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International Impact of COVID-19 on the Diagnosis of Heart Disease

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ABSTRACT

BACKGROUND The coronavirus disease 2019 (COVID-19) pandemic has adversely affected diagnosis and treatment of noncommunicable diseases. Its effects on delivery of diagnostic care for cardiovascular disease, which remains the leading cause of death worldwide, have not been quantified.

OBJECTIVES The study sought to assess COVID-19's impact on global cardiovascular diagnostic procedural volumes and safety practices.

METHODS The International Atomic Energy Agency conducted a worldwide survey assessing alterations in cardiovascular procedure volumes and safety practices resulting from COVID-19. Noninvasive and invasive cardiac testing volumes were obtained from participating sites for March and April 2020 and compared with those from March 2019. Availability of personal protective equipment and pandemic-related testing practice changes were ascertained.

RESULTS Surveys were submitted from 909 inpatient and outpatient centers performing cardiac diagnostic procedures, in 108 countries. Procedure volumes decreased 42% from March 2019 to March 2020, and 64% from March 2019 to April 2020. Transthoracic echocardiography decreased by 59%, transesophageal echocardiography 76%, and stress tests 78%, which varied between stress modalities. Coronary angiography (invasive or computed tomography) decreased 55% ($p < 0.001$ for each procedure). In multivariable regression, significantly greater reduction in procedures occurred for centers in countries with lower gross domestic product. Location in a low-income and lower-middle-income country was associated with an additional 22% reduction in cardiac procedures and less availability of personal protective equipment and telehealth.

CONCLUSIONS COVID-19 was associated with a significant and abrupt reduction in cardiovascular diagnostic testing across the globe, especially affecting the world's economically challenged. Further study of cardiovascular outcomes and COVID-19-related changes in care delivery is warranted. (J Am Coll Cardiol 2021;77:173-85) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

COVID-19 = coronavirus disease 2019

IAEA = International Atomic Energy Agency

INCAPS = International Atomic Energy Agency Noninvasive Cardiology Protocols Study

LMIC = low- and middle-income country

PET = positron emission tomography

PPE = personal protective equipment

The coronavirus disease 2019 (COVID-19) pandemic has markedly disrupted the delivery of health care and the lives of patients globally. Although continuous communicable threats, particularly COVID-19, are a central challenge for contemporary medicine and public health, noncommunicable diseases remain an equal priority (1). Noncommunicable diseases negatively affect global health and economies, and thereby compromise social gains in life expectancy, quality of life, and productivity (2). Cardiovascular diseases are the leading cause of morbidity and mortality worldwide, in high-income countries and low- and middle-income countries (LMICs) alike, with approximately 18 million deaths annually (3,4); this exceeds the deaths associated with communicable diseases, including the half million COVID-19 deaths estimated as of the end of June 2020 (5). Patient and population outcomes related to cardiovascular conditions are linked to early and effective diagnosis and evidence-based treatments, thus underscoring the importance of diagnostic and therapeutic cardiovascular procedures in promoting cardiovascular health (1,6). Delay in the delivery of these essential services will affect health outcomes and potentially reverse the declines observed in cardiovascular event rates over the past several decades (7). However, to date, the magnitude of the worldwide impact of COVID-19 on cardiovascular procedural volumes as well as changes in testing patterns and modality utilization have not been quantified.

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The mission of the International Atomic Energy Agency (IAEA) Division of Human Health includes supporting member states as they confront the burden of cardiovascular diseases, cancer, malnutrition, and other health conditions through the use of appropriate prevention, diagnostic testing, and treatment. The impact of COVID-19 on the worldwide delivery of cardiovascular care is of particular importance to the IAEA and its goal of promoting equitable global cardiovascular care. Quantifying the early impact of COVID-19 on cardiovascular testing volumes and modality utilization across a large, diverse range of countries and world regions is also important for ongoing and future studies aiming to assess the impact of the pandemic on long-term cardiovascular disease-related outcomes and to define specific needs for recovery of effective cardiovascular care delivery. Such information can also inform strategic interventions targeted at planning for and responding to future outbreaks (8,9). Therefore, in an effort led by the IAEA Division of Human Health, we performed a large-scale global Web-based survey to assess changes in noninvasive and invasive diagnostic procedural volumes and in safety practices resulting from the COVID-19 pandemic.

METHODS

STUDY DESIGN. The IAEA Noninvasive Cardiology Protocols Study (INCAPS) Group has for the past decade conducted numerous studies addressing the use of best practices and worldwide practice variation in cardiovascular disease diagnosis. With the emergence of COVID-19, IAEA Nuclear Medicine and Diagnostic Imaging section leadership and the INCAPS group convened an INCAPS COVID executive committee to survey the impact of the pandemic on worldwide cardiovascular diagnostic care delivery. The steering committee, comprising experts in clinical cardiology and cardiac imaging from around the world, devised a survey questionnaire including for each site: 1) descriptors of participating health care facility and health care professional; 2) use of personal protective equipment (PPE) and strategic plans for reopening; and 3) changes in procedural volume for a range of cardiovascular diagnostic procedures. The latter included transthoracic echocardiography and transesophageal echocardiography, cardiac magnetic resonance (CMR), stress testing (stress electrocardiography, echocardiography, single-photon emission computed tomography, positron emission tomography [PET], and CMR), PET infection studies,

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Kim A. Eagle, MD, served as Guest Associate Editor for this paper. P.K. Shah, MD, served as Guest Editor-in-Chief for this paper.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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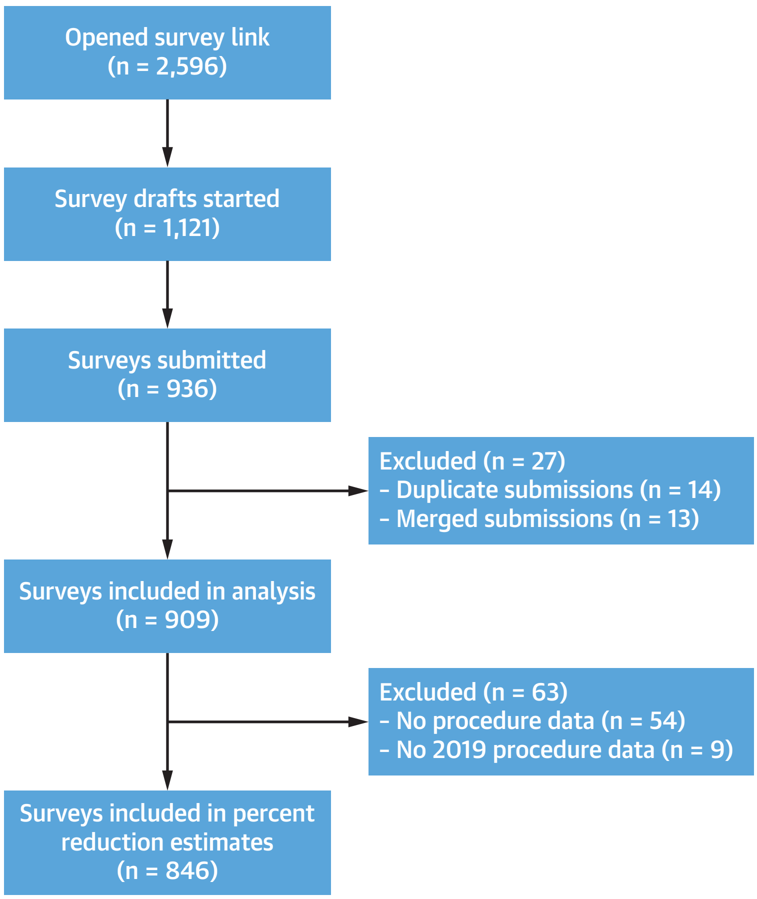
FIGURE 1 Flow Diagram Detailing Survey Completion



