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Recovery of cardiovascular testing in Asia during the COVID-19 pandemic: findings from the INCAPS COVID 2 study

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ABSTRACT

Background Understanding pandemic-related reductions and subsequent recovery of cardiovascular testing in Asia is important for guiding regional public health efforts.

Objectives This study sought to evaluate the recovery of cardiovascular testing in Asia 1 year into the COVID-19 pandemic.

Methods In this subanalysis of a worldwide survey on the impact of COVID-19 on cardiovascular diagnostic care in April 2020 and April 2021, recovery of testing volume in Asia was compared among subregions, World Bank income groups and imaging modalities.

Results Of 669 sites worldwide, 164 sites were in 33 Asian countries. Cardiovascular testing volumes in Asia decreased by 53% from March 2019 to April 2020, then recovered 96% of this decrease by April 2021, compared with 98% recovery in the rest of the world. Eastern Asia and Western and Central Asia reported recovery rates of 123% and 110%, compared with 50% and 80% recovery in Southern and South-eastern Asia. Testing volumes among high-income and upper-middle-income Asian countries recovered to 117% and 121% but remained depressed at 49% and 14% recovery in lower-middle and low-income countries, respectively. Stress ECG, stress echo and stress positron emission tomography studies experienced median reductions of 48%, 35% and 57% in testing volume between March 2019 and April 2021, while volumes of coronary artery calcium, coronary CT angiography and cardiac MR remained stable during this period.

Conclusions The recovery of cardiovascular testing in Asia 1 year into the COVID-19 pandemic lagged in the Southern and South-eastern subregions, as well as in lower-income countries. Recovery favoured advanced cardiac imaging modalities over standard stress testing modalities.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The COVID-19 pandemic caused significant reductions in cardiovascular diagnostic testing volumes worldwide, followed by unequal rates of recovery 1 year later.

WHAT THIS STUDY ADDS

⇒ In our study, the recovery of cardiovascular testing in Asia 1 year into the COVID-19 pandemic lagged in the Southern and South-eastern subregions, as well as in lower-income countries.

⇒ Recovery favoured advanced cardiac imaging modalities over standard stress testing modalities.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings highlight the need for targeted interventions in lower-income and Southern and South-eastern Asian countries to ensure adequate cardiovascular diagnostic testing in these populations.

INTRODUCTION

The COVID-19 pandemic caused significant harm to patients worldwide through the acute and long-term sequelae of viral infection, as well as through pandemic-related disruption of critical healthcare services. The disruption of cardiovascular disease (CVD) management has been of particular concern, given that CVD remains the leading cause of morbidity and mortality worldwide. Cardiovascular outcomes are closely linked to early and effective diagnosis.[1] Indeed, the excess

CVD mortality that has coincided with major waves of COVID-19 has been attributed to underdiagnosis, postponement of treatment and subsequently more complex presentations of acute coronary syndrome.[2–4]

To date, two large-scale, sequential studies of the impact of COVID-19 on cardiac testing volumes have been conducted by the International Atomic Energy Agency (IAEA). The initial INCAPS COVID study (IAEA Noninvasive Cardiology Protocols COVID) surveyed testing volumes in more than 900 sites across 108 countries in March and April 2020 and found a 64% total reduction in cardiac testing volume during the first 2 months of the pandemic compared with a prepandemic baseline in March 2019.[5] To assess intermediate-term trends 1 year into the pandemic, the follow-up INCAPS COVID 2 study then surveyed 669 sites in 107 countries in April 2021. Key findings were markedly delayed recovery of testing volume in lower-income countries compared with complete recovery in upper-middle and high-income countries, as well as a reduction in stress testing in favour of advanced imaging modalities, that is, positron emission tomography (PET) and magnetic resonance (MR).[6]

In addition to these overarching global trends in cardiac testing within the first year of the pandemic, significant regional differences were noted in the types of procedures affected and in the rate of recovery of testing volume.[5 6] Regional variations were attributed to multifactorial differences in healthcare systems, COVID-19 response strategies and time course of the pandemic. Therefore, subsequent studies have focused on obtaining actionable insights through regional analyses of INCAPS COVID and INCAPS COVID 2.[7–9] The first substudy focused on Asian countries found disruptions to cardiovascular testing following the onset of COVID-19 similar to worldwide trends but with a few notable differences, including an early recovery of procedure volume by nearly 1% between March 2020 and April 2020 not seen in other world regions.[8] It is unknown whether this early recovery signal persisted among Asian countries in the following months, or whether the degree of recovery varied by subregion or income level. The purpose of this INCAPS COVID 2 substudy is to evaluate intermediate-term changes in diagnostic testing volume in Asia compared with the rest of the world (RoW), 1 year into the pandemic.

