Stress testing and myocardial perfusion imaging for patients after recovery from severe COVID-19 infection requiring hospitalization: A single-center experience

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Background. As the coronavirus pandemic progresses, patients that have recovered from COVID-19-related hospitalization require resumption of care for other medical issues. Thus far, the literature has not detailed the experience of stress testing in this patient population.

Methods. We retrospectively reviewed patients that recovered from COVID-19-related hospitalizations and underwent SPECT MPI studies at the University of Alabama at Birmingham Medical Center.

Results. 15 patients (median age 60 years, 67% male) were identified with COVID-19-related hospitalization and then underwent SPECT MPI imaging after recovery. During COVID-19-related hospitalization (median length of stay 8 days), patients received various COVID-19 therapies; 3 required mechanical ventilation. Stress tests (4 Exercise, 11 Pharmacologic) were performed 65 days (interquartile range 31-94 days) after the diagnosis of COVID-19. None of the patients experienced serious adverse events during or after stress testing. One patient required regadenoson reversal using aminophylline due to chest pain.

Conclusion. Over time, more patients that recover from COVID-19 infection will require MPI testing for myocardial ischemia evaluation. Our study provides some information regarding performing stress testing in patients who have recently recovered from COVID-19 infections requiring hospitalization. Further studies are recommended to establish formal protocols for testing in this cohort. (J Nucl Cardiol 2021;28:2167–73.)

Key Words: CAD • SPECT • vasodilators • exercise testing

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INTRODUCTION

During the peak of the pandemic, in an attempt to preserve personal protective equipment while protecting patients and healthcare workers, there was a marked reduction in cardiovascular imaging studies and procedures including stress tests using single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI). The American Society of Nuclear Cardiology (ASNC) provided guidance on how best to navigate the initial phase of the pandemic when non-emergent evaluations were postponed and thereafter when nuclear cardiology laboratories began to resume testing.6,7 Now, as the pandemic progresses, providers are encountering patients that have recovered from COVID-19 infections and require MPI for multiple indications. Since recovery from COVID-19 is variable with many patients having persistent shortness of breath, reduced quality of life and fatigue for weeks, perceived inability to tolerate MPI can present a dilemma to providers.8 In this manuscript, we report on the initial data from a single institution regarding our experience in performing MPI in patients that recovered from severe COVID-19-related hospitalizations.

METHODS

We retrospectively identified patients at the University of Alabama at Birmingham who underwent stress MPI for all indications after recovering from COVID-19-related hospitalization from March to October 2020. Patient demographics, past medical history, indication for and findings on MPI were obtained from medical records.

Standard ASNC protocols were used for MPI testing.9 Performance and interpretation of MPI at our institution has been described previously.10-14 A stress-first protocol was used. Patients were provided a mask to wear during testing. Although we purposefully decreased the performance of exercise stress tests during the pandemic, when personal protective equipment (PPE) supplies were available, our institution offered exercise MPI in select patients that tested negative for COVID-19 using polymerase chain reaction within 72 hours prior to undergoing MPI while quarantining. Staff in the stress room were fitted with proper PPE including N95 masks, gowns, gloves, hair caps, and face shields.

We observed for the occurrence of serious complications during or following stress testing and for symptoms reported during the test. As summary statistics, the median [interquartile range] of continuous data and the frequency (percentage) of categorical data are shown.

RESULTS

During the study period, 15 patients underwent stress testing with MPI at our institution after recovering from COVID-19-related hospitalization. Summary statistics are shown in Table 1 and data for the individual patients are shown in Appendix 1A-B. The median age of the cohort was 60 years [51-68] and more than half of the patients were Black. There was a high prevalence of risk factors and comorbidities, but none of the patients had a prior history of myocardial infarction.

The vast majority of COVID hospitalizations (median length of stay 8 days) were related to respiratory distress or failure. Almost half of the patients required intensive-care-unit-level care during their hospitalization. Of the three patients that required mechanical ventilation, this was maintained for 16, 31, and 33 days, respectively. Patients received varied therapies for COVID-19 infection ranging from supportive care to dexamethasone/remdesivir as well as investigational therapies as part of clinical trials.

The majority of the stress tests were completed in the outpatient setting and were performed for evaluation of chest pain or shortness of breath (Table 1). The median duration between COVID-19 diagnosis and MPI was 65 days (earliest at 22 days). Two patients had MPI prior to discharge from their COVID-related hospitalization. Most patients (80%) had a negative COVID-19 test prior to undergoing stress testing with most of these occurring within 72 hours of MPI. Most of the studies were performed using regadenoson rather than exercise. All the exercise studies were terminated due to fatigue after achieving on average 95% of maximal age-predicted heart rate. The majority of the patients had normal perfusion with one (7%) demonstrating scar in the distribution of the left anterior descending artery. The average LVEF was 55%.

