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# Initial Findings From the North American COVID-19 Myocardial Infarction Registry

Santiago Garcia, MD,<sup>a</sup> Payam Dehghani, MD,<sup>b</sup> Cindy Grines, MD,<sup>c,d</sup> Laura Davidson, MD,<sup>e</sup> Keshav R. Nayak, MD,<sup>f</sup> Jacqueline Saw, MD,<sup>g</sup> Ron Waksman, MD,<sup>h</sup> John Blair, MD,<sup>i</sup> Bagai Akshay, MD,<sup>j</sup> Ross Garberich, MS, MBA,<sup>a</sup> Christian Schmidt, MS,<sup>a</sup> Hung Q. Ly, MD, SM,<sup>k</sup> Scott Sharkey, MD,<sup>a</sup> Nestor Mercado, MD,<sup>1</sup> Carlos E. Alfonso, MD,<sup>m</sup> Naoki Misumida, MD,<sup>n</sup> Deepak Acharya, MD,<sup>o</sup> Mina Madan, MD,<sup>p</sup> Abdul Moiz Hafiz, MD,<sup>q</sup> Nosheen Javed, MD,<sup>r</sup> Jay Shavadia, MD,<sup>s</sup> Jay Stone, MD,<sup>t</sup> M. Chadi Alraies, MD,<sup>u</sup> Wah Htun, MD,<sup>V</sup> William Downey, MD,<sup>w</sup> Brian A. Bergmark, MD,<sup>×</sup> Jospeh Ebinger, MD,<sup>y</sup> Tareq Alyousef, MD,<sup>z</sup> Houman Khalili, MD,<sup>aa</sup> Chao-Wei Hwang, MD, PHD,<sup>bb,cc</sup> Joshua Purow, MD,<sup>dd</sup> Alexander Llanos, MD,<sup>dd</sup> Brent McGrath, MD,<sup>ee</sup> Mark Tannenbaum, MD,<sup>ff</sup> Jon Resar, MD,<sup>gg</sup> Rodrigo Bagur, MD,<sup>hh</sup> Pedro Cox-Alomar, MD,<sup>ii</sup> Ada C. Stefanescu Schmidt, MD, MSc,<sup>jj</sup> Lindsey A. Cilia, MD,<sup>jj</sup> Farouc A. Jaffer, MD, PHD,<sup>jj</sup> Michael Gharacholou, MD,<sup>kk</sup> Michael Salinger, MD,<sup>ll</sup> Brian Case, MD,<sup>h</sup> Ameer Kabour, MD,<sup>mm</sup> Xuming Dai, MD,<sup>nn</sup> Osama Elkhateeb, MD,<sup>oo</sup> Taisei Kobayashi, MD,<sup>pp</sup> Hahn-Ho Kim, MD,<sup>qq</sup> Mazen Roumia, MD,<sup>rr</sup> Frank V. Aguirre, MD,<sup>ss</sup> Jeffrey Rade, MD,<sup>tt</sup> Aun-Yeong Chong, MD,<sup>uu</sup> Hurst M. Hall, MD,<sup>vv</sup> Shy Amlani, MD,<sup>ww</sup> Alireza Bagherli, MD,<sup>xx</sup> Rajan A.G. Patel, MD,<sup>yy</sup> David A. Wood, MD,<sup>zz</sup> Frederick G. Welt, MD,<sup>aaa,bbb</sup> Jay Giri, MD, MPH,<sup>pp</sup> Ehtisham Mahmud, MD,<sup>ccc</sup> Timothy D. Henry, MD,<sup>ddd</sup> on behalf of the Society for Cardiac Angiography and Interventions, the Canadian Association of Interventional Cardiology, and the American College of Cardiology Interventional Council

#### ABSTRACT

**BACKGROUND** The coronavirus disease 2019 (COVID-19) pandemic has impacted many aspects of ST-segment elevation myocardial infarction (STEMI) care, including timely access to primary percutaneous coronary intervention (PPCI).

**OBJECTIVES** The goal of the NACMI (North American COVID-19 and STEMI) registry is to describe demographic characteristics, management strategies, and outcomes of COVID-19 patients with STEMI.

