Clinical Trials

Effect of Intensive Blood Pressure Lowering on Left Ventricular Hypertrophy in Patients With Diabetes Mellitus
Action to Control Cardiovascular Risk in Diabetes Blood Pressure Trial

Elsayed Z. Soliman, Robert P. Byington, J. Thomas Bigger, Gregory Evans, Peter M. Okin, David C. Goff Jr, Haiying Chen

See Editorial Commentary, pp 1104–1105

Abstract—Left ventricular hypertrophy (LVH), a marker of cardiac end-organ damage, is a common complication of hypertension. Regression of LVH is achievable by sustained lowering of systolic blood pressure (BP). However, it is unknown whether a strategy aimed at lowering BP beyond that recommended would lower the risk of LVH. We examined the effect of intensive (systolic BP<120 mmHg), compared with standard (systolic BP<140 mmHg), BP lowering on the risk of LVH in 4331 patients with diabetes mellitus from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) BP trial, a randomized controlled trial. The outcome measures were electrocardiographic LVH defined by Cornell voltage (binary variable) and mean Cornell index (continuous variable). The baseline prevalence of LVH (5.3% versus 5.4%; P=0.91) and the mean Cornell index (1456 versus 1470 µV; P=0.45) were similar in the intensive (n=2154) and standard (n=2177) BP-lowering arms, respectively. However, after median follow-up of 4.4 years, intensive, compared with standard, BP lowering was associated with a 39% lower risk of LVH (odds ratio [95% confidence interval], 0.61[0.43, 0.88]; P=0.008) and a significantly lower adjusted mean Cornell index (1352 versus 1447 µV; P<0.001). The lower risk of LVH associated with intensive BP lowering during follow-up was because of more regression of baseline LVH and lower rate of developing new LVH, compared with standard BP lowering. No interactions by age, sex, or race were observed. These results provide evidence that targeting a systolic BP of <120 mmHg when compared with <140 mm Hg in patients with hypertension and diabetes mellitus produces a greater reduction in LVH.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00000620

Key Words: blood pressure ■ cardiovascular disease ■ Cornell medical index ■ diabetes mellitus ■ hypertension, left ventricular

Left ventricular hypertrophy (LVH), a marker of cardiac end-organ damage, is a common complication of hypertension and is associated with an increased risk of cardiovascular disease (CVD) morbidity and mortality.1–4 There is a strong line of evidence indicating that the risk of poor cardiovascular outcomes associated with LVH is significantly reduced with regression of LVH.5–12 Hence, regression of LVH is considered a clinically useful intermediate target for assessing the efficacy of antihypertensive treatment.13

LVH regression is achievable by sustained lowering of systolic blood pressure (SBP) by most antihypertensive agents, and selection of individual drugs seems to be not the key factor.14 However, it is not known whether lowering BP beyond what is recommended would be associated with more regression of LVH. Therefore, we examined the differential effect of intensive BP lowering (target SBP<120 mm Hg) versus standard BP lowering (target SBP<140 mm Hg) on LVH in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) BP trial, a randomized, multicenter trial involving middle-aged and older patients with type 2 diabetes mellitus (T2DM) who are at risk of CVD.15

We hypothesized that, compared with standard BP lowering, a strategy aimed at intensive BP lowering will be associated with lower risk of LVH. This expected reduction in the risk of LVH will be because of regression of existing LVH or prevention of developing new LVH.

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Given the common concomitant presence of hypertension and diabetes mellitus and the established risk of poor outcomes associated with hypertension-induced LVH, results from this analysis could be of potential importance from both clinical and public health perspectives.

Methods

Study Population and Design

ACCORD was a randomized trial conducted at 77 clinical sites organized into 7 networks in the United States and Canada. The trial enrolled 10251 patients with T2DM at high risk of CVD. Participants were eligible if they had T2DM and a glycohemoglobin level of ≥7.5% and were aged ≥40 years with CVD or ≥25 years with evidence of atherosclerosis, albuminuria, LVH, or ≥2 additional risk factors of CVD (dyslipidemia, hypertension, or obesity). All participants provided written informed consent.

