Chest pain in long covid disease. Insights from stress cardiovascular magnetic resonance

Francisco Dias Claudio Nuria Vallejo Lourdes Mateu Antoni Bayes-Genis Victoria Delgado Albert Teis

PII: S0870-2551(25)00284-7

DOI: https://doi.org/doi:10.1016/j.repc.2025.03.008

Reference: REPC 2480

To appear in: *Revista Portuguesa de Cardiologia*

Received Date: 22 January 2025

Please cite this article as: Claudio FD, Vallejo N, Mateu L, Bayes-Genis A, Delgado V, Teis A, Chest pain in long covid disease. Insights from stress cardiovascular magnetic resonance, *Revista Portuguesa de Cardiologia* (2025), doi: https://doi.org/10.1016/j.repc.2025.03.008

Chest pain in long covid disease. Insights from stress cardiovascular magnetic resonance.

Dor torácica em *Long Covid* em perspetiva a partir da Ressonância Magnética Cardíaca de *Stress*

Francisco Dias Claudio[1]; Nuria Vallejo[2]; Lourdes Mateu[3]; Antoni Bayes-Genis,[4]; Victoria Delgado[5]; Albert Teis[6]*.

1. Heart Institute. Cardiology Department. Germans Trias University Hospital. Badalona. Barcelona. Spain.
2. Heart Institute. Cardiology Department. Germans Trias University Hospital. Badalona. Barcelona. Spain.
3. Infectious Disease Department. Germans Trias University Hospital. Badalona. Barcelona. Spain;
4. Heart Institute. Cardiology Department. Germans Trias University Hospital. Badalona. Barcelona. Spain; Department of Medicine. Universitat Autònoma de Barcelona. Barcelona. Spain;
5. Heart Institute. Cardiology Department. Germans Trias University Hospital. Badalona. Barcelona. Spain; Centre de Medicina Comparativa i Bioimatge de Catalunya (CMCiB). Badalona. Barcelona. Spain;
6. Heart Institute. Cardiology Department. Germans Trias University Hospital. Badalona. Barcelona. Spain;

***Corresponding autor:**

Email address: a_teis@yahoo.es (A. Teis)

Keywords:

Long COVID; Chest pain; Microvascular Angina; Cardiac magnetic resonance

Long COVID; Dor torácica; Angina microvascular; Ressonância magnética cardíaca

Post-COVID-19 condition or "Long COVID" is a complex heterogeneous entity characterized by incomplete recovery after acute COVID-19 infection. Prevalence of chest pain varies from 21% to 53% and the potential pathophysiological mechanisms include myocardial infarction, myocarditis and pericarditis[1]. Preliminary reports suggest that microvascular dysfunction may be a cause of chest pain in these patients[2,3]. However, the extent of microvascular dysfunction contribution in relation to other factors causing chest pain in patients with long COVID has not been thoroughly characterized.

This prospective study included consecutive patients with long COVID reporting typical chest pain, from February 2021 to May 2023. The study was approved by the institution's human research committee (PI-21-065). Epicardial coronary artery disease was ruled out via coronary computed tomography angiography. Adenosine stress cardiac magnetic resonance (CMR) was performed in a 1.5 Tesla scanner. Medis software was used for CMR data analysis. Microvascular dysfunction was considered positive if first-pass stress perfusion showed a significant circumferential subendocardial perfusion defect. Statistical analysis was conducted using SPSS v.28, with significance set at $p<0.05$.

Of the 548 individuals with long COVID-19 symptoms at our center, 59 patients reported typical chest pain and underwent stress CMR. Median time between COVID infection and CMR was 13 months. Mean age was 46.9 years, and the majority were female (71%), and a low prevalence of cardiovascular risk factors was observed (Table 1). Most patients had experienced a previous mild form of COVID-19 infection. 23 patients (39%) were positive for microvascular dysfunction (Case A from Figure 1). No significant differences were observed in clinical or risk factors between patients with and without microvascular dysfunction. There were no disparities in cardiac chamber dimensions, myocardial T1 mapping or extracellular volume between the two groups. While all patients exhibited T2 mapping values within the normal range, those without microvascular dysfunction presented a slightly higher T2 mapping (47.6ms compared to 45.2ms, $p=0.022$). LGE was present in five patients (8.5%). The most common pattern of LGE was epicardial (three patients – see Case B from Figure 1). In five patients (8.5%), CMR data suggested the presence of prior myocarditis. Neither myocardial infarction nor pericardial disease were detected in any case.