The 8-page online survey, including changes in practice performance and procedure numbers, was emailed to participants via various organizations and completed by June 10, 2020. A total of 909 participants from 108 countries were included in the final analysis.

coronary artery calcium scanning, coronary computed tomography angiography, and invasive coronary angiography. Data were obtained from each participating site for March and April of 2020 and estimates were compared with those from March of 2019, which served as a baseline. Additional country-specific data compiled within the IAEA on COVID-19 include the number of confirmed cases, deaths, and number of recovered cases. Data were aggregated on a country-wide and region-specific level. Data from a territory (e.g., Puerto Rico, Faroe Islands) were counted toward that of the country of jurisdiction (United States and Denmark, respectively). We used IAEA standard country coding for 8 world regions (10): Africa, Eastern Europe, Far East, Latin America, Middle East and South Asia, North America (i.e. Canada and United States), South East Asia and the Pacific, and Western Europe. Participating countries in each world region are specified in the Appendix. Country classification into 4 economic levels (low, lower middle, upper middle, and high) was performed in accordance with the system of the World Bank (11).

DATA COLLECTION. Efforts were undertaken to ensure extensive and diverse site inclusion worldwide, including both private and public health care organizations, and practices of different sizes. Outreach to encourage participation from sites performing cardiac imaging was undertaken through a variety of methods. These included emails from the IAEA, INCAPS COVID executive committee, and national coordinators to potential participants and contacts including those registered in IAEA-compiled databases of health care facilities (12) incorporating sites from the INCAPS 1 (13) and forthcoming INCAPS 2 studies and past participants in IAEA cardiac imaging research and educational projects, such as technical cooperation projects, regional training courses,

TABLE 1 Characteristics of Participating Centers

	Africa	Eastern Europe	Far East	Latin America	Middle East and South Asia	United States and Canada	Southeast Asia and Pacific	Western Europe	Total	p Value
Centers	42	62	99	201	60	172	81	192	909	
Countries	11	22	8	19	16	2	9	21	108	
Procedures										
March 2019	17,278	24,131	140,323	109,209	41,557	190,146	37,175	118,819	678,638	
March 2020	7,632	14,896	74,569	69,991	18,797	116,161	28,385	64,194	394,625	
April 2020	3,646	7,698	91,072	19,397	6,552	61,592	17,694	36,785	244,436	
Median procedures per center										
March 2019	68 (17–439)	144 (40–562)	606 (168–1,205)	148 (60–500)	216 (88–790)	640 (235–1,709)	127 (43–778)	308 (87–993)	270 (80–861)	<0.001
March 2020	42 (10–180)	56 (15–215)	394 (108–908)	87 (28–242)	121 (51–389)	323 (112–1,067)	100 (40–503)	152 (41–405)	144 (41–503)	<0.001
April 2020	12 (2–42)	14 (2–92)	358 (78–930)	26 (7–97)	44 (0–173)	172 (49–570)	69 (21–288)	68 (20–268)	64 (13–272)	<0.001
Type of center										
Hospital inpatient only	3 (7)	11 (18)	1 (1)	8 (4)	2 (3)	4 (2)	2 (2)	11 (6)	42 (5)	
Hospital inpatient/outpatient	32 (76)	46 (74)	96 (97)	118 (59)	54 (90)	117 (68)	61 (75)	173 (90)	697 (77)	
Hospital outpatient only	0 (0)	0 (0)	1 (1)	7 (3)	0 (0)	2 (1)	3 (4)	1 (0.5)	14 (2)	
Outpatient imaging center	4 (10)	4 (6)	0 (0)	53 (26)	1 (2)	5 (3)	11 (14)	4 (2)	82 (9)	
Outpatient physician practice	3 (7)	1 (2)	1 (1)	15 (7)	3 (5)	44 (26)	4 (5)	3 (2)	74 (8)	<0.001
Teaching institution	23 (55)	48 (77)	72 (73)	96 (48)	40 (67)	109 (63)	57 (70)	152 (79)	597 (66)	<0.001
Median hospital beds	282 (200–800)	500 (222–1,099)	845 (480–1,800)	200 (116–364)	500 (300–950)	517 (250–745)	619 (350–812)	700 (355–988)	517 (235–877)	<0.001
Economic level by center										
Low/middle	42 (100)	36 (58)	49 (49)	189 (94)	42 (68)	0 (0)	14 (17)	2 (1)	372 (41)	
Low	2 (5)	0 (0)	0 (0)	0 (0)	2 (3)	0 (0)	0 (0)	0 (0)	4 (0.4)	
Lower middle	18 (43)	5 (8)	19 (19)	5 (2)	28 (47)	0 (0)	11 (14)	0 (0)	86 (9)	
Upper middle	22 (52)	31 (50)	30 (30)	183 (91)	11 (18)	0 (0)	3 (4)	2 (1)	282 (31)	
Upper	0 (0)	26 (42)	50 (51)	13 (6)	19 (32)	172 (100)	67 (83)	190 (99)	537 (59)	<0.001