METHODS

Study design

This study uses data from the INCAPS COVID 2 study, the study design for which has been described in detail elsewhere.[5 6] In brief, a web-based survey was conducted to assess the impact of COVID-19 on cardiovascular diagnostic care delivery. Procedure volumes were collected for the following tests: coronary artery calcium (CAC) scanning, coronary CT angiography (CCTA), transthoracic (TTE) and transoesophageal (TEE) echocardiography, cardiac MR (CMR), PET for infective endocarditis (IE) (PET infection), stress testing (stress ECG, stress echocardiography (Echo), stress single-photon emission CT, stress PET, and stress CMR), and invasive coronary angiography (ICA). Data were obtained from each participating site for the pre-COVID-19 baseline in March 2019 and for April 2020 and April 2021. Data were aggregated by country and region. In this subanalysis, the Asian countries participating in INCAPS COVID 2 were divided into four subregions (Eastern, Southeastern, Southern, and Central and Western) based on United Nations classification.[10] Country income level was defined according to World Bank classification.[11] A full list of countries grouped by subregion and income level is available in online supplemental table S1.

Data collection

Survey data were collected in the web-based International Research Integration System. Various methods of outreach to candidate sites, including emails from the INCAPS COVID executive committee and national coordinators, emails from the IAEA to cardiology and imaging societies, and communications from professional societies to their members and social media platforms (Twitter, LinkedIn and Facebook), were employed to increase the diversity of participating sites. Review by an ethics committee was not required given no patient-specific personal information or confidential data were collected, and all study sites participated voluntarily. The present study complied with the Declaration of Helsinki. Duplicate and incomplete entries were excluded, such that each site in the final data set is represented by one complete survey.

Statistical analysis

Recovery, defined as per cent return in 2021 to 2019 baseline from 2020 volumes at the initial phase of the pandemic, was calculated as: 100%×{1–[(March 2019 volume–April 2021 volume)/(March 2019 volume–April 2020 volume)]}. The per cent change in procedure volumes from March 2019 to April 2020 was calculated as: 100%×[(April 2020 volume–March 2019 volume)/(March 2019 volume)] and analogously for March 2019 to April 2021. The median per cent change was calculated for each testing modality and compared between Asia and the RoW, among the four Asian subregions, and among Asian countries of different income levels. Wilcoxon rank sum and Kruskal-Wallis tests were used to compare differences in continuous variables, while differences in survey response distributions were compared by Fisher's exact tests. Statistical analysis was performed using Stata/SE version 15.1 (StataCorp) and Microsoft Excel (Microsoft, Redmond, Washington, USA). A two-tailed $p<0.05$ was considered statistically significant. Maps were created using the rnaturalearth and tmap packages in R V.4.3.3 (R Development Core Team).

RESULTS

Site characteristics

Key characteristics of the Asian sites participating in INCAPS COVID 2 are described in table 1. Data were obtained from a total of 669 sites in 107 countries worldwide, including 164 sites in 33 Asian countries. Of these, 103 sites (63%) had previously participated in the first INCAPS COVID study. Eastern Asia continued to be the most represented subregion with 69 sites across 4 countries contributing data. Across all Asian sites, a total of 375 107 cardiovascular diagnostic procedures were performed during the 3 months considered—154 037 in March 2019, 71 988 in April 2020 and 150 504 in April 2021. Over 60% of these procedures were performed in Eastern Asia at all time points. A total of 816 397 procedures were performed in participating sites in the RoW during the same 3 months.

Recovery of cardiovascular diagnostic testing volumes in Asia

At INCAPS COVID 2 sites in Asia, cardiovascular diagnostic testing volumes decreased by 53% from March 2019 to April 2020, then recovered 96% of this decrease by April 2021 (figure 1). The 96% recovery rate in Asia was similar to the 98% recovery reported by INCAPS COVID 2 sites in the RoW. However, recovery rates within Asia varied widely by subregion. Sites in Eastern Asia and Western and Central Asia reported recovery rates of 123% and 110%, respectively. Sites in Southern Asia reported the lowest recovery rate of 50%.