All ACCORD participants were randomly assigned to either intensive or standard glycemic control (the ACCORD glycemia trial). In addition, 5518 participants were also randomly assigned (in a 2-by-2 factorial design) to either simvastatin plus fenofibrate or simvastatin plus placebo (the ACCORD lipid trial), and the remaining 4733 participants were randomly assigned (in a 2-by-2 factorial design) to either intensive or standard BP lowering (the ACCORD BP trial). This analysis is based on the ACCORD BP trial, which included ACCORD participants with an SBP between 130 and 180 mm Hg who were taking ≤3 antihypertensive medications and who had the equivalent of a 24-hour protein excretion rate of <1.0 g.

The ACCORD BP trial was a nonblinded trial in which participants were randomly assigned to intensive therapy that targeted an SBP of <120 mm Hg or standard therapy that targeted an SBP of <140 mm Hg. The ACCORD BP trial was a study of a treatment strategy to achieve specific SBP goals, rather than an evaluation of any specific drug regimen. Therefore, all available antihypertensive medications were used to lower BP. After the first year of therapy, the average SBP was 133.5 mm Hg in the standard therapy group and 119.3 mm Hg in the intensive therapy group, resulting in an average between-group difference of 14.2 mm Hg (95% confidence interval, 13.7–14.7). The corresponding mean diastolic BPs were 70.5 and 64.4 mm Hg for an average difference of 6.1 mm Hg (95% confidence interval, 5.7–6.5). These levels of BP control in the 2 groups were maintained throughout the study.

For the purpose of this analysis, we excluded participants with missing or uninterpretable (missing leads, major background noise, or lead location errors) baseline ECG (n=25) or without any follow-up (n=377) (Figure 1). Because the effect of intensive BP lowering would not be only on developing less new LVH but also on regression of existing LVH, we opted not to exclude those with LVH at baseline. Also, because ECG diagnosis of LVH in the presence of major ventricular conduction delay need to be made with caution as recommended by the current guidelines, we conducted sensitivity analysis in which we excluded 202 participants with ECG conditions leading to major ventricular conduction delay manifested as prolonged QRS duration. This included complete left and right bundle branch blocks, Wolf–Parkinson–White syndrome, pacemaker, or major nonspecific conduction delay (QRS duration>120 ms).

Ascertainment of LVH

LVH was ascertained from the 12-lead ECGs obtained at the biennial ACCORD follow-up visits and close-out visit using Cornell voltage (R amplitude in aVL+S amplitude in V3). LVH was considered present when Cornell voltage exceeded 2200 µV in women or 2800 µV in men. In addition to using LVH as a categorical/binary variable, Cornell voltage was also examined as a continuous variable and referred to in this article as Cornell index. Using Cornell index as a continuous variable has the advantage of being not dependent on the cut points selected to define LVH and is more sensitive to changes during follow-up than a categorical variable, such as LVH.

EGCs were digitally acquired using a GE MAC 1200 electrocardiograph (GE, Milwaukee, Wisconsin) at a calibration of 10 mm/mV and a speed of 25 mm/s. ECG reading was performed centrally at the Epidemiological Cardiology Research Center, Wake Forest School of Medicine, Winston-Salem, NC. All ECG tracings were initially inspected visually for technical errors and inadequate quality before being automatically processed using GE 12-SL Marquette version 2001 (GE, Milwaukee, WI).

Other Data

Details of the assessment of BP, the adjustment of medication doses, and antihypertensive drug regimens in the ACCORD BP trial are provided elsewhere. Race/ethnicity was self-reported. Blood samples were collected in the fasting state during visits and were used to assess lipid profile, hemoglobin A1c, serum glucose, and others. History of CVD included previous myocardial infarction, stroke, arterial revascularization, angina with ischemic changes on ECG at rest, changes on a graded exercise test, and positive cardiac imaging test results.

Statistical Analyses

Baseline characteristics were compared between the 2 trial arms using χ² test for categorical variables and 2-sample t test for continuous variables. The prevalence of LVH over time was examined and compared between the 2 trial arms. A generalized estimating equation approach that controls for within-subject correlations was used for this purpose while adjusting for baseline LVH status. Mean Cornell index during follow-up was compared in the intensive BP-lowering arm versus standard BP-lowering arm using linear mixed-effects models that control for within-subject correlations between time points while adjusting for baseline values.