**METHODS** A prospective, ongoing observational registry was created under the guidance of 3 cardiology societies. STEMI patients with confirmed COVID+ (group 1) or suspected (person under investigation [PUI]) (group 2) COVID-19 infection were included. A group of age- and sex-matched STEMI patients (matched to COVID+ patients in a 2:1 ratio) treated in the pre-COVID era (2015 to 2019) serves as the control group for comparison of treatment strategies and outcomes (group 3). The primary outcome was a composite of in-hospital death, stroke, recurrent myocardial infarction, or repeat unplanned revascularization.

**RESULTS** As of December 6, 2020, 1,185 patients were included in the NACMI registry (230 COVID+ patients, 495 PUIs, and 460 control patients). COVID+ patients were more likely to have minority ethnicity (Hispanic 23%, Black 24%) and had a higher prevalence of diabetes mellitus (46%) (all p < 0.001 relative to PUIs). COVID+ patients were more likely to present with cardiogenic shock (18%) but were less likely to receive invasive angiography (78%) (all p < 0.001 relative to control patients). Among COVID+ patients who received angiography, 71% received PPCI and 20% received medical therapy (both p < 0.001 relative to control patients). The primary outcome occurred in 36% of COVID+ patients, 13% of PUIs, and 5% of control patients (p < 0.001 relative to control patients).

**CONCLUSIONS** COVID+ patients with STEMI represent a high-risk group of patients with unique demographic and clinical characteristics. PPCI is feasible and remains the predominant reperfusion strategy, supporting current recommendations. (J Am Coll Cardiol 2021;77:1994-2003) © 2021 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

Dr. Valentin Fuster on

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atients with cardiovascular disease are more susceptible to severe forms of coronavirus disease 2019 (COVID-19) infection (1,2). Myocardial injury, detected by biomarkers of cardiac damage or cardiac magnetic resonance, is highly prevalent (20% to 30%) among hospitalized patients with COVID-19 infection (3,4). Myocardial injury may present with electrocardiographic features of STsegment elevation myocardial infarction (STEMI) (5). The management of these patients is controversial, with some advocating a shift to pharmacological reperfusion to mitigate delays in reperfusion and to protect essential health care workers and resources (6). However, this strategy has been associated with delays in reperfusion, increased mortality, and risk of heart failure (7). Furthermore, these patients more frequently have no culprit lesion on angiography and therefore are not expected to benefit from pharmacological reperfusion while being exposed to potentially harmful side effects associated with thrombolysis. The prognosis of STEMI patients with COVID-19 infection

is highly variable, with reported in-patient mortality ranging from 12% to 72% (7-12).

In order to fill these gaps in knowledge, the Society for Cardiovascular Angiography and Interventions (SCAI) and Canadian Association of Interventional Cardiologists in conjunction with the American College of Cardiology (ACC) Interventional Council collaborated to create the NACMI (North American COVID-19 Myocardial Infarction) registry. The goal of this registry is to provide real-time clinical, management, and outcome data on STEMI patients treated in the United States and Canada.

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### METHODS

**STUDY DESIGN.** The NACMI registry is a prospective, investigator-initiated, multicenter, observational registry of hospitalized STEMI patients with

