The Impact of the 2017 American College of Cardiology/American Heart Association and the 2018 European Society of Cardiology/European Society of Hypertension Guidelines on the Asian Population: Is it Time for Our Own Asian Hypertension Guidelines?

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Abstract

Hypertension (HTN) remains to be the single most important risk factor for the development of cardiovascular disease worldwide. Moreover, the global burden of disease is expected to rise even more in the coming years due to the obesity epidemic and the aging population. However, control rates of high blood pressure (BP) remain low. The American College of Cardiology/American Heart Association 2017 Guidelines and the European Society of Cardiology/European Society of Hypertension 2018 Guidelines have different thresholds and targets, with the US guideline “redefining” HTN to a new lower level, while the European guideline remains unchanged from its previous levels. There is now emphasis on proper BP measurement for accurate initial diagnosis, and the use of home and ambulatory BP monitors is encouraged to ensure strict 24-h (morning and evening) BP control. Lifestyle modifications are encouraged, especially in the elderly who are more responsive to salt restriction. Asian characteristics of HTN warrant further study. Enhanced salt sensitivity, high dietary salt intake, aging population, and obesity are just some of the different characteristics of Asian HTN. More importantly, stroke is a more common consequence of uncontrolled HTN in Asia (compared to coronary artery disease), with hemorrhagic stroke having a relatively higher prevalence. Hence, lower BP targets are needed since BP levels correlate more linearly with stroke. China, Japan, Taiwan, and Korea have come up with published guidelines, highlighting some key points and difference with the US and European guidelines. The Philippine Society of Hypertension also previously came out with the “140/90 Report,” locally attuning foreign guidelines. Several years back, there has been a call for the development of our own Asian HTN guidelines. With newer findings on the benefits of lower BP targets/goals and its possible benefits to the Asian population and more findings on the different Asian characteristics of HTN, it might be the best time now to heed that call.

Key words: American college of cardiology/americian heart association hypertension guidelines, asian hypertension guidelines, european society of cardiology/european society of hypertension guidelines, philippine society of hypertension

Introduction

Hypertension (HTN) remains to be the single most important risk factor for the development of cardiovascular (CV) disease, leading to premature death worldwide. It is said to be the most common, readily identifiable, and reversible risk factor for myocardial infarction, stroke, heart failure, atrial fibrillation, aortic dissection, and peripheral arterial disease, as well as chronic kidney disease and cognitive decline. The global burden of HTN is projected to rise even more in the future.
coming years due in part to the obesity epidemic and the aging population. Moreover, yet, despite its high prevalence and its associated deleterious effects on various organ systems of the body, treatment remains inadequate in majority of patients, and control rates remain low.\textsuperscript{[1,2]}

One area of concern with regard to HTN treatment is the control rate. Despite the availability of effective antihypertensive medications, and despite more aggressive campaigns to detect and treat HTN, control rates still remain low.\textsuperscript{[3]} Back in 2009, the term “HTN paradox” was used to describe the situation, wherein there is more uncontrolled disease despite improved therapy. It is paradoxical that despite the various therapeutic advances proven in clinical trials, the number of people with uncontrolled HTN has continued to rise. In part, a critical factor in this increase is the failure to adopt healthy lifestyles, which must be addressed more urgently. Other possible reasons for the low control rates might be poor management of elevated systolic blood pressure (BP).\textsuperscript{[4]} This might be due to poor compliance/adherence to medications and lifestyle modifications. Some authors blame physician inertia (or therapeutic inertia) as a cause of poor management of elevated BP.\textsuperscript{[5-7]}

The Joint National Committee (JNC) on Detection, Evaluation, and Treatment of High BP published its first report back in 1976.\textsuperscript{[8]} It was intended to give recommendations to help physicians who care for hypertensive patients achieve better results in prevention and management of HTN. Since then, these guidelines have been widely used by primary care physicians, who are the ones who handle the majority of hypertensive patients, and it has greatly improved the management of HTN since its introduction. Aside from JNC, the other two most commonly used guidelines are from the European Society of Cardiology and the National Institute for Health and Clinical Excellence (NICE) guidelines from the United Kingdom.

