I.F.C. Italian Federation of Cardiology

Autoptic prevalence of pericarditis in coronavirus disease 2019 patients

Marco Zuin[a,c], Gianluca Rigatelli[b], Claudio Bilato[c], Massimo Imazio[d] and Loris Roncon[b]

J Cardiovasc Med 2022, **23**:623–625

Keywords: myocarditis, coronavirus disease 2019, autopsy, prevalence, pericarditis

[a]Department of Translational Medicine, University of Ferrara, Ferrara, [b]Department of Cardiology, Santa Maria della Misericordia Hospital, Rovigo, [c]Department of Cardiology, West Vincenza Hospitals, Arzignano and [d]Cardiothoracic department University Hospital Santa Maria della Misericordia, Udine, Italy

Correspondence to Dr Marco Zuin, MD, FESC, FACC, FANMCO, Department of Translational Medicine, University of Ferrara, 44100 Ferrara, Italy.
E-mail: marco.zuin@edu.unife.it

Received 10 October 2021 **Accepted** 17 March 2022

To the Editor,

Data regarding the real prevalence of pericardial involvement, and especially acute pericarditis, in coronavirus disease 2019 (COVID-19) patients are currently scant.[1] The aim of the present manuscript is to perform a systematic review and meta-analysis to assess the pooled prevalence of pericarditis in COVID-19 patients at autopsy.

Methods

A literature search was performed using MEDLINE and Scopus databases from their inception to August 2021 to locate investigations in the English language reporting the autoptic prevalence of pericarditis in COVID-19 patients. The selection of studies to be included in our analysis was independently conducted by two authors (L. R., M.Z.) in a blinded fashion. Searches were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Supplementary file 1, http://links.lww.com/JCM/A451). The search terms included the following MeSH terms: 'COVID-19' OR 'SARS-CoV-2' AND 'pericarditis' AND 'autopsy'. Moreover, we searched the bibliographies of target studies for additional references. The final search was conducted on August 16, 2021.

We predefined the inclusion criteria for eligible studies as follows: investigations reporting the autoptic prevalence of pericarditis in patients with a confirmed diagnosis of SARS-CoV-2 infection. Conversely, studies were excluded if they were case reports, review articles, editorials, letters and case series with <20 participants or they did not report sufficient data regarding the autoptic prevalence of pericarditis.

The gathered data included author/s, sample size, mean age, gender, concomitant comorbidities such as arterial hypertension (HT), diabetes mellitus (DM), atrial fibrillation (AF), cancer, chronic obstructive pulmonary disease (COPD), heart failure (HF) and estimated prevalence of pericarditis at autopsy. The quality of included studies was graded using the Newcastle-Ottawa quality assessment scale (NOS).

The cumulative autoptic prevalence of pericarditis in COVID-19 patients (n/N) was defined as the ratio between patients with histopathological findings of pericarditis (n) and the number of patients enrolled in each study (N). Data were pooled using a random-effects model and presented with the corresponding 95% confidence interval (CI). Between study heterogeneity was assessed using the Higgins I^2 statistic and Q-value. The presence of potential publication bias was verified by visual inspection of the funnel plot. Due to the low number of included studies (<10), small-study bias was not examined as our analysis was underpowered to detect such bias. To further appraise the impact of potential baseline confounders, a meta-regression analysis was performed. All meta-analyses were conducted using Comprehensive Meta-Analysis software, version 3 (Biostat, USA).

