A case-control, multicentre study of consecutive patients with COVID-19 and acute (myo)pericarditis: incidence, risk factors, clinical characteristics and outcomes

Òscar Mirò,[1] Manel Sabaté,[2] Sònia Jiménez ,[1] Alexandre Mebazaa,[3] Gemma Martínez-Nadal,[1] Pascual Piñera,[4] Guillermo Burillo-Putze,[5] Alfonso Martín,[6] Francisco Javier Martín-Sánchez,[7] Javier Jacob,[8] Aitor Alquézar-Arbé,[9] Eric Jorge García-Lamberechts,[7] Pere Llorens ,[10] Juan González del Castillo,[7] on behalf of the Spanish Investigators on Emergency Situations TeAm (SIESTA) network

Handling editor David Metcalfe

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/emermed-2020-210977).

For numbered affiliations see end of article.

Correspondence to
Dr Òscar Mirò, Emergency Department, Hospital Clinic, 08036 Barcelona, Spain; omiro@clinic.cat

Received 4 December 2020
Accepted 30 November 2021

To cite: Mirò Ò, Sabaté M, Jiménez S, *et al*. *Emerg Med J* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/emermed-2020-210977

ABSTRACT

Objective To estimate incidence, risk factors, clinical characteristics and outcomes of acute (myo)pericarditis (AMP) in patients with COVID-19.

Methods Case-control, retrospective review, consecutive case inclusion performed in 62 Spanish EDs. All COVID-19 patients with AMP (cases) were compared in clinical characteristics and outcomes with COVID-19 without AMP (control group A) and non-COVID patients with AMP (control group B). We estimated unadjusted standardised incidence (SI, not adjusted by population's age/sex) of AMP in COVID-19 and non-COVID populations (per 100 000/year).

Results We identified 67 AMP in COVID-19 patients (SI=56.5, OR with respect to non-COVID patients=4.43, 95% CI=3.98 to 4.94). Remarkably, COVID-19 cases presented with chest pain less frequently than non-COVID patients and had less typical ECG changes, higher NT-proBNP (N-terminal prohormone of brain natriuretic peptide), more left and right ventricular dysfunction in echocardiography and more need of inotropic/vasopressor drugs. Admission to intensive care was higher than control group A (OR=3.22, 95% CI=1.43 to 7.23), and in-hospital mortality was higher than control group B (OR=7.75, 95% CI=2.77 to 21.7).

Conclusion AMP is unusual as a form of COVID-19 presentation (about 1‰ cases), but SI is more than fourfold higher than non-COVID population, and it is less symptomatic, more severe and has higher in-hospital mortality; therefore, rapid recognition, echocardiographic assessment of myopericardial inflammation/dysfunction and treatment with vasoactive drugs when needed are recommended in AMP in patients with COVID-19.

Key messages

What is already known on this subject

► Cases of acute (myo)pericarditis (AMP) have been reported in patients with COVID-19. Some authors have suggested that AMP would be triggered by SARS-CoV-2 infection, but data coming from large registries are still lacking precluding any conclusion on this potential relationship. In addition, the clinical characteristics and potential differences with AMP observed in the general population (patients without COVID-19) remain to be defined.

What this study adds

► In the present case-control, retrospective review, consecutive case inclusion study performed in 62 Spanish EDs, we identified 67 patients with COVID-19 developing AMP. From our data, we conclude that AMP in patients with COVID-19 is more frequent and it seems to be less symptomatic, more severe, and with increased in-hospital mortality than in general population with AMP. Therefore, rapid recognition, echocardiographic assessment and treatment are recommended in these patients.

INTRODUCTION

Infection by SARS-CoV-2 is mainly characterised by fever and respiratory symptoms, with dyspnoea and lung infiltrates being present in more than 50% of hospitalised cases.[1] A significant number of other signs and symptoms can be present, involving the gastrointestinal tract, liver, skeletal muscle or the coagulation cascade, biochemically detected by increased D-dimers, which is related to complications and worse prognosis.[1–4] Acute (myo)pericarditis (AMP) is a potential manifestation of some viral infections, including parvovirus B19, human herpes virus, Epstein-Barr virus, enterovirus, cytomegalovirus, adenovirus, HIV and hepatitis C virus. Isolated case reports have been recently published in patients with COVID-19;[5–12] however, as large case series are lacking, the actual frequency of AMP in patients with COVID-19 is currently unknown. Additionally, in some reported cases, the clinical course of AMP appeared after the patient had been admitted[7 10] and this could, to some extent, represent the expression of the increased number of complications that can be found in patients who

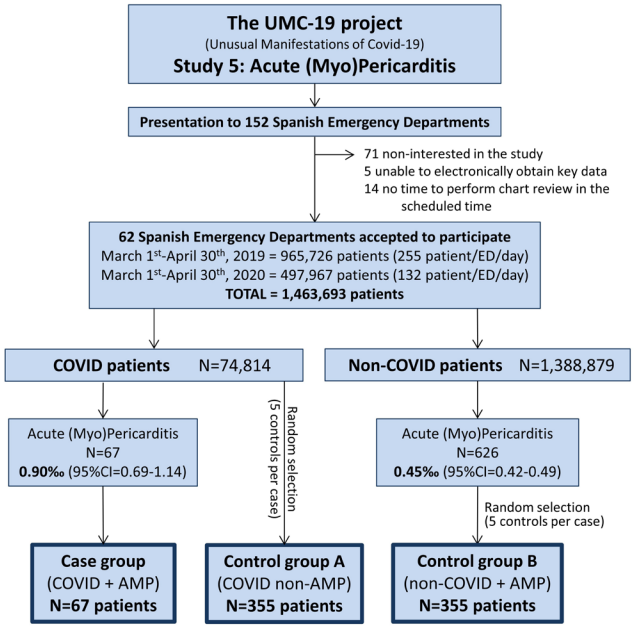

Figure 1 Study design and inclusion flow chart. AMP, acute (myo) pericarditis; UMC, Unusual Manifestations of COVID-19

are bedridden, multidrug treated, mechanically ventilated and/or in very poor condition. In this scenario, it is difficult to quantify the real association of AMP with the pathogenesis of the disease caused by SARS-CoV-2 infection. On the other hand, the clinical characteristics and potential differences between AMP observed in patients with COVID-19 and in the general population (patients not infected by SARS-CoV-2) remain to be defined. Bearing these uncertainties in mind, we aimed to (1) determine the frequency of AMP in patients with COVID-19; (2) uncover risk factors associated with the development of AMP in patients with COVID-19; (3) describe whether there is any distinctive clinical characteristic in these patients in comparison with AMP observed in non-COVID patients and (4) investigate the outcomes.

METHODS

Study design and setting

This case-control study is part of the multicentre Unusual Manifestations of COVID-19 (UMC-19) project, designed to investigate the potential relationship between COVID-19 and 10 different entities that could be influenced by SARS-CoV-2 infection itself.[13 14] This study, labelled UMC-19 Study 5 (UMC-19-S_5) is a retrospective, case-control, ED-based, multicentre study designed to describe the incidence, risk factors, clinical characteristics and outcomes for AMP in patients with COVID-19.