Differences among Asian countries and subregions are further highlighted in figure 2, which displays recovery rates on a country-by-country basis (figure 2, upper panel) and differences in the median percent change in testing volume among Asian subregions from March 2019 to April 2020 and from March 2019 to April 2021 (figure 2, lower panel). At both time points represented in INCAPS COVID 2, the median per cent change in cardiovascular diagnostic testing volume differed across the four Asian subregions. Of note, in April 2021, sites in Eastern Asia reported a median 10% increase from their March 2019 baseline testing volumes while other subregions continued to report median decreases in testing volume. The percentage recovery of cardiac procedure volumes tended to decrease with lower income levels among countries in the RoW (figure 3, lower panel), while in Asia (figure 3, upper panel) the rate of recovery of upper-middle-income countries was similar (121%) to that of high-income countries (117%).

Changes in procedure volumes by modality

Early in the pandemic in April 2020, sites in the RoW reported a significantly greater reduction in utilisation of nearly all cardiac testing modalities compared with sites in Asia (figure 4, upper panel). Exceptions to this trend were the per cent change in utilisation of stress echo, stress PET, stress CMR and PET infection between March 2019 and April 2020, which were not significantly different between Asia and the RoW. Additional comparisons between Asian subregions are available in online supplemental table S2.

One year later in April 2021, there was no longer a significant difference between Asia and the RoW with respect to the percent change in overall cardiac testing volumes from March 2019 (figure 4, lower panel). The imaging modalities that did show a significant difference in between Asia and the RoW were stress ECG, stress PET, TTE, TEE and PET infection. For each of these five modalities, sites in Asia reported a significantly larger decline in their utilisation in April 2021 from March 2019 compared with sites in the RoW.

DISCUSSION

The COVID-19 pandemic significantly impacted cardiovascular care worldwide, causing immediate, dramatic reductions in procedure volume followed by varied degrees of recovery across world regions and countries in the subsequent months. In the present study, we analysed data from Asian sites participating in INCAPS COVID 2 to determine the intermediate-term impact of COVID-19 on cardiovascular diagnostic testing volume in Asia. Key findings were as follows: (1) significant variations in recovery among Asian subregions, with Southern Asia being disproportionately impacted, (2) persistent reductions in cardiac testing among lower income Asian countries and (3) larger declines in the utilisation of certain imaging modalities in Asia compared with the RoW.

Changes in procedure volumes by subregion and country income level

We found significant differences in the recovery of cardiac procedure volume between Asian subregions and income groups. Among the four Asian subregions, Eastern Asia reported the greatest recovery by April 2021, while Southern Asia reported the least recovery. These subregional variations may be due to pre-existing differences in healthcare infrastructure, such as low numbers of physicians per capita in Southern Asia, and differences in socioeconomic status.[12 13] Indeed, in the present study, five out of the six countries (37 out of 43 sites) representing Southern Asia in this study are in the UN lower-middle-income group, while the vast majority of sites (68 out of 69 sites) representing Eastern Asia are in upper-middle-income or high-income countries. Low-income countries were poorly represented in this analysis, with data from only one low-income country in Asia and five low-income countries in the RoW, reflecting the limited access to cardiac testing in this strata. However, based on the well-represented high-income, upper-middle-income and lower-middle-income groups, it was clear that greater recovery of procedure volume by April 2021 was associated with higher-income groups in both Asia and the RoW. These findings suggest that the COVID-19 pandemic has exacerbated health disparities among lower-income countries in Asia. Indeed, the tendency for unequal recovery from COVID-19 to exacerbate existing

