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Integrated approach in assessment of valvular calcification activity in aortic stenosis

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Introduction: Calcification is the key pathological process in aortic stenosis (AS) development. Circulating biomarkers and nuclear imaging methods could characterize the valvular calcification activity.
Purpose: To compare diagnostic values of serum fetiun A level and PET/CT with 18F NaF in assessment of aortic valve calcification.
Methods: 88 pts with asymptomatic AS were included: 39pts with tricuspid aortic valve (TAV) and 49 pts with bicuspid aortic valve (BAV). ECHO was performed at baseline and in 16.6±4.2 months. At start serum level of fetuin A was measured by ELISA in all pts and PET/CT with 18F NaF was performed in 60 of these pts (29 TAV pts and 31 BAV pts). Maximum standardized uptake value (SUV) was measured within circular region of interest (ROI) of 3.52 square millimeters that was drawn around areas of maximal 18F-NaF uptake in the valve. Blood-pool activity was estimated using maximum SUV within the same ROI, which was drawn on the left atrium. Ratio between maximum tissue and background SUV (TBR) was calculated. CT calcium scoring was performed using dedicated software.
Results: Pts with TAV were significantly older then BAV pts (62.4±5.3 yrs vs 55.9±8.4 yrs, p=0.003). TAV and BAV groups were comparable in AS severity by ECHO (peak aortic jet velocity (Vmax): 3.1±0.6 m/s vs 3.1±0.7 m/s, p=0.72). Both groups did not differ in valvular calcification degree (Agatston score 1433.9±1327.9 vs 1617.7±1404.5, p=0.59) and 18F-NaF uptake level (TBR 1.6±0.3 vs 1.6±0.5, p=0.64). Agatston score and TBR max 18F NaF were associated with AS severity measured by Vmax (r=0.58; $p<0.0001$ and r=0.46; $p<0.0001$ respectively). Fetuin A was significantly lower in pts with BAV compared to TAV pts (307.4±55.1 vs 342.6±78.2, p=0.02). The sensitivity and the specificity of fetuin A level in predicting of AS progression were 67% and 66%, respectively (AUC = 0.644 [95% CI: 0.527–0.750], p=0.04) with a cut-off value of 313.4 ng/ml. In BAV pts for cut-off value 313.4 ng/ml sensitivity and specificity were 81.8% and 59.4% respectively (AUC = 0.719 [95% CI: 0.561–0.845], p=0.006). There was no association revealed between fetuin A level and Agatston score, TBR 18F NaF.
Conclusions: Despite comparable valve calcification activity measured by PET/CT with 18F NaF in TAV and BAV pts, decreased circulating fetuin A was observed only in BAV pts, that may be related to different underlying pathophysiological mechanisms. Low serum fetuin-A level was associated with progression of AS, particularly in BAV pts.