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EARLY AND MID-TERM FUNCTIONAL AND HEMODYNAMIC EVALUATION OF THE ST. JUDE MEDICAL REGENT 17-MM AORTIC VALVE MECHANICAL PROTHESIS

Edvin PRIFTI,
Giovanni MINARDI,
Altin VESHTI,
Francesco MUSUMECI

Abstract

Objective: The aim of the present study is to report the early and mid-term clinical and hemodynamic results of a prospective trial investigating the clinical performance of the St Jude Medical Regent 17-mm mechanical aortic valve prosthesis (SJMR-17).

Materials and Methods: Between January 2001 and January 2006, 20 patients with aortic valve stenosis underwent first time AVR with a SJMR-17. There were 18 females and two males. Mean age was 69.2±7.3 years and mean BSA was 1.68±0.2 m2. The mean follow-up was 18.7±9.2 months (range 10-32 months). All patients were monitored with serial echocardiograms; the first study was performed preoperatively, subsequent controls were at 2 months, 6 months, and within 1 year, respectively. All survivors underwent Dobutamine stress test at 1 year after surgery.

Results: There was one death. At six months follow-up the mean NYHA FC class was 1.3±0.6 significantly lower than preoperatively 2.75±0.86 (p<0.0001). The peak and mean transprosthesis gradients were 29±6.8 and 17.5±4.5 mmHg respectively, significantly lower than preoperatively. Left ventricular mass(gm) and indexed left ventricular mass (gm/m2) were 191±23.8 gm/m2 and 114.5±10.6gm/m2 significantly lower than preoperative values 258±43gm (p<0.0001) and 157±27.7 gm (p=0.00003).The M-TPG correlated well with the LVMi reduction (p=0.033). During DSE the P-TPG and M-TPG increased significantly to 73.8±17.7mmHg and 37±10.7mmHg respectively, significantly higher than at basal state. Differently, the EOA, EOAi and DVI increased during DSE but not significantly versus the values measured at rest. The multivariate regression analysis identified EOAi, BSA, age, postoperative LVMi as strong predictors for higher mean transprosthesic gradients.

Conclusions: The SJMR-17 prosthesis might be employed with satisfactory postoperative clinical and hemodynamic outcome in patients with small aortic annulus, especially in elderly patients, as an alternative to other valves' choice or alternative surgical strategies such as annulus enlargement.

Key words: St Jude Medical Regent 17-mm mechanical aortic prothesis, dobutamine stress test, indexed effective orficice area, indexed left ventricular mass.

Introduction

Aortic valve replacement (AVR) in patients with a small aortic annulus is often challenging for the surgeon in terms of prosthesis selection. AVR with a small prosthetic valve is technically straightforward and commonly performed, but it may result in a patient-prosthetic mismatch resulting in a high residual outflow gradient, the significance of which remains the subject of controversy (1-9). The use of stentless valves or homographs results in lower residual postoperative gradients, but implant procedures are technically more demanding, leading to increased total ischemic time (10-13). Annular enlargement allows for insertion of a larger aortic prosthesis, but it too may introduce increased surgical risks (14-15). On the other hand, bileaflet valves are still the most implanted cardiac valve substitutes in the aortic position. Their excellent durability and low incidence of cardiac-related complications have been widely reported in the medical literature (3,16-18). The St. Jude Medical Regent valve is the next-generation bileaflet mechanical prosthetic aortic valve, constructed of pyrolytic carbon which has a modified external profile that achieves a larger geometric orifice area without changing the existing design of the pivot mechanism or blood-contact surface areas.

The St Jude Medical Regent™ 17-mm aortic valve mechanical prosthesis (SJMR-17) is undergoing evaluation for clinical use by the US Food and Drug Administration, based also in the data provided by

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this study. The employment of a 17-mm mechanical prosthesis is very rare and usually is indicated in small aortic roots when all the other alternatives such as annulus enlargement are not effective. There are no data in the today literature regarding the postoperative outcome in patients undergoing AVR with a SJMR-17. The aim of the present study is to report the early and mid-term clinical and hemodynamic results of a prospective trial investigating the clinical performance of the SJMR-17.

