



Mini review series: Current topic in Hypertension

Hypertension management before and under the COVID-19 pandemic: lessons and future directions

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Abstract

Hypertension is a significant risk factor for cardiovascular diseases. The prevalence of hypertension and its complications is increasing yearly, yet it remains inadequately controlled worldwide. It has already been recognized that self-management, including self-measured blood pressure monitoring at home, is more important than office blood pressure monitoring. The practical application of telemedicine using digital technology was already underway. COVID-19 has promoted the popularization of these management systems in primary care, although the COVID-19 pandemic disrupted lifestyle and healthcare access. At the beginning of the pandemic, we were at the mercy of information on whether certain antihypertensive drugs, for example, might pose a risk of infection in the face of unknown infectious diseases. Over the past three years, however, much knowledge has been accumulated. It has been scientifically proven that there is no serious problem in managing hypertension in the same way as before the pandemic. That is to control blood pressure mainly through home blood pressure monitoring and continuing conventional drug therapy while modifying lifestyle. On the other hand, in the New Normal era, it is necessary to accelerate digital hypertension management and the establishment of new social networks and medical systems to prepare for the re-emergence of future pandemics while continuing to protect against infection. This review will summarize the lessons and future directions we learned from the impact of the COVID-19 pandemic on hypertension management.

Keywords Hypertension management · COVID-19 · Home blood pressure monitoring · Telemedicine · Digital hypertension

Before the COVID-19 pandemic

Hypertension is a major risk factor for cardiovascular diseases (CVDs). The prevalence of hypertension and its complications is increasing yearly, yet it remains inadequately controlled all over the world. Hypertension treatment and control rates were lower in men than in women in most countries (global control rates were 18% in men and 23% in women respectively) [1]. Only 7% of hypertensive patients are well controlled in China, 27% in Japan, about 40–65%, and relatively higher in South Korea, Canada, USA, and Germany [1–3]. In Japan, a rapidly growing super-aging country, controlling CVDs caused by

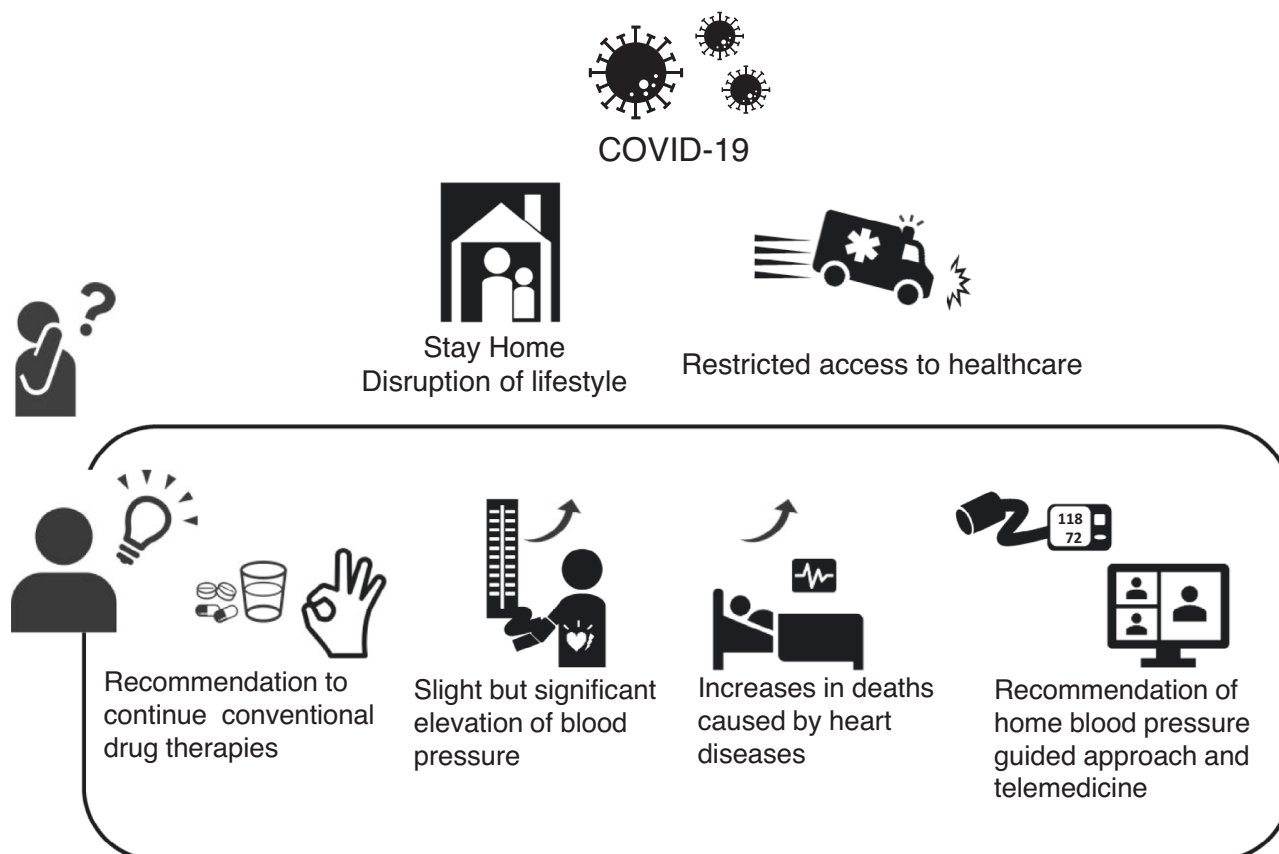
hypertension is an urgent issue, which needs advanced innovations in hypertension care. Hence, the Japanese Society of Hypertension (JSH) has newly established a “Future Plan” to conquer hypertension in 2018 [4]. Three components; medical system, academic research, and social edification were advocated. Hypertension management now and in the future will need to elucidate novel mechanisms, develop more effective treatments and therapeutics, and incorporate new future technologies by using artificial intelligence, big data, and telemedicine via the IoT. Thus, even before the COVID-19 pandemic, the practical application of telemedicine was already underway, but COVID-19 has dramatically changed hypertension management in the structure of primary care delivery. In recent years, national guidelines have emphasized the importance of home blood pressure monitoring in hypertension management, because home blood pressure monitoring has a high potential for improving the diagnosis of hypertension, reduction of blood pressure, and prediction of CVDs. Furthermore, it is useful in the selection of proper therapeutic agents [5]. Management by home blood pressure is even