Similar to previous ACCORD articles, all models accounted for the assignment to the intensive glucose-lowering intervention and each of the 7 clinical center networks.

Subgroup analysis by age, race, sex, previous CVD, and obesity (body mass index>30 kg/m²) was conducted to examine the consistency of the results in subgroups of the ACCORD participants.

Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC). All P values reported were 2-sided, and statistical significance threshold was chosen as 5%.
Results
A total of 4331 participants (mean age, 62.1 years; 47.1% women and 59.6% whites) from the ACCORD BP trial were included in the analysis; 2177 were randomly assigned to standard BP lowering, and 2154 were assigned to intensive BP lowering. Table 1 shows the baseline characteristics of the participants, overall and by treatment assignment. As shown, baseline characteristics of the study participants did not differ by treatment arms.

The baseline prevalence of LVH in the intensive BP-lowering arm was not different from that in the standard BP-lowering arm (5.3%, n=115 versus 5.4%, n=118, respectively; \( P=0.91 \)). However, during a median follow-up of 4.4 years, regression of LVH was more common in the intensive versus standard therapy arm: 55.6% of the participants with baseline LVH in the intensive BP-lowering arm no longer had LVH on their last follow-up ECG compared with 49.6% of the participants with baseline LVH in the standard BP-lowering arm (\( P<0.001 \)). In parallel fashion, development of new LVH in those with no baseline LVH was significantly less common in the intensive BP-lowering arm compared with standard BP-lowering arm (1.7% versus 3.0%; \( P<0.001 \)). In parallel fashion, development of new LVH in those with no baseline LVH was significantly less common in the intensive versus standard therapy arm: 55.6% of the participants with baseline LVH in the intensive BP-lowering arm no longer had LVH on their last follow-up ECG compared with 49.6% of the participants with baseline LVH in the standard BP-lowering arm (\( P<0.001 \)). In parallel fashion, development of new LVH in those with no baseline LVH was significantly less common in the intensive BP-lowering arm compared with standard BP-lowering arm (1.7% versus 3.0%; \( P<0.001 \)).

Table 2 shows the effect of intensive versus standard BP lowering on the prevalence of LVH during follow-up. As shown, intensive BP lowering was associated with a 39% lower risk of LVH compared with standard BP lowering (odds ratio [95% confidence interval], 0.61 [0.43–0.88]; \( P=0.008 \)). These results were consistent across subgroups of age, sex, race/ethnicity, previous CVD, and obesity (Figure 2).

Similarly, there was no difference between the intensive and standard arms in terms of baseline mean Cornell index (1456 versus 1470 \( \mu \)V, respectively; \( P=0.45 \)). However, the adjusted mean Cornell index during follow-up became significantly lower in the intensive arm compared with the standard arm (1352 versus 1447 \( \mu \)V, respectively; \( P<0.001 \); Table 3). These results were consistent across subgroups of age, sex, race/ethnicity, previous CVD, and obesity (Figure 3). The trends of regression of Cornell voltage followed the trends in SBP reduction during the trial (Figure S1 in the online-only Data Supplement).

In a sensitivity analysis in which we excluded 202 participants with major ventricular conduction delay, the effect of intensive versus standard BP lowering on LVH (odds ratio [95% confidence interval], 0.55 [0.41–0.73]; \( P=0.001 \)) and Cornell index (1353 versus 1449 \( \mu \)V; \( P<0.001 \)) was similar to that observed in the main analysis.

Discussion
In this analysis from the ACCORD BP trial, we examined the effect of intensive BP lowering (targeted SBP<120 mm Hg), compared with standard BP lowering (targeted SBP<140 mm Hg), on electrocardiographic measures of LVH. We found that intensive BP lowering, compared with standard BP lowering, resulted in lower risk of LVH. The lower risk of LVH in the intensive BP-lowering arm was because of more regression of existing LVH and lower rate of developing new LVH during follow-up, compared with standard BP-lowering arm.

