

Topic 04 – Valvular heart disease and general cardiology

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Gender specific profil of matrix metalloproteinase 3, tissue inhibitors and inflammatory markers on rheumatic mitral valve stenosis

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We investigated the profile and the relation of matrix metalloproteinase 3 (MMP-3), tissue inhibitors of matrix metalloproteinases (TIMP-1 and TIMP-2), and inflammatory markers (high-sensitive C-reactive protein) on rheumatic mitral valve stenosis (MVS) and restenosis post percutaneous mitral valve commissurotomy (PMC) in men and women.

We have enrolled 162 patients with rheumatic mitral stenosis (57 male, 45±11.56 y. old) and 88 healthy control subjects (46 male, 36±14 y.old.), previous PVC on 77% patients.

Peripheral blood samples were collected from these subjects to examine the plasma MMPs -3 and TIMP-1 and TIMP-2 by ELISA and high-sensitive C-reactive protein (hs-CRP). An echocardiography study was performed to evaluate area, anatomy and calcification degree of mitral valve. We observed a higher plasmatic levels of TIMP-2, hs-CRP and lymphocytes cells count on MVS patients than control (131.16±74 vs 71.34±47 ng/ml, p=0.02; 2.1 ±1.2 vs 4.6±2.8 mg/l, p=0.002 respectively) and lower level of MMP-3 (9.2±5.3vs 11.2±9.2 ng/ml, p=0.033). In case of restenosis, in men, the MMP-3 level was higher (16.39±5.7 vs 11.19±4.58 ng/ml, p=0.034), we observed a more severe MV calcification score. However, in women, we didn't relived a significant difference on MMP-3 level (7.47±3.6 vs 7.41±3.6 ng/ml), but a higher level of TIMP-2 and MMP-3 /TIMP-2 ratio. We observed also a significant higher levels of inflammatory markers but a lower calcification score. Positive correlation was found in women between calcification degree and MMP-3 plasmatic level (r=0.678, p<0.001), and between hs-CRP and MMP-3 (r=0.345, p=0.002). In men, only a correlation between MMP-3 and calcification degree were observed (r=0.456, p=0.05). This study suggest an implication of the MMP-3/TIMP system in ECM remodelling on rheumatic MS and demonstrates different patterns of association between inflammatory markers and MMP-3 in men and women, strengthening the hypothesis of gender specific differences in pathophysiological mechanisms of mitral stenosis evolution and calcification

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Relationship between anatomic and hemodynamic progression in aortic stenosis – impact of the degree of AS severity

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Background: Aortic stenosis (AS) is mainly caused by progressive calcium deposition within the valve leaflets. Aortic valve calcification (AVC) can be accurately measured using Multi-Detector-Computed-Tomography (MDCT) but the relationship between anatomic progression (calcium burden or AVC) and haemodynamic progression (aortic valve area (AVA)) has not been specifically evaluated.

Methods: In 146 patients with at least mild AS (AVA < 2 cm²) enrolled in an ongoing prospective cohort, we performed an echocardiographic evaluation of AS severity and a measurement of AVC using MDCT at study entry and at 2 years.

Results: At baseline mean AVA was 1.42±0.4 cm² and mean AVC 1082±871 AU. After 2 years of follow-up, mean AVC increase was 167±166 AU/year and mean AVA decrease -0.09±0.08 cm²/year. There was a significant correlation between hemodynamic and anatomic changes (r=0.26 p<0.001). Among the 146 patients, 46 had a mild AS (AVA>1.5 cm²), 82 a moderate AS (AVA 1-1.5 cm²), and 18 a severe AS (AVA<1cm²). Progression in each group was 120±122 AU/year and -0.10±0.09 cm²/year for mild AS, 166±141 AU/year and -0.08±0.07 cm²/year for moderate AS, and 317±265 AU/year and -0.06±0.05 cm²/year for severe AS. However; the association between hemodynamic and anatomic progression was not significantly different between the 3 groups of AS severity (p=0.37).

Conclusion: In this prospective cohort of patients with a wide range of AS severity we show that 1) there was a linear correlation between anatomic and hemodynamic changes and 2) that this association was similar among the 3 AS grades. Our results suggest that medical strategy aiming at preventing AVC progression may be useful in all subset of AS patients including those with severe AS.