The UMC-19-S_5 was carried out in 62 EDs (roughly, the 20% of Spanish EDs of the Public Health System; figure 1). Altogether these 62 hospitals provide health coverage to 15 094 000 citizens (32% of the population of 46.9 million of Spain) and make up a balanced representation of the Spanish territory, type of hospital and involvement in the pandemic.[13]

Participants

Cases

Cases were patients who attended the ED between 1 March and 30 April 2020 and had a diagnosis of SARS-CoV-2 and AMP. The diagnosis of AMP was based on the presence of at least two of the following four manifestations or findings according to the European Society of Cardiology guidelines criteria[15]: (1) chest pain, (2) pericardial friction rub, (3) characteristic ECG changes (new widespread ST elevation or PR depression) and (4) pericardial effusion. As supportive findings, we also considered inflammatory marker elevation of white cell count (WCC), the erythrocyte sedimentation rate, C reactive protein (CRP) and evidence of inflammation by imaging modalities. Diagnostic adjudication was made locally by the principal investigator of each centre, without external review. Mild cases that were entirely managed in the ED and directly discharged home without hospitalisation were included. Diagnosis of COVID-19 for this study was based on SARS-CoV-2 RNA detection in a nasopharyngeal swab by reverse transcriptase PCR (RT-PCR) and/or based on a clinically compatible clinical picture (including at least malaise, fever and cough) or the presence of typical lung parenchymal infiltrates in chest X-rays (bilateral interstitial lung infiltrates and ground-glass infiltrates) in patients with some clinical symptoms attributable to COVID-19. The initial COVID-19 clinical suspicion in patients without RT-PCR confirmation (due to shortage of tests at some time points of the first pandemic wave) was reviewed and finally adjudicated by the principal investigator of each centre, without external review.

Controls

We defined two different control groups. Control group A was formed by COVID-19 patients without AMP who presented to the ED during the same time period as the cases. This group was constituted by selecting five COVID-19 patients for every case with AMP detected by each centre. Selection (case:control ratio of 1:5) was performed by the inclusion of patients with COVID-19 seen immediately before or after each case.

Control group B was made up of patients with non-COVID diagnosed with AMP attending the ED during the same period as the cases (1 March to 30 April 2020) as well as patients with AMP diagnosed in the ED from 1 March to 30 April 2019.

Independent variables

We extracted 55 independent variables in cases and controls which included demographics, comorbidities, symptoms, vitals at ED arrival, blood parameters and radiological findings in CXRs. In patients with AMP (cases and control group B), we also recorded troponin and NT-proBNP blood concentrations, serological studies and the main ECG and echocardiographic findings if these tests were performed. Final aetiological diagnostic was recorded; of note, cases of AMP in patients with COVID-19 were not classified into the 'viral aetiology' group and they were computed into the 'idiopathic' group (unless they could be classified in any other specific category). We recorded the presence in the medical reports of each one of the four main diagnostic criteria of AMP, as well as of the additional supporting diagnostic findings. When the criteria were not described in the medical report, we assumed they were not present. Finally, we recorded the specific treatment provided to treat AMP, as well as the use of vasoactive drugs (either inotropes or vasopressors).

Outcomes

We defined four different outcomes for cases and controls which consisted of: (1) hospitalisation; (2) admission to intensive care unit (ICU); (3) prolonged hospitalisation (defined as a length of stay >7 days, which is the median length of stay of hospitalised patients in Spain), and (4) in-hospital all-cause mortality. We specified causes of death in patients with AMP, as into

Table 1 Baseline, clinical, analytical and radiological characteristics, and outcomes of patients with COVID-19 with acute (myo)pericarditis and comparison with patients with COVID-19 without acute (myo)pericarditis (control group A) and with patients without COVID-19 with acute (myo) pericarditis (control group B)

	Cases (COVID-19 and AMP) N=67 n (%)	Control group A (COVID-19 and non-AMP) N=335 n (%)	Control group B (non-COVID and AMP) N=335 n (%)
Demographics			
Age (years) (median (IQR)	51 (39–71)	65 (52–77)*	45 (30–66)†
Sex (male)	41 (61.2)	176 (52.5)	237 (70.7)
Comorbidities			
Hypertension	22 (33.8)	153 (45.7)	89 (26.6)
Dyslipidaemia	13 (19.4)	112 (33.4)*	72 (21.5)
Diabetes mellitus	10 (14.9)	60 (17.9)	36 (10.7)
Coronary artery disease	7 (10.4)	25 (7.5)	18 (5.4)
Chronic kidney disease	6 (9.0)	22 (6.6)	25 (7.5)
Active cancer	6 (9.0)	31 (9.3)	42 (12.5)
Obesity (clinically estimated)	5 (7.5)	52 (15.5)	32 (9.6)
Asthma	5 (7.5)	24 (7.2)	17 (5.1)
Chronic obstructive pulmonary disease	4 (6.0)	28 (8.4)	18 (5.4)
Active smoker	4 (6.0)	22 (6.6)	75 (22.4)†
Peripheral artery disease	4 (6.0)	15 (4.5)	15 (4.5)
Chronic liver disease	4 (6.0)	12 (3.6)	12 (3.6)
Chronic heart disease	3 (4.5)	28 (8.4)	22 (6.6)
Cerebrovascular disease	3 (4.5)	24 (7.2)	6 (1.8)
Dementia	1 (1.5)	30 (9.0)*	4 (1.2)
Symptoms at ED arrival			
Length of symptoms (days) (median (IQR)	5 (1–8)	7 (3–10)	2 (1–5)†
Chest pain	54 (80.6)	42 (12.5)*	307 (91.6)†
Dyspnoea	37 (55.2)	185 (5.2)	97 (29.0)†
Cough	26 (38.8)	196 (58.5)*	35 (10.4)†
Fever >38°C	20 (29.9)	198 (59.1)*	52 (15.5)†
Abdominal pain	9 (13.4)	17 (5.1)*	13 (3.9)†
Vomiting	9 (13.4)	24 (7.2)	13 (3.9)†
Diarrhoea	7 (10.4)	54 (16.1)	16 (4.8)
Expectoration	7 (10.4)	49 (14.6)	10 (3.0)†
Rhinorrhoea	5 (7.5)	23 (6.9)	10 (3.0)
Dysgeusia	3 (4.5)	26 (7.8)	1 (0.3)†
Anosmia	2 (3.0)	22 (6.6)	1 (0.3)†
Syncope	2 (3.0)	14 (4.2)	5 (1.5)
Signs at ED arrival (median (IQR)			
Temperature (°C)	36.4 (36.0–37.0)	36.6 (36.0–37.3)	36.2 (36.0–36.8)
SBP (mm Hg)	130 (115–146)	125 (114–140)	128 (117–140)
HR (bpm)	92 (80–106)	88 (78–100)	85 (75–99)†
RR (bpm)	19 (16–24)	18 (16–23)	16 (14–20)†
Room air pulse oximetry (%)	97 (94–99)	96 (92–98)*	98 (96–99)
Laboratory findings (median (IQR)			
Creatinine (mg/dL)	0.88 (0.73–1.19)	0.87 (0.72–1.10)	0.87 (0.75–1.05)
Sodium (mmol/L)	139 (135–141)	138 (136–140)	139 (137–141)
Potassium (mmol/L)	4.1 (3.7–4.4)	4.0 (3.7–4.4)	4.1 (3.9–4.4)
Aspartate aminotransferase (U/L)	31 (20–51)	30 (22–48)	23 (18–37)
Bilirubin (mg/dL)	0.72 (0.48–1.43)	0.50 (0.36–0.70)*	0.64 (0.40–0.97)
Alkaline phosphatase (U/L)	71 (54–94)	71 (57–95)	87 (61–107)
Lactate dehydrogenase (U/L)	262 (187–447)	278 (211–359)	205 (163–255)†
Haemoglobin (g/L)	135 (119–150)	139 (127–148)	140 (128–151)
Leucocyte ($\times 10^9$ cells/L)	8.2 (6.6–10.8)	6.7 (4.9–9.1)	9.3 (6.8–12.6)
Lymphocyte count ($\times 10^9$ cells/L)	1.4 (0.8–1.7)	1.1 (0.8–1.6)	1.7 (1.1–2.3)†
Platelets ($\times 10^9$ cells/L)	236 (191–304)	206 (161–259)*	241 (199–292)
D-dimer (ng/mL)	944 (302–2164)	640 (370–1280)	500 (285–1530)
C-reactive protein (mg/dL)	3.2 (0.3–10.4)	5.9 (1.9–12.2)*	2.0 (0.5–8.1)
Ferritin (ng/mL)	429 (44–870)	495 (270–1183)	184 (134–317)