None of the patients had serious adverse events after stress testing including no death, cardiac or respiratory arrest, myocardial infarction, stroke, hospitalization, significant arrhythmias (persistent or hemodynamically significant supraventricular or ventricular tachycardia, ventricular fibrillation, high-grade atrioventricular block, or asystole), seizures, or severe bronchospasm. Of the 11 patients who underwent pharmacologic stress, one patient reported chest pain after regadenoson administration and more than half had dyspnea, but these symptoms were not severe. The patient that experienced chest pain received aminophylline, but this was administered more than 2 minutes...
after tracer injection allowing for adequate imaging. Of the patients that underwent exercise, 75% reported non-limiting shortness of breath and 25% mild chest pain.

**DISCUSSION**

This is the first report in the literature describing the experience of performing stress testing and MPI in patients who were previously hospitalized with severe COVID-19. Laboratories, including our own, have started to encounter patients who have recovered from COVID-19 and are presenting for stress testing due to various indications. In this manuscript, we report on 15 patients who recovered from severe COVID infections that required hospitalization and thereafter underwent stress testing with MPI. Pharmacologic studies were preferred over exercise to help control the spread of the pandemic, but by incorporating safety protocols, we were able to perform exercise stress testing on some patients. We encountered no serious adverse effects in any of the patients regardless of stress modality, and none required transfer to an emergency department or admission to the hospital. Hopefully, our experience will serve as a template for other laboratories who are faced with increased demand to perform MPI testing on patients who have recovered from COVID-19 and require evaluation for ischemic heart disease.

**NEW KNOWLEDGE GAINED**

As we progress through the pandemic, more patients that have recovered from COVID-19 will be referred for MPI. We describe our experience in performing stress testing with exercise and regadenoson in patients who have recently recovered from severe COVID-19-related hospitalizations. Further data are needed in this regard to reassure referring providers regarding recommending stress testing with MPI in these patients. A multi-center registry guided by ASNC will provide useful information in this regard.

**APPENDIX 1A**

| Demographics                                      |  
|--------------------------------------------------|---
| Age                                              | 60 years [51-68]  
| Male gender                                      | 10 (66.7%)  
| Race                                             |  
| Caucasian                                        | 5 (33.3%)  
| Black                                            | 8 (53.3%)  
| Other                                            | 2 (13.3%)  
| Diabetes                                         | 7 (46.7%)  
| Hypertension                                     | 11 (73.3%)  
| Dyslipidemia                                     | 7 (46.7%)  
| ESRD                                             | 3 (20%)  
| Heart failure                                    | 1 (6.7%)  
| Myocardial infarction                            | 0  
| Coronary revascularization                       |  
| CABG                                             | 0  
| PCI                                              | 3 (20%)  
| Current tobacco use                              | 2 (13.3%)  
| SPECT MPI characteristics                        |  
| Outpatient                                       | 10 (67%)  
| Days between first positive test and MPI study   | 65 days [31-94]  
| Tested within 72 h before MPI                    | 9 (60%)  
| Type of study                                    |  
| Exercise                                         | 4 (27%)  
| Duration                                         | 8.3 minutes [6.10.2]  
| MET                                              | 10.7 METS [8.4-11.7]  
| Reported dyspnea                                 | 3 (75%)  
| Regadenoson                                       | 11 (73%)  
| Reported dyspnea                                 | 7 (63.6%)  
| Aminophylline administered                       | 1  
| Indication for study                             |  
| Chest pain                                       | 7 (46.7%)  
| Shortness of breath                              | 3 (20%)  
| Heart failure                                    | 2 (13.3%)  
| Pre-operative evaluation                         | 2 (13.3%)  
| Ventricular arrhythmia                           | 1 (6.7%)  

**Table 1. Baseline demographics, MPI study qualitative data**
| Patient | Demographics | Age (years) | Gender | Race | Hx of PC I= History of percutaneous coronary intervention |
|---------|--------------|-------------|--------|------|----------------------------------------------------------|
| 1       | 67           | F           | B      | W    | Heart failure with reduced ejection fraction            |
| 2       | 38           | M           | B      | B    | HTN, HLD, ESRD                                          |
| 3       | 71           | M           | B      | B    | DM, HTN, HLD                                           |
| 4       | 73           | F           | B      | B    | HTN, HLD, Hx of PCI                                     |
| 5       | 60           | M           | O      | O    | None documented                                         |
| 6       | 63           | M           | W      | W    | None documented                                         |
| 7       | 57           | M           | W      | W    | DM, HTN, HLD, CKD                                      |
| 8       | 65           | M           | B      | B    | DM, HTN, HLD, ESRD                                     |
| 9       | 68           | M           | W      | W    | HTN                                                     |
| 10      | 52           | M           | O      | O    | DM, HTN, HLD, ESRD, Hx of PCI                           |
| 11      | 77           | F           | B      | B    | DM, HTN, HLD, CKD, Hx of PCI                            |
| 12      | 48           | M           | B      | B    | DM, HTN                                                 |
| 13      | 51           | M           | W      | W    | HTN                                                     |
| 14      | 58           | F           | W      | W    | DM, HTN, CKD                                            |
| 15      | 51           | F           | B      | B    | None documented                                         |

