

RAPID RESEARCH IN COVID-19 PROGRAMME

CARDIAC IMAGING IN SARS CORONAVIRUS DISEASE-19 (CISCO-19)

AIMS

To investigate heart, lung and blood vessel involvement in patients with COVID-19

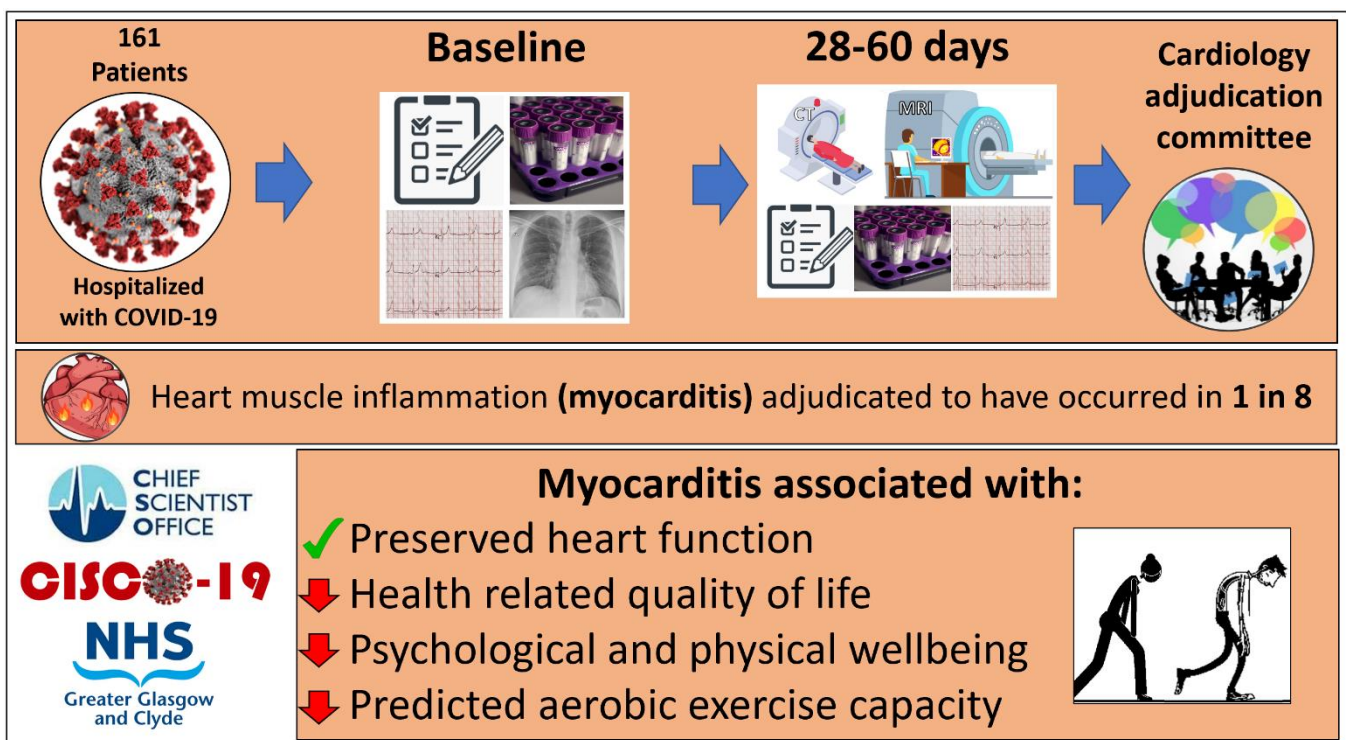
KEY FINDINGS

- Our study has described the illness trajectory of COVID-19.
- 267 patients who were treated in hospital and survived the acute COVID-19 infection were enrolled; their average age was 55 years, 91% were white, 41% were female, 39% lived in deprived areas and 16% were healthcare workers. 161 had heart, lung and kidney imaging using CT and MRI scans 28-60 days after discharge from hospital.
- Heart risk factors were very common: half were obese, half had high blood pressure and half had pre-diabetes or diabetes
- An independent adjudication committee of consultant cardiologists classified heart injury. Heart inflammation (myocarditis) was relatively common; 15% of patients had evidence of heart injury
- A blood test for heart injury differentiated patients according to their initial severity of illness e.g., need for respiratory support, wellbeing (quality of life) and exercise capacity one month after discharge
- Aerobic exercise capacity was markedly impaired initially and remained markedly reduced one month after discharge from hospital; this was especially the case in patients with heart inflammation.