Continued

Table 1 Continued

	Cases (COVID-19 and AMP) N=67 n (%)	Control group A (COVID-19 and non-AMP) N=335 n (%)	Control group B (non-COVID and AMP) N=335 n (%)
Procalcitonin (ng/mL)	0.06 (0.02–0.28)	0.10 (0.06–0.22)	0.08 (0.04–0.43)
CXR	**N=65**	**N=325**	**N=316**
Cardiomegaly	18 (27.7)	34 (10.5)*	73 (23.0)
Pleural effusion	8 (12.3)	14 (4.3)*	40 (12.6)
Interstitial lung infiltrates	21 (32.3)	143 (44.0)	9 (2.8)†
Ground-glass lung opacities	16 (24.6)	187 (57.5)*	8 (2.5)†
Outcomes			
Hospitalisation	43 (64.2)	253 (75.5)	174 (51.9)
Admission to ICU	11 (16.4)	22 (6.6)*	35 (10.4)
Prolonged hospitalisation	21 (34.4)	133 (39.9)	76 (22.8)
In-hospital mortality	11 (16.4)	55 (16.4)	8 (2.4)†

p values denote statistically significant differences (p<0.05).
*P values refer to comparison between cases and control group A.
†P values refer to comparison between cases and control group B.
AMP, acute (myo)pericarditis; ICU, intensive care unit.

Table 2 Magnitude of statistically significant associations found in the unadjusted analysis

	OR	95% CI
Comparison of baseline, clinical, analytical and radiological characteristics of COVID-19 patients developing acute (myo)pericarditis with respect to COVID-19 patients not developing acute (myopericarditis)		
Chest pain	13.346	7.331 to 24.30
Bilirubin>1 mg/dL	4.455	2.045 to 9.701
Cardiomegaly in CXR	3.280	1.710 to 6.270
Pleural effusion in CXR	3.120	1.250 to 7.770
Age <40 years	3.049	1.647 to 5.650
Abdominal pain	2.903	1.234 to 6.826
Leucocyte count >×10^9 cells/L)	2.187	1.205 to 3.969
Platelet count >300×10^9 elements/L)	2.181	1.149 to 4.138
Pulse oximetry at ED arrival <96%	0.573	0.329 to 0.996
C-reactive protein >5 mg/dL	0.549	0.311 to 0.969
Dyslipidaemia	0.479	0.251 to 0.915
Cough	0.450	0.263 to 0.770
Fever >38°C	0.294	0.167 to 0.519
Ground-glass lung opacities in CXR	0.241	0.131 to 0.442
Dementia	0.154	0.021 to 1.150
Comparison of baseline, clinical, analytical and radiological characteristics of COVID-19 patients developing acute (myo)pericarditis with respect to non-COVID patients developing acute (myo)pericarditis		
Lung interstitial infiltrates in CXR	16.33	7.035 to 37.92
Dysgeusia	15.66	1.603 to 152.9
Ground-glass lung opacities in CXR	12.61	5.125 to 31.04
Anosmia	10.28	0.918 to 115.0
Cough	5.436	2.973 to 9.937
Lactate dehydrogenase >300 U/L	4.442	1.928 to 10.24
Abdominal pain	3.844	1.571 to 9.404
Vomiting	3.844	1.571 to 9.404
Expectoration	3.792	1.389 to 10.35
Tachypnoea >20 bpm	3.379	1.844 to 6.192
Dyspnoea	3.026	1.770 to 5.174
Length of symptoms >7 days	2.890	1.565 to 5.348
Lymphocyte count <1 (x10^9 cells/L)	2.878	1.603 to 5.165
Aspartate aminotransferase >40 U/L	2.559	1.242 to 5.274
Fever >38°C	2.316	1.270 to 4.224
Tachycardia >100 bpm	1.819	1.017 to 3.254
Age <40 years	0.600	0.340 to 1.057
Chest pain	0.379	0.185 to 0.777
Active smoker	0.220	0.078 to 0.624

cardiovascular, non-cardiovascular or unknown, according to the Academic Research Consortium-2 consensus.[16]

Statistical analysis

Discrete variables were expressed as absolute values and percentages, and continuous variables as median and IQR. The incidence of AMP in COVID-19 and non-COVID patients were expressed per thousand (‰) and standardised incidence (not adjusted by population's age/sex) as cases per 100 000 per year, both with 95% CI. For non-COVID patients, partial calculations were made for the COVID-19 (2020) and non-COVID (2019) periods of patient inclusion. To estimate COVID-19 prevalence in each ED catchment area during COVID-19 period, we used the seroprevalence of SARS-CoV-2 in the province of that ED as determined in a wide Spanish study performed between 27 April and 11 May 2020.[17] We also used OR with 95% CI to compare the incidence of AMP in COVID-19 patients with respect to non-COVID patients globally, and for COVID-19 and non-COVID periods individually.

Differences between the case and the control groups were assessed by the χ^2 test (or Fisher's exact test as appropriate) for categorical variables and by the Mann-Whitney non-parametric test for continuous variables. The magnitude of associations was expressed as unadjusted OR with 95% CI. Continuous variables were dichotomized using clinically meaningful cut-offs or around the median of the distribution. As the number of patients with AMP we expected to identify was not large, we did not plan to go further in the investigation of the significant relationships identified in the unadjusted analysis using adjusted models, with the exception of outcomes, which were adjusted for age and sex.

In all comparisons, statistical significance was accepted if the p-value was <0.05 or if the 95% CI of the risk estimations excluded the value 1. The analyses were performed with the SPSS (V.24) statistical software package (IBM, Armonk, New York, USA).

