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Recovered COVID-19 Patients Show Ongoing Subclinical Myocarditis as Revealed by Cardiac Magnetic Resonance Imaging

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PII: S1936-878X(20)30729-4

DOI: https://doi.org/10.1016/j.jcmg.2020.08.012

Reference: JCMG 3582

To appear in: *JACC: Cardiovascular Imaging*

Received Date: 7 July 2020

Revised Date: 19 August 2020

Accepted Date: 21 August 2020

Please cite this article as: Ng M-Y, Ferreira VM, Leung ST, Yin Lee JC, Ho-Tung Fong A, To Liu RW, Man Chan JW, Alan Wu KL, Lung K-C, Crean AM, Fan-Ngai Hung I, SIU C-W, Recovered COVID-19 Patients Show Ongoing Subclinical Myocarditis as Revealed by Cardiac Magnetic Resonance Imaging, *JACC: Cardiovascular Imaging* (2020), doi: https://doi.org/10.1016/j.jcmg.2020.08.012.

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Recovered COVID-19 Patients Show Ongoing Subclinical Myocarditis as Revealed by Cardiac Magnetic Resonance Imaging

Running Title: Recovered COVID-19 Patients Show Subclinical Myocarditis Using CMR

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Conflict of Interest: MYN has receiving funding from Bayer AG and Circle Cardiovascular Imaging. CWS has received research funding from AstraZeneca. All other authors have no conflict of interest to declare.

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Keywords: Cardiac magnetic resonance imaging, COVID-19, Recovered, Troponin, myocarditis

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The cardiovascular complications of coronavirus disease 2019 (COVID-19) are still being established[1]. Expert guidelines recommend the use of cardiac imaging in the management of COVID-19 patients[2], and cardiovascular magnetic resonance (CMR) has demonstrated utility in the non-invasive detection of myocardial inflammation[3]. We present a case series of 16 recovered COVID-19 patients who underwent CMR to assess for evidence of myocardial involvement or ongoing myocarditis.

Ethics approval was obtained from the Hong Kong West Cluster (UW20-359) Institutional Review Board for this retrospective study. Inclusion criteria were COVID-19 patients admitted as inpatients to Queen Mary Hospital, referred for outpatient CMR post-recovery for raised troponin or electrocardiogram (ECG) changes during the acute illness. Exclusion criteria were poor quality CMR preventing assessment of ventricular function and late gadolinium enhancement (LGE). COVID-19 was diagnosed based on reverse transcription polymerase chain reaction (RT-PCR) tests of nasopharyngeal and throat swabs. Recovered COVID-19 status was based on (1) two negative nasopharyngeal swab RT-PCR results >24 hours apart and (2) absence of fever and improvement in respiratory symptoms. COVID-19 disease severity was defined according to World Health Organization (WHO) criteria[4]. CMR performed at 1.5T (GE Healthcare system) included cine, native T1-mapping ($SMART_1$), T2-mapping and LGE. T1/T2-mapping were analyzed in the mid-ventricular slice for an average value per patient. Images were reviewed independently by 3 cardiac radiologists.

16 patients were identified (median 68yrs, IQR 53-69yrs, 7 females), 15/16 (94%) had mild/moderate WHO-defined disease severity. On admission, 14 (88%) had ECG changes, and 7 (44%) had raised troponin levels. At ≥2 weeks post-discharge, 11 (69%) patients were asymptomatic. 5 (31%) had symptoms such as cough, shortness of breath and mild chest pain.

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CMR was performed at a median of 56 days post-recovery. Three (19%) patients had non-ischemic LGE with elevated global T2-mapping values (57-62 ms), fulfilling the Lake Louise criteria for myocardial inflammation[3]- one had chest discomfort with mildly elevated CRP; one was asymptomatic but with elevated troponin (figure 1); one was asymptomatic with no blood biomarkers of inflammation. The fourth patient with LGE had a known history of NSTEMI with circumflex artery stenting, showing a lateral wall infarct but no myocarditic changes. In the rest (all 12 without LGE), 4 patients had elevated T1 only, 1 had elevated T2 only, and 1 had both elevated T1 and T2. Of these, 4/6 had blood biomarkers of inflammation (high WBC, CRP or Troponin), and 3/6 had ongoing symptoms (1 cough, 1 cough/ SOB, 1 SOB/chest discomfort). The remaining 6 had normal T1, T2 and no LGE: 5/6 were asymptomatic, of which 2/5 still had elevated troponin, 1/5 had elevated CRP, and 2/5 had normal blood tests . None had pericardial thickening or effusion.