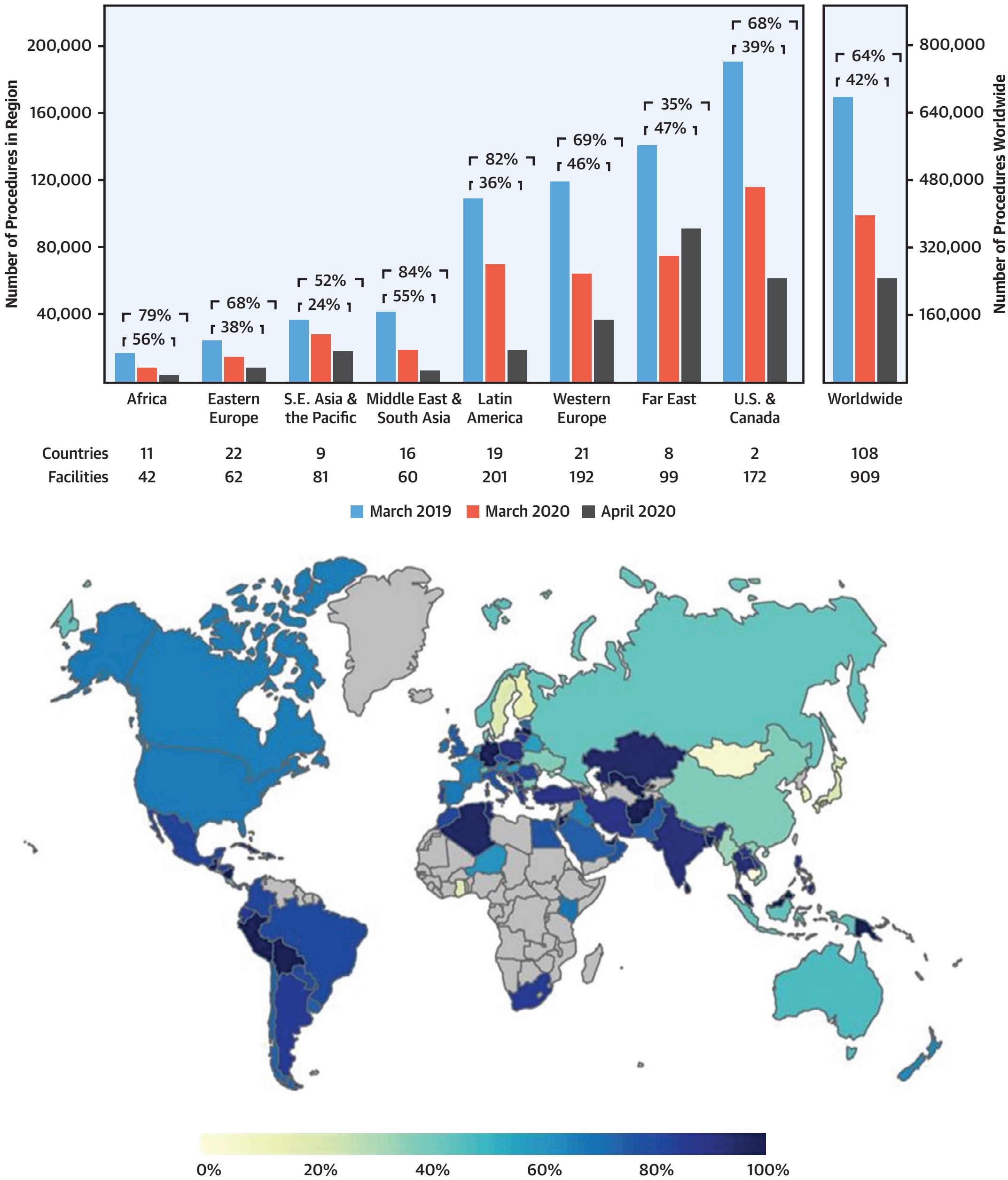
Values are n, median (interquartile range), or n (%). Procedure counts are for centers performing testing in March 2019. The p values are for Kruskal-Wallis tests comparing procedures and hospital beds per center between world regions, and for chi-square tests comparing types of center, teaching institution status, and economic levels between world regions.

and the triennial Integrated Medical Imaging in Cardiovascular Diseases meetings. Other outreach included emails from IAEA to cardiology and imaging societies, communication from professional societies to their memberships, and a marketing campaign on social media platforms (Twitter, LinkedIn, and Facebook) conducted by a dedicated Communications Committee experienced with cardiology and imaging social media. Based on the IAEA standardized methodology, a Web-based data entry system was devised to collect data on the impact around the world of the COVID-19 pandemic on cardiovascular testing practices. The IAEA employs a secure software platform, the International Research Integration System, for questionnaire data collection. In INCAPS COVID, no patient-specific or confidential data were collected, and all participation by study sites was voluntary; therefore, it was deemed that no external ethics committee review was required, and the study complies with the Declaration of Helsinki.

Throughout enrollment, the Data Coordination Committee reviewed entries on a daily basis and reached out to survey participants with questions regarding missing data, implausible-appearing data, and duplicate or inconsistent entries from the same institution. Participants were given an opportunity to clarify details and correct their response as needed. Only 1 entry from a given center was included in the final dataset. Final database cleaning was completed on July 1, 2020. Entries were largely excluded for reasons such as missing or incomplete responses to the questionnaire.

STATISTICAL ANALYSIS. Nonparametric statistics using the Kruskal-Wallis test with asymptotic 2-sided p values were calculated when comparing differences in test volume between 2019 and 2020 and differences in continuous variables between world regions, and generalized linear models were performed. Chi-square tests were performed to compare center characteristics between world regions. Linear regression models with stepwise selection related percent reduction in all procedures from March 2019 to April 2020 to facility characteristics. Statistical analysis was performed in R version 4.0.1 (R

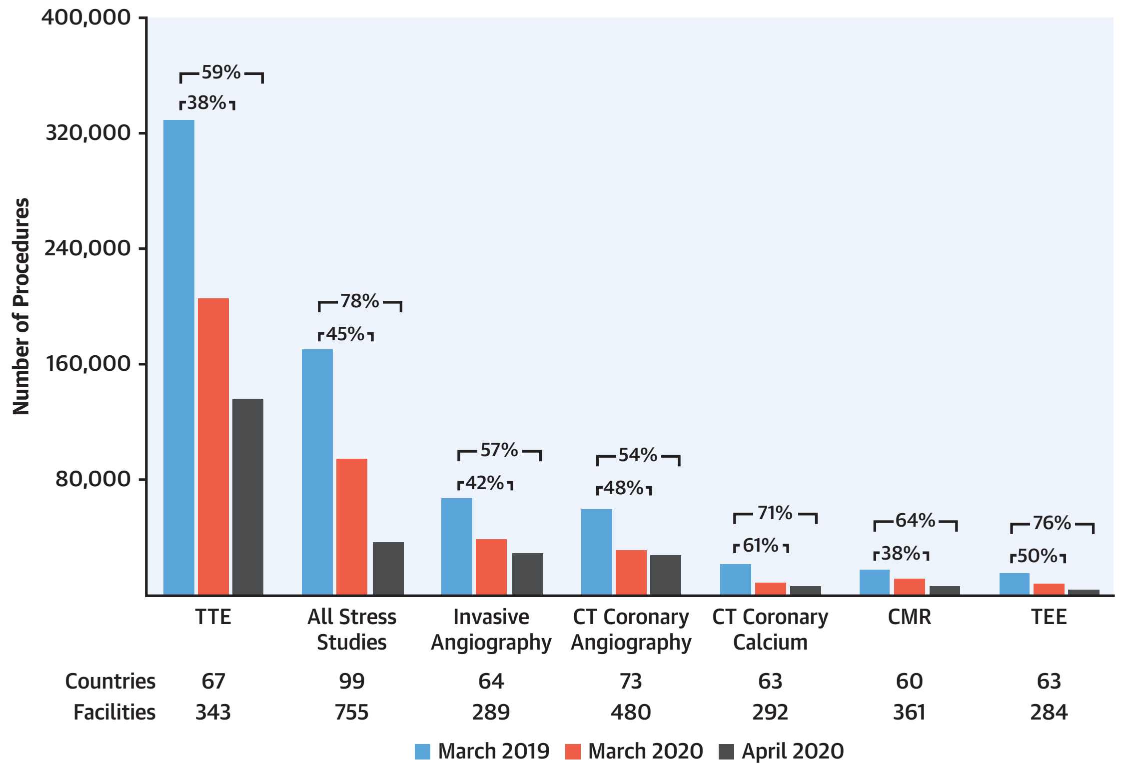
CENTRAL ILLUSTRATION **Reduction in Worldwide Cardiovascular Disease Diagnostic Testing Volume in the Beginning of the Coronavirus Disease 2019 Pandemic (March and April 2020)**



Einstein, A.J. et al. J Am Coll Cardiol. 2021;77(2):173–85.