Ethics

The UMC-19 project was approved by the Ethics Committee of the Hospital Clínic of Barcelona (Spain), with the reference number HCB/2020/0534, and it was carried out in strict compliance with the principles of the Declaration of Helsinki.

Patient and public involvement

Patients were not involved in the recruitment and conduct of the study. The authors are unable to disseminate the findings to study participants directly.

RESULTS

A total of 74 814 patients with COVID-19 attended the 62 Spanish EDs participating in the UMC-19-S_5 (figure 1) during the 61-day study period. In 67 of these patients, AMP diagnosis was adjudicated (incidence=0.90‰, 95% CI=0.69‰ to 1.14‰) and constituted the case group. Control group A included 335 COVID-19 patients without AMP during the same period. COVID-19 infection was confirmed by RT-PCR in 45 cases and 246 control group A patients (67.2% and 73.4%, respectively, p=0.30), while in the remaining patients, COVID-19 diagnosis was based on epidemiological context and clinical data.

During the 2020 study period, 423 153 non-COVID patients were seen, and 965 726 during the 61-day period in 2019 for a total of 1 388 879 non-COVID patients. Of these, 626 were diagnosed with AMP (230 in COVID-19 period and 396 in the pre-COVID period). Control group B was formed by 368 selected patients from these 626 non-COVID patients with AMP. Overall incidence of AMP in the study was 0.45‰ (95% CI=0.42‰ to 0.49‰), with a COVID-19 period incidence of 0.54‰ (95% CI=0.48‰ to 0.62‰) and a pre-COVID period incidence of 0.41% (95% CI=0.37% to 0.45%).

The median age of COVID-19 patients with AMP (cases) was 51 years; 61% were men, and the most frequent comorbidities were hypertension (34%), dyslipidaemia (19%), diabetes mellitus (15%) and coronary artery disease (10%) (table 1 and online supplemental table 1). The most frequent symptomatology was chest pain (66%), dyspnoea (55%), cough (39%) and fever (30%), and the median time from symptom onset to ED consultation (whichever was first) was 5 days.

There was a higher frequency of AMP in COVID-19 compared with non-COVID ED patients (control groups A and B) (OR of 1.99 (95% CI=1.55 to 2.56)). AMP was more frequent in COVID-19 patients than in non-COVID patients during the 2020 study period (OR 1.94 (95% CI=1.48 to 2.55)) and in patients in the pre-COVID period (OR 2.19 (95% CI=1.69 to 2.83)). The unadjusted standardised incidences of AMP were 56.5 per 100 000 COVID-19 individuals per year (95% CI=52.7 to 60.1) and 12.7 per 100 000 non-COVID individuals per year (95% CI=12.2 to 13.3, with partial unadjusted standard incidences of 9.6 in 2020–COVID-19 period and 15.7 in 2019 pre-COVID period). Consequently, the OR of AMP for COVID-19 with respect to non-COVID patients was of 4.43 (95% CI=3.98 to 4.94), with partial OR of 5.89, 95% CI=5.27 to 6.58, when compared with non-COVID patients from the COVID-19 period, and partial OR of 3.59, 95% CI=3.23 to 3.99, when compared with non-COVID patients from the pre-COVID period.

COVID-19 patients with acute (myo)pericarditis versus COVID-19 patients without acute (myo)pericarditis

COVID-19 patients with AMP were significantly different to COVID-19 patients without AMP (control group A) with regard to age, presence of chest pain, cardiomegaly, pleural effusion and elevated bilirubin, all with ORs over threefold greater (table 2) Although some biomarkers of inflammatory activity were significantly higher (WCC and platelet count), CRP was significantly lower. Compared with non-COVID patients with AMP (control group B patients), dysgeusia, anosmia and cough were more common in COVID-19 patients with AMP as were findings of COVID-19 infection on chest X-ray (lung interstitial infiltrates or ground-glass lung opacities), all with ORs over fivefold higher (table 3). Chest pain was not as frequent in COVID-19 patients with AMP as in non-COVID patients with AMP (OR of 0.38; 95% CI 0.19 to 0.78).

Table 3 Radiological characteristics of patients with COVID-19 with acute (myo)pericarditis (AMP) and comparison with non-COVID-19 patients with AMP (control group B)

	Cases (COVID-19 and AMP) N=67 n (%)	Control group B (non-COVID and AMP) N=335 n (%)	P value
Analytical data			
Raised troponin (above 99th of general population)	22 (32.8)	107 (31.9)	0.89
NT-proBNP >900 ng/mL (n=16/53)	11 (68.8)	18 (31.3)	**0.01**
ECG			
Diffuse ST elevation	32 (47.8)	202 (60.3)	0.06
Diffuse PR depression	14 (20.9)	75 (22.4)	0.79
Peaked T waves	13 (19.4)	46 (13.7)	0.23
ST depression	19 (28.4)	92 (27.5)	0.88
Atrial fibrillation	14 (20.9)	54 (16.1)	0.34
Echocardiography (n=54/251)			
Pericardial effusion	26 (48.1)	124 (49.4)	0.87
Pericardial inflammation	7 (13.0)	20 (8.0)	0.24
Right ventricular dysfunction	11 (20.4)	25 (10.0)	**0.03**
Left ventricular dysfunction	17 (31.5)	31 (13.9)	**0.002**
Ventricular hypokinesia/akinesia	13 (24.1)	36 (14.3)	0.08
Treatment			
Non-steroidal anti-inflammatory drugs	48 (71.6)	278 (83.0)	**0.03**
Colchicine	23 (34.3)	183 (54.6)	**0.002**
Corticosteroids	22 (32.8)	67 (20.0)	**0.02**
Need of inotropes	14 (20.9)	7 (2.1)	**<0.001**
Final aetiological diagnosis			
Idiopathic	51 (76.1)	262 (78.2)	0.75
Bacterial	5 (8.2)	20 (6.3)	0.59
Neoplasia	4 (6.6)	9 (2.8)	0.24
Viral (confirmed by serological studies; not including SAR-CoV-2)	3 (4.9)	6 (1.8)	0.18
Metabolic	3 (4.9)	1 (0.3)	**0.02**
Autoimmune	2 (3.3)	16 (5.0)	0.75
Drug related	1 (1.6)	5 (1.6)	1.0
Traumatism/iatrogenic	0 (0)	16 (5.0)	0.09
Causes of death			
All-cause death	11 (16.4)	8 (2.4)	**<0.001**
Cardiovascular death	3 (4.9)	2 (0.6)	**0.03**
Non-cardiovascular death	3 (4.9)	4 (1.2)	0.09
Unknown cause of death	5 (8.2)	2 (0.6)	**0.002**

Bold p values denote statistically significant differences (p<0.05).
NT-proBNP, N-terminal prohormone of brain natriuretic peptide.

COVID-19 acute (myo)pericarditis versus non-COVID acute (myo)pericarditis

COVID-19 patients with AMP were similar to non-COVID patients with AMP (control group B) with regard to elevated troponin l and ECG findings; the most frequent finding was diffuse ST elevation (48% vs 60%, p=0.06). However a NT-proBNP over 1000 ng/mL was more common in COVID-19 cases in 69% and 31% (p=0.01).