Our study demonstrates subclinical ongoing or resolving myocardial inflammation in recovered COVID-19 patients, as revealed by CMR. A Wuhan study showed that 58% of recovered COVID-19 patients had abnormal CMR findings, but all had cardiac symptoms[5]. In contrast, our study extends that, although 69% (11/16) of recovered COVID-19 patients were asymptomatic, a majority (56%, 9/16) showed abnormal CMR findings (high T1 and/or T2, +/- non-ischemic LGE), 67% (6/9) of whom had accompanying blood biomarkers of ongoing inflammation, even if asymptomatic (3/6). In asymptomatic patients, 45% (5/11) had abnormal CMR findings; 27% (3/11) of asymptomatic patients also had corroborating serological evidence of inflammation. In symptomatic patients, 80% (4/5) had abnormal CMR findings (high T1 and/or T2), 75% (3/4) of whom had corroborating serological evidence of ongoing inflammation. Overall, 6/16 (38%) patients had both imaging and serological evidence of myocardial inflammation, and may need follow-up within their individual clinical context. 3 (19%) patients had either high T1 and/or T2 on CMR, but

without blood biomarkers of inflammation; the abnormal T1 or T2 signals may represent residual or resolving myocardial inflammation. Thus, in COVID-19 patients deemed to have recovered, there remains a high index of suspicion of initial and ongoing myocardial inflammation, and CMR has demonstrable utility in identifying subclinical myocardial involvement post COVID-19.

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Figure Legend

Figure 1: CMR images from a recovered asymptomatic COVID-19 patient with myocardial inflammation.
(A&B) High global T1- and T2-mapping values. (C) Short-axis cine. (D) Small, subepicardial, basal anterolateral wall LGE (arrow). (E) CMR Results.

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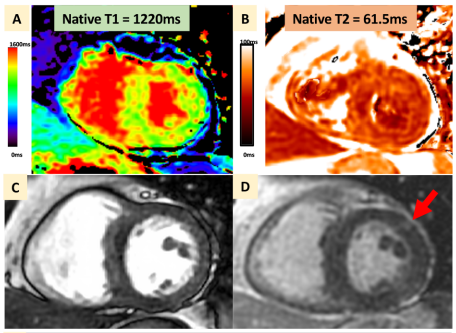

E	Cardiac Magnetic Resonance (CMR)
LV End-Diastolic Volume Indexed (ml/m²)	79 (IQR: 70-84)
LV Ejection Fraction (%)	59 (IQR 56-65)
RV End-Diastolic Volume Indexed (ml/m²)	88 (IQR 76-94)¶
RV Ejection Fraction (%)	53 (IQR 48-57)
Global mid-ventricular native T1 (ms)	1209 (IQR 1164-1219)#
Global mid-ventricular native T2 (ms)	52 (IQR 50-56)##
High global native T1 only (>1208 ms) (n, % cases)	4 (25%)
High global native T2 only (>54.8 ms) (n, % cases)	1 (5%)
High native T1 and T2 (n, % cases)	4 (25%)

Notes:

IQR= Interquartile range; LV= Left ventricle; RV = Right ventricle

¶=One patient had borderline dilated right ventricle and dilated main pulmonary artery (37mm), with no initial suspicion of pulmonary embolus, and a VQ scan post-CMR was normal.

#p<0.02 when compared to 15 healthy volunteers with a mean T1 of 1158±25ms (2SD range 1109 - 1208 ms)

##p<0.01 when compared to 15 healthy volunteers with a mean T2 of 48.2±3.4ms (2SD range 41.5 - 54.8 ms)

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