HTN guidelines such as the JNC provide recommendations for the prevention, detection, evaluation, and treatment of HTN, which aims to provide the greatest benefit to patients with the least amount of harm. It usually includes the best evidence available at that time. In 2014, the JNC passed on the responsibility of making HTN guidelines to the American College of Cardiology/American Heart Association (ACC/AHA), and 3 years later, in 2017, the ACC/AHA came up with a new set of guidelines which effectively “redefined” HTN. It was totally different from previous guidelines due to the lower threshold and targets. The following year, in 2018, the European Society of Cardiology/European Society of HTN (ESC/ESH) followed suit and came up with a much-awaited update to their own guidelines.

The recent change in HTN guidelines by the ACC/AHA in 2017, with its redefinition of HTN to a lower BP level of 130/80, has generated a lot of buzz in the medical world. In an article written by Poulter et al., for the International Society of HTN, they stated that these guidelines have many laudable recommendations but some, particularly the redefinition of the HTN threshold, are somewhat controversial.\textsuperscript{[9]} Indeed, the new BP classification with lowered BP thresholds and targets promptly attained great attention and controversy worldwide.\textsuperscript{[10]}

By coming up with a new diagnostic threshold and new therapeutic targets, it effectively introduced the concept of early treatment. Early detection of elevated BP and early management through non-pharmacologic/lifestyle modifications, pharmacologic treatment, or both can possibly delay the progression of HTN and in the long run promote CV protection and also minimize target organ damage. It was considered a shocking change because some of the evidence used were based on epidemiological evidence. On a positive note, the new guidelines emphasized the use of appropriate technique for BP measurement, which was discussed at length. Using the proper blood pressure equipment (especially correct sized BP cuffs) and using the proper technique for measurement (patient rested and seated quietly, feet flat on the floor, BP cuff at same level with the heart) invariably leads to an accurate diagnosis of hypertension. The guidelines strongly recommended the use of out-of-office BP measurements such as 24-h ambulatory BP monitoring (24-h ABPM) and home BP monitoring (HBPM). These are best used for white coat HTN, masked HTN, and nocturnal measurements to check for dipping. The use of CV risk stratification was reintroduced, which will help in deciding whether to use antihypertensive medications or not, especially in those with Stage I HTN, based on the patient’s 10-year CV risk profile. Screening for secondary HTN was also recommended.\textsuperscript{[11]}

Evidence to support the lower BP threshold of 130/80 mmHg came from two recent publications, the Systolic BP Intervention Trial (SPRINT) and the 2016 Lancet meta-analysis of randomized controlled trials (RCTs) of antihypertensive medications. The Lancet meta-analysis showed benefit in prevention of CV events with a BP reduction of 25%, while SPRINT, through the use of unattended automated office BP monitoring, yielded BP values 10–15 mmHg lower than routine clinic BP. Hence, the achievement of a systolic BP of 120 mmHg is postulated to be equivalent to 130–135 mmHg by routine clinic measurement. Recognizing the difference in the manner of BP measurement techniques, a BP value of 130/80 mmHg was deemed reasonable for use as both BP threshold and BP target. The core concept of earlier and tighter BP control is deemed to provide more sustained target organ protection and CV disease prevention. Strict BP lowering early in life is said to maintain vascular health, which is important later on in life as the patient ages. Focus was shifted to a practical approach through the use of HBPM which can help in determining efficacy of drug management when measured at trough levels early in the morning. Checking the BP in the clinic, at home, and the occasional use of ABPM will also help improve detection and management of white coat and masked HTN.\textsuperscript{[12]}

The central controversy in the 2017 ACC/AHA Guidelines revolves around the new lower levels of 130/80 mmHg, thereby increasing the prevalence of HTN and diagnosing more hypertensive subjects <65 years old. Along with this concern was the increased number of patients getting medication. However, as explained by the authors, therapy will only need

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In a commentary in the International Journal of Preventive Medicine AK Gupta said that, with the exception of the NICE guidelines, none of the existing HTN guidelines at that time took into account phenotypical characteristics such as race, age, obesity, and plasma renin activity. Racial differences, leading to differing responses to different classes of antihypertensives, include those who are of African American descent, who have higher salt sensitivity and low plasma renin activity, and South Asians with a higher prevalence of central obesity and insulin resistance, with HTN driven mainly by high sympathetic activity. African Americans respond better to CCBs and diuretics, while Asians fare better with angiotension-converting enzyme inhibitors.[17]

