SPECIAL REVIEW ARTICLE

Nuclear Cardiology in the Post-COVID Era: What Will Be Its Legacy?

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Abstract

The pandemic of Coronavirus disease 2019 (COVID-19) caused a substantial negative impact on patients with cardiovascular disease. The negative impact of the pandemic on daily clinical practices for cardiovascular diseases (CVD) cannot be underestimated. The CVD patients (without COVID-19 infection), whose diagnosis and treatment have been delayed or postponed by the pandemic, are victims of COVID-19. In this context, COVID-19 is a "syndemic" disease. Several studies already revealed that negative changes already occurred in CVD patient management, such as increased in-hospital death, supply shortage of ^{99m}Tc/^{99}Mo generator, etc. To clarify the impact of COVID-19 on the management of CVD, a global survey named "INCAPS-COVID" was conducted. This study revealed a substantial reduction (around 50%) of cardiovascular imaging practice in the early stage of the pandemic during March and April 2020. This pandemic has necessitated changes in cardiovascular management practices to adopt this condition. Some of those changes will become the legacy of the pandemic. Possible legacy will be; 1) Use of telemedicine; 2) Shift from exercise to pharmacological stress; 3) Shift from single photon emission computed tomography (SPECT) to positron emission tomography (PET). By adapting and changing to the challenges caused by the COVID-19 pandemic, nuclear cardiology will survive and will rise as an improved cardiovascular practice, even after the pandemic.

Keywords: Cardiovascular imaging, COVID-19, INCAPS-COVID, Syndemic
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Coronavirus disease 2019 (COVID-19) is a novel infectious respiratory disease caused by the emerging virus SARS-CoV-2. COVID-19 emerged in Eastern Asia at the end of 2019 (1), and rapidly spread throughout Asia and then worldwide. It is a highly infectious disease with a relatively high mortality rate, which necessitates careful responses (2). Several comorbidities increase the risk of death in patients with COVID-19 (3). Aging and pulmonary disease increases fatality. On the other hand, many researchers identified cardiovascular diseases (CVD) as one of the most significant risks of progression of COVID-19. A meta-analysis showed a nearly three-fold higher risk in patients with than in those without CVD (4).

A critical issue associated with COVID-19 is that although the disease itself has a marked impact on the community, its indirect effects have become equally important worldwide. Due to the high mortality rate and rapid spread of COVID-19 as a contagious disease, the community, society, and government have had to respond and prepare for the waves of increasing infected patients. The medical community is no exception for this. Furthermore, hospitals and medical communities have to maintain medical supplies in preparedness for the anticipated increase of infected patients. Due to its highly contagious nature, the need for personal protective equipment (PPE), medical staff, and expensive resources, such as ventilators and extracorporeal membrane oxygenation (ECMO), is greater than that required for usual infectious diseases. This has had a negative impact on the economy and daily clinical practices in hospitals, including the management of CVD. Due to the indirect effects of the COVID-19 pandemic, it may be regarded not merely as a pandemic, but also as "syndemic" (5).

"Syndemic" was the idea proposed by Singer (6). It is the concept of considering a disease as the synergistic effects of

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the disease itself, co-occurring disease, its impact on the community, and social conditions, such as poverty. The term "infodemic" has frequently been used in journalism during the COVID-19 pandemic, and is a portmanteau of "information" and "epidemic" that means the extensive and rapid spread of a mixture of accurate, inaccurate, and fake information. However, the use of the term "infodemic" in the context of COVID-19 appears to underestimate the severity of the disease itself. Therefore, we employ the term "syndemic".