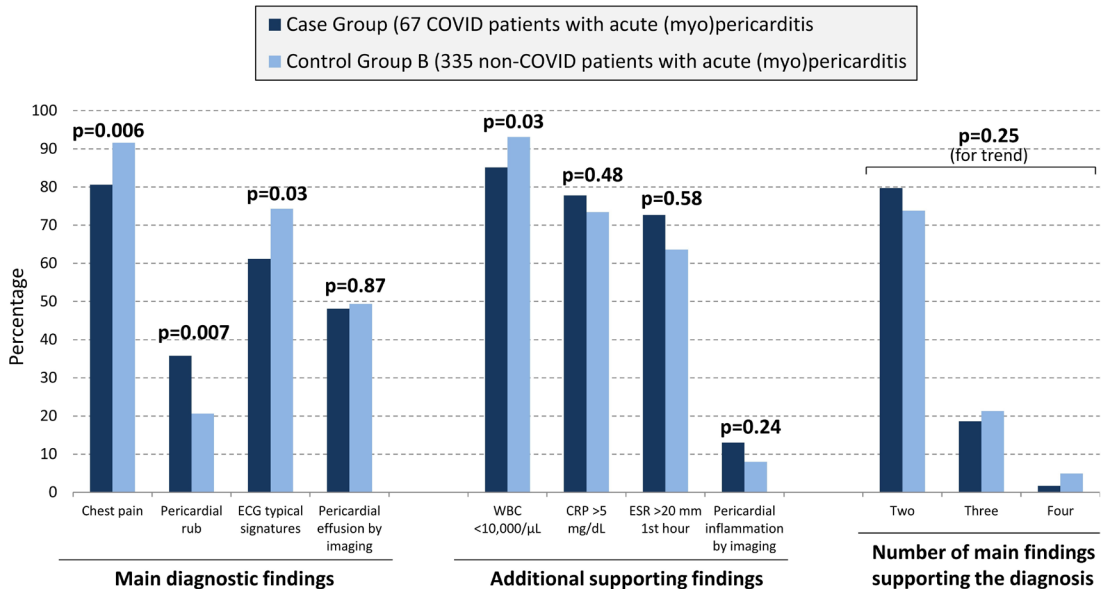

Figure 2 Main and additional supporting diagnostic findings in COVID patients with acute (myo)pericarditis (case group) and non-COVID patients with acute (myo)pericarditis (control group B). CRP, C-reactive protein; WBC, white blood cell

Echocardiography was performed in 54 COVID-19 and 251 non-COVID patients with AMP (81% and 75%, p=0.35), and the most frequent finding was pericardial effusion (48% and 49%, p=0.87). COVID-19 patients more frequently had right (20% vs 10%, p=0.03) and left (32% vs 14%) ventricular dysfunction.

COVID-19 patients with AMP were less frequently treated with non-steroidal anti-inflammatory drugs (72% vs 83%, p=0.03) and colchicine (34% vs 55%, p=0.002) and more frequently with corticosteroids (33% vs 20%, p=0.02) and inotropes/vasopressors (21% vs 2%, p<0.001) compared with non-COVID AMP patients. The most frequent aetiological diagnostic in both groups was idiopathic AMP (76% and 78%, p=0.75), and the only significant difference was found in metabolic AMP, which was more frequently seen in COVID-19 patients (5.1% vs 0.3%, p=0.02). Nine cases of AMP had a viral aetiology confirmed by serological studies, three in COVID-19 patients (all corresponding to cytomegalovirus) and six in non-COVID patients (three Epstein-Barr virus, two cytomegalovirus, one parvovirus). The number and distribution of the main diagnostic and supporting findings of AMP in COVID-19 and non-COVID patients are presented in figure 2.

Outcomes of COVID-19 patients with acute (myo)pericarditis

COVID-19 patients with AMP were hospitalised in 64% of cases, 16% were admitted to the ICU at some point during hospital stay, 34% experienced prolonged hospitalisation (>7 days) and 16% died during hospital stay (11 patients, 3 due to cardiovascular causes, 3 due to non-cardiovascular causes and 5 unknown; table 3). After adjustment, COVID-19 patients with AMP were more likely to have an ICU admission compared with COVID-19 patients without AMP (OR=3.22, 95% CI=1.43 to 7.26), but there was no difference in mortality. COVID-19 patients with AMP were more likely than non-COVID-19 patients with AMP who had higher in-hospital mortality (OR=7.75, 95% CI=2.77 to 21.7) (figure 3). However, significantly higher rates of all-cause mortality (with increased rates of cardiovascular mortality and mortality of unknown origin, but not of non-cardiovascular

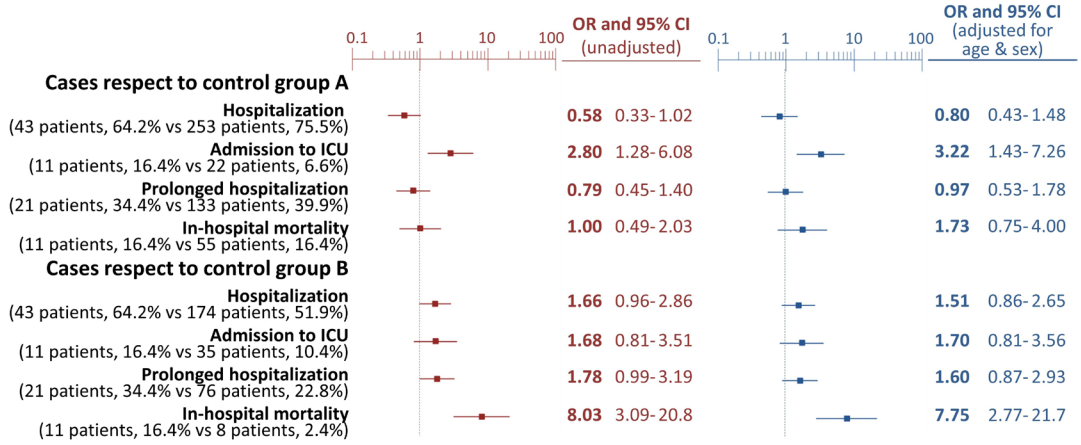

Figure 3 Outcomes of patients with COVID-19 and acute (myo)pericarditis compared with COVID-19 patients without acute (myo)pericarditis (control group A) and non-COVID patients with acute (myo)pericariditis (control group B), unadjusted (in red) and adjusted for age and sex (in blue).

origin) were observed in COVID-19 patients with AMP than in non-COVID patients (table 3).

DISCUSSION

To our knowledge, the UMC-19-S_5 is the largest series of consecutive AMP reported in COVID-19 patients, and there are four main findings that merit highlighting. First, the incidence of AMP in COVID-19 patients is double than the incidence of AMP in the general population (non-COVID patients) coming to ED, and unadjusted standardised incidence is over fourfold of that found n the non-COVID population. Second, young age is the main risk factor associated with the development of AMP in patients infected by SARS-CoV-2. Third, AMP in COVID-19 patients could be more difficult to diagnose than those without COVID-19, as chest pain and ECG typical signatures (key findings to suspect AMP) could be absent in up to one-fifth of cases. And fourth, based on clinical findings, including NT-BNP, echocardiogram and the use of vasopressors, the severity of AMP in COVID-19 patients seems to be greater.