LVH is an adaptive response to the wall stress associated with increased impedance to ventricular emptying because of increase in peripheral resistance, the hallmark of established hypertension.\(^1\)\(^2\) Hence, successful BP lowering is expected to alter the chances of new occurrence of LVH or enhance regression of existing LVH. This is supported by results from several

### Table 1. Baseline Characteristics of the Study Participants

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=4331)</th>
<th>Standard BP Lowering, (&lt;140) mm Hg (n=2177)</th>
<th>Intensive BP Lowering, (&lt;120) mm Hg (n=2154)</th>
<th>( P ) Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62.1±6.8</td>
<td>62.2±6.9</td>
<td>62.1±6.7</td>
<td>0.65</td>
</tr>
<tr>
<td>Female sex</td>
<td>2039 (47.1)</td>
<td>1030 (47.3)</td>
<td>1009 (46.8)</td>
<td></td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>2582 (59.6)</td>
<td>1272 (58.4)</td>
<td>1310 (60.8)</td>
<td>0.58</td>
</tr>
<tr>
<td>Latino</td>
<td>293 (6.8)</td>
<td>153 (7.0)</td>
<td>140 (6.5)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>986 (22.8)</td>
<td>510 (23.4)</td>
<td>476 (22.1)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>231 (5.3)</td>
<td>116 (5.3)</td>
<td>115 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>239 (5.5)</td>
<td>126 (5.8)</td>
<td>113 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1947 (45.0)</td>
<td>982 (45.1)</td>
<td>965 (44.9)</td>
<td>0.87</td>
</tr>
<tr>
<td>Past</td>
<td>1826 (42.2)</td>
<td>911 (41.9)</td>
<td>915 (42.9)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>554 (12.8)</td>
<td>283 (13.0)</td>
<td>271 (12.6)</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>32.18 (5.6)</td>
<td>32.10 (5.4)</td>
<td>32.25 (5.7)</td>
<td>0.40</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>139.07 (15.7)</td>
<td>139.17 (15.3)</td>
<td>138.98 (16.1)</td>
<td>0.69</td>
</tr>
<tr>
<td>Diastolic BP, mm Hg</td>
<td>75.97 (10.3)</td>
<td>75.93 (10.1)</td>
<td>76.02 (10.5)</td>
<td>0.77</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td>1433 (33.1)</td>
<td>719 (33.0)</td>
<td>714 (33.2)</td>
<td>0.93</td>
</tr>
<tr>
<td>Intensive glycemia lowering</td>
<td>2152 (49.7)</td>
<td>1095 (50.3)</td>
<td>1057 (49.1)</td>
<td>0.42</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>233 (5.4)</td>
<td>118 (5.4)</td>
<td>115 (5.3)</td>
<td>0.91</td>
</tr>
<tr>
<td>Cornell index, ( \mu )V</td>
<td>1463±594</td>
<td>1470±589</td>
<td>1456±598</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or mean±SD. BP indicates blood pressure.

* \( P \) value comparing participants' characteristics in the standard vs intensive BP-lowering arms.
cohort studies and clinical trials, indicating that LVH could be reversed by nonpharmacological and pharmacological interventions.\textsuperscript{22–37} However, none of these studies were designed to examine the effect of a strategy to lower BP beyond the recommended values (SBP<140 mm Hg) on regression of LVH in patients with diabetes mellitus. However, 1 trial compared an SBP goal of <130 mm Hg to a goal of <140 mm Hg in adults aged >55 years (n=1111 participants). That trial, Cardio-Sis trial, concluded that lowering of SBP to <130 mm Hg in non-diabetic patients with at least 1 additional risk factor decreased the likelihood of electrocardiographic LVH by 39%, compared with usual lowering to SBP <140 mm Hg,\textsuperscript{38} similar to our results in patients with diabetes mellitus. This is despite the fact that Cardio-Sis used different ECG-LVH criteria; Perugia score which generally yields higher prevalence estimates of LVH. To our knowledge, our results from the ACCORD BP trial is the first to provide evidence from a randomized clinical trial to suggest that intensive BP lowering (SBP<120 mm Hg) in patients with T2DM is associated with lower risk of LVH compared with standard BP lowering (SBP<140 mm Hg).