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From the <sup>a</sup>Minneapolis Heart Institute Foundation. Minneapolis, Minnesota, USA; <sup>b</sup>Prairie Vascular Research, Regina, Saskatchewan, Canada; <sup>c</sup>Northside Cardiovascular Institute, Atlanta, Georgia, USA; <sup>d</sup>Society for Cardiovascular Angiography and Interventions, Washington, DC, USA; <sup>e</sup>Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA; <sup>f</sup>Department of Cardiology, Scripps Mercy Hospital, San Diego, California, USA; <sup>g</sup>Vancouver General Hospital, Vancouver, British Columbia, Canada; <sup>h</sup>MedStar Washington Hospital Center, Washington, DC, USA; <sup>i</sup>University of Chicago, Chicago, Illinois, USA; <sup>i</sup>St. Michael's Hospital, Toronto, Ontario, Canada: <sup>k</sup>University of Montreal, Montreal, Ouebec, Canada: <sup>l</sup>University of New Mexico, Albuquerque, New Mexico, USA; "University of Miami, Miami, Florida, USA; "University of Kentucky, Lexington, Kentucky, USA; "University of Arizona Sarver Heart Center, Tucson, Arizona, USA; <sup>p</sup>Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada; <sup>q</sup>Southern Illinois University School of Medicine, Springfield, Illinois, USA; 'Southcoast Health System, New Bedford, Massachusetts, USA; <sup>s</sup>Royal University Hospital, Saskatchewan Health, Saskatoon, Saskatchewan, Canada; <sup>t</sup>Community Medical Center, RWJ Barnabas Health, Toms River, New Jersey, USA; <sup>u</sup>DMC Harper University Hospital, Detroit, Michigan, USA; <sup>v</sup>Gundersen Health System, La Crosse, Wisconsin, USA; "Sanger Heart and Vascular Institute, Atrium Health, Charlotte, North Carolina, USA; "TIMI Study Group, Brigham and Women's Hospital, Boston, Massachusetts, USA; <sup>y</sup>Cedars Sinai Heart Institute, Los Angeles, California, USA; <sup>z</sup>Cook County Health and Hospitals System, Chicago, Illinois, USA; aaDelray Medical Center, Tenet Healthcare, Delray Beach, Florida, USA; <sup>bb</sup>Frederick Health Hospital, Frederick, Maryland, USA; <sup>cc</sup>Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; <sup>dd</sup>Holy Cross Hospital, Fort Lauderdale, Florida, USA; <sup>ee</sup>Horizon Health Network, Saint John, New Brunswick, Canada; <sup>ff</sup>Iowa Heart, West Des Moines, Iowa, USA; gerrederick Health Hospital, Frederick, Maryland, USA, and Johns Hopkins University School of Medicine, Baltimore, Maryland, USA; hhLondon Health Sciences Centre, Western University, London, Ontario, Canada; <sup>ii</sup>Louisiana State University, New Orleans, Louisiana, USA; <sup>ji</sup>Massachusetts General Hospital, Boston, Massachusetts, USA; <sup>kk</sup>Mayo Clinic Jacksonville, Jacksonville, Florida, USA; <sup>II</sup>Medical College of Wisconsin, Wauwatosa, Wisconsin, USA; <sup>mm</sup>Mercy St. Vincent's Medical Center, Toledo, Ohio, USA; nnNewYork-Presbyterian Queens, Flushing, New York, USA; ooNova Scotia Health, Halifax, Nova Scotia, Canada; ppUniversity of Pennsylvania, Philadelphia, Pennsylvania, USA; qqSt. Mary's General Hospital, Kitchener, Ontario, Canada; "St. Vincent Hospital, Worcester, Massachusetts, USA; ssPrairie Heart Institute at HSHS St. John's Hospital, Springfield, Illinois, USA; <sup>tt</sup>UMass Memorial Medical Center, Worcester, Massachusetts, USA; <sup>uu</sup>University of Ottawa Heart Institute, Ottawa, Ontario, Canada; "VUT Southwestern Medical Center, Dallas, Texas, USA; "WWilliam Osler Health System, Brampton, Ontario, Canada; xxWindsor Regional Hospital, Windsor, Ontario, Canada; yyOchsner Medical Center, New Orleans, Louisiana, USA; <sup>zz</sup>Canadian Association of Interventional Cardiology, Ottawa, Ontario, Canada; <sup>aaa</sup>American College of Cardiology Interventional Cardiology Section Leadership Council, Washington, DC, USA; bbb University of Utah Health Sciences, Salt Lake City, Utah, USA; cccCsulpizio Cardiovascular Center, University of California San Diego, La Jolla, California, USA; and the dddCarl and Edyth Lindner Center for Research and Education, the Christ Hospital, Cincinnati, Ohio, USA.

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#### ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