(Top panel) Bar chart of cardiovascular disease test volumes by International Atomic Energy Agency world regions for 2019 and for 2 months in 2020. Note the different y-axis for world regions and worldwide. The percent reductions from 2019 are reported at the tops of the columns. **(Bottom panel)** World map demonstrating reductions in total cardiovascular procedural volume from March 2019 to April 2020 across the 108 participating countries. Countries or territories of a country shaded **gray** did not have data available. The procedures recorded included morphologic and other types of rest imaging (transthoracic echocardiography and transesophageal echocardiography, cardiac magnetic resonance, positron emission tomography for infective endocarditis), coronary imaging (coronary computed tomography angiography, coronary artery calcium, and invasive coronary angiography) and stress imaging (exercise electrocardiography, stress echocardiography, nuclear stress imaging [single-photon emission computed tomography and positron emission tomography], and stress cardiac magnetic resonance). S.E. = Southeast.

FIGURE 2 Worldwide Reduction in Individual Cardiac Procedure Types During the Beginning of the COVID-19 Pandemic



The bar graph demonstrates the reduction in the number of each procedure type for the entire world between March 2019, March 2020, and April 2020. All types of stress test modalities (exercise electrocardiography, stress echocardiography, nuclear stress imaging [single-photon emission computed tomography and positron emission tomography], and stress cardiac magnetic resonance) are grouped together. All modalities demonstrate a reduction in March 2020 and a further reduction in April 2020. CMR = cardiac magnetic resonance; COVID-19 = coronavirus disease 2019; CT = computed tomography; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

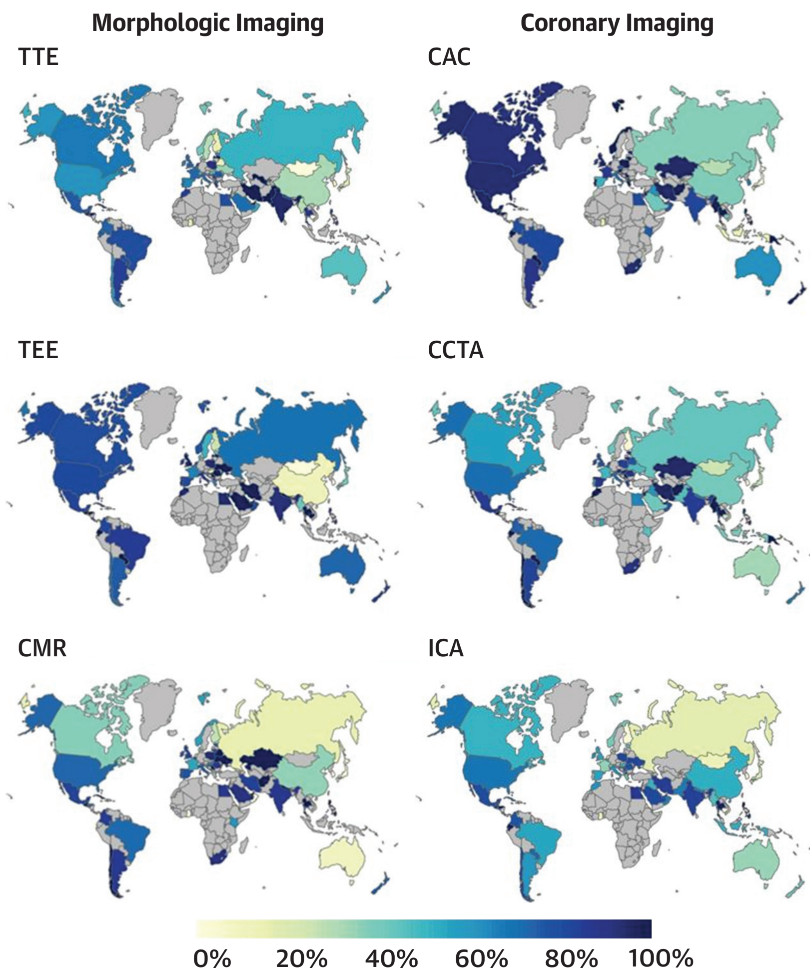
Foundation for Statistical Computing, Vienna, Austria), Stata version 16 (Stata Corporation, College Station, Texas), and Microsoft Excel 2016 (Microsoft, Redmond, Washington). Maps were created using rnaturalearth and tmap packages in R.

RESULTS

CENTERS. Data were obtained from 909 inpatient and outpatient centers in 108 countries, of which 846 centers in 106 countries provided data on procedure volumes. Figure 1 details the iterative exclusion criteria applied to select the final sample, and characteristics of these centers are summarized in Table 1. A total of 1.3 million cardiac diagnostic procedures were performed at participating sites during the 3 months considered. Countries contributing data had a combined population of 6.7 billion, and over 3.2 million cases of COVID-19, constituting 99% of the world's reported cases, as of the end of the study period.

PROCEDURE REDUCTION. Worldwide, cardiac diagnostic procedure volumes decreased by 42% from March 2019 to March 2020 and by 64% from March 2019 to April 2020. This varied markedly between world regions and countries (Central Illustration), with the greatest regional decreases in the Middle East and Latin America. In general, volumes decreased from March to April of 2020; only the Far East demonstrated recovery in April 2020, with further reductions seen in all other regions. Separate generalized linear models for world region and overall found significant declines in procedural volume ($p < 0.001$) using regression models weighted by 2019 procedural volume. The decrease in procedures also varied between specific procedure types (Figures 2 and 3). Transthoracic echocardiography decreased by