Table 1 Characteristics of participating sites and procedure numbers

	Asian Region					Worldwide		
	Eastern	South-eastern	Southern	Western and central	P value	Asia	Rest of world	P value
Number of sites	69	26	43	26		164	505	
Number of countries	4	9	6	14		33	73	
Participated in INCAPS COVID	57 (83)	13 (50)	20 (47)	13 (50%)		103 (63%)	346 (68%)	
Number of procedures								
March 2019	96 787 (63)	13 626 (9)	29 755 (19)	13 869 (9)		154 037	355 413	
April 2020	56 474 (78)	5091 (7)	5466 (8)	4957 (7)		71 988	111 483	
April 2021	106 135 (71)	11 946 (8)	17 711 (12)	14 712 (10)		150 504	349 501	
Number of sites performing each test type in April 2021								
Stress electrocardiography	27 (39)	7 (27)	15 (35)	12 (46)	0.970	61 (47)	212 (42)	0.678
Stress echocardiography	18 (26)	7 (27)	14 (33)	8 (31)	0.521	47 (29)	173 (34)	0.435
Stress SPECT	44 (64)	14 (54)	20 (47)	18 (69)	0.541	94 (57)	318 (63)	0.949
Stress PET	3 (4)	0 (0)	8 (19)	4 (15)	**0.009**	15 (9)	50 (10)	0.994
Stress CMR	5 (7)	2 (8)	4 (9)	2 (8)	0.860	13 (8)	104 (20)	**0.001**
CT coronary calcium	13 (19)	5 (19)	9 (21)	8 (31)	0.684	35 (21)	157 (31)	0.050
CT coronary angiography	51 (74)	7 (27)	13 (30)	13 (50)	**<0.001**	84 (51)	239 (47)	0.065
Transthoracic echocardiography	34 (49)	8 (31)	15 (35)	10 (39)	0.585	67 (41)	207 (41)	0.471
Transoesophageal echocardiography	29 (42)	5 (19)	14 (32)	7 (27)	0.282	55 (34)	170 (34)	0.547
PET infection	5 (7)	0 (0)	5 (12)	4 (15)	0.250	14 (9)	72 (14)	0.103
CMR	39 (57)	5 (19)	7 (16)	9 (35)	**<0.001**	60 (37)	197 (39)	0.907
Invasive coronary angiography	39 (57)	8 (31)	15 (35)	8 (31)	0.045	70 (43)	161 (32)	**0.001**
Baseline procedures per site	625 (169, 1096)	170 (32, 900)	325 (102, 1714)	315 (106, 500)	0.1525	439 (100, 1069)	247 (80, 993)	0.0505
Hospital beds	1000 (550, 2500)	700 (300, 1300)	400 (200, 1500)	390 (225, 871)	**<0.001**	700 (320, 1500)	460 (234, 867)	**<0.001**
Inpatient site	69 (100%)	25 (96%)	40 (93%)	26 (100%)	0.097	160 (98%)	418 (83%)	**<0.001**
Teaching institution	48 (79%)	26 (100%)	29 (67%)	23 (88%)	0.201	126 (77%)	349 (71%)	0.079

Values are n, n (%) or median (IQR). P values are calculated by Wilcoxon rank sum and Kruskal-Wallis tests for continuous variables or Fisher's exact tests for categorical variables. P values that reach statistical significance are bolded.
Data are presented as n, n (%), or median (IQR).
Baseline procedures per site=median (IQR) number of procedures performed in March 2019.
CMR, cardiac MR; INCAPS COVID, IAEA Non-invasive Cardiology Protocols COVID; PET, positron emission tomography; SPECT, single-photon emission CT.

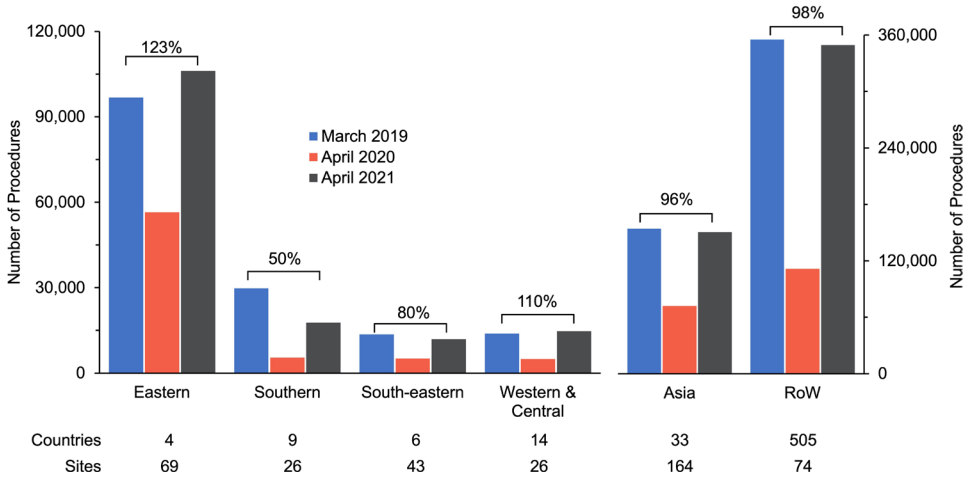

Figure 1 Recovery of cardiovascular diagnostic testing volume in Asia. Total procedure volumes performed in March 2019, April 2020 and April 2021 are displayed by world region. The left axis corresponds to procedure volumes in the four Asian subregions. The right axis corresponds to procedure volumes in Asia and the RoW. Recovery is defined as the percentage return in 2021–2019 baseline, from 2020 volumes at the initial phase of the pandemic. RoW, rest of the world.