Materials and methods

Between January 2000 and January 2006, 20 patients with aortic valve stenosis underwent first time AVR with a SJMR-17 at the San Camillo Hospital, Rome. Valve replacement was performed for rheumatic or degenerative valve disease and severe aortic valve stenosis with or without regurgitation. The investigational board approved the study protocol and written informed consent was obtained from all patients. For the past four years our practice has been to size the annulus and insert a SJMR-17 when indicated, without tempting the implantation of a 19-mm valve prosthesis by enlarging the aortic annulus.

Patients' characteristics. Preoperative demographic data are given in Table nr.1. There were 18 females and two males. Mean age was 69.2±7.3 years and mean body surface area(BSA) was 1.68±0.2 m2. The age, weight and BSA distribution are given in Figure nr.1A, nr.1B, nr.1C. Preoperative echocardiographic data are given in Table nr.3.

Anaesthesia and cardiopulmonary bypass. The inducement of anaesthesia consisted in: Fentanyl (25-30 γ/Kg), Diazepam (0,2 mg/Kg) and Bromure of Pancuronium (0,1 mg/Kg), and maintained with Ramifentanil (1-3 γ/Kg/min), Propofol and Isofluorane if necessary. The right atrium was cannulated using a double stage cannula. Normothermia and intermittent anterograde warm blood cardioplegia was employed. In cases undergoing mitral valve surgery, both caval veins were cannulated separately. The left ventricle was vented through the right superior pulmonary vein.

Operative techniques. The aortic annulus was debrided meticulously and measured with a snugly fitting sizer. Bicuspid aortic valve was found in 9 patients. Prosthesis size was selected according to the size of the aortic annulus. The AVR with a larger size aortic prosthesis such as 19-mm or 21-mm valves was tempted in all cases. In any of the 20 patients included in the study, the implantation of a 19-mm valve was not possibile. Then, it was decided the implantation of a SJMR-17. We rim the annulus with interrupted 2-0 Ethibond (Ethicon, Somerville, NJ) mattress sutures, with or without Teflon (Impra Inc, a subsidiary of L.R. Bard, Tempe, AZ) pledgets. The 17-mm mechanical aortic prosthesis were implanted in the supra-annular position in all cases. One patient required annulus enlargement. The operative and early postoperative data are given in Table nr.2.

Anticoagulation. All patients were anticoagulated with warfarin sodium from the second postoperative day. The international normalized ratio was used as control and kept between 2.5 and 3.5.

Follow-up. All patients were contacted and visited by the same investigator. The mean follow-up was 18.7±9.2 months (range 10-32 months). The INR, clinical status for any cardiac event were evaluated. Prior discharge all patients underwent echocardiographic examination. The second postoperative echocardiographic control was performed within 6 months after surgery. At one year after surgery, all patient but one underwent basal and dobutamine stress echocardiography. The other patient underwent basal and dobutamine stress echocardiography at 4 months after surgery. All preoperative and postoperative echocardiographic examinations were performed by the same investigator. At follow-up 20-mL blood sample was taken to perform the following measurements: (1) blood hemoglobin (in grams per deciliter); (2) serum lactic dehydrogenase (in units per liter); (3) percent-correlated reticulocyte fraction; (4) serum haptoglobin (in grams per liter). The criteria proposed by Skoularigis and colleagues (19) were used partially to define hemolysis. Patients were considered as having intravascular hemolysis when serum lactic dehydrogenase (LDH) levels were elevated (>460 U/L, major criteria) and at least 2 of the following minor criteria were observed: 1)blood hemoglobin of less than 13.8 g/dL for male patients and less than 12.4 g/dL for female patients; 2) reticulocyte fraction of greater than 2%; 3) serum haptoglobin level of less than 0.5g/L.

Echocardiography. Studies were performed with the use of 2.5-3.5 MHz transducer interfaced to SONOS 5500 (Agilent Technologies, Andover, Mass). All patients were monitored with serial echocardiograms; the first study was performed preoperatively, subsequent controls were at 2 months, 6 months, and 1 year, respectively. Images were stored on tape for late off-line analysis. M-mode, twodimensional, continuous pulsed-wave, and color Doppler were carried out and standard views were used.