FIGURE 3 **Reduction in Procedures Around the World for Nonstress Imaging**

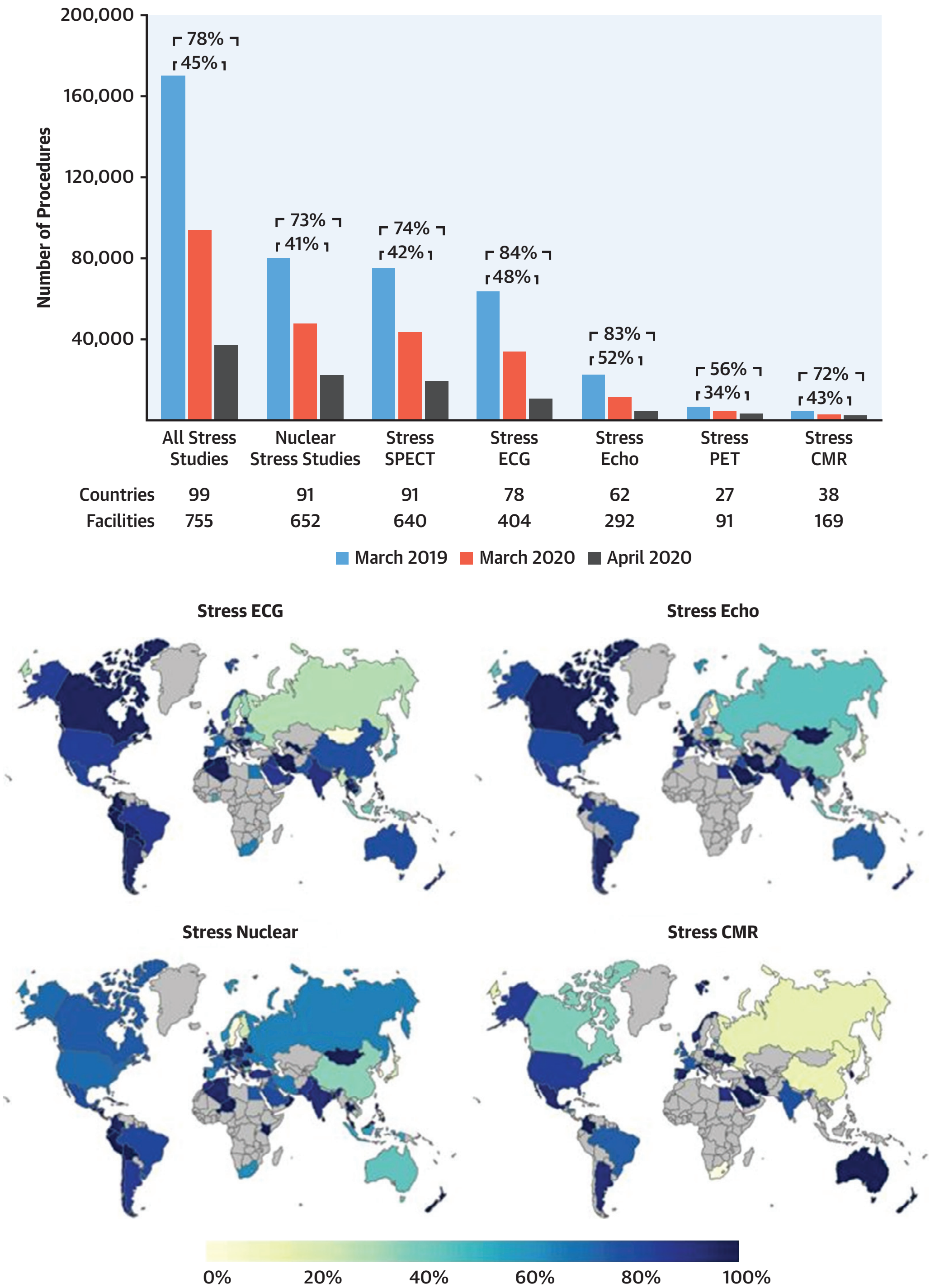


World maps are displayed to show reduction in nonstress imaging numbers (morphological and other indications on the **left**, coronary evaluation on the **right**) from March 2019 to April 2020. All modalities demonstrate significant reduction over this time period. Countries and territories of a country shaded **gray** did not have data available. CAC = coronary artery calcium score; CCTA = coronary computed tomography angiography; ICA = Invasive coronary angiography; other abbreviations as in Figure 2.

59%, transesophageal echocardiography by 76%, and stress tests by 78% overall, which was slightly more pronounced (Figure 4) for stress electrocardiography (84%) and echocardiography (83%) than for nuclear (73%) or CMR (72%) stress tests. Coronary angiography (invasive or computed tomography) decreased by 55%. These decreases were significant ($p < 0.001$) for each procedure. In the 845 facilities in our study reporting 2019 procedure volumes, an estimated 718,000 cardiac diagnostic procedures that would have been performed based on March 2019 procedure rates were not performed during these 2 months of the pandemic.

CENTER CAPACITY AND PRACTICE. Numerous changes in center capacity and practices were observed (Table 2). These were generally consistent worldwide, with modest differences between regions. Some outpatient activities were cancelled in most (83%) centers performing cardiac diagnostic testing, and all outpatient activities were cancelled at some point in nearly half (45%). Despite these cancellations, and additionally with most (73%) centers increasing time per study for cleaning and disinfection, extended hours (14%) and new weekend hours (10%) for cardiac testing during reopening were uncommon, suggesting challenges in catching up in

FIGURE 4 Worldwide Reduction in Stress Imaging Procedures



(Top panel) Bar graph demonstrating reduction in procedure numbers for all stress studies in 758 facilities in 99 countries, who performed at least 1 modality of stress imaging. Individual modalities are also displayed showing reduction in each in March 2020, compared with March 2019, and a further reduction to April 2020. **(Bottom panel)** The world maps further illustrate these reductions for individual countries for stress electrocardiography (ECG), echocardiography (Echo), nuclear (combined single-photon emission computed tomography [SPECT] and positron emission tomography [PET]) imaging, and cardiac magnetic resonance (CMR) imaging between March 2019 and April 2020. **Gray** shading indicates data not available from the country or territory.

TABLE 2 Changes in Center Capacity and Practice

	Africa	Eastern Europe	Far East	Latin America	Middle East and South Asia	United States and Canada	Southeast Asia and the Pacific	Western Europe	Worldwide
Change in capacity									
Some outpatient activities cancelled	28 (67)	53 (88)	74 (75)	167 (83)	46 (79)	155 (90)	66 (81)	163 (86)	752 (83)
All outpatient activities cancelled	22 (52)	27 (44)	38 (39)	89 (45)	32 (56)	86 (51)	26 (33)	85 (45)	405 (45)
Phased reopening after peak pandemic	17 (41)	32 (53)	60 (61)	66 (33)	32 (56)	118 (69)	43 (53)	114 (60)	482 (54)
Extended hours	2 (5)	12 (20)	18 (18)	18 (9)	9 (16)	21 (12)	5 (6)	38 (20)	123 (14)
New weekend hours	3 (7)	8 (13)	14 (14)	15 (8)	6 (10)	15 (9)	4 (5)	21 (11)	86 (10)
Use of telehealth for patient care	19 (45)	26 (43)	54 (55)	96 (48)	31 (53)	147 (86)	40 (49)	90 (48)	503 (56)
Increased time per study for cleaning/disinfection	25 (60)	42 (69)	54 (55)	171 (85)	39 (65)	135 (78)	48 (61)	143 (75)	657 (73)
Eliminate protocols requiring close contact	25 (60)	32 (52)	37 (37)	142 (72)	40 (67)	126 (74)	48 (60)	107 (56)	557 (62)
Change in practice									
Physical distancing	32 (78)	49 (79)	82 (83)	179 (90)	48 (83)	162 (95)	80 (99)	173 (92)	805 (89)
Separate spaces for patients with/without COVID	28 (70)	39 (64)	83 (84)	166 (83)	43 (74)	126 (76)	68 (84)	164 (87)	717 (80)
Reduced waiting room time	30 (73)	44 (72)	66 (67)	180 (90)	43 (74)	139 (82)	73 (90)	164 (86)	739 (82)
Limit visitors	36 (88)	53 (85)	89 (90)	187 (94)	49 (84)	162 (95)	77 (95)	181 (96)	834 (93)
Temperature checks	28 (68)	52 (84)	86 (87)	128 (64)	44 (76)	130 (76)	53 (65)	90 (47)	611 (68)
Symptom screening	24 (59)	48 (79)	88 (89)	150 (75)	40 (70)	160 (95)	73 (91)	124 (65)	707 (79)
COVID testing	7 (17)	6 (10)	29 (29)	17 (8)	9 (15)	43 (25)	7 (9)	19 (10)	137 (15)
Require masks	34 (81)	55 (89)	77 (78)	160 (80)	44 (73)	160 (93)	21 (26)	129 (68)	680 (75)