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Graphical Abstract

The COVID-19 pandemic has disrupted our daily life, restricted access to healthcare, and altered some of the conventional management of hypertension.



more important in the context of limited access to medical care during the COVID-19 pandemic.

Under the COVID-19 pandemic

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) changed the environment surrounding hypertension management dramatically. The COVID-19 pandemic has disrupted our daily life and routine medical care. SARS-CoV-2 is known to be transmitted via Angiotensin-converting enzyme 2 (ACE2) on the cell surface [6]. Since it has been reported in animal studies that renin-angiotensin system (RAS) inhibitors (ACE inhibitor and AT1 receptor blocker) potentially upregulate ACE2 expression, there was concern that RAS inhibitors might promote COVID-19 infection or be associated with the severity of illness in the early phase of the COVID-19 pandemic [7]. However, a subsequent comprehensive review had shown that ACE2 overexpression appears to be a rare rather than common consequence of RAS inhibitors in healthy animals and disease models [8]. And there are

also no clinical reports showing that oral RAS inhibitors make COVID-19 more likely or more severe. In this meaning, there is no clear rationale for changing or discontinuing RAS inhibitors [9–12]. It is now recommended by the various relevant societies that hypertension treatment with anti-hypertensive medication including RAS inhibitors should be continued in accordance with current guidelines [13–15]. Since hypertension is often associated with older age and other cardiovascular risk factors such as obesity, diabetes, and chronic kidney disease in the general population, which may also contribute to the susceptibility to SARS-COV-2 and worsening of comorbidities or mortality, hypertension was consistently reported to be an important risk factor for more severe disease and mortality in COVID-19 patients, however, this has now been ruled out. Although hypertension was comorbid in many COVID-19 patients, subsequent studies have not shown a direct role of hypertension as a risk factor for the SARS-COV-2 infection and COVID-19 outcome, particularly death, when adjusted for age and other comorbidities [16–18]. Differences in viral strains could affect the risk of susceptibility to infection and severity of diseases due to hypertension, and a similar result

reported very recently in 2022 demonstrated no association between preexisting hypertension and in-hospital mortality in COVID-19 patients after appropriate adjustment for confounding factors [19].