Among patients with long COVID-19 and typical chest pain, the prevalence of microvascular dysfunction, as assessed by stress CMR, is 39%. Furthermore, 8.5% patients exhibited sequelae of previous myocarditis, while none displayed myocardial

infarction or pericardial disease. Given the absence of cardiac structural or functional differences between patients with and without microvascular dysfunction, it is plausible that an immune-mediated inflammatory mechanism may underlie these findings[4]. In patients without COVID-19 infection, a recent meta-analysis showed a pooled prevalence of 43% microvascular dysfunction in a general cohort of patients without obstructive coronary artery disease[5]. Therefore, further research is needed to ascertain causality rather than just the coexistence of microvascular dysfunction and long COVID symptoms.

Any potential conflicts of interest, including related consultancies, shareholdings and funding grants:

Antoni Bayes-Genis reports personal fees and/or advisory board from AstraZeneca, Novartis, Boehringer Ingelheim, Abbott, Roche Diagnostics, and Vifor Pharma.

Victoria Delgado has received speaker fees from Abbott Vascular, Medtronic, Edwards Lifesciences, MSD, and GE Healthcare.

The remaining authors have nothing to disclose.

Ethics in publishing

1. Does your research involve experimentation on animals?:

No

2. Does your study include human subjects?:

Yes

If yes; please provide name of the ethical committee approving these experiments and the registration number. :

Germans Trias I Pujol Hospital's human research committee (PI-21-065)

If yes; please confirm authors compliance with all relevant ethical regulations. :

Yes

If yes; please confirm that written consent has been obtained from all patients. :

Yes

3. Does your study include a clinical trial?:

No

4. Are all data shown in the figures and tables also shown in the text of the Results section and discussed in the Conclusions?:

Yes

References

1. Petersen SE, Friedrich MG, Leiner T, et al. Cardiovascular Magnetic Resonance for Patients With COVID-19. *JACC Cardiovasc Imaging*. 2022;15(4):685-699. doi:10.1016/j.jcmg.2021.08.021

2. Drakos S, Chatzantonis G, Bietenbeck M, et al. A cardiovascular magnetic resonance imaging-based pilot study to assess coronary microvascular disease in COVID-19 patients. *Sci Rep*. 2021;11(1):15667. doi:10.1038/s41598-021-95277-z

3. Doeblin P, Steinbeis F, Scannell CM, et al. Brief Research Report: Quantitative Analysis of Potential Coronary Microvascular Disease in Suspected Long-COVID Syndrome. *Front Cardiovasc Med*. 2022;9. doi:10.3389/fcvm.2022.877416

4. Davis HE, McCorkell L, Vogel JM, et al. Long COVID: major findings, mechanisms and recommendations. *Nat Rev Microbiol*. 2023;21(3):133-146. doi:10.1038/s41579-022-00846-2

5. Mileva N, Nagumo S, Mizukami T, et al. Prevalence of Coronary Microvascular Disease and Coronary Vasospasm in Patients With Nonobstructive Coronary Artery Disease: Systematic Review and Meta-Analysis. *J Am Heart Assoc*. 2022;11(7). doi:10.1161/JAHA.121.023207