The presence of aortic regurgitation was quantified using color flow Doppler; ratios of either percent diameter or percent area of the jet to that of the left ventricular outflow tract (LVOT) in the long- or short-axis views were calculated. The regurgitant orifice was measured at its origin, just below the aortic valve. Aortic regurgitation was defined as trivial (grade I), mild (grade II), moderate (grade III), or severe (grade IV). Measurements of end-systolic diameter (ESD),

enddiastolic diameter (EDD), posterior wall thickness (WT), and interventricular septal thickness (IVST) were first made according to the recommendation of the American Society of Echocardiography using a leading edge-to-leading edge convention.

Left ventricular ejection fraction (LVEF) was calculated by using the apical four-chamber view and the application of the modified Simpson rule method. Beta-blockers were discontinued in 6 patients 24 hours before the test, whilst patients on Ace-inhibitors and Calcium antagonist continued their medication.

Soon after dobutamine was infused intravenously starting at 5 μg/kg/min and increasing by 5microg/Kg/min at 5 min interval up to 40 μg/kg/min. The dobutamine stress echocardiography (DSE) was terminated if any of the following end-points were met: target heart rate >85% of maximal predicted, angina or progressive dyspnoea, 2-mm ST-segment depression 80 msec after the J point or in case of hypertension (systolic blood pressure >220, diastolic blood pressure >120 mmHg), hypotension (drop in systolic blood pressure >30mmHg), frequent or polymorphous ventricular ectopic beats or supraventricular tachiarrhythmias or for intolerable symptoms. Heart rate (HR) and a 12-lead ECG were recorded continuously; blood pressure, cardiac output (CO), peak and mean gradients, effective orifice area (EOA), indexed EOA as well Doppler velocity index (DVI) were measured at baseline and at the end of each increment of dobutamine.

Doppler measurements and calculations. The maximal instantaneous pressure gradient across the prostheses was estimated by the modified Bernoulli equation; the mean pressure gradient was derived by planimetry of the Doppler envelope. Measurements from at least three velocity envelopes were averaged to assure consistency. The V_{LVOT} was obtained with pulsed-wave Doppler in the LVOT proximal to the aortic prostheses from the apical five-chamber view; the $V_{TRANSPROSTHETIC}$ was obtained with continuous-wave Doppler from the apical five-chamber view. The employed formulae for calculating the hemodynamic parameters are given in Table 3. Patient-prosthesis mismatch was defined as those patients indexed EOA below the 10th percentile ($\leq 0.60 cm^2/m^2$) (6).

Definitions. *Body surface area (BSA)* is body morphometric analysis indexing weights and heights. Indexed left ventricular mass reduction (R-LVM_i) is the difference between the preoperative value of the LVM_i and postoperative LVM_i. *Renal failure was* defined as a documented fasting serum creatinine level of 2.0 mg/dL. *Myocardial infarction was* defined either as the appearance of a new Q wave in 2 or more contiguous leads on the electrocardiogram or as clinical, angiographic, electrocardiographic, and/or laboratory isoenzyme evidence of myocardial necrosis if the electrocardiogram shows no new Q waves. *Reoperation* includes patients who had any prior cardiac operations. *Operative death* includes all deaths that occurred within 30 days of the AVR operation or death that occurred within the same admission. *Multiorgan system failure* indicates compromised function of 2 or more major organ systems. *Atrial fibrillation* indicates multiple atrial foci that discharge without a single uniform atrial depolarization documented by either monitor or electrocardiogram. *Bleeding* includes all patients who required surgical exploration, either in the operating room or in the intensive care unit, for postoperative continued hemorrhage.

- *Statistical Analysis.* Group statistics were expressed as mean ± SD. Fisher's exact test was used for the non continuous variables. The relationship between variables in different time points within the same group was assessed by the McNemar test. The Spearman linear regression test was employed for analyzing the correlations between variables. The multivariate logistic regression model was employed to determine the predictors for high transprothesic gradients at follow-up. The relationship between variables is represented by using the Statsoft 6-0 graphics. Significance between data was considered achieved when $p<0.05$.