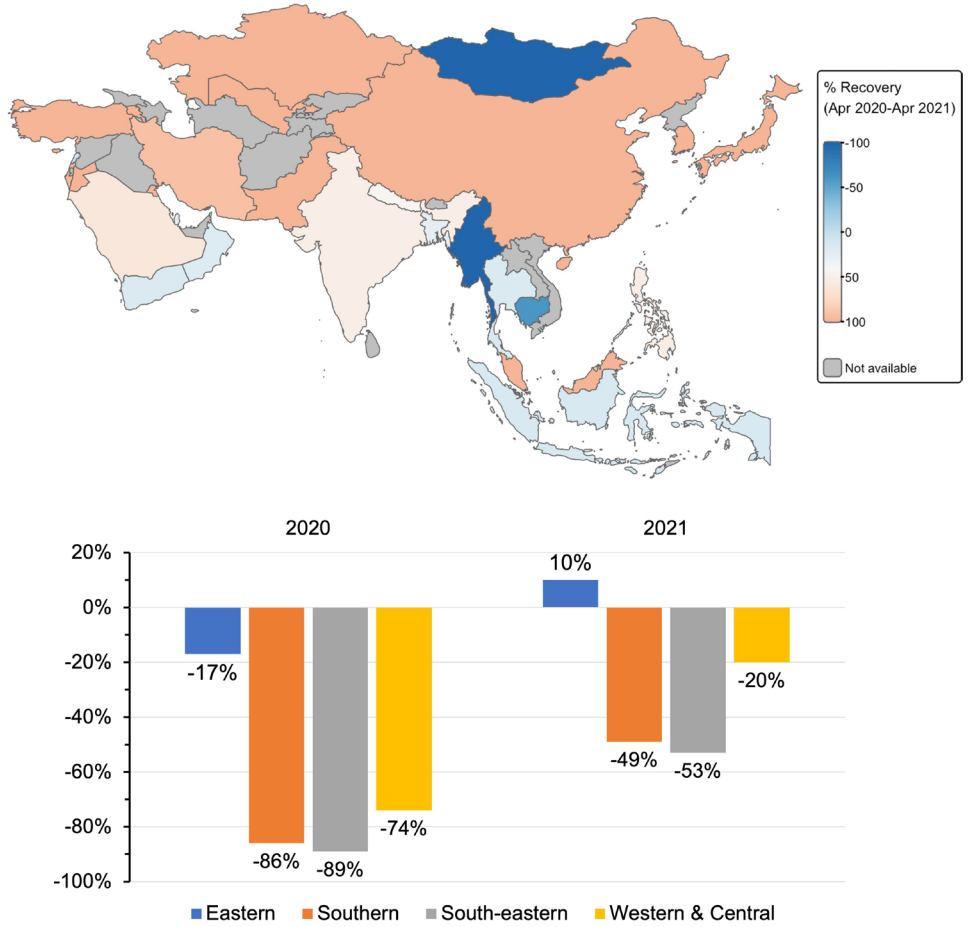

Figure 2 Recovery of cardiovascular diagnostic testing volumes by country and subregion among Asian sites participating in INCAPS COVID 2. Upper panel: Recovery is defined as percentage return in 2021 to 2019 baseline, from 2020 volumes at the initial phase of the pandemic. Darker red shades indicate greater recovery. Darker blue shades indicate less robust recovery. Countries in grey did not have data available. Lower panel: For each Asian subregion, the change in cardiovascular diagnostic testing volumes is represented as the median per cent change from March 2019 to April 2020 (left) and from March 2019 to April 2021 (right). INCAPS, IAEA Non-invasive Cardiology Protocols.

