with LGE ($P = 0.02$). Two cases of myocarditis, one from each analyzed time period, are shown in the Supplemental Figure.

In Fig. 1, the annual incidence per 100 000 inhabitants of myocarditis is shown for all the classes of age from 12 to

Table 1 General characteristics of patients prior to coronavirus disease 2019 and coronavirus disease 2019 time intervals

	PRECOVID ($n = 138$)	COVID ($n = 118$)	*P*-value
General features			
Age (years)	40 (24–63)	52 (33–64)	0.05
Males [*n* (%)]	93 (67)	76 (64)	0.61
Weight (kg)	74 ± 16	75 ± 17	0.72
Height (cm)	172 ± 9	170 ± 10	0.09
Family history of CAD [*n* (%)]	7 (5)	3 (2.5)	0.29
Hypertension [*n* (%)]	10 (7)	5 (4)	0.30
Diabetes mellitus [*n* (%)]	4 (3)	2 (2)	0.52
Dyslipidemia [*n* (%)]	6 (4)	5 (4)	0.96
Smoking [*n* (%)]	4 (3)	5 (4)	0.56
Clinical presentation			
Fever [*n* (%)]	60 (43,5)	47 (40)	0.61
Chest pain [*n* (%)]	138 (100)	118 (100)	-
Instrumental findings			
ECG ST-T abnormalities [*n* (%)]	105 (76)	85 (72)	0.48
ECG negative T waves [*n* (%)]	21 (15)	15 (13)	0.59
EMB [*n* (%)]	3 (2)	3 (2)	0.85
Laboratory findings			
WBC (10^3 cells/ml)	10.1 ± 4	9.7 ± 3	0.37
ESR (mm/h)	12 (1–28)	11 (2–26)	0.22
CRP (mg/l)	6 (6–24)	7 (1–26)	0.15
Hs TnT (pg/ml)	70 (65–1224)	61 (85–923)	0.90

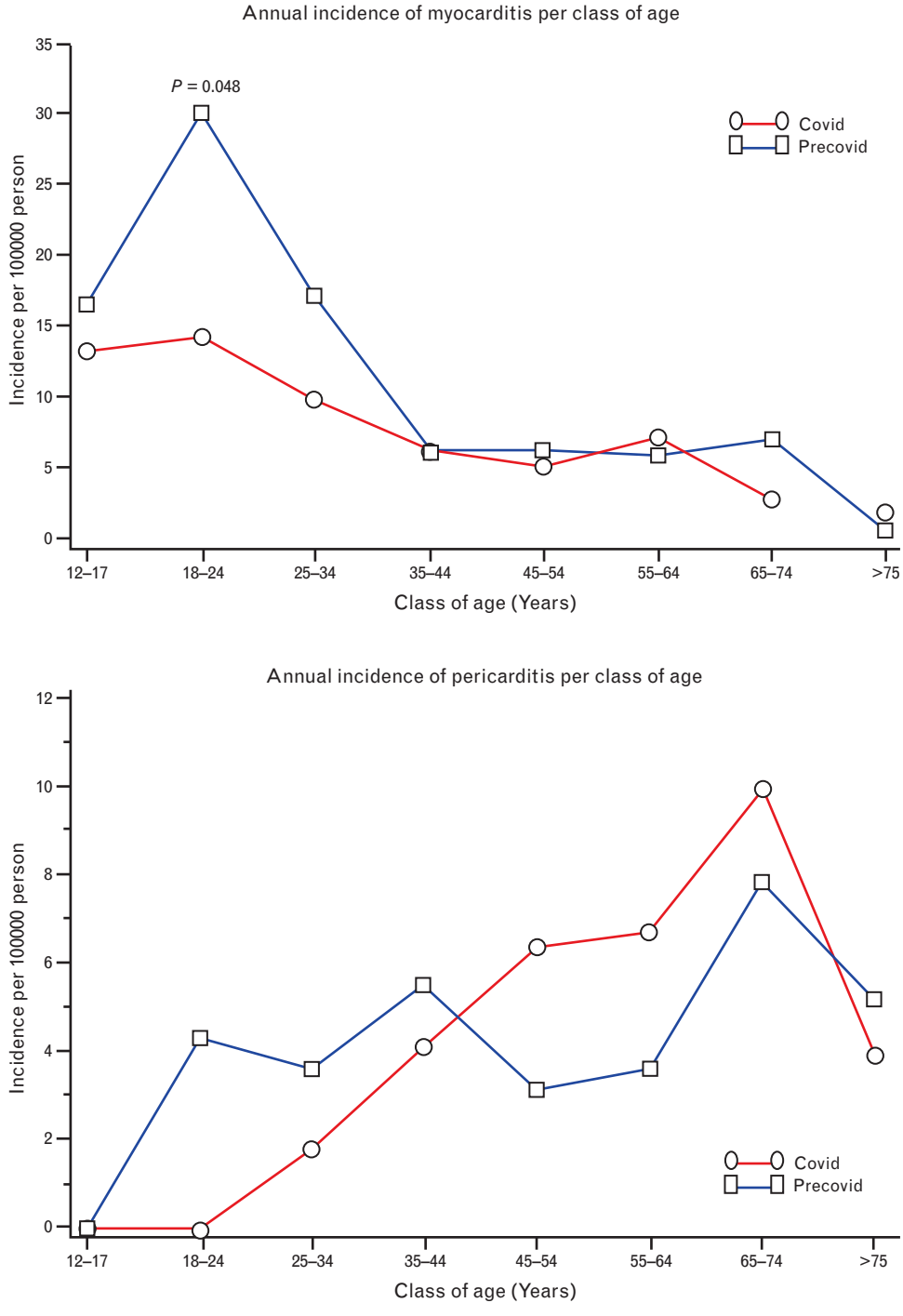
CAD, coronary artery disease; CRP, C-reactive protein; EMB, endomyocardial biopsy; ESR, erythrocyte sedimentation rate; HsTnT, high-sensitivity troponin T; WBC, white blood cells.