WHAT DID THE STUDY INVOLVE?

Our research idea was that infection with coronavirus-19 (COVID) led to release of virus from damaged lung tissue into circulating blood to directly infect the heart and blood vessels. Having gained ethics committee approval, we invited patients who had received treatment in 3 hospitals in Glasgow to attend the research unit approximately 1 month after discharge. The visit involved a heart, lung and kidney scan using MRI and CT. Uniquely, the protocol also involved measuring blood flow in the heart and lungs, giving insights into blood vessel function. The analyses focused on imaging heart, lung and kidney damage. The patients completed validated questionnaires and had a blood test at the time of giving informed consent in-hospital and then again during the second visit. We are planning to continue the follow-up of the patients for health and wellbeing in the longer term. Our '**Rapid Coronavirus Research**' aims to immediately clarify the links between the heart and lung injury and related risk factors. Our research will support the development of novel preventive therapies. In order to release the full potential of our research, we have established new research collaborations with companies involved in the life sciences, pharmaceutical and diagnostics sectors, and with other research groups.

CENTRAL ILLUSTRATION



WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

- The first patient was enrolled on May 22nd 2020, 3 days after receiving ethics committee approval and 3 weeks after receiving notice of research funding from the Chief Scientist Office. The last patient was enrolled on March 16, 2021 and the final 'control' patients were enrolled in July 2021.
- Three hospitals in the West of Scotland supported the project, including the Queen Elizabeth University Hospital and the Royal Infirmary in Glasgow, the Royal Alexandra Hospital in Paisley and Hairmyres Hospital in NHS Lanarkshire.
- Given the fall in disease prevalence from June to September, we presented an interim analysis in November 2020. The results in this report (October 2021) reflect the final population. Our research analyses involving the consultant adjudication committee and the core laboratory research data are ongoing. The analysis of our study has been undertaken by a statistician in the Robertson Centre for Biostatistics, University of Glasgow.

- Patients who were enrolled into our study had survived the acute illness. Following a screening process led by the healthcare staff, patients who were able to have a heart, lung and kidney scan involving MRI and CT 1 month after discharge were invited to take part.

267 patients were enrolled; their average age was 55 years, 90.5% were white, 4.0% were South Asian, 1.5% were East Asian and 4.0% were from other ethnic backgrounds. 41% were female, 39% lived in deprived areas and 16% were healthcare workers.

The diagnosis of COVID-19 was based on a positive virology laboratory test in 93% of the patients. The other patients were diagnosed based on radiology criteria from X-ray and/or CT scans. Considering the initial point of care, of 273 with available data, 206 (75.5%) attended A&E, 54 (19.8%) patients were admitted via the Acute Medical Receiving Unit, 13 (4.8%) patients were admitted to the acute medical wards, and none of the patients were admitted to other wards such as Care of the Elderly or Surgery. Allowing for 19 patients with incomplete data, 17 (6.5%) patients acquired COVID-19 in-hospital. Considering acute supportive therapy for COVID-19, 186 (71.3%) patients received oxygen, 22 (8.4%) patients received invasive ventilation, 40 (15.3%) patients received non-invasive respiratory support, 4 (1.5%) patients received haemodialysis and 1 patient received heart-lung support with extracorporeal membrane oxygenation (ECMO).

- Blood troponin is a heart muscle protein that is usually undetectable by a blood test (< 4 ng/L). A

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rise in troponin concentration reflects either heart injury or an impairment in the body's ability to clear troponin from the blood, as may happen during illness. The patients in our study have been categorised according to the initial troponin concentration, if measured as part of standard NHS care. We plan to re-measure troponin from the research blood sample that has been collected in all of the patients. This analysis will be undertaken at the end of the study. The standard care troponin results were available in 243 of 267 patients (reflecting the selective approach to troponin testing in the NHS). We have categorised the patients in our study according to the initial blood troponin concentration. A risk-based approach has been adopted based on prior research undertaken through our role in the HighSTEACS study (Bulgara A, ...Berry C, Mills N. *Circulation*. 2019 Nov 5;140(19):1557-1568). We have categorised the patients as Low Risk (<5 ng/L), Intermediate or High Risk (≥ 5 ng/L to the sex specific upper reference limit for troponin I), Myocardial Injury ($>$ sex-specific URL for troponin I). The sex-specific diagnostic threshold for troponin I concentration $>$ 99th percentile is 16 ng/L for women and 34 ng/L for men.

