

TOPIC 29 – Valvulopathies: mitral and others

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0266

Echocardiographic factors determining immediate results of percutaneous mitral balloon commissurotomy

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Objectives: Define echocardiographic predictors of the immediate results of percutaneous mitral balloon commissurotomy (PMC)

Methods : PMC by the Inoue balloon was attempted in 247 patients (mean age: 35 ans, 77% female) with severe mitral valve stenosis. All the patients had undergone echocardiographic examination before PMC to assess mitral anatomy, commissural calcification and to determine the Wilkins score.

Results: the mean value of Wilkins score was 7.98 ± 1.61 (range 5-13) and the mean mitral valve area (MVA) before PMC was $1 \pm 0.19 \text{cm}^2$ (range 0.5-1.4 cm^2). Twenty-nine patients (11.7%) had one-commissural calcification. After PMC, the mean MVA increased to $1.79 \pm 0.34 \text{cm}^2$ ($p < 0.001$) resulting in a success rate of 83%. Severe mitral regurgitation (MR) occurred in 5 patients (2%). Wilkins score was an independent predictor of the immediate result of PMC, but if > 8 , this score had a weak predictive value. Commissural morphology was another independent predictor of the immediate result of PMC.

Conclusion: Echocardiography is now the cornerstone in the assessment of mitral anatomy before PMC and should integrate Wilkins score and commissural morphology for the optimal selection of patients to PMC.

0098

Small GTPase deregulation and decreased $\beta 1$ -integrins expression might be involved in Fln A mutation associated to the valvulopathy

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Mutations in *FLNA* gene that encodes Filamin A (FlnA) an actin binding protein involved in actin cytoskeleton organization and many cellular signaling pathways were identified in X-linked Myxomatous Valvular Dystrophy (XMVD).

To analyze the effects of FlnA-P637Q mutation, I established stable cell lines expressing FlnA-WT and P637Q from a cell line that does not express endogenous FlnA. FlnA-P637Q cells exhibit impaired adhesion, spreading and migration capacities suggesting small Rho and Rac GTPase dysregulation. Using pull down experiments to evaluate Rho and Rac-GTPases activities and western blot to evaluate Rho and Rac effectors phosphorylation (MYPT and PAK, respectively), we showed increased RhoA activity and low Rac activity in FlnA-P637Q vs FlnA-WT cells. Rock inhibitor (Y27632 10 μM) and constitutively active Rac-G12V restored adhesion and spreading capacities of FlnA-P637Q cells, respectively. In addition, FlnA-P637Q cells exhibited decreased $\beta 1$ -integrins expression

In summary, FlnA mutations involved in valvular dystrophy modify the balance between RhoA and Rac activities and the expression of $\beta 1$ integrins. The potential roles of FilGAP (a GAP of Rac) and another small GTPase R-Ras which interacts with both $\beta 1$ -integrins and FlnA and participates to the adhesion process, are now under investigations.

In conclusion, our studies revealed FlnA mutations impair the regulation of two crucial players in extracellular matrix-cell crosstalk: integrin and GTPases. This suggests similar mechanisms may be at work in the valvulopathy.

0347

Subclinical right ventricular dysfunction in mild mitral stenosis

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Purpose: Mild mitral stenosis (MS) defined by a valve area between 1.5 and 2 cm^2 , usually does not have clinical consequences. The aim of this study is to assess right ventricular (RV) function in asymptomatic patients with mild mitral stenosis.

Method: We included 32 asymptomatic patients in sinus rhythm with pure mild MS (mean mitral valve area= $1.73 \pm 0.21 \text{cm}^2$) and 35 healthy subjects. The 2 groups had similar mean ages and sex ratio. All included subjects had no evidence of hypertension, diabetes mellitus, ischemic heart diseases or chronic pulmonary diseases. We used standard echocardiography and tissue Doppler imaging.

