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Progression of aortic valve stenosis is associated with bone remodeling and secondary hyperparathyroidism

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Background. There is currently no medical therapy that can prevent the progression of aortic valve stenosis (AS). Recent data highlight a possible relationship between bone metabolism and AS progression but prospective data are lacking.

Methods. Serum level of calcium, phosphorus, creatinine, vitamin D, intact parathormon (iPTH), C-terminal-telopeptide of type-I-collagen (CTX) and osteocalcin were assessed at baseline in 110 patients with at least mild AS. CTX/Osteocalcin ratio was calculated as a marker of bone remodeling balance. AS severity was assessed at baseline and 1 year based on mean gradient.

Results. AS progression was not associated with age, glomerular filtration rate, calcium and phosphorus levels, calcium-phosphorus product, but significantly with iPTH, CTX/Osteocalcin and vitamin D status (all $p < 0.01$). There was no correlation between iPTH and CTX/Osteocalcin ($R = 0.04$, $p = 0.70$) and AS progression was associated with CTX/osteocalcin ($R = 0.42$, $p = 0.009$) but not with iPTH ($R = 0.10$, $p = 0.55$) in patients with normal vitamin D level (33%), whereas it was associated with iPTH ($R = 0.47$, $p < 0.001$) and not with CTX/osteocalcin ($R = 0.04$, $p = 0.73$) in those with low vitamin D levels, especially if mild renal insufficiency was present ($R = 0.61$, $p < 0.001$).

Conclusion. In the present study, we observed an association between AS progression, vitamin D, iPTH and CTX/Osteocalcin ratio and their respective weight was function of the vitamin D status. In patients with low vitamin D, AS progression was associated with iPTH and secondary hyperparathyroidism, especially if mild renal insufficiency was present whereas in patients with normal vitamin D, AS progression was associated to a bone resorptive balance. These findings may have important therapeutic implications.

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Clinical outcome in asymptomatic severe aortic stenosis. Insights from the new proposed aortic stenosis grading classification

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Background: The management of patients with asymptomatic severe aortic valve stenosis (AS) remains controversial. Moreover, under the same denomination of severe AS, several entities may be identified according to transvalvular flow rates and pressure gradients, resulting in 4 flow-gradient patterns. We therefore studied the clinical course of patients with asymptomatic severe AS according to this new AS grading classification.

Methods and Results: Transthoracic echocardiography and measurement of BNP level from venous blood sample were performed in 150 consecutive patients with asymptomatic severe AS and normal exercise test. Patients were classified in 4 groups depending on LV flow state (normal flow vs. low flow: 35ml/m²) and pressure gradient levels (low gradient vs. high gradient: 40 mmHg). Patients with normal flow/low gradient (NF/LG) had significantly lower BNP than those with low flow/ high gradient (HG) and LF/LG. The mean follow-up was 27±12 months. At 2-year, cardiac event-free survival was 83±6%, 44±6%, 30±12% and 27±13% in NF/LG, NF/HG, LF/HG and LF/LG groups, respectively ($p < 0.0001$). On multivariable analysis, LF/LG (HR=5.26, 95% CI: 2.04-14.3, $p = 0.045$) and LF/HG (HR=2.38, 95% CI: 1.02-5.55, $p = 0.001$) were identified as strong independent determinants of poor prognosis as compared to NF/HG. By limiting the multivariable analysis to patients with LF, LF/LG was an independent predictor of markedly reduced cardiac event-free survival when compared to LF/HG (HR=5.4, 95%CI: 1.03-28.6, $p = 0.046$).

Conclusion: The use of the new AS grading classification integrating valve area and flow-gradient patterns allows a better characterization of the clinical outcome of patients with asymptomatic severe AS.

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Low flow-low gradient aortic stenosis associated with left ventricular dyssynchrony: impact on contractile reserve, and effects of cardiac resynchronization therapy

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Background: In low flow-low gradient aortic stenosis (LF-LG AS), assessment of contractile reserve (CR) using dobutamine stress echocardiography (DSE) is recommended to predict post-operative outcome. The prevalence and influence of left bundle branch block (LBBB) in this population has never been studied.

Purpose: 1) to evaluate the influence of LBBB on CR at DSE in LF-LG AS. 2) to assess the effects of cardiac resynchronization therapy (CRT) in patients with LF-LG AS associated with LBBB, without CR.

Methods. 25 patients with LF-LG AS were consecutively enrolled. CR was defined by an increase in stroke volume >20% on dobutamine. Patients with LBBB and high EuroSCORE >20% were proposed either surgical aortic valve replacement (AVR), transcatheter valve implantation (TAVI), or CRT prior to AVR.

Results: Seventeen patients (68%) had LBBB. Compared to patients with narrow QRS, these patients were older (83 vs 67 years, $p = 0.003$), more symptomatic (NYHA class 3.6 vs 2.5, $p = 0.002$), had higher logistic EuroSCORE (26.8 vs 16.8%, $p = 0.02$), lower mean aortic gradient (25 vs 36 mmHg, $p = 0.03$). CR was present in 46% of patients with LBBB, and 100% in those with narrow QRS ($p = 0.009$). Among 17 patients with LBBB, 15 underwent CRT: all of them had significant improvement in NYHA class, EuroSCORE, LVEF, mean aortic gradient, and Nt-proBNP. Ten of 15 CRT patients underwent subsequent AVR (6 surgical, 4 TAVI) with uneventful post operative outcome in all except 1 (mesenteric infarction). Four CRT patients refused AVR, 2 are doing well, 2 worsened and died 2 years post-CRT. One patient died suddenly 10 days post-CRT.

Conclusion: LBBB is highly prevalent in patients with LF-LG AS and may account for most cases of absent CR. CRT induces improvement in LVEF in all patients, including those with no CR on DSE, and should be considered prior to AVR to improve the status of patients with very high operative risk. However, the risk of sudden death following CRT remains to be determined.

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Changes in QRS duration during trans-catheter aortic valve implantation strongly predicts the risk of permanent pacing

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Purpose: Preventive pacing after TAVI (trans-catheter aortic valve implantation) exposes to the risk of severe complications, such as cardiac perforation. This can be avoided by limiting temporal lead placement in high risk patients. The purpose of this study is to identify clinical and electrical factors of permanent pacing.

Methods: The study included 35 patients (80±10 years, Euro-score=28.75±12%) free of permanent pacing before and immediately after TAVI procedure. Permanent pacemaker implantation was performed when complete atrioventricular block was observed at day 3 after TAVI procedure.