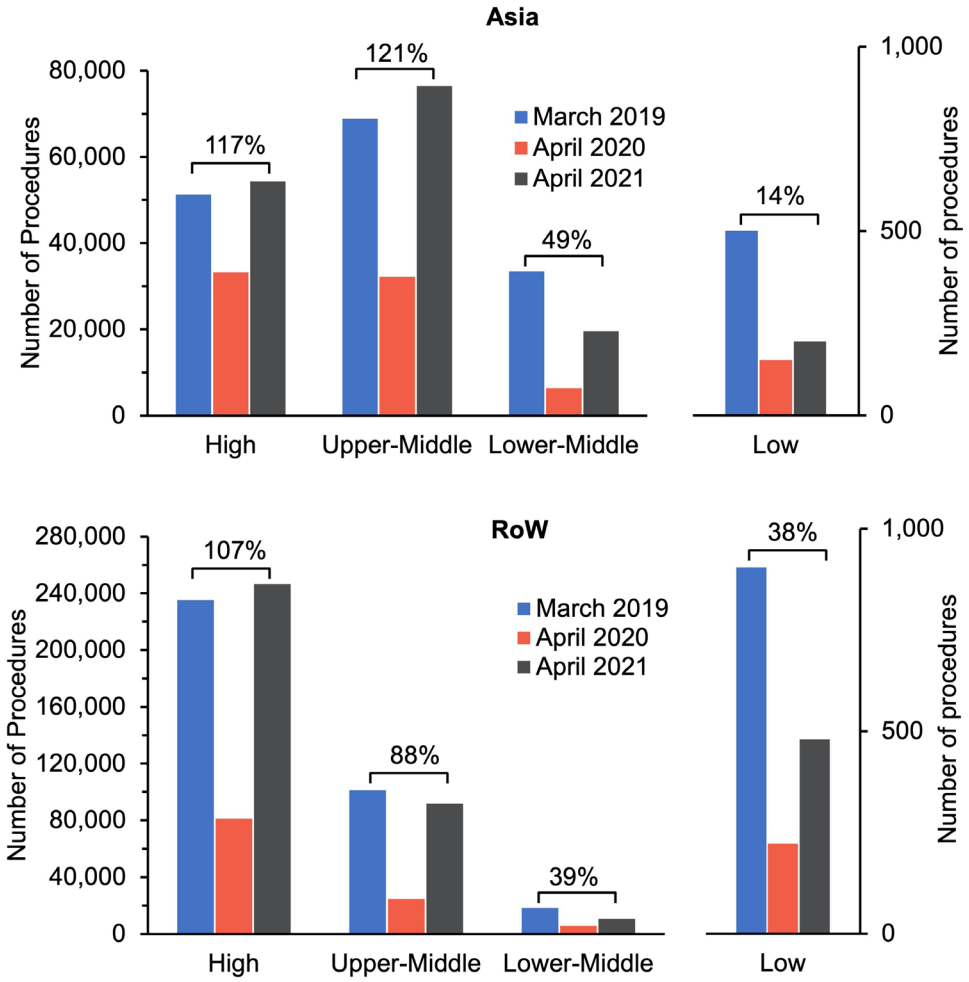

Figure 3 Recovery of cardiovascular diagnostic testing volume by income group. Total procedure volumes performed in March 2019, April 2020, and April 2021 are displayed by income groups among sites in Asia (upper panel) and by income groups among sites in the RoW (lower panel). Left axes correspond to procedure volumes in the high, upper-middle, and lower-middle-income groups. Right axes correspond to procedure volumes in low-income groups. Recovery is defined as the percentage return in 2021 to 2019 baseline, from 2020 volumes at the initial phase of the pandemic. RoW, rest of the world.

healthcare disparities between world income groups and regions has been reported in other medical fields after the pandemic, such as greater age-standardised cancer mortality in central and eastern European countries compared with the remaining European Union countries.[14] If not promptly addressed by policy-makers and leaders in the cardiovascular field, the persistent reduction in cardiac diagnostic testing we found in Southern Asia is likely to exacerbate the already disproportionate burden of CVD in this subregion.[15]

Of note, Mongolia was an outlier with respect to its degree of recovery among the Eastern subregion, which by UN classification also includes Japan, China and South Korea. While the Eastern subregion as a whole has the highest recovery rate among Asian subregions (123%), this is clearly driven by the latter three countries. Mongolia is the only country out of these four in the Eastern subregion that falls into the low-middle-income group per the World Bank, while Japan, China and South Korea fall into either the upper-middle or high-income groups. This suggests that income group plays a greater role than geographical subregion in determining recovery. Interestingly, upper-middle-income countries in Asia appeared to recover to a similar degree as did high-income countries in Asia (121% vs 117%), while the gap in recovery between upper-middle-income and high-income countries in the RoW was more pronounced (88% vs 107%). The reasons for upper-middle-income Asian countries displaying recovery greater than might be expected for this income group are unclear. It is likely driven in part by the robust recovery of procedure volume in China, which was the first country impacted by the pandemic and, therefore, had a longer time to adapt by April 2021 than other upper-middle-income countries in the RoW. It is also possible that cultural and political factors in Asian countries, such as heightened social cohesion and stringent lockdown policies, could have facilitated recovery in these countries.[16] Future studies are needed to better understand whether societal factors such as lockdown policies and vaccination rates can mitigate income-based disparities during the ongoing recovery from COVID-19 or lessen the impact of future pandemics.