Values are n (%).
COVID = coronavirus disease.

cardiac diagnostic procedures postponed during the pandemic. Nevertheless, plans for additional extended and weekend hours were expressed by many centers (29% and 21%, respectively). Most facilities across the world responded to COVID-19 with practices such as physical distancing, requiring masks, symptom screening, temperature checks, and limiting visitors. COVID-19 testing for all patients undergoing cardiac diagnostic testing is uncommon across the world, but with some regional variation, ranging from 8% in Latin America to 29% in the Far East. Shortages of surgical masks were reported in 22% of centers, high-filtration masks (e.g., N95/KN95/KF94/FFP2) in 52%, gloves in 7%, gowns in 27%, and eye shielding in 39%.

DIFFERENCES BETWEEN TYPES OF CENTERS. Procedure reductions differed between types of centers (Table 3). Of note, outpatient imaging-only centers noted a 78% reduction in all procedures, whereas outpatient centers with imaging and physician practices noted lesser reduction of 69%. University-affiliated teaching facilities noted less percent reduction than nonteaching facilities (62% vs. 70% overall), and larger hospitals noted less reduction than small hospitals (54% for hospitals in the highest tertile of number of beds, 69% for the middle tertile, and 75% for the lowest tertile, overall). Centers cancelling or postponing all nonurgent outpatient procedures evidenced a 13% greater reduction in procedures than did those not cancelling all nonurgent outpatient procedures.

DISPARITIES BETWEEN LEVELS OF ECONOMIC DEVELOPMENT. We observed a significant difference in procedure reduction between economically challenged and wealthier countries, with COVID-associated reduction in cardiac diagnostic procedures more prominent for the world's economically challenged (Figure 5). In the 4 low-income countries participating in the survey, overall reduction in procedures was 81%, and in lower-middle-income countries a reduction of 77% was noted. In contrast, procedural volume reduction was 62% in upper-middle-income countries and 63% in high-income countries. This trend was generally observed across procedure types. Another disparity noted between levels of economic status was in shortages of PPE, which were observed in a higher proportion of low- and lower-middle-income countries than in higher-income countries (surgical masks: 28% vs. 21%; high-filtration masks: 50% vs. 64%; gloves: 7% vs. 13%; gowns: 45% vs. 25%; and eye shielding: 60% vs. 37%). A third disparity noted was in use of telehealth. Telehealth for communicating with patients has been implemented in 60% of centers in high-income countries, about half of centers in both upper-middle-income and lower-middle-income countries, and none of the 4 centers in low-income countries.

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TABLE 3 Overall Percent Reductions in Cardiovascular Diagnostic Procedures by Type of Center

								Stress Tests							
	TTE	TEE	CMR	PET Infection	CAC	Coronary CTA	ICA	All	ECG	Echo	Nuclear	SPECT	PET	CMR	Total
Type of facility															
Hospital inpatient only	65	81	75	63	87	75	32	74	78	74	72	72	67	38	66
Hospital inpatient and outpatient	57	75	63	61	68	52	58	78	84	82	73	75	53	73	62
Hospital outpatient only	71	83	75		86	67	17	74	71	97	71	71	86	77	72
Outpatient imaging center	78	100	80	100	79	60		81	83	95	77	77	82	72	78
Outpatient physician practice	61	78	80	58	90	65	55	76	89	79	66	69	51	84	69
Teaching center status															
Teaching	57	75	63	63	67	52	56	79	85	83	74	75	58	67	62
Nonteaching	66	77	69	56	85	62	60	78	83	82	71	73	53	80	70
Hospital beds															
Lowest tertile	72	79	76	72	81	68	58	83	86	86	80	81	67	77	75
Middle tertile	63	80	71	66	88	62	60	80	84	83	76	78	58	77	69
Highest tertile	50	69	51	56	49	47	53	73	80	77	68	70	49	59	54
All nonurgent outpatient procedures															
Not cancelled	54	73	59	54	69	50	53	77	84	79	70	72	53	74	60
Cancelled	70	79	70	75	72	68	66	81	86	87	77	78	67	75	73

Values are n. Reductions are from March 2019 to April 2020.

CAC = coronary artery calcium; CMR = cardiac magnetic resonance; CTA = computed tomography angiography; ECG = electrocardiography; echo = echocardiography; ICA = invasive coronary angiography; PET = positron emission tomography; SPECT = single-photon emission computed tomography; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

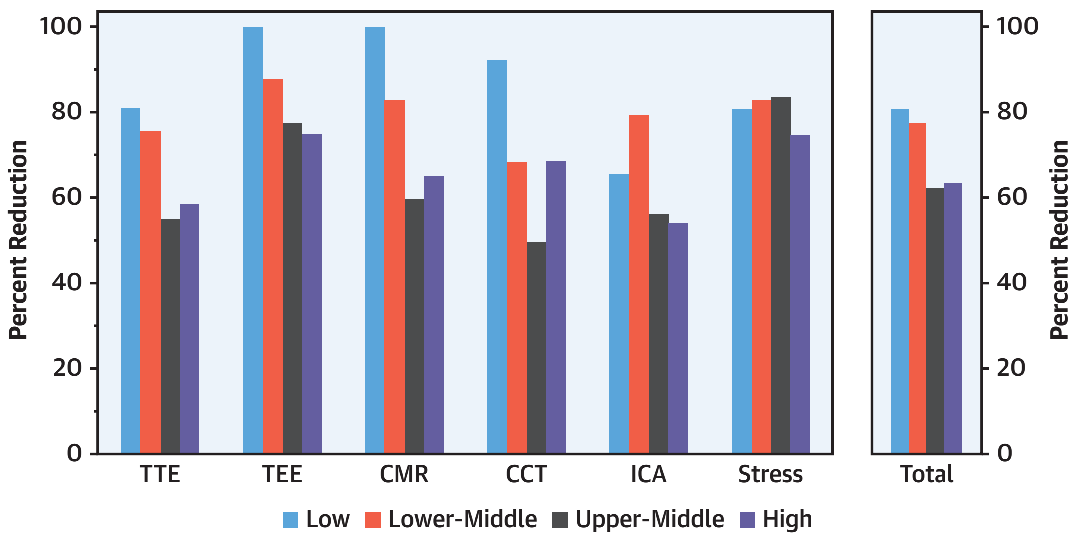
MULTIVARIABLE ANALYSIS. In multivariable regression, a statistically significantly greater reduction in cardiac procedure volume was associated with centers in countries with lower gross domestic product (9.4% lesser reduction in procedure volume per $\log_{10}$ of gross domestic product in dollars), centers avoiding exercise for stress testing (4.9% greater reduction in procedure volumes than in centers performing exercise stress testing), and centers in which the survey respondent was redeployed to COVID-19-related activities (6.7% greater reduction in procedure volumes than in centers where respondent was not redeployed). Significant differences in reduction were also noted among world regions. Country population, teaching hospital status, and shortage of PPE were not associated with a significant change in reduction in procedure volume. Location in a low-income or lower-middle-income country was associated with an additional 22% reduction in cardiac procedures.