Results

There was one death in the 8th postoperative day due to low cardiac output and multi organ failure in a female patient undergoing concomitant mitral valve replacement and coronary revascularization. The postoperative complications are given in Table nr.2. All survivors underwent echocardiographic examination at discharge. The mean transprosthesis gradient was 15.3±3.2mmHg (range 11-20 mmHg) significantly lower than preoperatively (Figure nr.2A).

At six months follow-up the mean NYHA FC class was 1.3±0.6 significantly lower than preoperatively 2.75±0.86 ($p<0.0001$). All survivors underwent transthoracic echocardiography examination at rest at 6 months after surgery (Table nr.4). The IVST and pulmonary artery pressure were significantly lower than preoperatively. The peak and mean transprosthesis gradients (P-TPG and M-TPG) were 29±6.8 and 17.5±4.5 mmHg respectively. The mean transprosthesis gradient was significantly higher than at discharge (Figure nr.2A). LVM and LVM_i were significantly lower than preoperatively (Figure nr.2B). Both LVM and LVM_i reduction for each patient is given in Figure nr.3A and nr.3B. The M-TPG correlated well with the LVM_i reduction (Figure nr.4A) and the M-TPG at basal and under stress conditions had a strong direct correlation with the postoperative LVM_i (Figure nr.4B and nr.4C).

Within 1 year after surgery all patients underwent a third postoperative TTE examination at rest and

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Number 2, Volume 44, 2013

under stress (dobutamine stress test). All patients terminated DSE without complications. Four patients had occasional premature atrial and/or ventricular beats; however such contractions were not the cause to stop the test. Two patients developed significant subvalvular or intraventricular gradients during DSE. One of two patients developing subvalvular gradients was undergone annulus enlargement during operation.

With dobutamine, HR, LVEF, CO, transprosthesis peak and mean flow velocities and gradients increased significantly as represented in Table nr.5. The P-TPG and M-TPG for each patient at rest and during DSE are given in Figure nr.3C and nr.3D. Differently, the EOA, EOA_i and DVI increased during DSE but not significantly versus the values measured at rest (Figure nr.2C and nr.2D). Strong inverse correlations were found between the P-TPG and M-TPG rest and during DSE versus EOA_i (Figure nr.5A, nr.5B, nr.5C and nr.5D).

The multivariate regression analysis identified EOA_i, BSA, age, preoperative and postoperative LVM_i as strong predictors for higher M-TPG as represented in Table nr.6).

Discussion

Management of the small aortic root is a challenge to the surgeon with regard to operative technique and selection of prosthesis. Many techniques have been described (14-15) to accommodate a larger prosthesis to circumvent this problem. These techniques potentially increase the risks of injury to the coronary arteries and conduction bundle, and of surgical hemorrhage. David et al (20) described techniques to accommodate a larger prosthesis with satisfactory short-term results; as yet the long-term results are not available. Homograft replacement of the aortic valve as a functional unit or root replacement (21) has an added advantage of freedom from anticoagulation. Replacement of the aortic valve with a pulmonary autograft may have some growth potential (22). Toronto SPV prostheses have early encouraging results(13), with a decrease in systolic gradient and good hemodynamics. However, these techniques require specialized training and experience and are not currently widely used. The mechanical valves still remain the most widely use prosthesis for AVR basically due to their proven long-durability, less technical difficulties and price. The employment of mechanical prosthesis in small aortic annulus is still an issue of controversies in the literature, however, most of surgeons confirm excellent postoperative aortic prosthesis hemodynamic in patients undergoing AVR with a small (19-mm) mechanical prosthesis. The question still remain, in patients in whom the aortic annulus can not accomodate a 19-mm mechanical prosthesis! In such cases, most of surgeons would indicate annulus enlargement (14-15), since the existing experience with the 17-mm mechanical prosthesis reveals significant postoperative gradients through the aortic prosthesis. We believe that with the newly produced SJMR-17 the annulus enlargement might be a second alternative in the surgeon's hands.