- Of the patients with a blood tests for heart injury available from the initial hospital visit, 136 (48.6%) were low risk, 64 (22.9%) were intermediate risk, 43 (15.4%) were higher risk (myocardial injury) and 37 (13.2%) had missing data.
- Heart risk factors were very common: half were obese, half had high blood pressure and half had pre-diabetes or diabetes.
- 1 in 8 patients had a diagnosis of heart injury based on the troponin result and clinical history.
- The blood troponin test of heart injury differentiated patients according to their initial severity of illness e.g., need for respiratory support, wellbeing (quality of life) and exercise capacity one month after discharge.
- Patient reported outcome measures (PROMS) included the Brief Illness Perception Score (BIPS), the PHQ-4 Anxiety and Depression score, the International Physical Activity Questionnaire (IPAQ), and the Duke Activity Index Score (DASI). The questionnaires were completed at Visit 1 and Visit 2. Health status, as reflected by the EQ5D Health Utility score (UK population norms ~0.78 men, 0.81 women, age 55-64 years, University of York) and aerobic exercise capacity are moderately depressed in-hospital and 28 days after discharge.
- Aerobic exercise capacity was markedly impaired initially and remained markedly reduced one month after discharge from hospital

- A diagnosis of heart inflammation (myocarditis) associated with lower health-related quality of life, and poorer physical and mental wellbeing and reduced aerobic exercise capacity one month after hospital discharge.

WHAT IMPACT COULD THE FINDINGS HAVE?

- **Patients** - Our results indicate that in patients who have received hospital care for COVID-19, heart injury is relatively common, affecting 1 in 8 patients. We have found associations with heart injury and patient well being; patients with heart injury are sicker, including in the post-COVID-19 phase after discharge. Our findings are relevant to post-COVID-19 syndromes (long COVID). The findings support the case for vaccination to prevent COVID-19.
- **Policy** – Our results highlight that a minority of hospitalised patients are experiencing clinically significant, persisting, health problems post-COVID and the majority of patients have a more modest impairments in exercise capacity and wellbeing, if any. A blood test for heart injury (troponin) appears to be a useful test for risk stratification. Heart imaging is not routinely indicated unless the blood troponin level is increased
- **Practice** – Our results support the case for targeted interventions to the subgroup of patients with significant persisting illness; they have an unmet therapeutic need and clinical trials of novel or repurposed therapy are urgently needed. Considering the majority of patients, more widely generalisable, community-based interventions may be helpful to improve exercise capacity and psychological health. We are currently running the CISCO-21 study of resistance exercise as a novel form of rehabilitation to prevent and treat ‘long COVID’. Public registration: <https://clinicaltrials.gov/ct2/show/NCT04900961>
- **Acknowledgement**
We are very grateful to the staff, patients and carers who supported this research project. We thank the CSO for funding this research.

HOW WILL THE OUTCOMES BE DISSEMINATED?

We have published the study design in a leading science journal, Cardiovascular Research.

We have shared information about our study through the Glasgow Science Festival.

<http://www.glasgowsciencefestival.org.uk/>

Our University website

<https://www.gla.ac.uk/researchinstitutes/icams/bhfcoeglasgow/themesprojectsandoutputs/covid19/cardiovascularresearch/>

The British Heart Foundation

<https://www.bhf.org.uk/what-we-do/news-from-the-bhf/news-archive/2020/may/glasgow-scientists-fast-track-coronavirus-research>

and in future scientific publications

in the BBC News (Reporting Scotland)

CONCLUSION

In patients who have been treated in hospital for COVID-19, 1 in 8 developed heart injury. This was associated with persisting breathlessness and exercise impairment one month later. Our ongoing research will clarify whether reductions in blood flow in the heart might contribute to exercise limitation post-COVID-19.