COVID-19 = coronavirus disease 2019

D2B = door to balloon

IQR = interquartile range

MI = myocardial infarction

**PPCI** = primary percutaneous coronary intervention

PUI = person under investigation

SCAI = Society for Cardiac Angiography and Interventions

**STEMI** = ST-segment elevation myocardial infarction

TABLE 1 Baseline Characteristics of the Study Cohort								
	COVID+ Patients (n = 230)	PUIs (n = 495)	p Value (COVID+ Patients vs. PUIs)	Control Patients (n = 460)	p Value (COVID+ Patients vs. Control Patients)			
Male	164 (71)	365 (74)	0.492	313 (68)	0.382			
Age group			0.226		0.906			
18-55 yrs	52 (23)	146 (29)		120 (26)				
56-65 yrs	73 (32)	149 (30)		137 (30)				
66-75 yrs	64 (28)	107 (22)		124 (27)				
76-85 yrs	33 (14)	72 (15)		64 (14)				
>85 yrs	8 (3)	21 (4)		15 (3)				
Race/ethnicity			<0.001	NA	NA			
White	89 (39)	355 (76)						
Black	54 (24)	49 (10)						
Asian	14 (6)	23 (5)						
Hispanic	53 (23)	26 (6)						
Indigenous	4 (2)	7 (2)						
Other/not reported	13 (6)	7 (2)						
Weight, kg	$\textbf{85.8} \pm \textbf{24.2}$	$\textbf{87.9} \pm \textbf{22.3}$	0.249	$\textbf{88.2} \pm \textbf{21.1}$	0.172			
BMI, kg/m <sup>2</sup>	$\textbf{29.3} \pm \textbf{7.6}$	$\textbf{29.9} \pm \textbf{7.5}$	0.388	$\textbf{29.5} \pm \textbf{6.4}$	0.699			
History of CAD	51 (24)	128 (27)	0.402	143 (31)	0.045			
Previous PCI	28 (13)	94 (20)	0.048	118 (26)	<0.001			
Previous MI	26 (13)	85 (18)	0.086	111 (24)	0.001			
Previous CABG	10 (5)	19 (4)	0.648	35 (8)	0.155			
Hypertension	166 (73)	349 (71)	0.783	317 (69)	0.162			
Dyslipidemia	101 (46)	277 (59)	0.002	277 (60)	0.001			
Diabetes	103 (46)	153 (32)	<0.001	130 (28)	<0.001			
Previous stroke/TIA	22 (10)	46 (10)	0.800	43 (9)	0.745			
Smoking history	94 (44)	291 (62)	<0.001	273 (59)	<0.001			
Current smoker	31 (15)	180 (38)	<0.001	173 (38)	<0.001			
History of CHF	33 (16)	47 (10)	0.026	41 (9)	0.009			
ASA	88 (38)	137 (28)	0.004	179 (39)	0.818			
Statin	89 (39)	172 (35)	0.303	159 (35)	0.305			

Values are n (%) or mean  $\pm$  SD.

ASA = acetylsalicylic acid; BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; CHF = congestive heart failure; COVID = coronavirus disease; MI = myocardial infarction; NA = not applicable; PCI = percutaneous coronary intervention; PUI = person under investigation; TIA = transient ischemic attack.

confirmed or suspected COVID-19 infection in North America. A detailed description of the study design has been previously published (13). At the time of data analysis (December 6, 2020), 64 sites were approved by local ethics committee (12 Canadian and 52 U.S. sites), of which 56 were actively enrolling patients. A complete list of active and enrolling sites with enrollment numbers is included in Supplemental Table 1.

COVID+ patients and persons under investigation (PUIs) were enrolled from January 1, 2020, to December 6, 2020. The primary endpoint was a composite of in-hospital death, stroke, recurrent myocardial infarction (MI), or unplanned revascularization. Nonfatal events were defined using National Cardiovascular Data Registry (NCDR Cath PCI Registry v4.4) definitions (Supplemental Appendix). **INCLUSION AND EXCLUSION CRITERIA.** Three groups of patients were included in the NACMI registry.

**Group 1 (COVID** + ). Group 1 comprised adult patients ( $\geq$ 18 years of age) with: 1) ST-segment elevation in at least 2 contiguous leads (or new onset left bundle branch block); 2) a clinical correlate of myocardial ischemia (e.g., chest pain, dyspnea, cardiac arrest, shock, mechanical ventilation); and 3) confirmed COVID+ by any commercially available test during, or 4 weeks before, the index STEMI hospitalization.