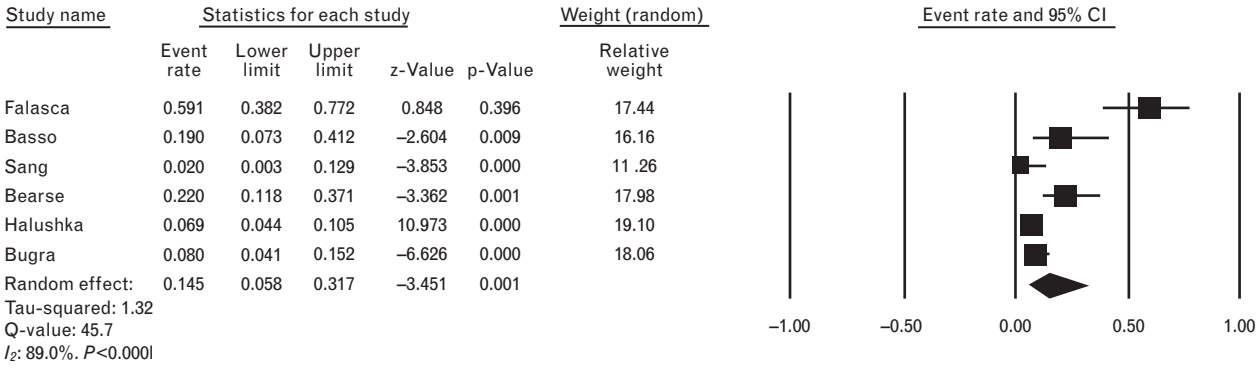
Results

Using our search strategy, six studies met the inclusion criteria and were included into the final analysis (Fig. 1).[2–7] Overall, 511 autopsies of COVID-19 patients (mean age 65.2 years, 345 males) were included in the analysis (Table 1). Quality assessment showed that all studies were of moderate-high quality according to the NOS scale.

Estimates for the prevalence of pericarditis at autopsy in COVID-19 patients ranged from 2.0% to 59.1% while the random-effects overall pooled estimated prevalence was 14.5% (95% CI: 5.8–31.7, I^2: 89.0%, $P < 0.0001$) (Fig. 1). Visual inspection of the relative funnel plot did not reveal significant evidence of publication bias (Supplementary file 2, http://links.lww.com/JCM/A452). Meta-regression showed a direct correlation with age (coefficient 0.015, $P = 0.002$) and gender (male vs. female, coefficient 0.016, $P = 0.03$), but no effect when considering arterial

 DOI:10.2459/JCM.0000000000001306

Fig. 1



Forest plot investigating the pooled autopsy prevalence of myocarditis in patients with COVID-19 infection. COVID-19, coronavirus disease 2019.

hypertension ($P = 0.08$), and diabetes mellitus ($P = 0.60$) as moderating variables.

Comment

Our results showed that the overall pooled prevalence of pericarditis among COVID-19 patients who underwent autopsy is 14.5%. Moreover, the histopathological findings were more common in male patients and influenced by increasing age, as demonstrated by the meta-regression performed. Probably, our results underestimate the real prevalence of acute pericarditis since they mainly reflect the prevalence in patients with more severe infection. Unfortunately, no specific data regarding the severity of the disease or need for intensive care unit hospitalization were reported in the original manuscripts as well as the concomitant prevalence of myocarditis. However, to date, the larger part of data on the prevalence of pericarditis in COVID-19 subjects has been obtained from clinical and radiological investigations, rather than from histopathological analyses.[2,8] Most treatments for pericarditis do not appear contraindicated also in the presence of possible COVID-19 infection and should not be discontinued, and some (corticosteroids, colchicine, and anakinra) can be considered to treat both conditions.[9]

The observed epidemiological aspects are in accordance with previous studies performed in non-COVID-19 subjects, which demonstrated that acute pericarditis is more common in male patients; furthermore, also aging resulted to be associated with a higher in-hospital mortality among these patients.[10] Notably, the same demographical issues have been also related to a higher mortality risk in COVID-19 patients,[11] representing a common risk factor. The high heterogeneity observed may be also due to the limited number of studies satisfying the inclusion criteria of our analysis as well as the relatively few numbers of enrolled patients. In addition, also the inherited biases derived from the original investigations may have further contributed to the heterogeneity level observed. Moreover, different levels of methodological quality, sampling methods, professional level of the pathologists as well as adequate coverage of the identified sample may have produced significant difference among studies. The absence of a systemic autoptic screening in these patients may have underestimated the prevalence of pericarditis in COVID-19