Regression of ECG-LVH has been repeatedly shown to be associated with lower risk of cardiovascular morbidity and mortality.\textsuperscript{5–12} With our results in mind, intensive BP lowering compared with standard BP lowering should have been associated with better outcomes in the ACCORD BP trial. However, on contrary, intensive BP lowering did not significantly reduce the primary cardiovascular outcome (composite of nonfatal myocardial infarction, nonfatal stroke, or death from cardiovascular causes) or the rate of death from any cause in the ACCORD BP trial.\textsuperscript{38} Nevertheless, intensive BP lowering did reduce the rate of total stroke and nonfatal stroke, 2 of the pre-specified secondary outcomes. Unlike a composite of CVD\textsuperscript{39} or coronary heart disease,\textsuperscript{40} LVH is an established predictor of stroke and a component of the Framingham stroke risk prediction score.\textsuperscript{41} This could explain why intensive BP lowering in the ACCORD BP trial selectively reduced the risk of stroke but not of CVD or coronary heart disease. However, it is unclear why intensive BP lowering did not reduce the risk of fatal and nonfatal heart failure in the ACCORD BP trial, although LVH is an established predictor of heart failure and a component of the Framingham heart failure risk prediction score\textsuperscript{42} similar to stroke. This might be explained by the notion that in some pathological conditions, the development of mild levels of hypertrophy might be beneficial. For example, in myocardial infarction, the presence of LVH worsens prognosis. However, it is the lack of an increase in wall thickness to compensate for the increase in chamber radius, which leads to the progressively increased diastolic stress that begets the remodeling that is accompanied by LV systolic dysfunction and increased morbidity and mortality from heart failure.\textsuperscript{43}

Evaluating the benefit of intensive BP lowering on different types of heart failure (preserved versus low ejection fraction heart failure) may shed light as why intensive BP lowering did not reduce the risk of heart failure despite its favorable benefit on LVH and the established risk of heart failure associated with LVH.

Taken altogether considering our results showing favorable effect of intensive BP lowering on LVH and

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Odd Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65 years</td>
<td>0.55 (0.39, 0.80)</td>
</tr>
<tr>
<td>≥65 years</td>
<td>0.61 (0.41, 0.92)</td>
</tr>
<tr>
<td>Male</td>
<td>0.52 (0.31, 0.86)</td>
</tr>
<tr>
<td>Female</td>
<td>0.39 (0.43, 0.82)</td>
</tr>
<tr>
<td>Non-White</td>
<td>0.68 (0.46, 1.00)</td>
</tr>
<tr>
<td>White</td>
<td>0.48 (0.33, 0.71)</td>
</tr>
<tr>
<td>No prior CVD</td>
<td>0.58 (0.41, 0.81)</td>
</tr>
<tr>
<td>Prior CVD</td>
<td>0.55 (0.35, 0.88)</td>
</tr>
<tr>
<td>Obese</td>
<td>0.65 (0.48, 0.92)</td>
</tr>
<tr>
<td>Non-obese</td>
<td>0.45 (0.28, 0.70)</td>
</tr>
</tbody>
</table>

Figure 2. Effect of intensive vs standard blood pressure lowering on the prevalence of left ventricular hypertrophy in subgroups during follow-up. All models accounted for the assignment to the intensive glucose-lowering intervention and each of the 7 clinical center networks. Model was also adjusted for baseline left ventricular hypertrophy (LVH) status. No significant interaction between subgroups. LVH is defined from the study ECG using Cornell voltage criteria. CI indicates confidence interval; and CVD, cardiovascular disease.
Intensive BP Lowering and LVH

Table 3. Effect of Intensive vs Standard Blood Pressure Lowering on the Mean Cornell Index During Follow-Up

<table>
<thead>
<tr>
<th>Study Visit</th>
<th>Standard BP Lowering Mean (SE), μV</th>
<th>Intensive BP Lowering Mean (SE), μV</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1470 (13)</td>
<td>1456 (13)</td>
<td>0.45</td>
</tr>
<tr>
<td>Follow-up</td>
<td>1447 (8)</td>
<td>1352 (9)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