At the same time, it was also of great interest to know whether the COVID-19 pandemic has resulted in a worsening of blood pressure control. In the acute phase of COVID-19 infection, the impact of infection on blood pressure is not clear. In patients with moderate to severe COVID-19 who present with cytokine storms, it is very difficult to prove a causal relationship between the viral infection and the blood pressure because a variety of factors affect circulatory dynamics, including mechanical ventilation and associated sedation, repeated inotropic administration, fluid management, fever, hypoxia, inflammation, ischemia, vasculitis, and dehydration. COVID-19 infection is a CVD risk in COVID-19 survivors in the subacute or chronic phase, but the mechanisms or the association between COVID-19 and the development of CVDs in the post-acute phase of the disease are not entirely clear. Further efforts are needed to elucidate the mechanisms, which are presumed to include viral infection of myocardial cells, endothelial damage, abnormalities in the coagulation system, microvascular damage, downregulation of ACE2, dysregulation of the renin-angiotensin-aldosterone system, and autonomic nervous system damage [20]. It was reported that Ang II levels were significantly higher in elevated blood pressure groups and concluded that RAS plays a major role in hypertension and COVID-19 infection [21]. Flow-mediated dilation (FMD) is a noninvasive tool to identify endothelial dysfunction by changes in brachial artery diameter in response to ischemia through ultrasound. Pulse wave velocity (PWV) including brachial-ankle pulse wave velocity (baPWV) and carotid-femoral pulse wave velocity (cfPWV) is indices of arterial stiffness. The result of a systematic review of the association between COVID-19 infection and vascular function determined by FMD and PWV implied that COVID-19 infection impairs vascular function, and exacerbates arterial stiffness and these effects persist after COVID-19 recovery [22]. The detailed mechanisms of how COVID-19 affects blood pressure through inflammation, sympathetic nervous system dysregulation, RAS activation, and even organ or vascular damage are unknown. In fact, clinical evidence of whether COVID-19 infection causes the new onset of hypertension is still lacking. A few studies demonstrated that COVID-19 infection leads to increase BP and causes new onset hypertension [23, 24]. Most studies were retrospective cohort and single-arm studies, and further investigations are needed.

COVID-19 pandemic may also have resulted in a worsening of blood pressure control since it has restricted access to healthcare for hypertensive patients and altered

their lifestyles (worsened eating habits, decreased exercise habits, and increased obesity) due to a life of self-restraint. The refraining of individuals from participating in social activities during the COVID-19 pandemic has also had a negative impact on mental health that may lead to the worsening of hypertension management. In the USA, there have been marked increases in deaths caused by ischemic heart disease and hypertensive heart disease but not in heart failure and CVDs during the early onset of the COVID-19 pandemic compared to before the pandemic [25]. On the other hand, delayed diagnosis of health conditions, hospitalization, and urgent coronary revascularization rates in patients with acute coronary syndrome were markedly decreased [26–28]. In addition, the COVID-19 pandemic was associated with a significant and abrupt reduction in diagnostic testing related to cardiovascular and hypertensive diseases during the first year of the COVID-19 pandemic [29, 30]. These findings suggested that the refusal or refrain from hospitals and delays in examinations and diagnosis during the COVID-19 pandemic may have indirectly contributed to the increase in the number of fatal CVD cases outside of hospitals [31]. In Japan, blood pressure increased by approximately 1–2/0.5–1 mmHg due to the COVID-19 pandemic [18]. This result was similar to that reported from the USA [32]. Although the increase in blood pressure is slight, it is a population-wide increase and can have a significant prognostic impact, including the development of cardiovascular complications. Blood pressure elevations were greater in women than in men, suggesting that the pandemic placed greater psychological stress on women [33]. These findings are consistent with previous reports that disasters increase the risk of hypertension and CVDs [34, 35]. COVID-19 outbreak is truly a global catastrophe and should be closely monitored for further developments. Many patients with hypertension not only in Japan but also throughout the world were rapidly shifted to online or telephone-based assessment and management [36]. The home blood pressure-guided approach and making good use of the telemedicine are widely recommended [14, 37, 38].

The “New Normal” after COVID-19 pandemic

In Japan, the environment surrounding hypertension treatment has changed dramatically with the COVID-19 pandemic, while a new way of hypertension treatment in the near future was already being explored, as described in the “Future plan” published by the Japanese Society of Hypertension in 2018. Although there was a great deal of controversy at the beginning of the pandemic, as noted above, it is now believed that the presence of hypertension or the prescription of certain antihypertensive medications does not pose a risk of COVID-19 infection or a risk of