Table 2 Cardiac magnetic resonance parameters in patients with acute myocarditis

	PRECOVID ($n = 92$)	COVID ($n = 67$)	*P*-value
Age (years)	38 ± 18	41 ± 19	0.24
Male sex [*n* (%)]	63 (69)	51 (76)	0.29
LVEDVi (ml/m^2)	78 (67–92)	75 (65–85)	0.16
LVESVi (ml/m^2)	29 (25–37)	26 (22–33)	0.11
LVEF (%)	61 ± 10	62 ± 11	0.36
LVEF less than 50% [*n* (%)]	8 (9)	7 (10)	0.71
LV mass index (g/m^2)	66 (54–75)	72 (63–78)	**0.01**
WM abnormalities [*n* (%)]	6 (7)	11 (16)	**0.047**
RVEDVi (ml/m^2)	77 (66–92)	79 (69–87)	0.88
RVESVi (ml/m^2)	31 (25–38)	31 (24–38)	0.87
RVEF (%)	60 ± 8	59 ± 9	0.84
Number of segments with edema	3 (1–5)	3 (2–5)	0.42
Positive pericardial edema [*n* (%)]	3 (3)	3 (4)	0.70
Positive myocardial LGE [*n* (%)]	64 (70)	55 (82)	0.07
Number of segments with LGE	1 (0–4)	2 (1–4)	**0.02**
Septal midwall/ring LGE [*n* (%)]	16 (17)	15 (22)	0.54
Subepicardial or other LGE [*n* (%)]	48 (52)	40 (60)	0.42
Positive pericardial LGE [*n* (%)]	0	0	

LGE, late gadolinium enhancement; LV, left ventricular; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; RVEDVi, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; RVESVi, right ventricular end-systolic volume index; WM, wall motion.

Fig. 1



In the upper panel annual incidence of acute myocarditis per class of age: compared with the prior to coronavirus disease 2019 period (grey line), the incidence of acute myocarditis in the COVID period (light grey line) decreased significantly, particularly in the class of age 18–24 years but remained substantially unchanged for subjects aged greater than 35 years. In the lower panel annual incidence of acute pericarditis per class of age: no significant difference was found in any class of age between the COVID (light grey line) and the PRECOVID period (grey line).

greater than 74 years old. As is evident from the graph, most of the differences in the incidence of myocarditis are because of a significant decrease in cases of myocarditis in the ages between 17 and 34 years. Particularly, the incidence of myocarditis was significantly lower in COVID than in PRECOVID in the class of age 18–24 <th>years ($P = 0.048$).