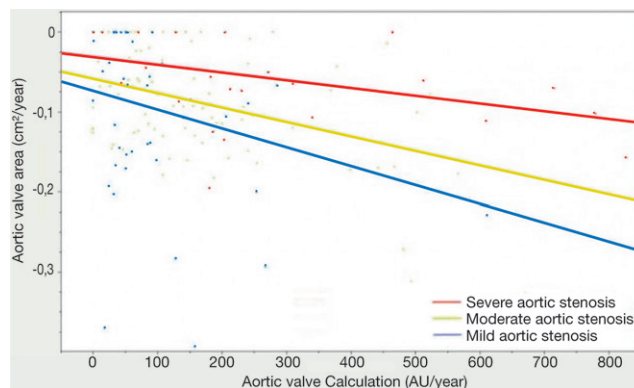


Figure – Relationship between AVC and AVA changes

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Effect of volume overload elimination on LV reverse remodelling after mitral valve surgery in organic MR

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Background: The short and long-term effects of volume overload elimination on left ventricular (LV) volume, function and systemic hemodynamic after surgery for chronic organic MR have been poorly explored.

Methods: 224 pts (64±13 years, 70% males) with severe organic MR referred to surgery underwent serial MR and LV measurements at baseline, early after surgery and at late follow-up (428 [355-688] days). Peripheral vascular function was also evaluated. Four pts with recurrent MR were excluded from analyses.

Results: There was a phased response of the LV. Elimination of volume overload led to an early drop in LV end-diastolic volume (EDV index: 119±25 to 75±14 mL/m², P<0.0001) after surgery while end-systolic volume (ESV) did not change. LV EF decreased (71±8 to 54±12%, P<0.0001) but forward stroke volume increased (38±8 to 40±9 mL/m², P=0.02). Early decline in EDV was related to pre-op MR volume (r=0.88, P<0.0001). In the late phase, LV ESV index decreased to 28±9 mL/m² (P<0.0001) while EDV index decreased further and LV EF increased to 60±8% (P<0.0001). Systemic vascular compliance and resistance improved. Surgery was performed early (Early) in 80 pts and later in 140 pts (Classical). Pre-op LV remodeling was worse in the Classical group. Despite a significant LV reverse remodeling in both groups, LV volumes remained higher and LV EF lower in the Classical group

compared with the Early group at late follow-up and vascular function remained impaired.

Conclusion: LV reverse remodeling after surgery for organic MR is a phased process. The initial step is driven essentially by the elimination of regurgitant volume with a proportional decline in EDV while ESV does not change and LV EF decreases. Long-term improvement of LV EF depends on a further decrease in EDV associated with a decrease in ESV. Patients operated early experience a more complete LV reverse remodelling, and a greater LV EF and vascular function recovery compared with classical indications.

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Impact of valve surgery in patients with infective endocarditis and neurological complications

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Neurologic complications (NC) are a major cause of morbidity and mortality in pts with infective endocarditis (IE) and may prevent pts from receiving valve surgery.

Methods: Among 399 cases of Li definite left-sided IE collected during a one-year prospective population-based survey, 100 had at least one symptomatic neurological complication (SNC). NC included transient ischemic attack, ischemic stroke, cerebral hemorrhage, meningitis, brain abscess and intracranial mycotic aneurysm. A neuroimaging procedure was performed in 183 of the remaining pts which diagnosed 35 asymptomatic (As) NC and was considered normal in 148 pts (NoNC).

Results: Among pts with SNC, 40 episodes occurred after the beginning of IE antibiotic therapy (21 during the first 48 hours). Mechanical prosthetic IE (OR 3.4, $p=0.007$), *S.aureus* IE (OR 1.8, $p=0.03$) and mitral IE (OR 2.0, $p=0.008$) were predictive of the occurrence of NC. Among the 135 NC pts, age, renal failure, septic shock and *S.aureus* as responsible micro-organism were predictive of in-hospital (33%) and 1-year mortality (38%). Furthermore, a symptomatic NC was also predictive of 1-year mortality. Rate of surgery was not different between pts with and without NC (52% vs 57%) but was significantly higher in AsNC than in SNC (77% vs 43%). In hospital mortality was higher in pts with NC than in noNC pts (33% vs 17%, $p=0.001$) and in SNC than in AsNC (42% vs 9%, $p=0.0003$). Among the 135 NC pts, 95 had a surgical indication (71%) which was performed in 70 (mortality 20%) and not performed in 25 (mortality 68%).

