

Noncardiac Production of Soluble ST2 in ST-Segment Elevation Myocardial Infarction

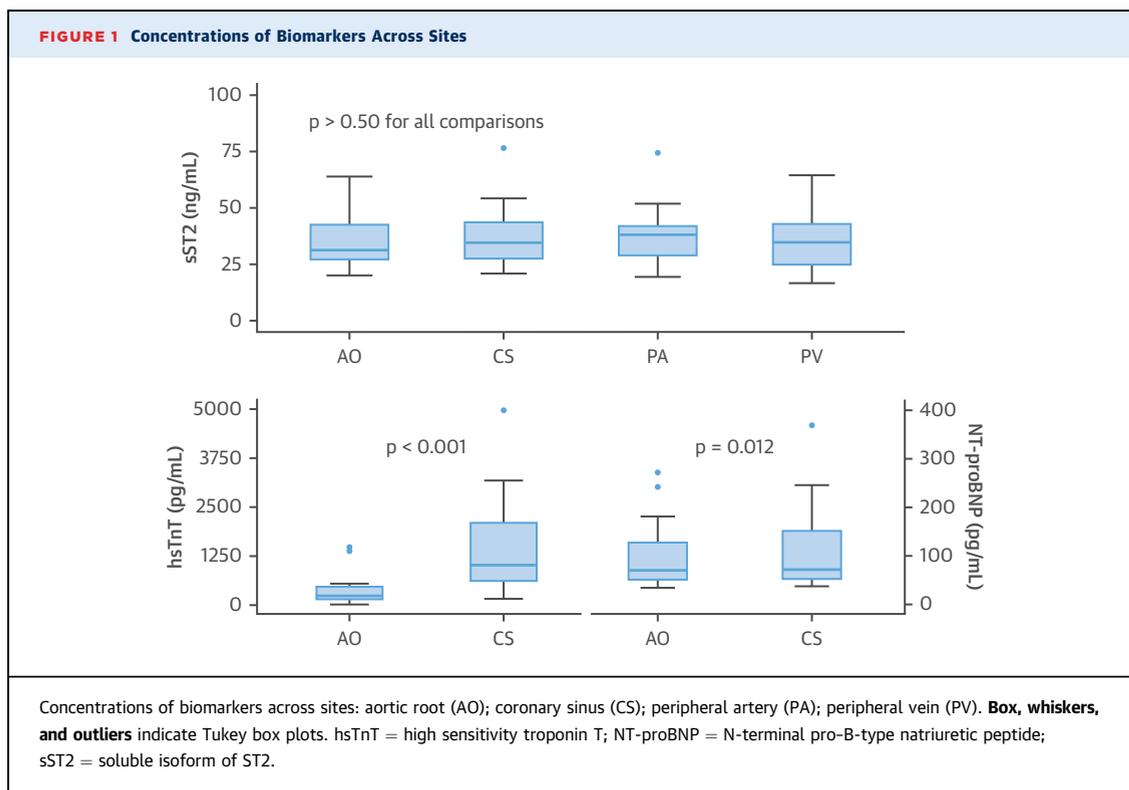


also obtained. Commercial assays were used for measuring sST2 (Presage ST2, Critical Diagnostics, San Diego, California) and other cardiac markers. Median time from symptom onset to sampling was 167 min (interquartile range [IQR]: 114 to 233 min; range: 75 to 265 min). Most patients were Killip class I (11 of 12); median left ventricular ejection fraction at discharge was 60% (IQR: 56% to 65%; range: 40% to 74%).

The soluble isoform of ST2 (sST2) represents a powerful prognostic biomarker in patients with heart failure and acute coronary syndromes. In patients with ST-segment elevation myocardial infarction (STEMI), concentrations of sST2 are elevated early and identify a higher risk of death, adverse myocardial remodeling, and heart failure in the follow-up (1-3). However, the source of circulating sST2 remains debated (3).

The concentrations of biomarkers are detailed in Figure 1. Friedman test and pairwise Wilcoxon signed-ranked test with Bonferroni-Holm correction were used to study differences. Both biomarkers of necrosis troponin T and creatine kinase-myocardial band showed a significant transcardiac gradient ($p < 0.001$); N-terminal pro-B-type natriuretic peptide (median: 64 pg/ml; IQR: 54 to 126 pg/ml) also had a small but significant gradient ($p = 0.012$). Median sST2 concentration was 34.7 pg/ml (IQR: 27.7 to 43.3 pg/ml; range: 21.0 to 76.4 pg/ml), but did not exhibit any significant transcardiac gradient and, considering all sites, no significant differences were observed ($p > 0.50$). No differences were found when considering the culprit artery or patients >35 pg/ml. We explored all clinical correlates of sST2, and the only significant was higher sST2 concentration at reperfusion was associated with lower left

Twelve STEMI patients (11 male, age 62 ± 10 years) who underwent a primary angioplasty according to clinical practice were recruited in this prospective study. The culprit artery was the right coronary artery in 8 patients, the circumflex in 3, and the left anterior descending in 1. Blood samples were collected immediately after reperfusion and simultaneously from the aortic root and coronary sinus to allow calculation of the transcardiac gradient. Peripheral blood samples from the radial artery and brachial vein were



ventricular ejection fraction at discharge for all sites ($r > 0.70$; $p < 0.001$).

The sST2 concentrations in the peripheral circulation are increased within the first few hours after symptoms onset in STEMI (1-2). In our study, sST2 was measured within the first 5 h and one-half of patients were above the prognostic cutoff of 35 pg/ml, but sST2 concentrations were similar in all sites. Therefore, sST2 concentrations rise early in the setting of myocardial ischemia and necrosis, but the source may be from organs other than the myocardium. Bartunek et al. (4) showed that venous and arterial endothelial cells had the ability to secrete ST2 protein and hypothesized that diastolic load is the main determinant. The absence of augmented levels of natriuretic peptides is against diastolic load as main determinant of ST2 production. ST2 secretion is also stimulated by inflammatory cytokines in endothelial cells, which might explain the early and systemic elevation of sST2 in STEMI (4). Among the limitations of our study, the unknown half-life of sST2 and the catheter position might influence the results; although we found no sign of a transcardiac gradient, it is possible subtle differences exist that might be obscured due to the nature of our study design. Though tissue-based autocrine and paracrine ST2 is important in the reparative processes after MI (5), our current results suggest the majority of circulating sST2 is secreted in organ beds other than the heart. The sST2 levels measured early predict heart failure and medium-term left ventricular functional recovery and remodeling (1,2). The correlation we found between sST2 levels at reperfusion and left ventricular ejection fraction at discharge also supports the previously identified tissue based role of ST2 in post-MI recovery (5).

In summary, sST2 concentrations are elevated early in the circulation of patients experiencing STEMI, but the lack of a transcardiac gradient supports the hypothesis that the majority of circulating sST2 may not be of cardiac origin. More data are needed to better understand the ST2 system.

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50 Years From Bench to Bedside



His Bundle Pacing Versus Right Ventricular Apical Pacing

Abdelrahman et al. (1) reported the clinical results of a comparative study in patients receiving permanent His bundle pacing with those implanted with right ventricular pacemakers. They were able to achieve permanent His bundle pacing in 92% of the 304 patients in consecutive studies compared with 433 who had right ventricular pacing. During the follow-up period, mortality, heart failure hospitalizations, and upgrades to biventricular pacing were all significantly reduced in patients with His bundle pacing compared with those with right ventricular pacing. Although His bundle pacing in patients was reported as early as 1970 (2), it was not until 2000, when Deshmukh et al. (3) used a fixed, screw-in lead