Results: We observed no difference in conventional indices of global left ventricular function between the 2 groups. Also, RV ejection fraction, the conventional Tei index and the tricuspid annular plane systolic excursion were similar in both groups. Conversely, the tricuspid annulus systolic velocities obtained at the basal RV free wall were significantly decreased in mild MS patients ($11.3 \pm 1.3 \text{cm/s}$ vs. $14.9 \pm 1.6 \text{cm/s}$, $p < 0.01$). In addition tricuspid annulus early diastolic velocities were significantly reduced in mild MS subjects ($-7.5 \pm 1.4 \text{cm/s}$ vs. $-10.9 \pm 1.3 \text{cm/s}$, $p < 0.01$) with lower ratio of early to late diastolic velocities (0.7 ± 0.15 vs. 1.24 ± 0.18 , $p < 0.01$). Among mild MS patients, impaired RV systolic and diastolic indices are significantly pronounced in the subgroup with mitral valve area $< 1.7 \text{cm}^2$.

Conclusion: Our data show the presence of subclinical systolic and diastolic RV dysfunction in pure mild mitral stenosis patients. Tissue Doppler imaging is a useful tool to demonstrate RV abnormalities and seems to be a powerful technique to monitor disease process.

0240

Surgery in infective endocarditis in a Tunisian high-volume tertiary care center: epidemiologic profile and predictors of mortality

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Introduction: 50% of infective endocarditis (IE) requires surgery during its active phase.

Objectives: to describe the demographic characteristics of patients who underwent a surgical treatment for IE in our center and to analyse predictors of mortality.

Methods: Our study is retrospective enrolling 297 patients, hospitalized in our institution between January 2001 and January 2010 for infective endocarditis. According to the modified DUKE criteria. 136 patients (49%) required surgery during the active phase of IE.

Results: 58% of the patients were men, The Mean age was 45.45 ± 12.17 years. The mean diagnosis delay was 9 ± 8 days. The Mean delay from diagnosis to surgery was 6 ± 4 days. The mean logistic Euro Score was 3. The Main valve involvement was aortic endocarditis (77.2%). Left-sided native valve IE, left-sided prosthetic valve IE, right-sided IE were involved respectively in 77.2% cases, in 22% cases, in 1.4% cases. Most often surgical indication was persistent heart failure due to severe valvular regurgitation (73%). Global mortality of IE was 16.1%, being 22% in the surgical group. In comparison with survivors, patients who died had more hyperleucocytosis ($p = 0.01$) and more severe anemia ($p = 0.01$), high logistic EuroScore ($p = 0.03$), early prosthetic endocarditis ($p = 0.01$) and septic shock ($p = 0.01$).

Conclusion: Our series demonstrate that the strongest predictors of mortality were: leukocytosis, anemia EuroScore value, early prosthetic IE, and septic shock.

0022

**Immediate and middle results of percutaneous mitral valvuloplasty
An experience of a Tunisian tertiary center (354 patients)**

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Introduction: Percutaneous mitral valvuloplasty (PVM) is an effective alternative of surgery in selected patients with rheumatic mitral stenosis but the result of the procedure is widely depend on the operator experience. Our aim is to analyse the immediate and the middle results of PVM in a Tunisian center.

Patients and methods: it is a retrospective study including 354 patients undergoing PVM for the first time between 1996 and 2004, in our department. The clinical, echocardiographic and hemodynamic data were obtained from medical files.

Results: the mean age was 33.9 years and most patients were women (81.07%). Forty two patients had a history of commissurotomy (12%). The main symptom was dyspnea class II NYHA (72%) whereas only 28 patients (7.9%) suffered from pulmonary edema at clinical follow up. The transthoracic echocardiography was achieved in all patients and beside mitral stenosis, it showed an aortic valvulopathy in 39%. The transoesophageal echocardiography performed in 304 patients (85.5%) and concluded at wilkins score >8 in 32%. The hemodynamic exam was systematic before the procedure. The PVM succeeded in most time. The mitral valve area moved from a mean of 1.23 cm² to a mean of 2.04cm² after PVM, the transmittal gradient moved from a mean of 20.44mmhg to a mean of 7.24mmhg, the systolic arterial pulmonary pressure moved from a mean of 50.44mmhg to a mean of 33.22mmhg. The procedure was complicated of a cardiac tamponnade in two cases (0.56%). A mitral regurgitation was appeared in 115 patients (34.6%) and was aggravated in 31 patients (10.7%). A severe mitral insufficiency was noted in 23 patients only (6.5%). During a mean follow up of 92 months, a restenosis was noted in 117 patients (33.1%), surgery was needed in 37 patients (10.54%) and PVM was repeated in 72 patients (20.33%). The cumulative event-free survival rate was estimated at 68%.