Differently from myocarditis, the annual incidence of pericarditis (including myopericarditis having only

Table 3 Cardiac magnetic resonance parameters in patients with acute pericarditis

	PRECOVID ($n=46$)	COVID ($n=51$)	*P*-value
Age (years)	56 ± 18	59 ± 13	0.38
Male sex [*n* (%)]	30 (65)	25 (49)	0.11
LVEDVi (ml/m2)	70 (62–87)	69 (54–78)	0.19
LVESVi (ml/m2)	26 (20–34)	22 (16–28)	**0.02**
LVEF (%)	60 ± 13	66 ± 10	**0.02**
LVEF less than 50% [*n* (%)]	6 (13)	3 (6)	0.21
LV mass index (g/m2)	61 (50–70)	63 (52–72)	0.94
WM abnormalities	7 (16)	5 (10)	0.39
RVEDVi (ml/m2)	68 (58–82)	68 (58–78)	0.55
RVESVi (ml/m2)	27 (20–34)	25 (19–32)	0.52
RVEF (%)	61 ± 9	62 ± 7	0.43
Positive pericardial edema [*n* (%)]	43 (94)	44 (86)	0.25
Positive pericardial LGE [*n* (%)]	35 (76)	39 (77)	0.96
Pericardial effusion [*n* (%)]	22 (48)	36 (71)	**0.02**
Pericardial effusion max dimension (mm)	16 (6–22)	12 (8–16)	0.58
Positive myocardial edemaa [*n* (%)]	10 (22)	8 (16)	0.45
Positive myocardial LGEa [*n* (%)]	14 (30)	23 (45)	0.14

LGE, late gadolinium enhancement; LV, left ventricular; LVEDVi, left ventricular end-diastolic volume index; LVEF, left ventricular ejection fraction; LVESVi, left ventricular end-systolic volume index; RVEDVi, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; RVESVi, right ventricular end-systolic volume index; WM, wall motion. [a] One or fewer myocardial segments involved.

minimal myocardial involvement) was not significantly different between the two periods of time (46 cases in PRECOVID and 51 in COVID, 4.03/100 000 vs. 4.47/100 000, $P=0.61$, IRT 0.9, 95% CI 0.5–1.4). The CMR characteristics of patients with pericarditis are reported in Table 3. Pericarditis during the COVID period were associated with higher LV EF ($P=0.02$), lower LV ESVi ($P=0.02$) and more often pericardial effusion ($P=0.02$) than in PRECOVID time interval.

The annual incidence of pericarditis per 100 000 inhabitants is shown in Fig. 1 for all the classes of age from 12<th> years to greater than 74 years old. As is evident from the graph, the incidence of pericarditis was not significantly different in all the classes of age between the COVID and PRECOVID periods.

Discussion

We have analyzed the impact of the pandemic on the incidence of acute inflammatory heart diseases in a definite area with a population of more than 1 million inhabitants. The main findings of our study show that: compared with the PRECOVID period, a 27% decrease in the annual incidence of myocarditis was found during the COVID pandemic; the greater decrease in the incidence of myocarditis was recorded in young patients and particularly in those under the age of 34 years; myocarditis observed in the COVID period showed greater severity of LV involvement with higher wall motion abnormalities, a greater number of LGE segments and higher ventricular mass index than those observed in PRECOVID period; finally, no difference regarding pericarditis was observed between the COVID and PRECOVID periods.

This is the first study showing the incidence of acute inflammatory heart diseases during the COVID pandemic. We decided to consider as the 'COVID period' the time between 1 June 2020 and 31 May 2021 based on several reasons: to avoid the effect of the 'strict' lockdown of the first months of 2020; stopping the evaluation on 31 May 2021 was also useful to exclude patients with myocarditis following anti-COVID vaccination that could have been a confounding factor, altering the incidence and prevalence of myocarditis; in the last months of 2021 a great percentage of the Italian population was vaccinated for COVID-19 and the vaccination could have mitigated the risk of myocarditis caused by COVID-19.

In Italy, during the first months of the pandemic, there was a strict lockdown associated with a marked reduction in admissions into emergency departments also for cardiovascular diseases.[15] Therefore, to exclude the negative impact of lockdown on hospitalization for myocarditis and pericarditis, we have excluded the first 6 months of the pandemic. Similarly, for the assessment of the PRECOVID period, we excluded the last 6 months of 2019 as we could not rule out the presence of the SARS-CoV-2 virus in Italy during that time. Then, we compared a 1-year period before the pandemic, from 1 June 2018 to 31 May 2019 (PRECOVID), with a 1-year period during the pandemic period, from 1 June 2020 to 31 May 2021 (COVID).