We found that AMP is diagnosed in around 0.5‰ of the general population (non-COVID patients) entering EDs, with very similar incidences in the pre-COVID and COVID-19 periods (0.41‰ and 0.54‰, respectively). These figures are within the relative frequencies reported in previous ED-based studies (0.15‰–0.81‰).[18–21] Therefore, our finding of around 1‰ AMP in COVID-19 patients coming to the ED during the COVID-19 outbreak is double than that observed in non-COVID patients. Similarly, the unadjusted standardised incidence of AMP for general (non-COVID) population found in the UMC-19-S_5 of 12.7 per 100 000 per year (9.6 and 15.7 for the COVID-19 and pre-COVID periods, respectively) is within the range of previously reported general incidences: 27.7 in a prospective, observational cohort study involving two general Italian hospitals,[22] 18.0 in a Swedish registry of the general population[23] and 7.4 in retired US military personnel.[24] Therefore, the unadjusted standardised incidence of 51.9 AMP cases per 100 000 COVID-19 patients per year, which is more than fourfold higher than in non-COVID population, is also remarkably high. Additionally, 76% of AMP in COVID-19 patients were diagnosed as idiopathic in the present study, in agreement with the figure of 80%–90% labelled idiopathic in Western Europe and North America.[25] Two-thirds of the idiopathic cases of AMP in our study had a positive RT-PCR, and thus our findings strongly suggest a pathogenic role of SARS-CoV-2, and the need to add this pathogen to the list of viral causes of AMP.

COVID-19 patients developing AMP were younger than COVID-19 patients who did not develop AMP, and they less frequently had cough and fever and more frequently presented abdominal pain. Surprisingly, although leucocytes and platelets were increased compared with COVID-19 patients without AMP, lymphocytes, procalcitonin and ferritin were not significantly elevated, and CRP values were lower. Therefore, although AMP implies an inflammatory process, the presence of myopericarditis does not appear to be a marker of increased inflammation beyond that of SARS-CoV-2.

The clinical characteristics of AMP in COVID-19 patients differed from AMP in non-COVID patients. Remarkably, COVID-19 patients presented with chest pain less frequently (OR of 0.38). Imazio *et al* found that in idiopathic AMP 99% of patients presented with chest pain, 35% had pericardial rubs, ST-segment elevation was identified in 90% and pericardial effusion in 60%.[25] Some of these findings (chest pain, typical ECG signatures) were less common in our COVID-19 patients, which could make AMP more difficult to diagnose in COVID-19 patients.[26 27] On the other hand, although the percentage of patients with myocardial involvement detected by raised troponin levels was similar in COVID-19 and non-COVID patients with AMP (33% and 32%, respectively), the increments were higher in COVID-19 patients. COVID-19 patients with AMP more frequently had increased NT-proBNP, right and left ventricular dysfunction and need of inotropes/vasopressors than non-COVID AMP patients. All these data suggest a higher severity ofAMP in COVID-19 patients. However, due to the observational nature of the UMC-19-S_5, it cannot be excluded that inotropic/vasoactive drugs were used because of the severity of other organ dysfunction linked to COVID-19 rather than to AMP itself. Nevertheless, our data support a high index of suspicion, and rapid echocardiography-based management with vasoactive treatment for AMP in COVID-19 patients.

With respect to the outcomes of cases, admission to the ICU was higher for COVID-19 patients with AMP than for COVID-19 patients without AMP (OR of 3.22), but hospitalisation, prolonged hospitalisation or in-hospital mortality rates did not differ. However, COVID-19 patients with AMP had a higher in-hospital mortality than AMP in the general population (OR of 7.75), even taking into account that in-hospital mortality found in our non-COVID population (2.3%) is higher than that reported in developed countries (around 1%).[25] Although this increased mortality could be as its severity is greater in COVID-19 than in non-COVID patients. The increased rate of cardiovascular deaths in COVID-19 patients also supports this hypothesis.

Limitations

First, as this is a retrospective review, some cases of mild, paucisymptomatic AMP could have remained undiagnosed. Indeed, as ED visits tended to decrease during the COVID-19 period due to population lockdown and/or fears of COVID-19 contagion, some patients with AMP could have stayed home, and thus the real incidence of AMP could be underestimated. Second, we did not adjust the incidence of baseline and clinical AMP variables, and outcomes were only adjusted by age and sex. Therefore, other unexplored confounders could modify our findings in some extend. Third, in around one-third of patients with COVID-19 the diagnosis was based exclusively on clinical/radiological findings, with no microbiological confirmation, due to the shortage of RT-PCR tests. Fourth, although the case abstraction form was standardised, there was no monitoring of data collection methods, and diagnosis and outcome adjudication were done locally. Fifth, extensive aetiological study of all AMP cases was not carried out, and some cases classified as idiopathic could correspond to other categories.

CONCLUSIONS

The present data demonstrate an incidence of AMP in patients with COVID-19 higher than expected in the general population and support previous reports suggesting that SARS-CoV-2 should be added to the list of viruses able to cause AMP.[28 29] In addition, other relevant findings of present study are that COVID-19 patients with AMP are more likely to be admitted in ICU than COVID-19 patients without AMP. They are also less likely to present with typical myopericarditis symptoms and more likely to die than patients with AMP without COVID-19. Therefore, special attention should be paid when patients with COVID-19 are evaluated in the ED. Although the size of our case series is limited and confounding cannot be effectively

excluded, we believe that rapid diagnosis, echocardiographic assessment of myopericardial inflammation and/or dysfunction and treatment with vasoactive drugs has to be recommended in AMP in patients with COVID-19.

Author affiliations
[1]Emergency Department, Hospital Clínic, IDIBAPS, Universitat de Barcelona, Barcelona, Spain
[2]Cardiology Department, Hospital Clínic, Barcelona, Spain
[3]Department of Anaesthesiology and Critical Care Medicine, Saint Louis and Lariboisière University Hospitals, Paris, France
[4]Emergency Department, Hospital Reina Sofia de Murcia, Murcia, Spain
[5]Emergency Department, Hospital Universitario de Canarias, Universidad Europea de Canarias, Tenerife, Spain
[6]Hospital Universitario Severo Ochoa, Leganes, Madrid, Spain
[7]Emergency, Hospital Clinico San Carlos, Madrid, Spain
[8]Emergency Department, Hospital Universitario de Bellvitge, Barcelona, Spain
[9]Emergency Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[10]Emergency Department, Hospital General Universitario de Alicante, Alicante, Spain