Conclusion: The results of PVM in our department confirm that it is an excellent treatment option in mitral stenosis. It is minimally invasive, well-tolerated and has a high success rate.

0371

Addressing the role of blood flow and klf2a during zebrafish valvulogenesis

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Heart contractility and blood flow are essential for valve formation in zebrafish (Hove, 2003). As these parameters are highly interdependent, it has been difficult to precisely characterize the influence of blood flow during zebrafish valvulogenesis. High resolution imaging showed the presence of a bidirectional flow or reversing flow, in the atrio-ventricular canal (AVC) where valvulogenic progenitors are located. In cell culture, submitted to pulsatile flow, numerous genes are up-regulated, suggesting that endothelial cells are able to interpret flow patterns (Dekker et al., 2002). Among these pulsatile flow inducible genes, *klf2a* localize in the AVC in zebrafish (Vermot, 2009). When heartbeating and reversing flow are reduced and when *klf2a* is knock down in the AVC, valvulogenesis is impaired. Our hypothesis is thus that reversing flow controls *klf2a* expression in the AVC to form functional valves.

To characterise the flow inducible control of *klf2a* expression in vivo we generated different *klf2a* expression reporter through transgenesis using *klf2a* promoter. We first explored the expression pattern in the AVC to address the specificity of the different promoters. We next tested the flow dependency of these *klf2a* promoters by modulating hemodynamic forces. When playing on velocity, heartbeating and reversing flow are respectively absent or reduced, resulting in a decrease in the number of GFP positive cells in the AVC and an absence of functional valves. According to these results, we isolated the *klf2a* line with the most specific expression pattern. Our results suggest that this line will provide a good tool to study *klf2a* expression in the AVC function of flow and indicate that both reversing flow and contractility are important to maintain *klf2a* expression in the AVC and proper valvulogenesis.

0040

Endocarditis admitted to a surgical tertiary care center ICU: one year prospective study

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During a 1 year period, 61 patients were admitted with a proven (Duke major criteria) complicated endocarditis that needed ICU hospitalisation

Patients were admitted from other services of the Bordeaux University Hospital (21/61- 34%) or transferred from local hospitals (40/61- 66%)

Admissions were motivated by : High grade valve failure that needed prompt surgery (53/61- 87%), most of them were aortic insufficiency (35/61- 57%)

Heart failure (killip 2 14/61- 23% killip 3 16/61 - 26% killip 4 8/61- 13%)
Septic shock with the need of amines (21/61 - 31%)

Embolic complications (25/61 - 41%) mainly neurological ones (16/61 - 26%)

Patients frequently required reanimation measures before surgery :
Mechanical ventilation (15/61 - 25%)

Renal epuration represented by veno venous continuous hemofiltration (19/61 - 31%)

Use of pressive amines (22/61 - 36%)

Ecological datas showed that staphylococci (and enterococci were the 2 predominant germs. Oral streptococci were rare. (cf. diagram)

Native valves accounted for 2/3 of endocarditis.

Health care acquired endocarditis were frequent (18/61 - 31%).

Surgery was performed in 44/61 patients (71%). The median delay was 5.8 +/- 7.2 days. Patients with neurological complication median delay for surgery was 32 +/- 9 days.

Surgery was elective (20/61 - 32%), urgent (35/61 - 58%) or emergency (6/61 - 10%). No salvage procedure was performed.

In hospital death was 15/61 (24%). Patients that benefited of surgery In hospital mortality was 7/44 (16%).

Three months mortality in the medical treatment group was high: 8/12 (72%).

