



**Abstract N°:** ESOC25-685 / P315

**Track:** 04.00 - DIAGNOSIS / ETIOLOGY

**Category:** 04.06 - CARDIOEMBOLISM & HEART-BRAIN INTERACTIONS

**Title:** STROKE-HEART SYNDROME AND RISK OF WORSENING STROKE: A REPORT FROM VISTA

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**On behalf of:**

**Disclosure of Interest:** All authors: nothing to disclose

**Background and Aims:** Early adverse cardiac events (i.e. stroke-heart syndrome, SHS) and neurological deterioration are serious complications in patients with acute ischaemic stroke. We investigated the impact of SHS on the subsequent complication of worsening stroke.

**Methods:** We analysed data from the Virtual International Stroke Trials Archive (VISTA). We defined SHS as the incidence of cardiac complications within 30 days post-stroke, including acute coronary syndrome/myocardial injury, heart failure/left ventricular dysfunction, atrial fibrillation/flutter, other arrhythmia/electrocardiogram abnormalities, and cardiorespiratory arrest. We evaluated the impact of SHS on worsening stroke (defined as stroke progression [an increase in National Institutes of Health Stroke Scale score  $\geq 4$ ]). Using Cox models, we assessed the association between SHS onset and the risk of worsening stroke.

**Results:** Among 14,905 patients with acute ischaemic stroke (mean age  $69 \pm 12$  years; 55% male), 1,653 (11.0%) experienced SHS and 662 (4.4%) developed worsening stroke. The cumulative incidence of worsening stroke was significantly higher in patients with SHS than those without (cumulative incidence free from the event [95% confidence interval]: 85.7% [84.0–87.7] vs. 96.1% [95.8–96.5],  $p < 0.001$ ). Time-dependent multivariate analysis showed strong association between SHS incident with worsening stroke (adjusted hazard ratio, aHR 1.70 [1.40–2.04],  $p < 0.001$ ). Patients who developed SHS within the first two days after admission had the highest risk of worsening stroke (aHR 1.57 [1.10–2.24],  $p = 0.012$ ) compared to those with later SHS onset (days 3 to 4 post-admission).

**Conclusion:** Stroke-heart syndrome is significantly associated with an increased risk of worsening stroke, particularly when SHS occurs within the first two days of hospital admission.