Twitter Sònia Jiménez @sonia_austen_70

Collaborators The SIESTA network is formed by the following researchers and centres (all from Spain): Steering Committee: Òscar Miró, Sònia Jiménez (Hospital Clínic, Barcelona), Juan González del Castillo, Francisco Javier Martín-Sánchez (Hospital Clínico San Carlos, Madrid), Pere Llorens (Hospital General de Alicante), Guillermo Burillo-Putze (Hospital Universitario de Canarias, Tenerife), Alfonso Martín (Hospital Universitario Severo Ochoa de Leganés, Madrid), Pascual Piñera Salmerón (Hospital General Universitario Reina Sofía, Murcia), E. Jorge García Lamberechts (Hospital Clínico San Carlos, Madrid), Javier Jacob (Hospital Universitario de Bellvitge, L'Hospitalet de Llobregat, Barcelona), Aitor Alquézar-Arbé (Hospital de la Santa Creu i Sant Pau, Barcelona). Participating centres: (1) -Hospital Universitario Doctor Peset Aleixandre de Valencia: María Luisa López Grima, Mª Ángeles Juan Gómez. (2) Hospital Universitario y Politécnico La Fe de Valencia: Javier Millán, Leticia Serrano Lázaro. (3) Hospital Universitario General de Alicante: Tamara García, Ana Belen Paya. (4) Hospital Clínico Universitario de Valencia: José Noceda. (5) Hospital Arnau de Vilanova de Valencia: María José Cano Cano, Rosa Sorando Serra. (6) Hospital Francesc de Borja de Gandía, Valencia: María José Fortuny Bayarri, Francisco José Salvador Suárez. (7) Hospital General Universitario de Elche, Alicante: Matilde González Tejera. (8) Hospital Marina Baixa de Villajoyosa de Alicante: Juan Miguel Marín Porrino, Monica Valera Varea, Rosa María Hernández Sánchez. (9) Hospital Virgen de los Lirios, Alcoy Alicante: Napoleón Meléndez, Patricia Borrás Albero. (10) Hospital Universitario Vinalopó de Elche (Alicante): Blas Jiménez, Karen Josefina Angarita Manrique, Rafael Esteve Solano. (11) Hospital Universitario de Torrevieja de Alicante: Rigoberto del Río, Alexandra Milan Mestre, Fernando Lajara Navarro. (12) Hospital Lluis Alcanys de Xativa: Carles Pérez García, Pilar Sánchez Amador. (13) Hospital Universitario de La Ribera de Valencia: José Vicente Brasó Aznar, José Luis Ruiz López. (14) Hospital de la Vega Baja Orihuela de Alicante:María Carmen Ponce. (15) Hospital Universitario Sant Joan Alicante: Elena Díaz Fernández. (16) Hospital General de Requena de Valencia: Laura Ejarque Martinez, Carol Cuenca Valero. (17) Hospital de Lliria de Valencia: Ana Peiró Gómez, Elena Gonzalo Bellver. (18) Hospital de la Santa Creu i Sant Pau (Barcelona): Carla Cabrera Suarez, Laura Balcells Argilag. (19) Hospital Clinic (Barcelona): Carlos Cardozo. (20) Hospital Universitari de Bellvitge de Hospitalet de Llobregat (Barcelona): Ferran Llopis-Roca, Antonio Haro-Bosch. (21) Hospital Universitari Germans Trias i Pujol de Badalona (Barcelona): Josep Maria Mòdol Deltell, Samuel Olmos Soto. (22) Hospital de Terrassa (Barcelona): Josep Tost. (23) Hospital del Mar (Barcelona): Alfons Aguirre Tejedo, Silvia Minguez Masó. (24) Hospital Universitari Joan XXIII (Tarragona): Anna Palau, Ruth Gaya Tur. (25) Hospital Universitari de Girona Dr. Josep Trueta (Girona): Maria Adroher Muñoz, Ester Soy Ferrer. (26) Hospital Universitari de Vic (Barcelona): Lluís LLauger García. (27) Hospital de Sant Pau i Santa Tecla (Tarragona): Enrique Martín Mojarro, Brigitte Silvana Alarcón Jiménez, Silvia Flores Quesada. (28) Clinica Sagrada Familia (Barcelona): Arturo Huerta. (29) Hospital Clínico San Carlos (Madrid): Marcos Fragiel. (30) Hospital Universitario La Paz (Madrid): Alejandro Martín Quirós, Elena Muñoz del Val, Angelica Rivera Núñez. (31) Hospital Universitario de la Princesa (Madrid): Carmen del Arco Galán, Guillermo Fernández Jiménez. (32) Hospital Universitario Severo Ochoa de Leganés (Madrid): Irene Cabrera Rodrigo, Dolores Corbacho Loarte. (33) Hospital Universitario Rey Juan Carlos (Madrid): Verónica Prieto Cabezas, Mª José Venegas De L'Hotellerie. (34) Hospital Universitario del Henares (Madrid): Cristobal M. Rodriguez Leal, Patricia Fraga Rivas. (35) Hospital Universitario de Fuenlabrada (Madrid): Marta Álvarez Alonso, Cristina Latorre Marco. (36) Hospital Universitario Infanta Cristina de Parla (Madrid): Ruth Calderón Hernaiz, Mary Gaby Llaro Casas. (37) Hospital Comarcal El Escorial (Madrid): Silvia Ortiz Zamorano, Frida Vallejo Somohano. (38) Clínica Universidad Navarra de Madrid: Raquel Piñero Panadero, Nieves López-Laguna. (39) Hospital Universitario de Salamanca: Angel García García, Cristina Gil Castillo. (40) Complejo Asistencial Universitario de León: Marta González Calabaza, Begoña Carmona Ayuela. (41) Hospital Universitario de Burgos: María Pilar López Díez. (42) Hospital Universitario Rio Hortega (Valladolid): Irena Cebrián Ruiz, Lorena Delgado Alonso, Rocío Ruiz Merino. (43) Complejo Asistencial de Soria: Fahd Beddar Chaib,Ikram Samira Mohamedi Abdelkader. (44) Hospital Universitario Regional de Málaga: Manuel Salido, Iván Villar Mena. (45) Hospital Universitario Juan Ramón Jiménez: María Angeles Garrido López, Setefilla Borne Jerez. (46) Hospital Costa del Sol de Marbella: Carmen Agüera Urbano, Ana Belen García Soto. (47) Hospital Valle de los Pedroches de Pozoblanco (Córdoba): Jorge Pedraza García. (48) Hospital Virgen del Rocío de Sevilla: Amparo Fernández de Simón Almela. (49) Complejo Hospitalario Universitario de A Coruña: Ricardo Calvo López. (50) Hospital Universitario Lucus Augusti Lugo: Juan José López Díaz. (51) Complejo Hospitalario Universitario de Vigo. Hospital Álvaro Cunqueiro: María Teresa Maza Vera, Raquel Rodríguez Calveiro. (52) Hospital Universitario General de Albacete: Francisco Javier Lucas-Galan, Francisco Javier Lucas-Imbernón. (53) Hospital Virgen de la Luz (Cuenca): Félix González Martínez, Diana Moya Olmeda. (54) Hospital Nuestra Señora del Prado de Talavera de la Reina (Toledo): Ricardo Juárez. (55) Hospital Universitario de Canarias (Tenerife): Patricia Eiroa Hernandez, Jose Francisco Fernandez Rodriguez. (56) Hospital Universitario de Gran Canaria Dr. Negrín: José Pavón Monzo, Nayra Cabrera González. (57) Hospital Universitario Central Asturias: Pablo Herrero Puente, Desire María Velarde Herrera. (58) Hospital Universitario de Cabueñes (Gijón): Carmen Elvira Menéndez, Ana Murcia Olagüenaga. (59) Hospital Clínico Universitario Virgen de la Arrixaca: Eva Quero Motto, Nuria Tomas García. (60) Hospital General Universitario Reina Sofía de Murcia: Ines García Rosa, María Encarnación Sanchez Canovas, María Consuelo Quesada Martínez. (61) Hospital San Pedro de Logroño: Noemí Ruiz de Lobera. (62) Hospital Clínico Universitario Lozano Blesa: Jose María Ferreras Amez, Belen Arribas Entrala.

