Concerns for the Heart Failure Reduction in the NAGOYA HEART Study Based on Meta-Regression From the Evidence

To the Editor:

The NAGOYA HEART Study\(^1\) compared the efficacies of an angiotensin II type 1 receptor blocker (ARB) valsartan and a calcium channel blocker amldipine on cardiovascular morbidity and mortality as a primary outcome in Japanese hypertensive patients with glucose intolerance. Time-to-event curves for primary outcomes did not significantly differ between the 2 groups (hazard ratio, 0.97; 95% confidence interval [CI], 0.86–1.09; \(P=0.56\)). Despite no significant differences in the risk of myocardial infarction, stroke, coronary revascularization, or sudden cardiac death between the 2 groups, the incidence of admission because of heart failure was significantly less in the valsartan group than in the amlodipine group (hazard ratio, 0.85). Despite no significant confidence interval [CI], 0.66–1.40; \(P=0.56\)) for the effects of ARB (log OR for heart failure) were modulated by the achieved SBP difference using the 11 comparisons (not including the NAGOYA HEART Study).\(^1\) The meta-regression coefficient (slope of the meta-regression line) was positive and statistically significant (0.02701; 95% CI, 0.00474–0.04929; \(P=0.01746\)) with an intercept of –0.10935 (95% CI, –0.16776 to –0.05093; Figure), which would indicate that as a given factor decreases, the OR decreases, that is, ARB is more beneficial in reducing the outcome of interest. In the meta-regression graph, we simply added (without altering the result of the meta-regression analysis) the NAGOYA HEART Study (achieved SBP difference, –0.05093; Figure), which is an extraordinarily long way from the area enclosed by the 95% CI curves of the meta-regression. Thus, we confirmed the specificity of the significant relative risk reduction for heart failure with the achieved SBP difference of nearly zero shown in the NAGOYA HEART Study, which is irreconcilable with the result of the current meta-regression analysis of the data set included in the most robust evidence\(^2\) for BP-lowering treatment with agents inhibiting the renin–angiotensin system.

In a study by the Blood Pressure Lowering Treatment Trialists’ Collaboration (BPLTTC),\(^2\) there were 17 angiotensin-converting enzyme inhibitor trials (n=101,626), 9 ARB trials (n=45,212), and 3 direct head-to-head trials (n=18,477). We selected 11 comparisons from 10 of the 12 ARB trials (including 3 direct head-to-head trials) for the All-Literature Investigation of Cardiovascular Evidence (ALICE) Group,\(^3\) with the area of each circle inversely proportional to the variance of the log odds ratio. A fitted line with curves represents the summary meta-regression measure with lower and upper limits of its 95% confidence interval for the trials included in the BPLTTC study (not including the NAGOYA HEART Study). because both an odds ratio (OR) for heart failure and an achieved SBP difference (mm Hg) were stated in the BPLTTC study. A fixed-effects meta-regression analysis was performed to determine whether the effects of ARB (log OR for heart failure) were modulated by the achieved SBP difference (mm Hg) in the valsartan group and more incidents of disease in the amlodipine group at 54 months). Herein, we would like to assess the specificity of the significant relative risk reduction for heart failure with the achieved systolic BP (SBP) difference of only –1 mm Hg shown in the NAGOYA HEART Study by means of a novel meta-regression analysis of a data set included in the most robust evidence\(^2\) for BP-lowering treatment with agents inhibiting the renin–angiotensin system.

Figure. Associations of blood pressure reduction with risk reduction for heart failure in trials of angiotensin II type 1 receptor blockers. Open circles represent trials included in the study by the Blood Pressure Lowering Treatment Trialists’ Collaboration (BPLTTC),\(^2\) and a closed circle represents the NAGOYA HEART Study,\(^1\) with the area of each circle inversely proportional to the variance of the log odds ratio. A fitted line with curves represents the summary meta-regression measure with lower and upper limits of its 95% confidence interval for the trials included in the BPLTTC study (not including the NAGOYA HEART Study).

Disclosures

None.

Hisato Takagi
Takuya Umemoto
for the All-Literature Investigation of Cardiovascular Evidence (ALICE) Group
Department of Cardiovascular Surgery
Shizuoka Medical Center
Shizuoka, Japan

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Hisato Takagi and Takuya Umemoto
for the All-Literature Investigation of Cardiovascular Evidence (ALICE) Group

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