Ernesto Schiffrin, MD, from McGill University in Montreal, emphasized that ethnicity may affect an individual’s response to treatment, and instead of universal application, stressed that guidelines should be adapted to the local setting. Likewise, George Bakris, MD, from University of Chicago Medicine, stated that culture and location must be considered in the interpretation of clinical trial data, so it is not a one-size-fits-all proposition. This is the reason why Japan requires that studies in Japanese people should be done before guidelines are accepted.

In 2015, Jeong Bae Park, MD, from Cheil General Hospital/ Dankook University College of Medicine, stated the need for Asian guidelines on HTN, enumerating various characteristics of Asians and Asian HTN, namely rapid aging of their societies, a high prevalence of metabolic diseases constituting a “metabolic pandemic,” due in part to adoption of Western lifestyles, high salt intake in diets despite various efforts by their own governments, and a relatively high risk of stroke compared to coronary artery disease, with a stronger relationship between BP level and stroke (compared to Westerners).[18]

Back in 1979, Dr. Ramon F. Abarquez, Jr., founder of the Philippine Society of HTN (PSH), was the first one who pushed for the treatment of HTN starting at a level of 140/90 mmHg, which was then still considered by international experts as normal BP. At a time, when HTN was still defined as a BP of 160/100 or higher, Dr. Abarquez and his team at the University of the Philippines-Philippine General Hospital presented a paper showing that at a level as low as 140/90 mmHg, there were already abnormal changes in the heart and arteries of the individual.[19]

To date, the following countries have published their own guidelines on hypertension: China (2011), Korea (2013), Japan (2014) and Taiwan (2015, with focused update in 2017). The Philippine Society of Hypertension launched their own guidelines in 2012, called the Philippine Clinical Practice Guidelines (CPG) on the Detection and Management of Hypertension (also called “140/90 Report: MultiSectoral Task Force Consensus on Hypertension”), which is due for update anytime soon.[20]

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to be initiated in only a small percentage more, because at the lower BP levels in Stage I, pharmacological treatment only needs to be initiated for those with high CV risk. This will not significantly affect cost-effectiveness ratio. From the clinical point of view, patients who are detected early will benefit with closer and earlier follow-up, and in the future, earlier initiation of antihypertensive medications will prevent HTN-mediated organ damage (HMOD).[13]

Probably as a result of the controversy, the 2017 ACC/ AHA Guidelines effectively increased the awareness with regard to importance of elevated BP as a cause for CV morbidity and mortality throughout the world.[9] Suddenly, people all over the world started talking about their BP levels and their CV risk profile. It effectively forced people to take charge and be in control of their BP. One author puts it quite nicely: Changing the cutoff values for HTN diagnosis might be an important way to force patients to follow-up with their doctors, and persuade them to change their lifestyle and use non-pharmacologic methods to reduce BP and thereby prevent, protect from, or delay onset of HMOD.[13] However, caution should also be exercised because inappropriately labeling people as hypertensives might cause undue anxiety, or there might be unnecessary antihypertension medications that will be given to younger people who are low risk.[9]

Last September 2018, the ESC/ESH came out with an update to their own HTN guidelines. In general, the European guidelines are more conservative, using the same traditional BP categories from their previous guideline, thereby using a higher threshold for Stage 1 HTN defined as office BP values of 140–159/90–99 mmHg compared to the 2017 US guidelines. This is actually based on evidence from multiple RCTs showing clearer benefit with higher thresholds. Like the US guidelines, it also recommends lifestyle interventions, as well as regular use of HBPM, with ABPM as an option.[14] Based on the guidelines, it is recommended that treatment be initiated with a two-drug single-pill combination treatment, except in the low-risk, the frail, and very old hypertensive patient. This is meant to enhance compliance and control rates. Likewise, simple algorithms replaced complicated guidelines for primary care physicians who see majority of patients. Traditional BP categories were maintained, primarily due to clearer benefits from RCTs using these thresholds. Finally, in contrast to the American guidelines, the European guidelines are not as aggressive in lowering target BP to reflect SPRINT data.[15]

Recognizing the difference in recommendations and the level of evidence used in these guidelines, the concern was shifted to implementation of these same guidelines at the last year’s Annual AHA Convention. Taking into account differences in genetics, race, diet, etc., the more important question now is if these guidelines could apply to other populations.[16] Some Asian countries, namely China, Japan, Korea, and Taiwan, recognizing differences in genetic makeup, lifestyle, diet, etc., adapted some of the recommendations from the previous US and European guidelines and tried to modify it to suit the needs of their specific countries.