The SJMR heart valve represents an enhancement to existing SJM mechanical heart valves. The currently marketed Standard and Hemodynamic Plus(HP) valve prostheses have excellent in vitro and in vivo hemodynamics (23), with an excellent record for safety and freedom from adverse events (24). Like currently available SJM mechanical heart valves, the SJMR heart valve is a bi-leaflet design with the same leaflet pivot mechanism. The SJMR heart valve is also manufactured from the same pyrolytic carbon, and has a rotatable polyester sewing cuff. The SJMR heart valve features a modified outer profile as compared to the standard SJM mechanical heart valve carbon orifice. This modification allows for an increase in the inside lumen area while maintaining the same tissue annulus diameter and sewing cuff diameter as a SJM mechanical heart valve HP valve or a SJM standard mechanical heart valve (Figure nr.6). This modification has been accomplished without changing the inner surfaces of the valve that have direct contact with blood flow. The hinge pivot mechanisms, valve leaflets, and profile of the inside diameter of the valve have remained unchanged. The only modification to these features is that they have been dimensionally scaled to accommodate the larger valve inside diameter.

In-vitro studies, have identified a lower pressure gradient and greater EOA in Regent valve confirming the gain of the SJMR valve over the HP valve that is expected based on the increased geometric orifice area (25). In another in vitro study (26), the experimental measurements conducted in the hinge and near-hinge flow regions of the SJMR-17 and SJMHP 17-mm valves provided a description of the flow fields in this hinge design. The flow field at the mid-acceleration phase of diastole in the SJMR-17 hinge showed the possible beginning formation of a rotating structure, whereas the corresponding flow field in the SJMHP-17 hinge showed a more distinct rotating structure. During diastole, the slightly higher velocities in the SJMR-17 hinge contributed to slightly larger turbulent shear stress levels than those measured in the SJMHP-17 hinge. However, the higher forward flow velocities in the SJMR-17 hinge may lead to more improved forward flow washout of the hinge pockets compared with that of the SJMHP-17 hinge. Similar peak flow

velocities and qualitatively similar flow features were observed in the two hinges. The authors concluded that based on the findings of this study and the consistency of the two valve designs, the hinge flow characteristics of the SJMR-17 series should be superior to those of the SJMHP-17 series.

Recently, different authors have reported excellent clinical and hemodynamic outcome in patients undergoing AVR with a SJMR mechanical aortic prosthesis (27-29). However the reported series did not include any patient undergoing SJMR-17 implantation except one in the series of 361 patients reported by Bach et al (27), this probably due to a lower incidence of small aortic root in selected series of patients, or rather due to surgeons' preference. In the present study we report a series of 16 patients undergoing SJMR-17 which represents the largest series ever reported. The early postoperative outcome were excellent, taking into the consideration the age, female sex, small BSA, the number of combined operations and double valve surgery (30-31). Postoperative bleeding events predominantly comprised early procedure-related events that were not directly related to the prosthesis. The assessment of clinical outcomes relies on long-term assessment for years and decades. However, within the available follow-up of just more than 18 months, there were excellent clinical outcomes among patients after implantation with the SJMR-17. Functional status assessed by New York Heart Association classification was excellent, and there were no adverse events in terms of embolic, bleeding and endocarditis. The intravascular hemolysis is another adverse effect in patients undergoing AVR with mechanical prosthesis. It must be pointed out that because bileaflet valves as the SJMR valves, in the aortic position usually carry low degrees of hemolysis (32), the presence of the blood cell damage might be attributed to high gradients and flow turbulence (32-33). At follow-up were identified almost normal hematologic parameters in our patients. A slightly increased LDH suggests for a subclinical blood cell damage but not significant.

Two-dimensional and Doppler echocardiography is an accurate, reliable and non invasive tool for assessing prosthetic heart valves. However, the ideal means for testing valve function require basal and stress hemodynamic evaluation, under various flow conditions. Recently, DSE has been proposed as an alternative means for evaluating valve hemodynamics (33-39). In the present study we used basal and dobutamine 2-dimensional and Doppler echocardiography for assessing aortic SJMR-17, implanted in patients with a small aortic root. The basal transprothesis peak and mean gradients were similar to other series of patients undergoing AVR with SJM standard mechanical prosthesis (5,17,37,39-40), SJMHP (37, 41), as well as with 19-mm Carpentier-Edwards pericardial bioprosthesis (36), 19-mm Carbomedics valves (42), but higher than the SJMR-19 (27-29) in patients with similar EOAi. Such data confrontation demonstrates that the SJMR-17 enables one-size-up hemodynamic performance.