**Group 2 (suspected COVID + or PUI).** Group 2 comprised adult patients with STEMI who were suspected positive but subsequently tested negative for COVID-19 infection. The definition of PUI was left to the discretion of local hospitals but in general

TABLE 2 Clinical and Angiographic Characteristics at Presentation							
	COVID+ Patients (n = 230)	PUIs (n = 495)	p Value (COVID+ Patients vs. PUIs)	Control Patients (n = 460)	p Value (COVID+ Patients vs. Control Patients)		
COVID-19 symptoms				NA	NA		
Dyspnea	125 (54)	180 (36)	<0.001				
Chest pain	119 (52)	386 (78)	<0.001				
Syncope	6 (3)	29 (6)	0.057				
Abnormal chest x-ray findings				NA	NA		
Infiltrates	105 (46)	90 (18)	<0.001				
Pleural effusion	17 (7)	31 (6)	0.569				
Cardiomegaly	20 (9)	25 (5)	0.058				
Cardiac arrest pre-PCI	23 (11)	79 (16)	0.088	34 (7)	0.095		
Cardiogenic shock pre-PCI	36 (18)	67 (14)	0.203	44 (10)	0.002		
Presented in-hospital STEMI	13 (6)	9 (2)	0.004	24 (5)	0.735		
No angiography	50 (22)	19 (4)	<0.001	0 (0)	< 0.001		
Door-to-balloon time, min	79 (52-125)	77 (55-119)	0.989	66 (46-93)*	0.008		
Door-to-balloon time $\leq$ 90 min	58	63	0.422	73	0.006		
Ejection fraction, %	45 (35-55)	45 (35-52)	0.816	45 (35-55)	0.474		
Reperfusion strategies among patients undergoing angiography	n = 179	n = 463		n = 459	<0.001		
Thrombolytics	6 (3)	3 (1)	0.017	0 (0)			
Primary PCI	127 (71)	375 (81)	0.006	425 (93)			
Facilitated/rescue PCI	7 (4)	16 (3)	0.781	14 (3)			
Medical Tx	36 (20)	51 (11)	0.003	9 (2)			
CABG	3 (2)	18 (4)	0.158	11 (2)			
Culprit artery			0.013		< 0.001		
LMCA	1 (1)	4 (1)		5 (1)			
LAD/diagonal	52 (29)	164 (35)		173 (38)			
LCx/OM/PDA	12 (7)	37 (8)		62 (14)			
RCA/PDA	44 (25)	136 (29)		196 (43)			
Bypass graft	0 (0)	4 (1)		13 (3)			
Ramus	0 (0)	2 (0)		0 (0)			
Multiple	29 (16)	65 (14)		0 (0)			
No culprit	41 (23)	51 (11)		5 (1)			
TIMI flow grade post-PCI			0.534		0.010		
0/1	7 (6)	17 (5)		8 (2)			
2/3	106 (94)	343 (95)		436 (98)			
Number of stents	1 (1-2)	1 (1-2)	0.958	1 (1-2)	0.805		
Drug-eluting stent	113 (97)	346 (96)	0.820	398 (98)	0.359		

Values are n (%), median (interquartile range), or %, unless otherwise indicated. \*Door-to-balloon time after exclusion of transfer patients (>60 miles from primary PCI center). LAD = left anterior descending artery; LCx = left circumflex artery; LMCA = left main coronary artery; OM = obtuse marginal branch; PDA = posterior descending artery; RCA = right coronary artery; STEMI = ST-segment elevation myocardial infarction; TIMI = Thrombolysis In Myocardial Infarction; Tx = treatment; other abbreviations as in Table 1.

included a combination of possible COVID signs and symptoms (fever or respiratory symptoms such as cough, shortness of breath, sore throat), or exposure to a confirmed case or cluster of suspected COVID-19 cases.

**Group 3 (control group).** Group 3 comprised contemporary STEMI patients without COVID 19 infection treated in the Midwest STEMI Consortium 5 years before the onset of the pandemic (January 2015 to December 2019). The control patients were age and sex matched to the 230 STEMI patients with a

confirmed COVID-19 diagnosis (2:1 ratio of control patients to COVID+ patients).

The Midwest STEMI Consortium is a collaboration of 4 large regional STEMI programs: Iowa Heart Center in Des Moines, Iowa; Minneapolis Heart Institute Foundation in Minneapolis, Minnesota; Prairie Cardiovascular in Springfield, Illinois; and The Christ Hospital in Cincinnati, Ohio. Each has similar standardized STEMI protocols and together include >100 referral hospitals and several emergency medical services (14). A comprehensive database includes



traditional risk factors, detailed angiographic characteristics, time-to-reperfusion data, and short- and long-term clinical outcomes up to 5 years for MI, stroke, severe bleeding, and all-cause mortality and up to 10 years for mortality. For the comparison of reperfusion strategies, including door-to-balloon (D2B) time, and clinical outcomes, only patients presenting to a primary percutaneous coronary intervention (PPCI) hospital, or referring hospital within 60 miles of a PPCI hospital, were included in the metric, and other long-distance (>60 miles) transfer patients receiving protocol-driven pharmacoinvasive therapy were excluded. Otherwise, there were no exclusion criteria for any of the 3 groups.