CVD are the leading cause of morbidity and mortality worldwide in high- and low-and-middle-income (LMIC) countries. The early diagnosis and effective treatment for CVD is continuously improving according to the early and appropriate delivery of a precise diagnosis and effective treatment (7, 8). However, COVID-19 has disrupted the provision of proper medical support to communities. Since 18 million deaths occur annually due to CVD and there have been approximately 8 million COVID-19 deaths worldwide as of August 2020 (9), the negative impact of the pandemic on daily clinical practices for CVD cannot be underestimated. In the "syndemic" context, CVD patients (without COVID-19 infection), whose treatment has been affected by the pandemic, are victims of this syndemic disease. A survey performed in Italy revealed that the number of out of hospital cardiac arrests (OHCA) was markedly higher during the COVID-19 pandemic than in 2019 (10). The findings obtained also showed that the mortality rate increased during the pandemic. A survey that focused on elective surgeries estimated the cancellation of 80% of surgeries for benign diseases, including coronary artery bypass grafting, if the peak of the COVID-19 pandemic continued for more than 12 weeks (11). A multicenter study on ischemic heart disease management reported increases in the number of in-hospital deaths and door-to-door balloon times during the COVID-19 pandemic (12). These findings indicate that the syndemic nature of COVID-19 may nullify extensive efforts for CVD care. Therefore, the lack of sufficient and inappropriate responses to COVID-19 may be detrimental for patients with CVD.

Influence on medical and cardiovascular diagnostic practices

The rapid spread of the COVID-19 pandemic has necessitated adaptations to medical practices (13). The American Society of Nuclear Cardiology (ASNC) and Society of Nuclear Medicine and Molecular Imaging (SNMMI) have issued a joint guidance for best practices during the COVID-19 pandemic (14). It lists not only changes to practices during examinations (such as rapid protocols with minimal contact and the use of pharmacological instead of exercise tests, etc.), but also changes to practices before a patient's arrival (including triage), on arrival (such as screening on arrival), and after examinations (including the use of telehealth). These changes need to be adopted under pandemic conditions, but cannot be achieved without some level of sacrifice. Several global surveys have already been performed and estimated this "sacrifice" on diagnostic practices during the COVID-19 pandemic. In nuclear medicine, a study published in the Journal of Nuclear Medicine surveyed estimated changes in study volumes on diagnostic and therapeutic nuclear medicine practices (15). This survey was performed between April 16 and May 3, 2020, which corresponded to the early stage of the COVID-19 pandemic, and showed decreases in the number of nuclear medicine practices due to the pandemic (54.4% in diagnosis and 45% in therapy). The findings obtained also revealed that declines in positron emission tomography/computed tomography (PET/CT) (mainly for cancer management) were moderate, whereas that in myocardial scintigraphy was very large. These efforts to maintain malignancy management are concordant with the findings of other surveys, which estimated a decline in the number of elective surgeries (11). The survey on elective surgeries also estimated a slight decrease in the number of surgeries for malignant diseases, but marked reductions in those for benign diseases. These studies suggested that medical communities respond to a pandemic by allocating more medical resources to the management of malignant diseases and less to non-malignant diseases, including CVD. The study on nuclear medicine also revealed that the supply of radioisotopes, particularly ^{123}I and ^{99m}Tc/^{99}Mo generators, became insufficient during the pandemic. The delivery of radioisotopes relies on international flights, which have been restricted since the emergence of COVID-19. ^{99m}Tc is an essential radioisotope for nuclear cardiology, and its shortage will have a devastating impact on clinical practices. These "syndemic" effects of COVID-19 will be prominent in the management of CVD.

To more directly clarify the impact of COVID-19 on the management of CVD, Dr. Andrew Einstein and The IAEA Non-invasive Cardiology Protocols Study (INCAPS) group in IAEA conducted an extensive international web-based survey called "INCAPS-COVID" (16–18).

