BIOMARKERS OF EXTRACELLULAR MATRIX IN LOW FLOW, LOW GRADIENT AORTIC STENOSIS: RELATIONSHIP TO HEMODYNAMIC, FUNCTIONAL, AND CLINICAL OUTCOMES - RESULTS FROM THE MULTICENTER TOPAS (TRULY OR PSEUDO SEVERE AORTIC STENOSIS) STUDY

ACC Poster Contributions
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Background: Patients with low LV ejection fraction (LVEF), low flow, low gradient, aortic stenosis (LFLG AS) have a poor prognosis with conservative therapy but a high operative mortality if treated surgically. We previously demonstrated that type B Natriuretic Peptide (BNP) provides important information for risk stratification and therapeutic decision-making in this population. The objective of this study was to evaluate the prognostic value of biomarkers of extracellular matrix metabolism in LFLG AS.

Methods: In the TOPAS study, 198 patients with LFLG AS (AVA≤1.2cm2, LVEF≤40%, and mean gradient≤40 mmHg) underwent dobutamine stress echocardiography, blood sample, and evaluation of functional capacity with the use of Duke Activity Status Index (DASI) and 6-minute walk test at entry in the study. Plasma level of type I Collagen Degradation Marker (ICTP) were measured in a subset of 30 patients. The severity of the stenosis was assessed using the projected aortic valve area at a normal transvalvular flow rate (AVAproj), which has been shown to be superior to traditional echocardiographic indices for evaluating the actual stenosis severity.

Results: There was a good correlation between the plasma levels of ICTP and BNP (r=0.64; p=0.0001). However, plasma levels of ICTP correlated better than BNP with (1) baseline AS severity assessed by AVAproj (r=-0.44; p=0.01 vs. r=-0.38; p=0.04), (2) DASI (r=-0.52; p=0.003 vs. r=0.18; p=0.35) and (3) 6-minute walk test distance (r=-0.80; p<0.0001 vs. r=-0.53; p=0.02). Baseline level of ICTP predicted the change in DASI at 1 year follow-up (r=-0.49; p=0.04) whereas BNP did not (r=0.04; p=0.89). On univariate analysis, predictors of mortality were DASI (HR: 0.76 per 5 unit increase; p=0.005), 6-minute walk distance (HR: 0.81 per 10m increase; p<0.0001), BNP (HR: 1.01 per 10pg/ml increase; p=0.05) and ICTP (HR: 1.22 per 1ng/ml increase; p=0.004). After adjustment for BNP, ICTP remained a significant predictor of mortality (HR: 1.21; p=0.02).

Conclusion: Biomarkers of extracellular matrix metabolism may be useful in the risk stratification of patients with LFLG AS and may provide additional information for clinical decision making beyond that achieved using BNP.