To avoid selection biases related to the ethnic-race composition of the Midwest STEMI Consortium, group 3 (pre-COVID STEMI control patients) was used exclusively for comparisons of treatment strategies and clinical outcomes and group 2 (PUI), representative of same NACMI registry sites enrolling COVID+ patients, was used for ethnic-race comparisons.

**DATA COLLECTION.** We used standardized data collection forms, modeled after the ACC National Cardiovascular Data Registry definitions, and a secure Web-based application (REDCap [Research Electronic Data Capture]) for building and managing the dataset. The data coordinating center at the Minneapolis Heart Institute Foundation had full access to the dataset and performed the statistical analysis. The protocol was approved by each local Institutional Review Board. Informed consent was waived.

STATISTICS. Results are reported with regard to COVID-19 diagnosis among NACMI registry patients (COVID+ and PUI) and compared with age- and sexmatched control patients from the Midwest STEMI Consortium. Discrete variables are reported as count and percentages and are compared using a chi-square test or Fisher exact test, where appropriate. Continuous variables are reported as mean  $\pm$  SD if normally distributed, and as median (interquartile range [IQR]) if skewed. Differences in continuous variables are assessed using Student's t-test or Wilcoxon rank sum test depending on the distribution. Stata version 15.1 (StataCorp, College Station, Texas) and R version 3.6.0 (R Foundation for Statistical Computing, Vienna, Austria) in RStudio version 1.1.463 (RStudio, Boston, Massachusetts) were used in the analysis.

### RESULTS

A total of 230 COVID-confirmed cases (COVID+) and 495 COVID-suspected cases (PUI) were enrolled from April 28, 2020, and were compared with 460 age- and sex-matched control patients. Baseline characteristics are presented in **Table 1**. COVID+ patients were typically male (71%) and between 56 and 75 years of age. The majority of COVID+ patients were ethnic minorities (23% Hispanics, 24% Blacks, 6% Asians), with Whites representing only 39% of patients. Dyspnea was the most common presenting symptom (54%), and 46% of patients had infiltrates on chest x-ray film (**Table 2**). A significant proportion of COVID+ patients presented with high-risk pre-PCI conditions,

TABLE 3 In-Hospital Outcomes							
	COVID+ Patients (n = 230)	PUIs (n = 495)	p Value (COVID+ Patients vs. PUIs)	Control Patients (n = 460)	p Value (COVID+ Patients vs. Control Patients)		
Primary endpoint (composite of in-hospital death, stroke, recurrent MI, repeat unplanned revascularization)	80 (36)	64 (13)	<0.001	24 (5)	<0.001		
In-hospital death	73 (33)	54 (11)	<0.001	18 (4)	<0.001		
Stroke	5 (3)	7 (2)	0.271	2 (0)	0.017		
Recurrent myocardial infarction	3 (2)	5 (1)	0.690	2 (0)	0.119		
Unplanned revascularization	7 (4)	29 (7)	0.260	17 (4)	0.733		
Length of ICU stay, days	3 (1-10)	2 (1-4)	<0.001	NA	NA		
Total length of stay, days	6 (3-15)	3 (2-6)	<0.001	2 (2-4)	<0.001		
Values are n (%) or median (interquartile range). ICU = intensive care unit: other abbreviations as in <b>Table 1</b> .							

including cardiogenic shock (18%) and cardiac arrest (11%) (Table 2).

**REPERFUSION STRATEGIES, TREATMENT TIMES,** AND CULPRIT VESSEL. Of the 230 COVID+ patients, 179 (78%) underwent angiography and 127 (71% of patients undergoing angiography) received PPCI. Other reperfusion strategies included facilitated or rescue PCI (n = 7, 4%), thrombolytic therapy (n = 6, 3%), and coronary artery bypass grafting surgery (n = 3, 2%). Among the 179 patients who underwent angiography, 36 (20%) received medical management alone without reperfusion (Figure 1). In contrast, ageand sex-matched control patients were more likely to receive PPCI (93%; p < 0.001) and less likely to management receive medical alone (2%: p < 0.001) (Table 2).