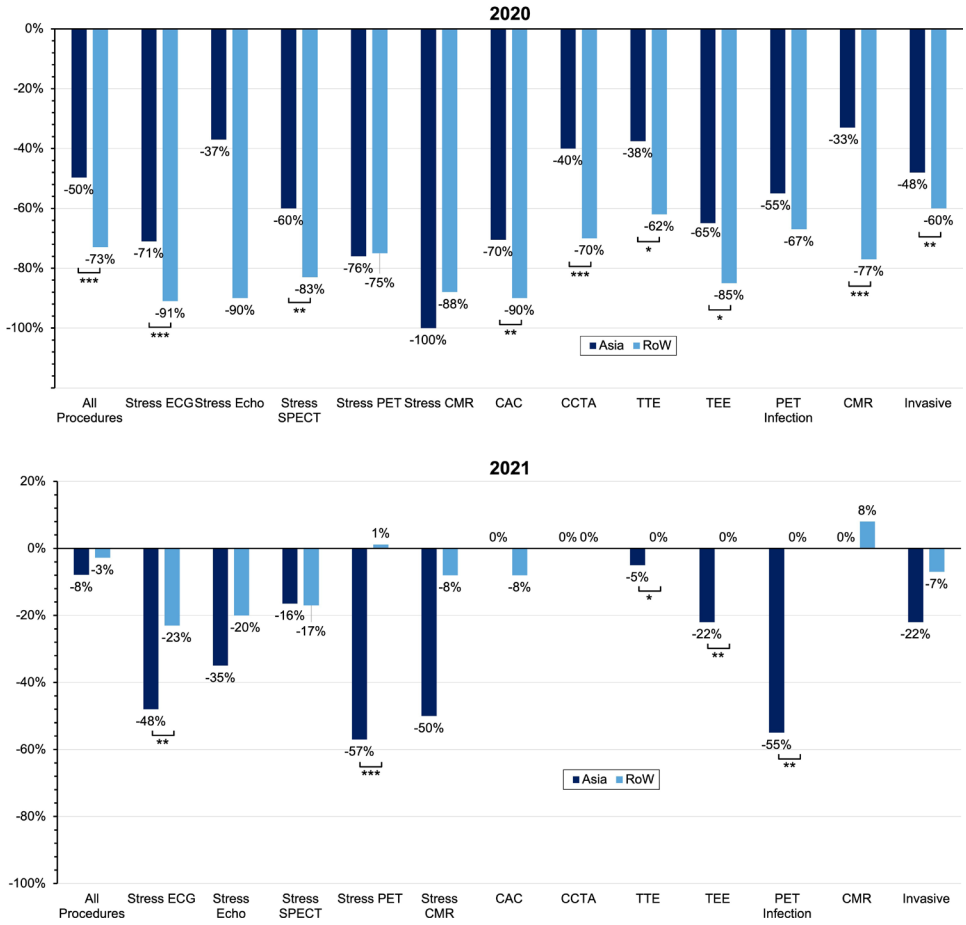

Figure 4 Changes in baseline testing volumes by modality in Asia vs the RoW. For each modality, the median per cent change from March 2019 to April 2020 (upper panel) and from March 2019 to April 2021 (lower panel) are displayed for sites in Asia and sites in the RoW. *p<0.05, **p<0.01, ***p<0.001 respectively. CAC, coronary artery calcium; CCTA, coronary CT angiography; CMR, cardiac MR; PET, positron emission tomography; RoW, rest of the world; SPECT, single-photon emission CT; TEE, transoesophageal echocardiography; TTE, transthoracic echocardiography.

Modality-specific reductions in procedure volume persisting in Asia

It was previously reported that Asian countries experienced a nearly 1% recovery in cardiac procedure volumes between March 2020 and April 2020, while procedure volume in the RoW continued to decline by 52%.[8] In the present study, we found this difference in trajectories between Asia and the RoW during the first 2 months of the pandemic resulted in a significantly smaller median decline in overall procedure volume by April 2020 in Asia compared with the RoW. However, the difference between Asia and the RoW was no longer present 1 year later; by April 2021, the median per cent change in procedure volume was −8% in Asia compared with −3% in the RoW. This is notably in contrast to subanalyses of other world regions in April 2021. For example, the USA had a significantly larger increase in the median per cent change from baseline procedure volume compared with the RoW (+4% in the USA vs −9% in RoW; p<0.01),[9] while Latin America remained far below baseline (−21% in Latin America vs 0% in RoW; p<0.01).[17] The similarity between Asia and RoW may be due to the wider distribution of income groups among Asian countries than in other world regions.[18]