| Patient | Current smoker | Hospitalization outcomes | Length of stay (days) | ICU level care required | Intubation required (days) |
|---------|----------------|--------------------------|-----------------------|-------------------------|----------------------------|
| 1       | Y              |                          | 26                    | Y                       | N                          |
| 2       | N              |                          | 8                     | N                       | N                          |
| 3       | N              |                          | 33                    | Y                       | Y (33)                     |
| 4       | N              |                          | 2                     | N                       | N                          |
| 5       | N              |                          | 11                    | N                       | N                          |
| 6       | N              |                          | 6                     | N                       | N                          |
| 7       | N              |                          | 6                     | N                       | N                          |
| 8       | N              |                          | 54                    | Y                       | Y (31)                     |
| 9       | N              |                          | 25                    | Y                       | Y (16)                     |
| 10      | N              |                          | 8                     | Y                       | N                          |
| 11      | Y              |                          | 4                     | N                       | N                          |
| 12      | N              |                          | 15                    | Y                       | N                          |
| 13      | N              |                          | 11                    | Y                       | N                          |
| 14      | N              |                          | 2                     | N                       | N                          |
| 15      | N              |                          | 6                     | N                       | N                          |
| Patient | COVID treatment therapies delivered | MPI study | Inpatient (I) vs outpatient (O) | Indication for study | Exercise (E) vs pharmacologic (P) (regadenoson) |
|---------|------------------------------------|-----------|---------------------------------|----------------------|-----------------------------------------------|
| 1       | 10 days dexamethasone + 5 days remdesivir | I         | I                               | Heart failure evaluation | P                                             |
| 2       | Supportive care                     | O         | O                               | Pre-operative evaluation for kidney transplant | P                                             |
| 3       | 10 days dexamethasone               | O         | O                               | Non-sustained ventricular tachycardia | P                                             |
| 4       | Supportive care                     | O         | O                               | Shortness of breath | E                                             |
| 5       | Enrolled in blinded remdesivir trial| O         | O                               | Chest pain | E                                             |
| 6       | 10 days dexamethasone + 5 days remdesivir | I         | I                               | Chest pain | E                                             |
| 7       | 5 days dexamethasone + enrolled in canakinumab trial | O         | O                               | Chest pain | E                                             |
| 8       | 1 day remdesivir, 1 unit of convalescent plasma | O         | O                               | Shortness of breath | P                                             |
| 9       | 10 days dexamethasone + 10 days remdesivir | O         | O                               | Pre-operative evaluation for kidney transplant | P                                             |
| 10      | Supportive care                     | O         | I                               | Heart failure evaluation | P                                             |
| 11      | Supportive care                     | I         | I                               | Chest pain | P                                             |
| 12      | 5 days dexamethasone + 5 days remdesivir | I         | I                               | Shortness of breath | P                                             |
| 13      | 10 days dexamethasone + 5 days remdesivir | O         | O                               | Chest pain | P                                             |
| 14      | Supportive care                     | O         | O                               | Chest pain | P                                             |
| 15      | Supportive care                     | I         | I                               | Chest pain | P                                             |

| Patient | Symptoms during MPI study | Other notes | Days between first positive COVID-19 test and MPI study | Days between COVID-related hospitalization discharge and MPI study |
|---------|---------------------------|-------------|-------------------------------------------------------|---------------------------------------------------------|
| 1       | Dyspnea, abdominal cramping |             | 24                                                    | n/a                                                     |
| 2       | Dyspnea                   |             | 171                                                   | 164                                                     |
| 3       | None                      |             | 59                                                    | 24                                                      |
| 4       | Fatigue                   |             | 94                                                    | 93                                                      |
| 5       | Dyspnea, fatigue          |             | 191                                                   | 188                                                     |
| 6       | Fatigue, shortness of breath, chest pain | | 34                                                    | 25                                                      |
| 7       | Dyspnea, fatigue          |             | 65                                                    | 60                                                      |
| 8       | None                      |             | 96                                                    | 70                                                      |
| 9       | None                      |             | 79                                                    | 55                                                      |
| 10      | Dyspnea                   |             | 86                                                    | 78                                                      |
| 11      | Dyspnea, headache         |             | 62                                                    | 58                                                      |
| 12      | Dyspnea                   |             | 22                                                    | n/a                                                     |
| 13      | Dyspnea                   |             | 88                                                    | 74                                                      |
| 14      | Chest pain                | Aminophylline administered for chest pain | 31                                                    | 30                                                      |
| 15      | Palpitations              |             | 22                                                    | 17                                                      |
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