Among patients who received PPCI with available treatment time data (COVID+, n = 106; PUIs, n = 347), we observed only slightly longer D2B times in COV-ID+ patients (median 79 min [IQR: 52 to 125 min]) and PUIs (median 77 min [IQR: 56 to 119 min]) relative to control patients (median 66 min [IQR: 46 to 93 min]) (p = 0.008 and p < 0.001, respectively). The distribution of culprit vessels is presented in **Table 2**. COVID+ patients were more likely to have no culprit vessel identified on angiography relative to control patients (COVID+ patients 23% vs. control patients 1%; p < 0.001) and PUIs (COVID+ patients 23 % vs. PUIs 11%; p < 0.001).

**IN-HOSPITAL OUTCOMES.** The primary endpoint (composite of in-hospital death, stroke, recurrent MI, or unplanned revascularization) occurred in 80 (36%) COVID+ patients, 64 (13%) PUIs, and 24 (5%) control patients (p value<sup>COVID+ patients vs. PUIs</sup> <0.001, p value<sup>COVID+ patients vs. control patients</sup> <0.001) (**Table 3**, **Figure 2**). This difference was driven primarily by increased in-hospital mortality (COVID+ patients 33%, PUIs 11%, and control patients 4%; p value<sup>COVID+</sup>

patients vs. PUIs <0.001, p value<sup>COVID+</sup> patients vs. control patients <0.001) and stroke (COVID+ patients 3%, PUIs 2%, and control patients 0%; p value<sup>COVID+</sup> patients vs. PUIs <0.27, p value<sup>COVID+</sup> patients vs. control patients = 0.03). Among COVID+ patients, mortality was higher for those who did not undergo coronary angiography (n = 24 of 50, 48%) versus those who did (n = 49 of 179, 28%) (p = 0.006). COVID+ patients also had longer length of stay and intensive care unit stay (Table 3).

#### DISCUSSION

In a collaborative effort between 3 North American cardiology societies representing 2 countries and 64 clinical sites, we were able to compare 230 STEMI patients confirmed to have COVID-19, with 495 patients suspected but ultimately confirmed not to have COVID-19, and 460 age- and sex-matched control patients treated in the pre-COVID era. There are several important findings of this prospective, multicenter NACMI registry (Central Illustration). First, STEMI in COVID+ patients disproportionately affects ethnic minorities (50%) with diabetes mellitus, which was present in 46% of COVID+ patients. Second, COVID+ patients with STEMI are more likely to present with atypical symptoms such as dyspnea (54%), pulmonary infiltrates on chest x-ray film (46%), and high-risk conditions such as cardiogenic shock (18%). Third, despite these high-risk features, COVID+ patients are less likely to undergo invasive angiography when compared with STEMI patients who are COVID- or PUIs. Fourth, PPCI is the dominant revascularization modality (71% of COVID+ patients referred for invasive angiography and 55% of overall COVID+ group) with reported D2B times slightly longer than non-COVID patients among those with available data. Medical therapy was recommended to 20% of COVID+ patients versus 11% of PUIs and 2% of



control patients. Finally, the combination of STEMI and COVID-19 infection confers a poor prognosis, with 1 in 3 patients succumbing to the disease, even among patients selected for invasive angiography (28% mortality).

As both Canada and the United States enter second and third waves of the COVID-19 pandemic (15), our study highlights important practical and actionable messages. First, ethnic minorities are at increased risk of this devastating complication, a finding of public health significance. Second, PPCI is feasible in COVID 19 patients with limited delays in D2B times among patients with available data. Our findings are consistent with current SCAI/ACC/American Heart Association recommendations to pursue PPCI in STEMI patients during the COVID-19 pandemic (16). Third, among COVID+ patients undergoing invasive angiography, 1 in 5 did not have a culprit vessel and therefore did not receive PCI. The non-PPCI group may represent different etiologies of ST-segment elevation including microemboli, myocarditis, takotsubo cardiomyopathy, and others (a list of available diagnoses from the NACMI registry can be found in the Supplemental Appendix). Importantly, the stroke rate was significantly higher in COVID+ patients than in age- and sex-matched control patients, which is consistent with a systemic procoagulant state, an issue of importance when balancing the risks of bleeding (i.e., hemorrhagic conversion) and benefits (1 in 5 with no culprit vessel) in patients exposed to thrombolytic therapy.