DISCUSSION

The COVID-19 pandemic represents an unprecedented challenge to global health and modern health care delivery. Owing to the resources required to treat patients with COVID-19 and efforts to prevent its spread, the ability of world health care systems to concomitantly diagnose and treat noncommunicable diseases has been strained. Prior to the COVID-19 pandemic, declines in heart disease mortality have been documented in many regions of the world. Diagnostic evaluation pathways predicated on tests for cardiovascular disease are widely employed to guide the use of effective, life-saving treatments. However, to date, the impact of COVID-19 on the performance of invasive and noninvasive cardiovascular testing volumes during the COVID-19 pandemic has been unknown.

We observed a marked disruption in cardiovascular diagnostic services around the world, potentially impacting care for millions of patients who are at risk for or living with heart disease conditions. To our knowledge, this study represents the first large-scale global assessment of the early impact of COVID-19 on worldwide cardiovascular diagnostic testing volumes. Through survey respondents from 108 countries, representing 909 inpatient and outpatient health care facilities, we document that COVID-19 was directly associated with a 64% reduction in invasive and noninvasive diagnostic tests for heart diseases during the first 2 months of the pandemic (March to April 2020; COVID-19 was declared a pandemic on March 11) (14) as compared with March 2019 baseline testing volumes. The reductions in testing were abrupt, of significant magnitude across all world regions, and most significantly affected low-income and lower-middle-income countries. Testing reductions were most significant for the performance of stress electrocardiography (84%), stress

FIGURE 5 **Reduction in Cardiac Diagnostic Procedures by Income Level**



The bar graph demonstrates the reduction between March 2019 and April 2020 in the number of cardiac diagnostic procedures, in low-income, lower-middle-income, upper-middle-income, and high-income countries. Abbreviations as in Figures 2 and 3.

echocardiography (83%), and transesophageal echocardiography (76%), likely due to the aerosolization risk related to these tests at a time when PPE is limited. We noted some regional differences; for example, in China, echocardiography volumes decreased considerably less than they did in North America, although the decrease in invasive coronary angiography volumes was more similar. The reasons for regional differences are complex, and may include differences in health care systems, types of responses to COVID-19, and time course of the pandemic.

These data have several important implications for cardiovascular health care delivery going forward. First, this report may serve to better inform studies evaluating the short- and long-term effects of COVID-19 on global cardiovascular disease outcomes. The cumulative impact of the current pandemic will likely result in consequences in delayed cardiovascular diagnosis that, if persistent, may not only erase prior population declines for this condition, but also hasten premature morbidity and mortality for millions of patients from low- to high-income countries alike. Already, COVID-19-associated increases in out-of-hospital cardiac arrest have been documented (7), and prolonged limitation in cardiovascular diagnosis will likely exacerbate this phenomenon and long-term adverse heart health outcomes. Moreover, the significant decline in cardiovascular testing capacity in lower-income countries warrants close observation given the increasing incidence and prevalence of cardiovascular diseases in LMICs (3).

These data may also provide insight for health care leaders involved in current planning for additional waves or recurrences of COVID-19 and for future pandemics. For example, with better access to PPE, improvements in patient and staff safety protocols, and experience, it is probable that patient access to cardiovascular testing and health care testing capacity will improve, with these data serving as an initial call to action regarding the magnitude of impact on potentially undiagnosed cardiovascular diseases to date. We observed that there was a small increase in diagnostic testing in the Far East region from March to April 2020, perhaps reflective of a decreased effect of the pandemic and adaptations by health systems.

Avoidance of tests that involve aerosolization (exercise stress tests and transesophageal echocardiogram) likely reflect operating procedures to limit staff exposure as well as PPE shortages in some locales, but may also signify a paradigm shift in cardiovascular testing away from such tests to alternatives. For example, the performance of transesophageal echocardiography to rule out left atrial thrombus has been replaced by cardiac computed tomography angiography for appropriately selected patients at many centers (15). With a move toward pharmacologic rather than exercise stress testing (16,17), the major advantage to patients of single-photon emission computed tomography over PET stress testing in most centers where the latter is available, namely the assessment of functional capacity, is no longer operative, which should foster a preference for PET. Such changes, if persistent, may require modifications globally in staffing, equipment acquisition, and the design of cardiovascular product lines.

Finally, we observed that the global health care system was not prepared for the PPE demands imparted by such a highly contagious virus. The majority of respondents (52%) described significant shortages in high-filtration (e.g., N95) masks early during the pandemic, although shortages in other supplies (gloves, gowns, and face shields) were less common. Low- and lower-middle-income countries were most likely to have faced significant PPE shortages and were less likely to be able to implement telehealth strategies to attempt to continue patient visits. Strategies for prioritization of diagnostic testing in the setting of limited resources have been addressed in professional society guidelines, which recommend case-by-case triage involving both testing and referring physicians, reflecting indication, urgency, patient clinical status, and results of other tests (16).

A strength of our study was its true global coverage, which enables evaluation of the impact of the pandemic on LMICs and high-income countries alike. Although representation of low-income countries in the survey was small, limited to sites in Afghanistan, Nepal, Niger, and Uganda, little cardiac testing is performed in low-income countries, in many the record-keeping systems do not easily enable estimation of monthly procedure volumes, and equipment availability is poor. We had good representation (41% of centers) from middle-income countries, including a range of nations with modest gross domestic product per capita, such as Bangladesh, Ghana, Laos, Mongolia, Nicaragua, Papua New Guinea, and Ukraine, all of which have gross domestic product per capita of <$5,000. Further study of the impact of the pandemic on cardiovascular testing and outcomes in LMICs is essential and planning to mitigate the disproportionate impact of COVID-19 on cardiovascular care in LMICs is needed.