Conclusion: The presence of NC is associated with a poor prognosis when it is symptomatic. However, when NC is discovered on systematic neuroimaging, it is associated with a very high rate of surgery and a better prognosis than that of pts with SNC and even without NC, suggesting a protective role of surgery.

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Mid-term results of the self-testing of the international normalized ratio in adults with a mechanical heart valve

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The study protocol on the use of Dabigatran in patients with mechanical valves was interrupted by the laboratory Boehringer Ingelheim. The vitamin K antagonists (VKA) remain currently the only molecules used for the prevention of complications related to thromboembolism in this group of patients.

The quality of life of patients with mechanical valve prosthesis mainly depends on the stability of the INR (international normalized ratio), which is achieved by an optimal biological monitoring, and guarantees the absence of unwanted events related to anticoagulation. The objective of this study is to show that INR self-measurement at home is reliable and feasible and that it is the key to improve the patients' medical care.

Methods: All patients in the study concerning the INR self-measurement (clinicaltrials.gov: NCT00925197) conducted between the years 2004 and 2007 were contacted again to allow the medium term follow-up. In total, 178 patients among the 192 patients who participated to the study answered the questionnaire. The average patients follow-up was 4.2 years for the self-measurement group and 4.9 years for the control group.

Results: Among these patients, only 26 (group A) continued to use the INR self-measurement to monitor their VKA treatment. The main reasons for the interruption of the use of INR self-measurement mentioned by the patients are the high cost and the difficulty to get bandages supply. There were significantly fewer bleeding complications ($p=0.04$) and fewer complications related to VKA ($p=0.01$) for patients in group A compared to the control group (group B).

Conclusion: Despite the lack of the cost covering of the INR monitoring by self-measurement in adults with a mechanical heart valve, some patients continue to use this method for their long-term follow-up. These patients present a significant reduction of the bleeding accidents rate and / or thromboembolism associated to VKA and a significant improvement of their quality of life.

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Aortic root diameter in patients with spontaneous cervical artery dissection

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Background: Spontaneous cervical artery dissections (SCAD) are a well-recognized cause of ischemic stroke among young and middle-aged individuals. The exact pathogenesis of this condition remains unknown. It was proposed that an underlying vasculopathy originating from disturbed development of extra cellular matrix could exist. Aortic remodelling is usually seen in such extracellular matrix abnormalities. The aim of the study was to compare aortic dimensions in patients with SCAD and healthy controls.

Methods: We designed a retrospective single-center case control study. 63 patients with SCAD were identified and compared to a control group matched to case patients for age (± 5 years) and sex. Aortic morphology was assessed using Trans thoracic echocardiograms (TTE). The diameters of the aorta were assessed at four levels: aortic annulus, sinuses of Valsalva, sino tubular junction and proximal ascending aorta.

Results: For men and women, aortic diameters did not differ between the two groups (aortic annulus: 12.7 ± 1 vs 12.2 ± 1.1 mm/m², $p=0.09$; sinuses of Valsalva: 17.8 ± 1 vs 18.6 ± 1.9 mm/m², $p=0.7$; sino tubular junction: 15.3 ± 0.9 vs 15.9 ± 2.3 mm/m², $p=0.67$; proximal ascending aorta 17.3 ± 1.6 vs 17.4 ± 2.1 , $p=0.87$). Unexpectedly, we found 3 patients with bicuspid aortic valve.

Conclusion: In our study, SCAD is not associated to an enlargement of the aortic root. Bicuspid aortic valve may represent a risk factor for SCAD.

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Covered stent graft for vessel injury after transfemoral aortic valve implantation

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Access site complications remain the most frequent adverse event after transcatheter aortic valve implantation (TAVI) and are often treated percutane-

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