During the COVID period, an elevated number of restrictions and recommendations were entered to prevent the spread of the pandemic. The main strategy was reducing in-person contact, promoting social distancing and the use of facial masks. As previously demonstrated, all these activities are associated with a marked reduction in both SARS-CoV-2 and all respiratory pathogens.[16,17]

The reduced incidence of non-COVID myocarditis during the COVID period is supported by a reduction the respiratory pathogens (i.e. adenovirus, influenza) with myocardial trophism. Furthermore, the use of sanitizing gel and/or medical gloves may have contributed also to the decrease in the incidence of some gastrointestinal viruses with some aptitude to myocarditis such, as coxsackie virus and echovirus. Indeed, during the COVID period, we have observed a greater reduction in myocarditis particularly in young patients, aged less than 34 years. The decrease in myocarditis incidence of such a group of young patients, representing the most involved class of age in PRECOVID, could be partially explained by the restriction on social life that were imposed during our COVID period of observation (closure of discotheques, disco-bars, pubs, etc.).

We observed only nine cases (8%) of myocarditis in patients with recent COVID; the overall reduced

incidence of myocarditis during the pandemic is strongly related to restrictions and recommendations of the Italian government.

In this period of restrictions, the only six cases observed and hospitalized for myocarditis had LV dysfunction. Interestingly, myocarditis observed in the COVID period had a greater myocardial involvement because of wall motion abnormalities and myocardial segments with LGE.

Also, the higher LV mass index observed in the COVID group than in PRECOVID is the result of greater myocardial damage. In fact, many studies have demonstrated that the presence of both myocardial edema and post contrast enhancement because of viral infection is associated with an increase in LV mass, as a myocardial 'tumefaction'.[18] The reasons for this more severe presentation of myocarditis during COVID could be because of great virulence and/or a higher virus load of pathogens necessary to infect patients despite the antiviral prophylaxis measures. Moreover, during COVID, patients' fear of going to hospital may have led to hospitalization of only those with worse symptoms and cardiac involvement.

Differently from myocarditis, the incidence of pericarditis was similar in the COVID and PRECOVID periods. A possible explanation for this finding could be that the etiological spectrum of pericarditis is wider than that of myocarditis and includes many very frequent noninfective conditions such as, for instance, rheumatological disease, that were probably not influenced by the COVID pandemic.

The identification of all the causes of pericarditis was beyond the scope of the present study, thus we can neither confirm nor exclude this hypothesis.

Study limitation

The main limitation of our retrospective study is because of the absence of a definite etiological diagnosis of myocarditis and pericarditis in all the population. However, the majority of our patients were stable and with normal cardiac function. Endomyocardial biopsy, the only method able to identify cause, was indicated only in a few patients with severe LV dysfunction or hemodynamic instability.

For the same reasons, we were unable to assess whether myocarditis during the COVID period was caused by direct SARS-CoV-2 infection, by other viruses, or by nonviral causes.

However, the finding of a decrease in the overall incidence of myocarditis during COVID could be considered as indirect proof of the absence of a substantial impact of SARS-CoV-2 on the risk of myocarditis.

In order to avoid confounding factors, we decided to exclude from the analysis patients with myocarditis or pericarditis occurring within 10 days of SARS-CoV-2 vaccination as potential iatrogenic conditions. However, we have observed a low incidence (3/1<th>000 000) of postvaccine myocarditis that was very similar to those observed in Israel.[19] Our period of observation includes only the first 6 months of the SARS-CoV-2 vaccination program in Italy. During this initial phase of the vaccination program, patients of the younger classes of age were excluded from vaccination (with the exception of healthcare personnel or patients with chronic disease). In the last 6 months, the vaccination program was extended to those aged greater than 12 years, and an increased incidence of vaccination-related myocarditis was reported in young adults or adolescents.[20] However, the assessment of the prevalence of such vaccination-related myocarditis was beyond the scope of our study.

We chose a time period from 1 June 2020 to 31 May 2021 as the COVID period. We were well aware that this time was only a small part of the pandemic that is still ongoing. However, this choice was motivated by the need for removing many confounding facts as discussed above.

Finally, our study is limited to a relatively small population and it has a geographical representation. Incidence of myocarditis in other Italian regions or in other countries could be different.

Conclusion

During the COVID period, the incidence of myocarditis apparently decreased by 27% compared with a PRECOVID period of time. The social distancing and restrictions as well as the prophylactic procedures (i.e. face masks, medical gloves and sanitizing gel) could have contributed to mitigation of the incidence of acute myocarditis. On contrast, the incidence of pericarditis did not change during COVID.

Authors' contributions

Writing the original draft, formal analysis, data curation, visualization: G.D.A., R.A., G.D.B. Conceptualization, funding acquisition, review and editing, supervision: A. M., T.G., D.S. Writing, review and editing, investigation, and validation: I.U., R.L., G.C., B.A.

Conflicts of interest

There are no conflicts of interest.

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