Findings of and lessons to be learned from INCAPS-COVID

INCAPS-COVID was performed in May 2020. It collected information on cardiology practice volumes in March 2019, March 2020, and April 2020 and compared practice numbers before and during the pandemic. This survey also collected descriptors of facilities, the use of PPE, and plans for re-opening. INCAPS-COVID collected information on the actual number of each cardiology practice conducted, which differed from the previously discussed nuclear medicine survey (15),

Table 1 The legacy of changes in nuclear cardiology that will persist after the pandemic

	pre-pandemic	during the pandemic	post-pandemic
Telemedicine	not frequent	increased usage	Will become a legacy of the pandemic
Pharmacological stress test	exercise preferable	Pharmacology preferable	Return to pre-pandemic or become a legacy?
PET for nuclear cardiology	not frequent	shortage in ^{99m}Tc, resulting in a shift to PET	PET becomes more central to nuclear cardiology.

which obtained information on the "estimated" percentage of reductions. Data from 108 countries and 909 facilities were included and analyzed in this survey.

The significant finding of INCAPS-COVID is the substantial impact of COVID-19 on cardiovascular imaging practices and its geometrical/economic variance. Cardiovascular imaging practices showed an overall reduction of 42% in March 2020 and 64% in April 2020 from those performed in March 2019. The cardiovascular imaging practices defined in the study were transthoracic echo (TTE), transesophageal echo (TEE), coronary CT, CT for calcium scoring, cardiac magnetic resonance imaging (MRI), nuclear cardiology practices, including stress myocardial perfusion imaging (MPI) and stress PET, and invasive angiography. The rates of reductions were high in stress studies (45% in March 2020 and 78% in April 2020), indicating that in preparedness for COVID-19, the protective behavior of medical communities resulted in decreases in medical imaging practices for cardiovascular medicine.

INCAPS-COVID also revealed a geometrical difference in responses to the COVID-19 pandemic. Reductions in the volumes of procedures were severe in the Middle East and South Asia (55 and 82% reductions in March and April 2020, respectively). On the other hand, in Eastern Asia, from which the COVID-19 pandemic initially emerged, marked decreases occurred in March 2020 (47% from March 2019), but showed some recovery in April 2020 (35% reduction from March 2019). This recovery was unique to Eastern Asia, it was not observed in other areas. Another important finding from INCAPS-COVID was the disparity in the impact of the pandemic between the different economic levels in each country. When data were divided into low-, lower-middle, upper-middle, and high-income country groups according to the World Bank database, lower-income countries were more likely to show severe reductions in procedure volumes.

Strategies to adopt during the pandemic. What will be its legacy?

The COVID-19 pandemic has necessitated changes in cardiovascular management practices. Some of these changes are positive. Some of those changes are not necessarily negative but can be seen as a positive changes. INCAPS-COVID provided some clues for positive recommendations. Three changes may become the legacy of this pandemic (Table 1).

The ASNC/SNMMI guidance stated that the adaptation of practices during the pandemic needs to include changes to practices before and after examinations. Before arrival, patients must be carefully screened, and imaging tests are only to be performed on those who undoubtedly require them. After examination, patients must be informed of the results of their examination, but it can be performed without face-to-face contact. Telemedicine (or telehealth) is a very beneficial countermeasure to the pandemic. An INCAPS-COVID US sub-study showed that the frequency of telemedicine increased during the pandemic (18). It is a very natural and unavoidable response to this highly contagious disease. However, the use of telemedicine is not merely a countermeasure for COVID-19. Telemedicine was expected to expand the patient friendliness of medicine even before the COVID-19 pandemic, and may continue after the COVID-19 pandemic. Therefore, the expanded use of telehealth will become a legacy of the pandemic (19).

Nuclear cardiology may have one advantage over invasive modalities for the diagnosis of CVD, namely, it provides more protection against infection than exercise ECG, invasive angiography, and endoscopic ultrasound. An exercise or pharmacological stress test may be selected in stress single-photon emission computed tomography (SPECT) MPI. Exercise stress is a more straightforward method to choose for stress-induced ischemia. However, due to the increasing number of elderly/very elderly patients, the pharmacological stress test is being selected more frequently, and this was the case even before the COVID-19 pandemic (7). Since the pharmacological stress test is more patient-friendly than the exercise stress test with similar sensitivity/specificity, this change may be positive. As noted in the ASNC/SNMMI joint guidance and also in the statement from American Society of Echocardiography (14, 20), exercise stress tests should be replaced by pharmacological stress under the pandemic condition. Using the pharmacological stress test under well-prepared conditions, SPECT MPI may be safely performed even during the COVID-19 pandemic. It currently remains unclear whether the accelerated adoption of this preference for the pharmacological stress test will persist after the pandemic.