Contributors All the authors discussed the idea and design of study and provided patients. Data analysis and first draft writing were done by ÒM. All authors read the draft and provided insight for the final version. ÒM is the guarantor of the paper, taking responsibility for the integrity of the work as a whole, from inception to published article.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval This study involves human participants and was approved by the UMC-19 project with reference number HCB/2020/0534 by the Ethics Committee of the Hospital Clínic of Barcelona (Spain) that acted as the central ethical committee. The UMC-19-S9 was carried out in strict compliance with the Declaration of Helsinki principles. The retrospective characteristics of the study do not require the patient consent, as indicated by the Ethics Committee of the Hospital Clínic.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. Data are available from the authors with the permission of respectively intitutions. The data that support the findings of this study are available from the corresponding author, (ÒM), on reasonable request.

ORCID iDs
Sònia Jiménez http://orcid.org/0000-0002-8332-7492
Pere Llorens http://orcid.org/0000-0002-9291-7179

REFERENCES

1 Guan W-J, Ni Z-Y, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708–20.
2 Chen N, Zhou M, Dong X, *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020;395:507–13.

3 Richardson S, Hirsch JS, Narasimhan M, *et al*. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the new York City area. *JAMA* 2020;323:2052.
4 Lodigiani C, Iapichino G, Carenzo L, *et al*. Venous and arterial thromboembolic complications in COVID-19 patients admitted to an academic hospital in Milan, Italy. *Thromb Res* 2020;191:9–14.
5 Hua A, O'Gallagher K, Sado D, *et al*. Life-Threatening cardiac tamponade complicating myo-pericarditis in COVID-19. *Eur Heart J* 2020;41:2130.
6 Marschall A, Concepción Suárez R, Dejuan Bitriá C, *et al*. Acute pericarditis secondary to COVID-19. *Emergencias* 2020;32:221–2.
7 Asif T, Kassab K, Iskander F, *et al*. Acute pericarditis and cardiac tamponade in a patient with COVID-19: a therapeutic challenge. *Eur J Case Rep Intern Med* 2020;7:001701.
8 Inciardi RM, Lupi L, Zaccone G, *et al*. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. In Press 2020;5:819.
9 Doyen D, Moceri P, Ducreux D, *et al*. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. *Lancet* 2020;395:1516.
10 Tung-Chen Y. Acute pericarditis due to COVID-19 infection: an underdiagnosed disease? *Med Clin*. In Press 2020;155:44–5.
11 Cizgici AY, Zencirkiran Agus H, Yildiz M. COVID-19 myopericarditis: It should be kept in mind in today's conditions. *Am J Emerg Med*. In Press 2020;38:1547.e5–1547.e6.
12 Buja LM, Wolf DA, Zhao B, *et al*. The emerging spectrum of cardiopulmonary pathology of the coronavirus disease 2019 (COVID-19): report of 3 autopsies from Houston, Texas, and review of autopsy findings from other United States cities. *Cardiovasc Pathol* 2020;48:107233.
13 Miró Òscar, González Del Castillo J. Collaboration among Spanish emergency departments to promote research: on the creation of the SIESTA (Spanish Investigators in emergency situations team) network and the coordination of the UMC-19 (unusual manifestations of COVID-19) macroproject. *Emergencias* 2020;32:269–77.
14 Gil-Rodrigo A, Miró Òscar, Piñera P, *et al*. Analysis of clinical characteristics and outcomes in patients with COVID-19 based on a series of 1000 patients treated in Spanish emergency departments. *Emergencias* 2020;32:233–41.
15 Adler Y, Charron P, Imazio M, *et al*. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2015;36:2921–64.
16 Garcia-Garcia HM, McFadden EP, Farb A, *et al*. Standardized end point definitions for coronary intervention trials: the Academic Research Consortium-2 consensus document. *Circulation* 2018;137:2635–50.
17 Pollán M, Pérez-Gómez B, Pastor-Barriuso R, *et al*. Prevalence of SARS-CoV-2 in Spain (ENE-COVID): a nationwide, population-based seroepidemiological study. *Lancet* 2020;396:535–44.
18 Hooper AJ, Celenza A. A descriptive analysis of patients with an emergency department diagnosis of acute pericarditis. *Emerg Med J* 2013;30:1003–8.
19 Patel B, Shah M, Sheikh T, *et al*. Regional and seasonal variations in the US emergency department visits for acute pericarditis. *Am J Emerg Med* 2019;37:997–9.
20 Martínez-Nadal G, Prepoudis A, Miró Òscar, *et al*. Clinical features of pericarditis with and without myocardial involvement diagnosed in the emergency department and factors associated with need for hospitalization. *Emergencias* 2020;32:97–104.
21 López-Barbeito B, Martínez-Nadal G, Bragulat E, *et al*. Changes in cases of nontraumatic chest pain treated in a chest pain unit over the 10-year period of 2008-2017. *Emergencias* 2019;31:377–84.
22 Imazio M, Cecchi E, Demichelis B, *et al*. Myopericarditis versus viral or idiopathic acute pericarditis. *Heart* 2008;94:498–501.
23 Elfström P, Hamsten A, Montgomery SM, *et al*. Cardiomyopathy, pericarditis and myocarditis in a population-based cohort of inpatients with coeliac disease. *J Intern Med* 2007;262:545–54.
24 Lin AH, Phan H-AL, Barthel RV, *et al*. Myopericarditis and pericarditis in the deployed military member: a retrospective series. *Mil Med* 2013;178:18–20.
25 Imazio M, Gaita F, LeWinter M. Evaluation and treatment of pericarditis: a systematic review. *JAMA* 2015;314:1498–506.
26 Kytö V, Sipilä J, Rautava P. Clinical profile and influences on outcomes in patients hospitalized for acute pericarditis. *Circulation* 2014;130:1601–6.
27 Povar Marco J. Organizing the emergency care of patients with chest pain. *Emergencias* 2019;31:371–2.
28 Mostafavi A, Tabatabaei SAH, Zamani Fard S, *et al*. The incidence of myopericarditis in patients with COVID-19. *J Cardiovasc Thorac Res* 2021;13:203–7.
29 Singer ME, Taub IB, Kaelber DC. Risk of myocarditis from COVID-19 infection in people under age 20: a population-based analysis. *medRxiv* 2021. doi:10.1101/2021.07.23.21260998. [Epub ahead of print: 27 Jul 2021].