worsening prognosis. The basic approach for hypertension management, which is to set antihypertensive goals based on home blood pressure according to age and comorbid diseases, modify lifestyle habits, and use conventional drug therapy mainly with RAS inhibitors, calcium channel blockers, and antihypertensive diuretics to prevent the onset of cardiovascular diseases, also remains unchanged. In fact, there is no need to revise the direction in which the “Future Plan” is targeting in the big picture. During the pandemic, actions to prevent infection were of utmost importance, and people were required to refrain from social activities such as visiting doctors and going out, which inevitably led to a major change in lifestyle. In this context, the introduction of online medical care and medical support using smartphone applications, which had been promoted over the years, has also dramatically accelerated. Three years have finally passed since the beginning of the COVID-19 outbreak, and normal pre-pandemic social activities have gradually resumed, but even if the outbreak is contained in the future, it is unlikely that medical practices will be completely the same as they were before the COVID-19 outbreak. Health maintenance efforts must take into account adaptation to the “new lifestyle,” or the “New Normal,” while striking a balance between taking measures to prevent infection, and at the same time maintaining individual access to medical care and activity. In particular, older people, who have many comorbidities and are at high risk of serious illness, are the most vulnerable not only during the COVID-19 pandemic but also under the New Normal. They lost the opportunity to receive appropriate medical care despite the worsening of their chronic diseases, and the quality of treatment for chronic diseases deteriorated further as a result of prolonged hospitalization and repeated hospital transfers due to the infection, which forced them to leave their traditional living environment and medical care. In the New Normal, the effective use of digital technologies, including online medical services and smartphone applications, which are expected to have the potential to fundamentally solve these problems, is of utmost importance. Telemedicine,

which until now has only been a complementary service to outpatient care, may in the future be established as a form of medical care that differs from inpatient, outpatient, and home healthcare (Fig. 1). Meanwhile, the usefulness of digital devices should be demonstrated more in older people, who have many problems during the pandemic, but ironically, there are also digital literacy problems: older people are less familiar with digital devices.

Challenges emerging in the use of digital in healthcare

During the COVID-19 pandemic, medical institutions were forced to suspend or reduce outpatient services due to a rapid increase in the number of patients and infection control efforts, and telemedicine attracted attention and expanded its use around the world. As an emergency response, telemedicine has been rapidly deregulated and available in countries where its use had been slow to spread due to legal and regulatory obstacles. But whether it will continue to spread in the future remains to be seen. In Japan, insurance coverage for telemedicine for chronic diseases was approved as a temporary special exception in April 2020. However, according to the White Paper on Information and Communications published by the Ministry of Internal Affairs and Communications in 2021, the penetration rate of telemedicine in Japan only increased from about 5 to 15% before and after the COVID-19 pandemic. The COVID-19 pandemic may have been a catalyst for the spread of telemedicine, but there are many problems that need to be solved for telemedicine to continue to spread.

In Japan, reading, writing, and abacus skills are high by global standards, but on the other hand, digital literacy, which includes not only the ability to operate digital tools but also the ability to identify and solve problems using digital tools, is considered significantly lower than in Western countries. The importance of improving access to health care and digital literacy, especially for older people

Fig. 1 Telemedicine is not just a complementary but can be an alternative to outpatient care