All models accounted for the assignment to the intensive glucose-lowering intervention and each of the 7 clinical center networks. Model was also adjusted for baseline Cornell index values. Cornell index is defined as the sum of the R amplitude in aVL and S amplitude in V3 in microvolt. BP indicates blood pressure.

given the ACCORD BP trial results showing only benefit of intensive BP lowering on stroke, it might be reasonable to consider intensive BP lowering in selected patients with T2DM at higher risk of stroke. This suggestion is in agreement with a recent meta-analysis that showed reduction in risk of stroke but not other cardiovascular outcomes, with BP lowering to <130 mm Hg in patients with diabetes mellitus. Notably, the same meta-analysis showed reduction in the risk of all cardiovascular outcomes with BP lowering <140 but >130 mm Hg.

Our results should be read in the context of certain limitations and methodological considerations. By design, the ACCORD BP trial included only patients with diabetes mellitus at high risk of CVD. Our results may not be generalized to all patients with diabetes mellitus or nondiabetic populations. Also, the ACCORD BP trial had an open-label design that could lead to some bias. However, it is unlikely that the open-label design could have a significant effect on the ascertainment of LVH, which was measured from ECGs that were read centrally at an ECG core laboratory blinded to the treatment assignment.

In the ACCORD BP trial, LVH was defined from ECG not imaging (echocardiography or cardiac magnetic resonance imaging). Although imaging provides a more accurate assessment of LVH than does the ECG, this does not obviate the clinical use of the ECG, which is the most accessible cardiac investigation tool. More importantly, LVH detected by ECG has been shown to be predictive of poor outcomes in a similar way as LVH detected by imaging.45–46 Also, in addition to its established role as a predictor of poor outcome, regression of LVH defined by ECG has been shown to be associated with better prognosis.31–33 These findings along with the wide availability of ECG put ECG-LVH in a position to be an ideal tool to indicate a more advanced clinical state, predict a more serious clinical course, and predict improvement with therapy in patients with hypertension.

Despite these limitations, this is the first report from a well-designed large clinical trial in which the effect of intensive BP lowering on LVH in patients with hypertension and diabetes mellitus is examined. The strengths of our study include large sample size, racially/ethnically diverse population with representation of both sexes, random assignment of participants to treatment arms resulting in a balanced groups at baseline, standardized data collection including ECG data that were centrally read, and achievement and maintenance of an average between-group difference in an SBP of 14 mm Hg throughout the study.

**Perspectives**

This analysis from the ACCORD BP trial shows that intensive BP lowering (SBP<120 mm Hg), compared with standard lowering (SBP<140 mm Hg), reduces the risk of LVH in patients with hypertension and T2DM who are at high risk of CVD. The lower risk of LVH in the intensive BP lowering arm was because of more regression of existing LVH and lower rate of developing new LVH during follow-up, compared with standard BP-lowering arm. These findings suggest a potential benefit of intensive BP lowering in prevention of LVH-related comorbidities in patients with hypertension and T2DM.

**Acknowledgments**

We thank the staff and participants of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study for their important contributions.

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**Novelty and Significance**

**What Is New?**

- This is the first report from a well-designed large clinical trial in which the effect of intensive blood pressure (BP) lowering on left ventricular hypertrophy in patients with hypertension and diabetes mellitus is examined.

**What Is Relevant?**

- Our findings indicate that intensive BP lowering (systolic BP<120 mmHg), compared with standard lowering (systolic BP<140 mmHg), reduces the risk of left ventricular hypertrophy in patients with hypertension and type 2 diabetes mellitus.
Effect of Intensive Blood Pressure Lowering on Left Ventricular Hypertrophy in Patients With Diabetes Mellitus: Action to Control Cardiovascular Risk in Diabetes Blood Pressure Trial

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Supplemental Materials

Effect of Intensive Blood Pressure Lowering on Left Ventricular Hypertrophy in Patients with Diabetes: the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Blood Pressure Trial

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Short title: Intensive BP lowering and LVH

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Time trend of mean Cornell voltage index and systolic blood pressure during follow up