Heart failure (HF) is associated with an increased risk of ischemic stroke; however, the extent to which atrial fibrillation (AF) contributes to that risk is unclear, as most analyses of stroke in individuals with HF combined those with and without AF. In this pooled analysis of 2 randomized controlled HF trials, the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA) and the Gruppo Italiano per lo Studio della Sopravvivenza nell’Insufficienza cardiaca—Heart Failure trial (GISSI-HF), Abdul-Rahim et al determined the incidence of stroke in individuals with HF with or without AF, performed predictor analyses, developed a risk score using the predictors, and validated the predictive model using data from Candesartan in Heart Failure: Reduction in Mortality and morbidity (CHARM) trial.

Of the 9585 total patients with HF in the 2 trials, 6054 (63%) did not have AF. Cumulative incidence of stroke was 4.7% in those with AF and 3.4% in those without AF (rates 16.8 and 11.1 per 1000 patient-years, respectively). Independent predictors of stroke in patients without AF were age (hazard ratio, 1.34; 95% confidence interval, 1.18–1.63 per 10 years), New York Heart Association class (1.60, 1.21–2.12 class III/IV versus II), insulin-dependent diabetes mellitus (1.87, 1.22–2.88), body mass index (0.74, 0.60–0.91 per 10 years), and previous stroke (1.81, 1.19–2.74).

Individuals without AF had a lower stroke risk (1.2% per year) compared with those with AF (1.6% per year); however, when stratified by risk tertiles, individuals in the upper third tertile had a stroke rate of 2.0% per year; of these, 15% versus 11% had their BP actively lowered, whereas 158 (71%) were in the conservative group (adjusted odds ratio, 4.39; 95% confidence interval, 2.05–9.41). The proportion of men was higher in the active group compared with the conservative group (59% versus 55%). The median systolic BP on admission was higher in the active group compared with the conservative group (153 versus 146 mm Hg). These findings suggest that there may be a subset of high-risk HF patients without AF in whom the potential reduction in stroke with anticoagulants outweighs the risk of major bleeding.

The study strengths include its sample size and robust statistical analyses used to construct the predictive model and validate the model in a separate data set. The study is limited by generalizability as it only included individuals with systolic HF meeting the selection criteria of the trials. Prospective randomized controlled trials are needed to further evaluate the potential role of anticoagulation for high-risk HF individuals without AF.


The proportion of stroke patients receiving intravenous tissue plasminogen activator (IV tPA) remains low, and elevated blood pressure (BP) above 185/110 mm Hg remains a common reason for withholding IV tPA. In this study, Dirks et al evaluated whether an active BP-lowering strategy was associated with higher IV tPA administration rates compared with a conservative watch and measure strategy. In addition, they assessed safety and functional outcomes of these 2 treatment strategies. They performed post hoc analyses of 2 randomized controlled stroke trials, Promoting Acute Thrombolysis in Ischemic Stroke (PRACTISE) and the Preventive Antibiotics in Stroke Study (PASS). The primary outcome was the proportion of patients treated with IV tPA. Secondary outcomes were door-to-needle time, rate of symptomatic intracranial hemorrhage, and modified Rankin score at 3 months.

Of 2097 individuals who presented within the thrombolysis time window, 231 were eligible for IV thrombolysis but had a pretreatment BP >185/110 mm Hg at presentation. Seven received thrombolitics despite their elevated BP; of the remaining 224 individuals, 66 (29%) had their BP actively lowered, whereas 158 (71%) were monitored conservatively. In the active BP-lowering group, 55 (83%) received thrombolysis compared with 87 (55%) in the conservative group (adjusted odds ratio, 4.39; 95% confidence interval, 2.05–9.41). The proportion of men was higher in the active group than the conservative group (59% versus 46%) and the proportion of individuals with atrial fibrillation was higher in the conservative group compared with the active group (15% versus 11%). The median systolic BP on admission was higher in the active group than the conservative group (210 versus 200 mm Hg). There was no difference in door-to-needle time (70 versus 68 minutes). Symptomatic intracranial hemorrhage occurred in 6% and 4% of the patients in the active versus conservative group.
When the analysis was limited to those treated with IV tPA, the symptomatic intracerebral hemorrhage rate was 7% in both groups. A favorable clinical outcome at 3 months (modified Rankin score ≤2) was observed in 56% of the patients in the active BP-lowering group versus 46% of those in the conservative group.

In this retrospective analysis of 2 randomized controlled trials, active BP lowering was associated with higher likelihood of IV tPA administration without higher rates of symptomatic intracranial hemorrhage and trended toward better functional outcome at 3 months. These results should be interpreted with caution given the retrospective nature of this analysis and nonrandomized design. Furthermore, the method and intensity of hypertension treatment was not disclosed, and the decision whether to use BP-lowering or conservative measure was left to the discretion of the treating physician and in accordance with local hospital treatment guidelines, potentially introducing selection bias (particularly given the uneven distribution of known prognostic factors between groups). The multicenter, prospective, cluster-based Thrombolysis and Uncontrolled Hypertension (TRUTH) study may address these limitations and provide more definitive answers.
Stroke Literature Synopses: Clinical Science
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