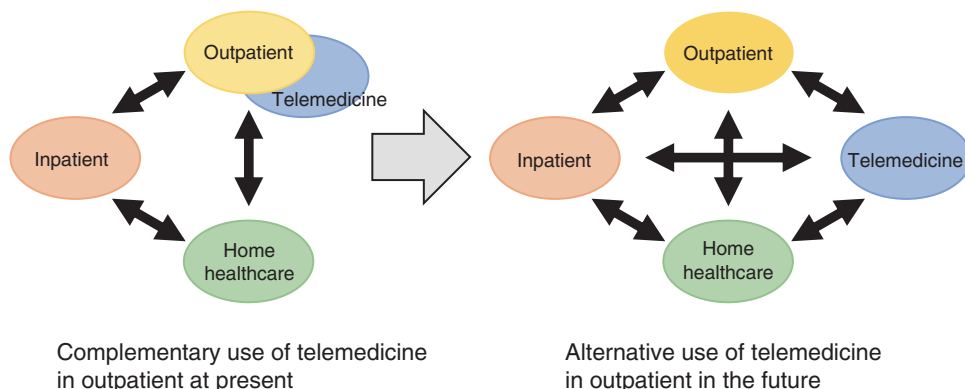
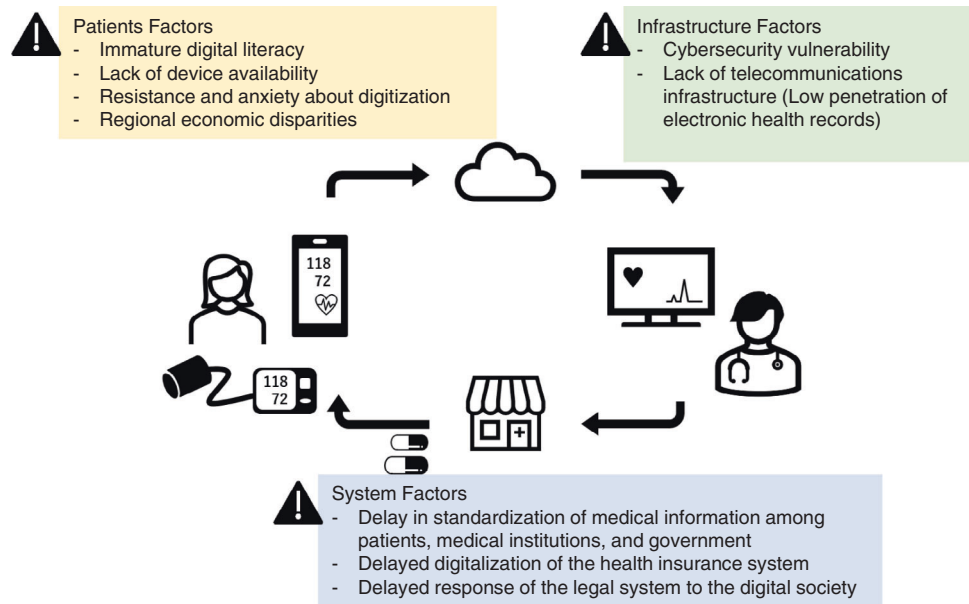


Fig. 2 Hypertension management in digital era and inherent problems with patients, infrastructure, and systemic factors



and the economically and geographically disadvantaged, has already been noted in order to actually reduce health disparities [39].

Rapid digitization was promoted throughout society during the COVID-19 pandemic, but this was accompanied by the emergence of more serious challenges in various aspects to realize a digital society. In Japan, the White Paper on Information and Communications in 2021 by the Ministry of Internal Affairs and Communications lists the following factors hindering digitalization: Factors on the user side: (1) immature digital literacy in an aging society and lagging digital education, (2) problems with the spread of devices (ICT tools such as smartphones, tablet PCs, and applications), (3) resistance to digitization and anxiety about privacy leaks against the backdrop of practices such as procedures based on written documents, (4) disparities due to geographical and economic conditions. Social infrastructure and technological factors, (5) vulnerability of information security such as personal information protection, (6) inadequate development of communication infrastructure and securing communication environment. Other social system factors included (7) Inadequate management system or platforms for safe and secure digital information (data collection, sharing, analysis, and storage), (8) the legal system is not yet ready for digitalization, and (9) the insurance and medical systems are lagging behind in responding to digitalization (Fig. 2). The main approaches to improve digital health literacy are (1) digital education in schools, (2) reeducation of patients and healthcare professionals, (3) expansion of digital education programs for older people, as well as (4) efforts to dispel anxiety as much as possible, (5) provision of digital services that make people want to actively use them, and (6) encouragement

from family members and other familiar figures, healthcare professionals, and others.

In controlling chronic diseases such as hypertension, it is important to improve adherence to outpatient visits and medication, including preventing patients from dropping out of outpatient visits and making them more aware of their disease. Telemedicine and home blood pressure remote monitoring systems are expected to play an important role in this regard [40–42]. It was reported that lifestyle modification using a hypertension management application on mobile devices in the HERB-DH1 pivotal trial was effective in promoting behavioral change that resulted in antihypertensive treatment in Japan [43]. This trial was novel in that it was the world's first multicenter randomized controlled trial of a therapeutic application for regulatory approval in the field of hypertension. On the contrary, the use of smartphone-based management of hypertension in the follow-up of patients with myocardial infarction did not have an effect on improved blood pressure control in the Netherlands [44]. A systematic review of the effectiveness of smartphone apps in hypertension management found mixed results across trials and may be influenced significantly by national characteristics, culture, and living and digital environments [45]. There is still a need to accumulate evidence on the usefulness of digital technology in health promotion and disease prevention/treatment, and digital healthcare is still in the process of development as an academic field. It is expected that the establishment of appropriate evaluation methods for digital healthcare services and research on whether interventions using digital tools for lifestyle-related diseases, such as hypertension, can change behavior and prevent development and progression of diseases, will be strongly promoted in the future.

Compliance with ethical standards

Conflict of interest The authors declare no competing interests.

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