While the change in overall procedure volumes in Asia and the RoW had equalised by April 2021, we found that the utilisation of five imaging modalities (stress ECG, stress PET, TTE, TEE, PET infection) remained significantly more depressed in Asia. Two of these were stress testing modalities, which were felt unlikely to alter short-term management and recommended to be postponed during the height of the pandemic.[19] Persistent reductions in these high-risk testing modalities suggest a more conservative approach to resuming prepandemic clinical practice patterns among sites in Asia compared with the RoW. Similarly, TEE was considered a very high droplet risk exposure for healthcare personnel and discouraged in favour of PET for evaluation of IE.[20] Despite this guidance from the American Society of Nuclear Cardiology and Society of Nuclear Medicine and Molecular Imaging, our study finds that even the volume of PET infection studies remained significantly reduced in Asia compared with the RoW. This trend may be due in part to the dependence of PET on radiotracer availability, especially at centres without local cyclotrons, and the international guidance to prioritise the provision of uninterrupted PET services for oncological patients.[21 22] The persistent reduction of both TEE and PET infection studies is concerning for lower

rates of detection and treatment of IE during the pandemic, which was reported in other world regions.[23 24] Future studies should investigate the long-term impact of reduced testing for IE during the COVID-19 pandemic in Asia.

Of note, there was no imaging modality with an overall increase in testing volume in April 2021 compared with March 2019 among participating Asian sites. At best, we found that volumes of CAC, CCTA and CMR had returned to their prepandemic baselines. The preferential recovery of these modalities in Asia is consistent with the greater use of advanced imaging modalities reported worldwide, as well as a larger paradigm shift in recent years favouring the use of CCTA as the first line for diagnosing coronary artery disease.[6 25 26]

Study limitations

This study has several limitations, including the possibility of biased responses (eg, non-response or selection bias) and inaccurate data due to recall error, unverified answers, or incomplete data that applies to all survey-based studies. To mitigate this, a data coordination committee was formed to scrutinise responses for potential errors, exclude duplicate and incomplete entries, and contact individual sites for clarifications when necessary. Another limitation is that the responding sites in Asia and the RoW may not be fully representative of the countries and regions in which they are located. Various efforts, as described in the Methods section, were taken to diversify participating sites and collect as representative a sample as possible. However, low-income countries remain poorly represented in this study and in prior INCAPS COVID studies, partly reflecting the lack of access to many advanced diagnostic tests, high testing costs and lack of insurance coverage in low-income countries. Lastly, this study collected data regarding cardiovascular testing volumes at discrete 1-month time points in March 2019, April 2020 and April 2021, while pandemic-related changes occurred continuously and at varying times for Asian countries. Assessment of longer-term trends will be enabled by the forthcoming INCAPS COVID 4 study, which will provide updated data on worldwide cardiac testing several years into the pandemic.

CONCLUSIONS

In this subanalysis of the INCAPS COVID 2 study, we observed a 96% recovery in cardiovascular testing volume in Asia 1 year into the COVID-19 pandemic, similar to the 98% recovery rate in the RoW. The recovery of testing volume was unequally distributed among Asian subregions, with Southern and South-eastern Asia experiencing lower recovery rates of 50% and 80%, respectively, as of April 2021. Rates of recovery varied even more when compared across income groups based on World Bank classification, with the lowest recovery rate of 14% reported among low-income Asian countries. As of April 2021, Asian sites reported larger persistent reductions in the volume of stress ECG, stress PET, TTE, TEE, PET infection studies compared with the RoW. Future studies should assess the clinical outcomes following pandemic-related reductions in cardiovascular testing volume, especially the long-term impacts of reduced testing for IE in Asia. In addition, further studies are needed to better understand the interactions between societal norms, pandemic response policies and income in causing different degrees of health system disruption among Asian countries.

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Contributors KZD, MD, DP and AJE devised the study and wrote the manuscript. LB and KZD performed the data analyses and designed the figures. All other authors contributed equally in data collection. AJE is the guarantor.

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Competing interests SD has received honoraria from Pfizer and GE HealthCare and has received grants to her institution from Pfizer and GE HealthCare. TCV is

a former employee of Elucid Biomining. MCW has given talks for Canon Medical Systems, Siemens Healthineers, GE HealthCare, and Novartis and performed consultancy for FEOPS and Canon Medical Systems. AJE reports receiving a speaker's fee from Ionetix, consulting for W. L. Gore & Associates and Artrya, authorship fees from Wolters Kluwer Healthcare—UpToDate, and serving on scientific advisory boards for Axcellant and Canon Medical Systems USA; his institution has grants/grants pending from Alexion, Attralus, BridgeBio, Canon Medical Systems USA, GE HealthCare, Intellia Therapeutics, Ionis Pharmaceuticals, Neovasc, Pfizer, Roche Medical Systems and W. L. Gore & Associates. None of the other authors reported any disclosures.

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Ethics approval Columbia University IRB AAAT3701 exempted this study from need for informed consent, in accordance with US law and as detailed in the manuscript.

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