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Editorial

# Coronary artery calcium score to guide hypertension therapy!

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Hypertension is the most prevalent non-communicable disease, estimated to affect 1.13 billion individuals nowadays. It is the leading preventable cause of mortality worldwide and a major risk factor for coronary artery disease, heart failure, stroke and chronic renal diseases in developed and developing countries [1,2]. Worldwide, the aging population, decreased fitness and obesity epidemic have contributed to the increased prevalence of hypertension [3]. Given that, it poses a significant health and economic challenge to both developed and developing countries [2].

The definition of hypertension was widely accepted till 2017, when new guidelines for the treatment of hypertension were released by the American heart association and American college of cardiology (AHA/ACC). For the first time, there was a disagreement between cardiac scientific societies in regards to the definition of hypertension. While the new guidelines adopted a lower threshold for definition of hypertension (SBP of 130 mmHg–139 mmHg or and diastolic BP (DBP) of 80 mmHg–89 mmHg) [4], the European Society of Cardiology (ESC) retained the old definition (SBP of 140 mmHg–149 mmHg or and DBP of 90 mmHg–99 mmHg) [5]. The new AHA/ACC guidelines led to a significant increase in the prevalence of hypertension, particularly among young subjects. Thus, the prevalence of hypertension is expected to reach 3.5 billion people [6] if this new definition is applied.

Given that, clinicians globally are now facing two sets of guidelines when individualizing management goals for their patients. In addition, there is randomized clinical trial data suggesting that treating to lower targets is associated with lower event rate. The SPRINT (Systolic Pressure Intervention Trial) tested the hypothesis that treatment to a systolic blood pressure (SBP) goal $< 120$ mm Hg (intensive treatment) in patients $\geq 50$ years of age is superior to a target SBP $< 140$ mm Hg in reducing myocardial infarction, acute coronary syndrome, stroke, acute compensated heart failure, or death from cardiovascular causes [7]. Patients in the intensive-treatment arm had a 25% lower incidence of the primary outcome and a 27% reduction in all-cause mortality. However, there were some increases in some of the adverse events including acute renal failure. A *post-hoc* analysis of the SPRINT trial showed that stratification of the SPRINT population may identify a group which could benefit the most from intensive treatment while having the least side effects [8]. Patients with lower baseline 10-year CVD risk had more harm than benefit from intensive treatment, whereas those with higher risk had more benefit. However, several studies have shown that the risk score may overestimate patients' risk [9]; thus, better tools may be needed to better identify those patients who may benefit the most from the intensive therapy.

Coronary artery calcium (CAC) score is a direct measure of subclinical atherosclerosis [10]. It is widely available and can be done with low radiation exposure [11]. It has been extensively studied and adopted in contemporary cardiac practice including the new prevention guidelines [12]. The low cost, reproducibility across various vendors and the ease at which it can be obtained, make CAC scoring a very attractive tool for risk stratification [13]. Multiple large-scale studies demonstrated the independent value of CAC prognosis and risk reclassification of coronary artery disease as well as outcomes. A CAC score of zero confers a very low risk of future cardiovascular events including death, myocardial infarction and stroke, and the risk increases with higher CAC score, particularly CAC score $> 400$ [14]. However, it is unclear how often patients recommended for intensive hypertension therapy have detectable CAC.

In this issue of *Atherosclerosis*, Kang et al. present an interesting study of the burden of subclinical atherosclerosis measured by CAC score in a large population of otherwise healthy young Korean adults [15]. In this large cohort of more than 96 thousand subjects, predominantly males, the authors demonstrated an independent association between systolic BP and CAC even in patients without hypertension irrespective of age or risk category. The association between BP and CAC score persisted in young subjects (20–39 years) and low-risk groups (estimated 10-year cardiovascular risk of 10%). The same association was found between AHA/ACC 2017 blood pressure categories and CAC in patients with hypertension.

The authors should be congratulated for putting together this large cohort of young patients who underwent CAC imaging. These patients are mostly considered normotensive by the prior guidelines, but a significant proportion would be re-classified into prehypertension or hypertension using the new ACC/AHA guidelines. Most patients ($> 90\%$) in the non-hypertensive group have low cardiovascular risk score $<$

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10%. Similarly, most of the non-hypertensive patients (> 75%) had zero calcium score. These patients are known to have low event rates, even in the presence of symptoms. Using the ACC/AHA guidelines to treat these patients aggressively will result in overtreating a cohort who has been documented many times to have a low event rate. However, reserving the intensive treatment to only patients with CAC would be associated with a targeted treatment of a group that is known to have higher event rate and thus would draw higher benefit of intensive therapy.

However, the study has some limitations, including the inclusion of a patients from single ethnicity which makes the findings not generalizable to the general population. The included group is relatively younger and healthy (compared to other primary prevention cohorts) with low rates of obesity and metabolic syndrome. Two other studies examined the association between high BP readings according to the 2017 AHA/ACC and cardiac outcomes in young adults. When participants of CARDIA study (mean age of 35 years) were categorized according to the new AHA/ACC guidelines, stage 1 hypertension was associated with an almost 2-fold increase in cardiovascular events including coronary artery disease, heart failure, stroke and peripheral artery disease [16]. Another investigation by Son et al. from Korea also studied more than 2.5 million Korean subjects (median age of 31 years) using the new AHA/ACC guidelines, reporting an independent increased risk of cardiovascular death with stage 1 hypertension [17]. However, the rate of cardiovascular events in both studies was relatively low making the number needed to treat to prevent an event very high.

Another limitation of this study is the lack of outcomes data. Thus, this data cannot be used to support the hypothesis that CAC score can be used to guide intensive hypertension therapy. However, recently presented data from the CAC Consortium [18] included 5163 were SPRINT-eligible (age > 50 years, Framingham Risk Score > 15%, and no diabetes mellitus) patients would support this hypothesis. Over a mean follow-up of 11.6 ± 3.6 years, there were 409 cardiovascular deaths [19]. A CAC score of 220 was associated with the age-standardized cardiovascular mortality rate observed in SPRINT. Additionally, increasing CAC scores were associated with increased cardiovascular mortality suggesting that CAC could risk stratify adults with hypertension.

A similar approach was used to determine whether CAC can guide statin therapy for primary prevention. In a large registry of almost 17 thousand patients considered for primary prevention, the presence and extent of CAC score successfully identified patients who will benefit from statin therapy. Patients with CAC score > 100 had significant reduction of MACE with statin, while patients with CAC = 0 had no benefit [20]. In fact, the most recent AHA/ACC guidelines on the management of blood cholesterol advocate the use of CAC score to determine statin therapy in patients with intermediate 10-year risk [12].

The work of Kang et al. paves the road for the use of CAC scoring in individualizing hypertension therapeutic goals when treating patients with hypertension. Like the primary prevention story with statins, CAC may help identifying patient who may benefit of intensive blood pressure control and hence my help reconcile the BP target differences between AHA/ACC and ESC. Further outcome studies are needed to support the use of such approach. Until such studies are available, CAC remains a promising discriminator to adopt either set of guidelines when tailoring care of hypertensive patients.

## Conflict of interest

The authors declared they do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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