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on a possible common hypertension guidelines for Asia. At that time, there was increased prevalence of hypertension in China but awareness and control rate remain unchanged. Such an increase was brought about by an increase in the elderly population, and also abrupt changes in lifestyle like high salt, sugar, fat and calories in the diet, plus low physical activity and increased anxiety and stress in work. The Korean guidelines identified sodium reduction as the most important lifestyle change needed to help curb HTN. The risks for cerebrovascular disease and coronary artery disease (CAD) were highest in Korea. Their guidelines classified pre-HTN further into Stage 1 and Stage 2 prehypertension based on office BP because they have shown that CV risks are significantly different in both stages. The Japanese had the highest intake of salt in the diet, coupled with genetically high salt sensitivity. They also recognized the higher prevalence of stroke in Asian hypertensives (vs. CAD in Caucasians), and the steeper association between level of BP and stroke, such that they emphasized the importance of strict 24-h BP control, taking into account both the morning BP surge and nocturnal BP increase. They were one of the first to advocate the use of HBPM in the Ohasama study. Likewise, it was recommended that obesity and related metabolic syndrome should be addressed by lifestyle modifications. The Taiwanese guidelines recommend the use of both traditional office BP measurements and unattended automated office BP measurements (AOBPM) and, in 2017, revised their BP treatment targets to more intensive levels. Using intensive BP strategies will benefit a large group of hypertensive patients and with aggressive BP targets foresee that CV events in Taiwan will substantially decrease. The use of AOBPM is recommended for intensive BP targets, with HBPM as surrogate.

Differing characteristics of Asian HTN underscore the need for HTN guidelines developed specifically for the Asian population. The rapidly aging population, prevalence of obesity and metabolic syndrome as a consequence of adoption of Western lifestyle, high salt intake, and the different stroke/CAD profile represent major differences compared to Western hypertensives. Stroke, especially hemorrhagic stroke, and non-ischemic heart failure are commonly seen in Asia as a result of HTN, with a stronger association between BP levels and stroke. This might be related to early morning BP surge and to high sodium intake. Higher salt sensitivity due to salt-sensitive gene polymorphism of the renin-angiotensin system also plays a role. Strict 24-h BP control is, therefore, important in Asia, and a practical step for strict control on an individual level is HBPM. To better understand the management of HTN in Asians, more clinical studies should be done to investigate Asian characteristics of HTN.

In summary, the recent change in diagnostic threshold and treatment targets of the US guidelines might benefit the Asian hypertensive more than the European guidelines. Considering that stroke is the more common sequelae of HTN in Asians, a lower target will definitely benefit them more since stroke and BP exhibit a linear relationship. Strict BP control for the whole 24-h will also be beneficial, and this can be achieved by checking home BP, as recommended by both the US and European guidelines. The early morning BP surge as well as nocturnal HTN will be detected early and appropriate treatments given early, too. Salt plays a major role in causing HTN in Asians, who have high salt intake in the diet aside from higher salt sensitivity. In this regard, elderly patients have been shown to respond well with salt restriction, although younger hypertensives and even those without HTN will benefit from salt restriction. People who are diagnosed to have Stage 1 HTN will benefit from lifestyle modifications, and with regular follow-up, the transition to higher levels of BP will be detected early; hence, medications can be started early depending on the CV risk of the individual. However, cost-effectiveness of such a strategy is subject to debate. Increased awareness is the key to earlier detection, prevention, and management.

Several years back, there has been a call for the development of Asian HTN guidelines, considering the differences in clinical phenotypes of HTN, and response to treatment. Now might be the best time to heed that call.

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