Tables

Table 1. Clinical and cardiac magnetic resonance findings

	Cohort (N=59)	**No Microvascular Dysfunction (N= 36)**	**Microvascular Dysfunction (N= 23)**	**p-value**
Age (years)	46.9 (8.9)	45.9 (9.6)	48.4 (7.6)	0.310
Sex (male)	17.0 (28.8)	13.0 (36.1)	4.0 (17.4)	0.150
BMI (kg/m2)	27.2 (5.6)	27.4 (6.1)	27.0 (4.9)	0.825
Family history of coronary artery disease	10.0 (16.9)	5.0 (13.9)	5.0 (21.7)	0.490
Smoking	20.0 (23.9)	11.0 (30.6)	9.0 (39.1)	0.551
Hypertension	11.0 (18.6)	5.0 (13.9)	6.0 (26.1)	0.310
Dyslipidemia	10.0 (16.9)	7.0 (19.4)	3.0 (13.0)	0.725
Type 2 diabetes	5.0 (8.5)	4.0 (11.1)	1.0 (4.3)	0.639
COVID-related inappropriate tachycardia	15.0 (25.4)	9.0 (25.0)	6.0 (26.1)	0.925
Asthma	1.0 (1.7)	1.0 (2.8)	0.0 (0.0)	0.610
CMR Findings				
LVDVi (ml/m2)	74.0 (17.4)	71.6 (18.3)	77.8 (15.6)	0.188
LVSVi (ml/m2)	28.3 (9.2)	28.1 (9.8)	28.8 (8.2)	0.779
LVEF (%)	62.5 (5.4)	63.0 (8.0)	63.0 (6.0)	0.629
LVMi (g/m2)	55.3 (24.1)	55.2 (21.1)	64.9 (26.4)	0.351
RVDVi (ml/m2)	72.4 (19.1)	68.8 (19.0)	78.2 (18.1)	0.065
RVSVi (ml/m2)	29.0 (14.5)	27.9 (10.0)	30.8 (9.3)	0.280
RVEF (%)	60.3 (8.0)	59.9 (5.9)	61.0 (6.1)	0.497
T1 mapping (ms)	989.0 (49.0)	984.0 (66.0)	991.0 (38.0)	0.731

T2 mapping (ms)	46.7 (4.2)	47.6 (4.7)	45.2 (2.8)	0.022
ECV (%)	25.0 (3.7)	24.8 (3.2)	25.2 (4.4)	0.702
LGE	5.0 (8.5)	3.0 (8.3)	2.0 (8.7)	0.654
Epicardic	3.0 (5.1)	2.0 (66.7)	1.0 (50.0)	
Mid-myocardial	2.0 (3.4)	1.0 (33.3)	1.0 (50.0)	

BMI: body mass index; COVID: coronavirus disease; CMR: cardiovascular magnetic resonance; ECV: extracellular volume; LGE: late gadolinium enhancement ; LVDVi: indexed left ventricular end-diastolic volume; LVSVi: indexed left ventricular end-systolic volume; LVEF: left ventricular ejection fraction; LVMi: left ventricular mass index; RVDVi: indexed right ventricular end-diastolic volume; RVSVi: indexed right ventricular end-systolic volume; RVEF: right ventricular ejection fraction.

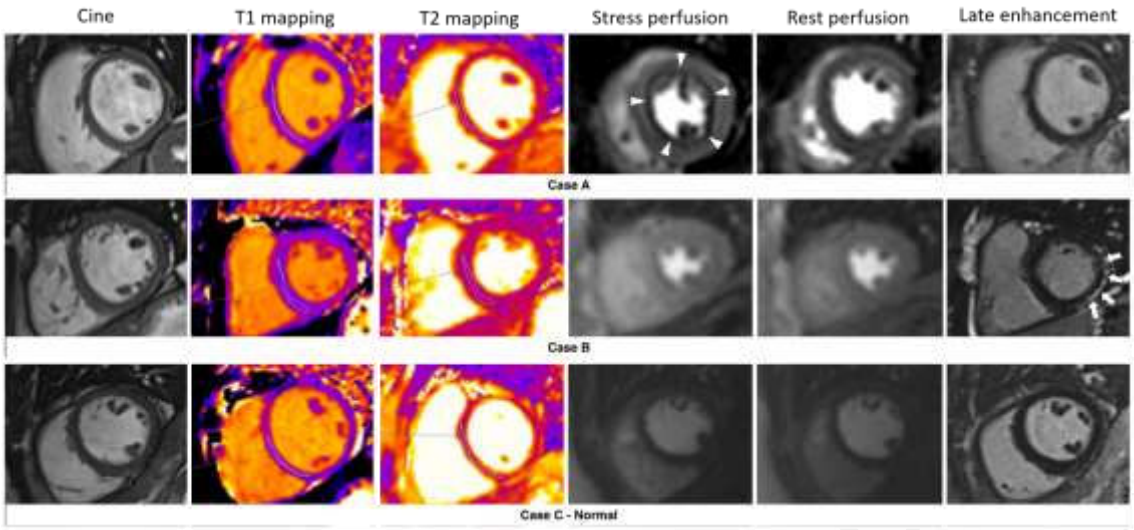

Figure 1