Table 1 General characteristics of the population enrolled

Author	No. of patients	Age (SD) [range]	Males, *n* (%)	HT, *n* (%)	DM, *n* (%)	AF, *n* (%)	Obesity, *n* (%)	Cancer, *n* (%)	COPD, *n* (%)	HF, *n* (%)	NOS
Falasca *et al.*[3]	22	76 (15)[a] 48.5 (13.0)[b]	15 (68.1)	4 (22.3)	4 (22.3)	1 (4.5)	NR	8 (44.5)	6 (33.3)	NR	8
Basso *et al.*[4]	21	69 [44–86]	15 (71)	16 (76)	7 (33)	4 (19)	NR	NR	NR	NR	7
Sang *et al.*[5]	50	63.5 [31–94]	36 (72)	45 (90)	28 (56)	NR	25 (50)	NR	NR	5 (10)	8
Bearse *et al.*[6]	41	67 [21–89]	27 (65.8)	27 (65.8)	13 (31.7)	NR	NR	NR	NR	NR	7
Halushka *et al.*[7]	277	75 [22–27]	172 (62.1)	152 (54.9)	89 (32.1)	NR	44 (15.9)	44 (15.9)	70 (25.3)	NR	8
Diaz-Arocutipa *et al.*[8]	100	54.8 (18.9)	80 (80)	NR	NR	NR	NR	NR	NR	NR	6

[a] With comorbidities. [b] Without comorbidities. COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HF, heart failure; HT, arterial hypertension; NOS, Newcastle-Ottawa quality assessment scale [investigations were classified as having low (<5 stars), moderate (5–7 stars) and high quality (>7 stars)].

patients who died as well as in those who survived since the diagnosis was suspected only in patients with evident clinical symptoms and/or high degree of suspicion. Therefore, despite the limited generalizability of our results to a non-autoptic COVID-19 population, acute pericarditis remains an important and underrecognized cardiovascular complication in COVID-19 patients which requires a proper workup and specific management.

Conflicts of interest

There are no conflicts of interest.

References

1 Furqan MM, Verma BR, Cremer PC, Imazio M, Klein AL. Pericardial diseases in COVID19: a contemporary review. *Curr Cardiol Rep* 2021; **23**:90.

2 Guo T, Fan Y, Chen M, *et al.* Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; **5**:811–818.

3 Falasca L, Nardacci R, Colombo D, *et al.* Postmortem findings in Italian patients with COVID-19: a descriptive full autopsy study of cases with and without comorbidities. *J Infect Dis* 2020; **222**:1807–1815.

4 Basso C, Leone O, Rizzo S, *et al.* Pathological features of COVID-19-associated myocardial injury: a multicentre cardiovascular pathology study. *Eur Heart J* 2020; **41**:3827–3835.

5 Sang CJ 3rd, Burkett A, Heindl B, *et al.* Cardiac pathology in COVID-19: a single center autopsy experience. *Cardiovasc Pathol* 2021; **54**:107370; doi: 10.1016/j.carpath.2021.107370.

6 Bearse M, Hung YP, Krauson AJ, *et al.* Factors associated with myocardial SARS-CoV-2 infection, myocarditis, and cardiac inflammation in patients with COVID-19. *Mod Pathol* 2021; **34**:1345–1357.

7 Halushka MK, Vander Heide RS. Myocarditis is rare in COVID-19 autopsies: cardiovascular findings across 277 postmortem examinations. *Cardiovasc Pathol* 2021; **50**:107300.

8 Diaz-Arocutipa C, Saucedo-Chinchay J, Imazio M. Pericarditis in patients with COVID-19: a systematic review. *J Cardiovasc Med (Hagerstown)* 2021; **22**:693–700.

9 Imazio M, Brucato A, Lazaros G, *et al.* Anti-inflammatory therapies for pericardial diseases in the COVID-19 pandemic: safety and potentiality. *J Cardiovasc Med (Hagerstown)* 2020; **21**:625–629.

10 Kytö V, Sipilä J, Rautava P. Clinical profile and influences on outcomes in patients hospitalized for acute pericarditis. *Circulation* 2014; **130**:1601–1606.

11 Mallapaty S. The coronavirus is most deadly if you are older and male - new data reveal the risks. *Nature* 2020; **585**:16–17.