Another possible trend is a shift from SPECT to PET. PET requires less time to perform than SPECT, which is advantageous for infection management. A reduction in the

time spent in close contact with a patient will be enormously beneficial for medical staff, who are under a constant risk of infection. The delivery shortage in ^{99m}Tc/^{99}Mo was already very disruptive in the nuclear medicine community before the pandemic. Due to this shortage, nuclear cardiology has been gradually shifting from SPECT to PET. The delivery shortage for ^{99m}Tc/^{99}Mo generators during the pandemic has accelerated this change. Due to the combination of these two factors, namely, the benefits of PET for infection protection and the shortage of ^{99m}Tc, the use of PET has increased during the COVID-19 pandemic. Once physicians become proficient in the use of PET, SPECT will become obsolete. Therefore, the shift towards PET from SPECT is another legacy of the pandemic.

Stress MPI itself may become a legacy of the pandemic. Invasive tests, such as coronary angiography (CAG) and percutaneous coronary intervention (PCI), are more hazardous for infection control than other less-invasive tests, including MPI, CT, MRI and echo. The pandemic has necessitated the careful selection of patients requiring invasive testing and treatment. Elective CAG/PCI is more frequently performed in Japan than in other countries, with the rate of elective PCI in contemporary practice being 2-fold higher in Japan than in the United States (21). During the pandemic, the number of emergent CAG conducted in Japan was not markedly affected, whereas elective CAG was more likely to be postponed (22). The necessary reductions in the number of patients undergoing elective CAG/PCI warrant the use of proper screening techniques with evidence. Stress MPI is a well-known screening test for coronary artery disease that prevents unnecessary invasive angiography. Careful screening may not be solely attributed to the pandemic, it was a common requirement even before the pandemic (23, 24). However, the pandemic has enforced the careful screening of patients for CAG/PCI for the management of ischemic heart disease. Even after the pandemic, this will be a strong driving force for the use of MPI before invasive tests.

According to INCAPS-COVID, recovery from the negative impact of COVID-19 is possible. The findings of INCAPS-COVID revealed that the number of cardiovascular diagnostic practices in Eastern Asia markedly decreased in March 2020, but recovered in April 2020. Since COVID-19 initially emerged in Eastern Asia, these findings indicate that with proper responses, medical practices may be quickly restored after the pandemic.

On the other hand, the pandemic is a “pan” demic. Therefore, considerations and responses need to be global, not local. INCAPS-COVID identified many factors, such as PPE shortages and reductions in procedure numbers, that are markedly worse in LMIC than in high-income countries. The increased usage of telehealth in the INCAPS-COVID US sub-study also revealed significant differences in its usage between the US and the rest of the world. A sophisticated measure, such as telehealth, cannot be widely used in low-income countries. These findings indicate the necessity of proper reallocation and support from the global community to heavily impacted countries/societies in order to minimize the global effects of the COVID-19 pandemic.

The COVID-19 pandemic has not yet ended. It is an ongoing event that has exceeded optimistic estimations from last year. INCAPS-COVID has only described the effects of the pandemic on cardiovascular practices in the very early stage of the pandemic. More than one year has passed since the declaration of the pandemic, and medical communities have adopted adequate responds in some areas, but not in others. To assess the long-term influence of the pandemic, the second stage of INCAPS-COVID (INCAPS-COVID-2) is now underway.

Conclusion

The COVID-19 pandemic has had many negative impacts on cardiovascular diagnostic and management practices. However, recovery from the negative consequences of COVID-19 is vital. By adapting and changing to the challenges caused by the COVID-19 pandemic, nuclear cardiology will survive and will rise as an improved cardiovascular practice, even after the pandemic.

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Conflicts of interest

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