STUDY LIMITATIONS. Our study is not without limitations. We only obtained procedure volumes during the pandemic in March and April 2020, whereas in China the peak occurred earlier and in some Latin American countries and the United States it is peaking later. Nevertheless, COVID-19-related changes in practice likely preceded this peak in many centers. Further study of testing patterns throughout the evolving pandemic is of significant interest, and the INCAPS COVID Investigators Group is planning further data collection later in 2021 to address this desideratum; sites interested in participating are welcome to contact INCAPS@iaea.org. Our study was also based on self-reported responses and not on measured procedural volumes using claims or other verifiable methods. Although sites were asked to accurately report study volumes, the potential for inaccurate reporting exists and inclusion of procedural estimates was allowed. Nonetheless, we feel that the observed trends and large-scale size of our analysis represents the best available data collection processes currently available for such a large-scale global study. Some of the reductions in testing noted may in fact represent elimination of inappropriate studies; for example Ward et al. (18) noted a reduction in rarely appropriate transthoracic echocardiography from 7% to 1% with the institution of a new workflow protocol responding to hospital- and state-issued pandemic guidelines. However, it seems unlikely that such desirable reductions in testing constitute more than a small proportion of the total reductions observed. Additionally, study investigators attempted to eliminate spurious data through meticulous review of the data with targeted site queries and data integrity procedures. Finally, as with any study based on survey methodology, there is the risk of sampling, response, and nonresponse bias. Although we attempted to ensure broad participation globally by utilizing multiple methods to reach potential participants, the number of sites providing cardiovascular testing in the world is not fully known, making the survey response rate impossible to be calculated.

CONCLUSIONS

COVID-19 was associated with a rapid reduction in cardiovascular diagnostic procedure volumes across the world. Decreases in cardiac testing and the unavailability of PPE and telehealth were most notable in lower-income countries. The impact of these and ongoing changes in cardiovascular diagnostic care related to COVID-19 requires further study, although they raise serious concerns for long-term adverse cardiovascular health outcomes resulting from decreased diagnosis. Efforts to improve timely patient access to cardiovascular diagnosis in this and future pandemics, particularly in low- and middle-income countries, are warranted.

ACKNOWLEDGMENTS The INCAPS COVID Investigators Group, listed by name in the Supplemental Appendix, thank cardiology and imaging professional societies worldwide for their assistance in disseminating the survey to their memberships. These include alphabetically, but are not limited to, the American Society of Nuclear Cardiology, Arab Society of Nuclear Medicine, Australasian Association of Nuclear Medicine Specialists, Australia-New Zealand Society of Nuclear Medicine, Belgian Society of Nuclear Medicine, Brazilian Nuclear Medicine Society, British Society of Cardiovascular Imaging, Conjoint Committee for the Recognition of Training in CT Coronary Angiography, Consortium of Universities and Institutions in Japan, Gruppo Italiano Cardiologia Nucleare, Indonesian Society of Nuclear Medicine, Japanese Society of Nuclear Cardiology, Philippine Society of Nuclear Medicine, Russian Society of Radiology, Society of Cardiovascular Computed Tomography, and Thailand Society of Nuclear Medicine.

AUTHOR DISCLOSURES

Dr. Einstein has received consulting fees from W.L. Gore and Associates; has received institutional grant support from Canon Medical Systems, GE Healthcare, Roche Medical Systems, W.L. Gore and Associates, and XyloCor Therapeutics; and has received travel/accommodations/meeting expenses from HeartFlow. Dr. Dorbala has received honoraria from Pfizer and GE Healthcare; and has received institutional research grant support from Pfizer and GE Healthcare. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: The COVID-19 pandemic reduced the frequency of diagnostic testing for heart disease, especially in resource-constrained countries, reflecting challenges in access to care.

TRANSLATIONAL OUTLOOK: Further research is needed to assess the impact of patient behavior and limited access to diagnostic, preventive, and therapeutic services on cardiovascular outcomes during and after the pandemic.

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KEY WORDS cardiac testing, cardiovascular disease, coronavirus, COVID-19, global health

APPENDIX For a complete list of the INCAPS COVID Investigators Group as well as survey questions, please see the online version of this paper.

Update

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CORRECTIONS

Einstein AJ, Shaw LJ, Hirschfeld C, Williams MC, Villines TC, Better N, Vitola JV, Cerci R, Dorbala S, Raggi P, Choi AD, Lu B, Sinitsyn V, Sergienko V, Kudo T, Nørgaard BL, Maurovich-Horvat P, Campisi R, Milan E, Louw L, Allam AH, Bhatia M, Malkovskiy E, Goebel B, Cohen Y, Randazzo M, Narula J, Pascual TNB, Pynda Y, Dondi M, Paez D, on behalf of the INCAPS COVID Investigators Group

International Impact of COVID-19 on the Diagnosis of Heart Disease

J Am Coll Cardiol 2021;77:173–85

The INCAPS COVID Investigators Group, listed in the appendix, was not coded properly when this article initially published. As a result, they were not indexed on PubMed. Their names have now been coded properly to facilitate inclusion in the PubMed indexing.

The publisher apologizes for this error.

https://doi.org/10.1016/j.jacc.2021.05.030

Giudicessi JR, Ackerman MJ, Fatkin D, Kovacic JC

Precision Medicine Approaches to Cardiac Arrhythmias: *JACC* Focus Seminar 4/5

J Am Coll Cardiol 2021;77:2573–91

In the print issue, reference citations are missing in 2 sentences.

In the following sentence, the citation for reference 10 should have included citations for references 21-23.

However, the majority of these minor LQTS susceptibility genes were discovered with the use of hypothesis-driven candidate gene-based approaches rather than less biased methods (e.g., linkage analysis, next-generation sequencing trio/pedigree analysis) and before the true burden of rare, and presumably innocuous, nonsynonymous genetic variants was illuminated fully by large-scale next-generation sequencing projects (10,).

The correct sentence is as follows.

However, the majority of these minor LQTS susceptibility genes were discovered with the use of hypothesis-driven candidate gene-based approaches rather than less biased methods (e.g., linkage analysis, next-generation sequencing trio/pedigree analysis) and before the true burden of rare, and presumably innocuous, nonsynonymous genetic variants was illuminated fully by large-scale next-generation sequencing projects (10,21-23).

In the following sentence, the second citation for references 57 and 58 should cite references 59-61.

The majority of remaining minor BrS susceptibility genes encode pore-forming α- and accessory β-subunits that impart either a loss of function to the depolarizing L-type calcium current (*CACNA1C*, *CACNA2D1*, and *CACNB2*) (57,58) or a gain of function to the repolarizing transient outward (I_{to}; *KCND3*, *KCNE3*, and *KCNE5*) (57,58) and ATP-sensitive potassium (*ABCC9* and *KCNJ8*) (62,63) currents (**Figure 2B**).

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The publisher apologizes for these errors and accepts full responsibility.

The online version of the article is correct.

https://doi.org/10.1016/j.jacc.2021.05.032