Previous studies have reported heterogeneous findings in the management and prognosis of STEMI in COVID-19 patients due to small samples, lack of standardized enrollment criteria, and a control group (7-12). The NACMI registry was prospectively designed with these considerations in mind as an investigator-initiated, collaborative effort encompassing 3 North American societies (SCAI, Canadian Association of Interventional Cardiologists, and the ACC Interventional Council) and 64 clinical sites to date. Because early in the COVID-19 pandemic we noted a significant decline in cardiac catheterization laboratory activations for STEMI in the United States (17), the NACMI registry was purposely designed to include all STEMI patients irrespective of revascularization modality and utilization of invasive angiography. Similarly, because of long turnaround times in diagnostic tests used to confirm COVID-19 infection, and local practice determining different triaging systems for STEMI patients suspected of COVID-19 infection (18), the NACMI registry was designed to



COVID-19 and STEMI; PUI = person under investigation.

include PUIs in order to examine treatment delays and its potential impact on outcomes relative to prepandemic period and to compare baseline characteristics with COVID+ patients. The PUI group more closely resembled age- and sex-matched control patients with regard to baseline characteristics (76% White), and utilization of angiography (96%) and PPCI (81%). However, clinical outcomes were significantly worse for PUIs relative to age- and sex-matched control patients (in-hospital mortality 11% vs. 4% for control patients; p < 0.01) a finding that requires further investigation. The higher prevalence of cardiac arrest pre-PCI (PUIs 16% vs. control patients 7%) may account for these differences in mortality, as many out-of-hospital cardiac arrests might have been labeled PUI during the pandemic.

**STUDY LIMITATIONS.** The NACMI registry is the largest prospective, multicentric, STEMI COVID registry to date. The current paper is the first description of short-term outcomes and current management strategies, but important subgroup analyses remain to be conducted. These include independent electrocardiographic and angiographic

core laboratory assessment as well prospective follow-up of discharged patients up to 1 year after STEMI. Previous studies have revealed high thrombus burden in patients with COVID-19 presenting with STEMI (10). A planned, independent angiographic core lab analysis will shed light on this important issue, which may have therapeutic implications. Another important limitation is the lack of pre-hospital data regarding total ischemic and transfer times for patients presenting to a non-PPCI hospital. Late STEMI presentations have been reported during the pandemic (19,20). In many patients, D2B time could not be accurately estimated because of atypical presentations (i.e., dyspnea instead of chest pain) that could not be timed to STEMI onset per se in the setting of COVID 19 infection. Finally, we cannot rule out delayed symptom-hospital presentation as a contributor to worse outcomes.

#### CONCLUSIONS

COVID+ patients with STEMI represent a high-risk group of patients with unique demographic and clinical characteristics. Timely PPCI is feasible and remains the predominant reperfusion strategy, supporting current recommendations.

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ADDRESS FOR CORRESPONDENCE: Dr. Santiago Garcia, Minneapolis Heart Institute Foundation, 920 East 28th Street, Suite 300, Minneapolis, Minnesota 55407, USA. E-mail: santiagogarcia@me.com. Twitter: @MHIF\_Heart, @jaygirimd, @HenrytTimothy, @SCAL Prez.

#### PERSPECTIVES

#### COMPETENCY IN PATIENT CARE AND

**PROCEDURAL SKILLS:** Patients with STEMI and concomitant COVID-19 infection are more likely to have diabetes mellitus and belong to an ethnic minority. PPCI is feasible for these patients, who are at high risk of stroke and in-hospital mortality.

**TRANSLATIONAL OUTLOOK:** Further studies are needed to understand the pathophysiologic mechanisms leading to STEMI, its predilection for ethnic minorities, and high mortality in patients with COVID-19.

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**KEY WORDS** COVID-19, outcomes, ST-segment myocardial infarction

**APPENDIX** For expanded Methods and Results sections as well as a supplemental table, please see the online version of this paper.