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## A risk score for prediction of TIA/ischemic stroke in patients with heart failure and sinus rhythm

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**Background:** Prediction of ischemic cerebral events in patients with heart failure (HF) in the absence of atrial fibrillation (AF) is challenging.

**Purpose:** To prospectively test a staged approach to identify patients with HF and sinus rhythm who are at high risk of developing TIA/ischemic stroke (TIA/IS) during the first two years after diagnosis.

**Methods:** The analysis is based on patient data reported in the Swedish Heart Failure Register from January 2003 until December 2013. Patients with AF and those treated with anticoagulants were excluded. The study population was categorized in two groups according to left ventricular ejection fraction: LVEF  $\leq$ 40% and LVEF >40%. Factors associated with TIA/IS were determined by univariate proportional hazard regression. The risk score included: age (1p for 65–74y; 2p for 75–84y; 3p for  $\geq$ 85y), previous ischemic heart disease (1p), hypertension (1p), diabetes mellitus (1p), TIA/IS (2p), and kidney dysfunction (1p). Two-year hazard ratios with death as competing risk were computed. The probability of observing the outcome was calculated using the cumulative incidence function.

**Results:** A total of 16,865 patients (mean age 72.1 $\pm$ 13.2y) were included in the study, 39.9% women; 59.7% had LVEF  $\leq$ 40%. The two-year crude rate of TIA/IS, hemorrhagic stroke, and all-cause mortality were 3.3%, 0.3%, and 26%, respectively.

An incremental absolute risk for TIA/IS was observed for patients with LVEF

 $\leq\!\!40\%$  and score 1-  $\geq\!\!6$ : 1.6, 2.3, 3.6, 2.9, 6.3, and 7.1%, respectively. The corresponding HRs with 95% confidence interval (CI) and the patients with 0 points as reference group were: 2.8 (1.1–7.3), 4.0 (1.6–10.1), 6.6 (2.7–16.2), 5.5 (2.2–13.8), 14.4 (5.8–35.9) for score 1-  $\geq\!\!6$ , where all p-values were less than 0.05 and Wald  $\chi^2$  for overall model fit <0.0001. The cumulative incidence per 1000 person-years was: 8.2 (5.4–12.5), 11.8 (3.3–61.7), 19.4 (15.1–24.8), 16.3 (12.6–21.1), 36.6 (29.4–45.4), and 42.1 (33.0–53.8), respectively.

In patients with LVEF >40% and score 1–≥6, the absolute TIA/IS risk was: 1.3, 3.1, 3.1, 3.3, 4.6, and 5.3%, respectively. The corresponding HRs with 95% CI and patients with 1 point as reference group was: 2.4 (1.1–5.2), 2.5 (1.2–5.3), 2.7 (1.3–5.7), 3.9 (1.8–8.2); and 4.6 (2.2–9.8), for score 1- ≥6 (all p<0.05 and Wald  $\chi^2$  for overall model fit p=0.0002). The cumulative incidence per 1000 person-year was: 6.7 (3.4–13.2), 16.0 (10.8–23.8), 16.7 (12.5–22.2), 18.0 (13.9–23.4), 25.8 (19.4–34.3), and 30.6 (21.7–43.0), for score 1- ≥6, respectively.

**Conclusion:** In the current study, a risk score compiling age and specific comorbidity was shown to predict increased risk of TIA/IS, regardless of LVEF, during the first two years after diagnosis in patients with incident HF in sinus rhythm.