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Editorial Commentary

Cardiac Benefits of an Intensive Blood Pressure Control in Diabetes Mellitus

Paolo Verdecchia, Fabio Angeli, Gianpaolo Reboldi

In the current issue of Hypertension, Soliman et al1 present a post hoc analysis of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. The analysis compares the 2 groups randomized to an intensive (<120 mm Hg) or standard (<140 mm Hg) reduction in systolic blood pressure (SBP) in the changes of left ventricular hypertrophy (LVH) diagnosed by standard ECG. LVH was diagnosed by a Cornell voltage (RaVL+SV3 amplitude) >2200 μV in women and >2800 μV in men and also by using the Cornell voltage as a continuous variable. Over a median follow-up of 4.4 years, the risk of LVH was 39% lower (P=0.008) in the intensive than in the standard SBP arm. The median Cornell voltage during follow-up was significantly lower in the intensive than in the standard SBP arm (P<0.001). Not only was LVH regression more common but also the new development of LVH less frequent (P<0.001), in the former group.1 The greater reduction in the Cornell voltage went in parallel with the greater reduction in BP in the more intensive SBP arm, supporting the notion of a quantitative biological gradient (ie, dose–response relationship) between the extent of BP reduction and the amount of LVH regression.2

These findings are consistent to those obtained in another randomized study that compared an intensive (<130 mm Hg) with a standard (<140 mm Hg) BP goal in hypertensive patients without diabetes mellitus.3 Risk of ECG LVH (a composite of Cornell voltage and strain), the primary outcome of the study, was 37% lower (P=0.013) in the intensive than in the standard BP group, a value comparable with that found in ACCORD.3

The study by Soliman et al1 should be discussed in the context of the current debate on the most appropriate BP goal in hypertensive patients with type 2 diabetes mellitus. The Eighth Joint National Committee recommended a BP goal of <140/90 mm Hg, but the strength of recommendation was E (evidence unclear or conflicting). The 2013 European Society of Hypertension/European Society of Cardiology guidelines recommended a BP goal of <140/85 mm Hg (class I, level of evidence A). The Canadian Guidelines seemed to adopt a more intensive approach, with a recommended BP goal of <130 mm Hg (grade C) for SBP and <80 mm Hg (grade A) for diastolic BP.

It is likely that a barrier to the acceptance of a more intensive BP goal for hypertensive patients with diabetes mellitus might be because of the failure of the ACCORD trial to demonstrate superiority of the intensive over the standard BP arm in reducing the risk of the primary cardiovascular outcome, a composite of myocardial infarction, stroke, and cardiovascular death.4 However, the ACCORD study also found a significant 41% reduction (P=0.01) in the risk of stroke, a prespecified secondary outcome, in the more intensive compared with the less intensive BP group.4 The ACCORD study might have been underpowered to detect a statistically significant difference between the 2 arms in the risk of the composite primary outcome. Such limitation that can be overcome by the ongoing Systolic Blood Pressure Intervention Trial (SPRINT), that compares similar SBP goals (<120 mm Hg versus <140 mm Hg) in high-risk hypertensive patients without diabetes mellitus.5

The different impact of an intensive BP goal on the risk of stroke and coronary artery disease in patients with diabetes mellitus has been investigated in a systematic review of studies, which compared different antihypertensive drugs and different BP goals in these patients.6 Allocation to a more intensive, compared with less intensive, BP goal reduced the risk of stroke by 39% (P<0.001), whereas the reduction in myocardial infarction approached, but did not achieve, statistical significance. In a meta-regression analysis, the risk of stroke decreased by 13% (P=0.002) for each 5-mm Hg reduction in SBP and by 11.5% (P<0.001) for each 2-mm Hg reduction in diastolic BP.6 In contrast, the risk of myocardial infarction did not show any association with the extent of BP reduction.

The study by Soliman et al1 is timely and important because it provides convincing evidence, from a well-designed randomized intervention trial, that ECG LVH regression occurs more frequently and, conversely, new-onset LVH develops less frequently, in association with an SBP goal of <120 mm Hg as compared with a standard goal of <140 mm Hg in hypertensive patients with diabetes mellitus. Unfortunately, the authors could not demonstrate a direct relationship between LVH regression and outcome in the context of their study. However, the link between ECG LVH and subsequent outcome is being supported by a growing number of studies conducted in the general population and in specific subsets of patients, including those with hypertension.7,8

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Framingham Heart study was the first to demonstrate that a progressive reduction of ECG voltages over time predicts a better outcome than the progressive increase in the voltages. Other studies have confirmed the favorable prognostic impact of regression of ECG LVH. For example, in patients at high vascular risk enrolled in the Ongoing Telmisartan Alone and in Combination With Ramipril Global End Point Trial (ONTARGET), the risk of primary outcome during follow-up, a composite of composite of cardiovascular death, myocardial infarction, stroke, or hospitalization for congestive heart failure, increased progressively when the diagnosis of ECG LVH at entry was based on high voltage alone, strain alone and their combination (P<0.001) compared with the absence of LVH (all P<0.001). In that study, patients with new-onset ECG LVH during follow-up showed a 77% higher risk of subsequent primary outcome events (P 0.0001) than those with persistent absence of LVH.

In conclusion, an intensive SBP goal in hypertensive patients with diabetes mellitus (<130 mmHg or, even more intensively, <120 mmHg) is currently supported by studies focused on important intermediate end points, such as LVH, as this study, or meta-analyses based on a significant reduction in the risk of stroke. Large adequately powered studies are urgently needed to confirm these encouraging indications.

Disclosures
None.

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