Three months mortality was also high in the group with neurological complications: (6/16) 36%

0402

Preoperative atrial fibrillation is an independent predictor of post-operative left ventricular dysfunction after valve repair for mitral valve prolapse

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Background: Left ventricular (LV) dysfunction is the first cause of late mortality after mitral valve surgery. Patients with severe organic mitral regurgitation (MR) and preoperative atrial fibrillation (AF) have increased post-operative mortality. Guidelines recommend surgery, preferably mitral valve repair (MVR), for patients with severe organic MR and severe symptoms or overt LV dysfunction or occurrence of AF. In this analysis, we studied the association between preoperative atrial fibrillation and occurrence of LV dysfunction after MVR.

Methods: Between 1991 and 2009, 335 consecutive patients underwent MVR for severe mitral regurgitation due to leaflet prolapse in our institution. Echocardiography was performed preoperatively and at 10.8 (9 - 12 months) after surgery in 306 patients who represented the study population. Cardiac events were recorded during follow-up. LV dysfunction was defined by LV ejection fraction (EF) <50%.

Results: LVEF decreased from 67.1±9.7% before surgery to 58.9±10.1% post operatively (p<0.0001). There were 79 patients (23.6%) in AF at baseline.

Patients in AF at baseline were older (70 ± 9 vs. 65 ± 10 years old, $p < 0.0001$), more often in NYHA III - IV class ($p=0.027$), had a higher EuroSCORE (4.5 ± 5.8 vs. 2.8 ± 2.4 , $p<0.001$), and lower preoperative EF (64 ± 11 vs. $68\pm 9\%$, $p=0.002$). On univariate analysis, AF at baseline was associated with post-operative LV dysfunction during follow-up ($p=0.008$). On multivariate analysis adjusted for gender, EuroSCORE, NYHA III - IV class, preoperative EF, preoperative AF and EF were the 2 parameters associated with LV post-operative dysfunction (OR 2.06, $p=0.038$ and OR 1.04, $p=0.027$ respectively). Post-operative LV dysfunction was associated with more than 2.5 - fold increase in the risk of cardiac death or cardiac heart failure during follow - up (HR 2.67 (1.41 - 5.08); $p=0.0003$).

Conclusion: Preoperative AF is an independent predictor of post - operative LV dysfunction after valve repair for mitral valve prolapse.

0408

Preoperative atrial fibrillation predicts outcome after valve repair for mitral valve prolapse

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Background: Guideline recommend surgery, preferably mitral valve repair (MVR) for patients with severe organic MR, and severe symptoms or overt LV dysfunction or occurrence of AF. However, the impact of preoperative AF on outcome is not well defined. The aim of this study is to assess the impact of preoperative AF on outcome in patients undergoing MVR for mitral valve prolapse.

Methods: Between 1991 and 2009, 335 consecutive patients underwent MVR for severe MR due to leaflet prolapse. Univariate and multivariate logistic regression analyses were performed to evaluate predictors of early mortality, long term mortality, and occurrence of heart failure after the surgery (Follow-up:mean duration, 105 ± 52 months).

Results: The 79 patients (23.6%) in AF at baseline. were older (70 ± 9 vs. 65 ± 10 years, $p<0.0001$), more often in NYHA III - IV class ($p=0.027$), had a significantly higher EuroSCORE (4.5 ± 5.8 vs. 2.8 ± 2.4 , $p<0.001$). At baseline, mean preoperative ejection fraction (EF) was 64 ± 11 and $68\pm 9\%$ in patients in AF and sinus rhythm, respectively ($p=0.002$). Incidence of early mortality was 6.3% of patients with preoperative AF ($n=10$) vs. 1.9% of patients in sinus rhythm ($n=5$, $p=0.046$). Multivariate analysis did not identify AF as a predictor of early mortality whereas EuroSCORE ($p < 0.0001$) and low preoperative EF $< 60\%$ ($p=0.019$) were independent risk factors for early mortality. On multivariate analysis adjusted for EuroSCORE, NYHA III - IV class and preoperative LVEF, preoperative AF was IDENTIFIED AS an independent predictors of overall mortality (OR 1.372; $p=0.02$). AF was ALSO identified as an independent predictor of occurrence of heart failure (OR 1.548, $p=0.028$).

Conclusion: Preoperative AF is an independent predictor for long term mortality and occurrence of heart failure during follow-up after MVR for MR.