The postoperative LVM and LVM_i were significantly lower than preoperatively, indicating that the implanted SJMR-17 had reduced significantly the pressure gradient across the AV. It may well be argued that during the follow-up, favorable ventricular remodeling as a result of sustained relief of outflow obstruction has occurred inducing a near normalization of systolic load following valve replacement associated with a rapid rate of reduction in myocyte hypertrophy and left ventricular mass This was demonstrated even by a significant reduction of the IVS hypertrophy. Previous studies, performed in patients receiving larger size mechanical prothesis or bioprothesis showed similar results at follow-up (16, 40,43). Similar LVM_i reduction has been also reported in SJMR mechanical valves of larger dimensions (27-29). In our series of patients we found a strong inverse correlation between the LVM_i quantified reduction and the M-TPG at rest. Also, high preoperative and postoperative LVM_i were strong predictors for higher M-TPG at rest and under stress. A strong direct correlation was found in our patients between the M-TPG at rest and under stress and postoperative LVM_i as already demonstrated in other series of patients undergoing AVR with larger size mechanical prothesis. However the opinions of authors regarding such correlation remains still controversial (17,47-48). These data confirm that the SJMR-17 offers acceptable transprothesis gradients at rest, which are compatible with an almost normal systolic load of the LV.

During DSE peak and mean flow velocities and gradients rose markedly. Similar results were obtained in previous reports studying different valve types and size under stress conditions, exercise or DSE (33-39). These studies clearly demonstrated higher flow velocities and TPG in patients undergoing AVR with small aortic prostheses, especially in patients with large BSA (37). Most of the authors agree that a large BSA is a predictor for higher postoperative TPG at rest in patients undergoing AVR with small aortic valve (33-39), others did not find a strong inverse correlation at rest (3) or during stress (35). In our small series we were not able to demonstrate a clear relationship between BSA and TPG, probably due to the small number of patients.

The hemodynamic performance of currently available aortic valve prostheses remains inferior to those of the native aortic valve. With the exception of homografts, and probably stentless valves, all current prosthetic valve designs produce measurable TPG that, potentially, could place persistent additional demands on the LV, and may hinder or delay the regression of LV hypertrophy.

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This is said to occur more frequently when the size of the implanted prosthesis is limited by the presence of a small aortic annulus, particularly in a patient with a large BSA, when there is a mismatch between prosthesis and patient. Although most of authors have found the patient-prosthesis mismatch a strong predictor for higher postoperative TPG and late survival the opinions are still controversial (5-7). In our series of SJMR-17 we found a strong inverse correlation between the postoperative TPG at rest and under stress and EOA_i similarly to other reported studies (38). Also, a low EOA_i was found to be a strong predictor for high postoperative TPG at rest and EOA_i, BSA and AV area were strong predictors for high TPG under stress in our series of SJMR-17. Therefore most of our patients had patient-prosthesis mismatch by current definitions (6-9) yet overall they experienced a significant reduction in symptom class, acceptable TPG and normalization of LVM.

Because the TPG may depend on the valve type and size, the diastolic filling period, and the LV loading conditions, it is important to keep in mind that high TPG do not necessarily mean prosthetic stenosis. Since the volumetric flow in the LVOT equals the volumetric flow through the prosthetic valve ($Q_{LVOT}=Q_{AVPROSTHESIS}$), the rise in CO generated by DSE increases the flow velocities on the two sides of the valve orifice, maintaining the EOA basically unchanged. This principle of conservation of mass was clearly demonstrated in this study when the continuity equation (Q_{LVOT} x A_{LVOT}= $Q_{TRANSPROSTHETIC}$ x $A_{TRANSPROSTHETIC}$) was applied at baseline and at peak stress: the AV area remained relatively unchanged despite a significant increased in TPG. These results confirmed previously reported data derived from patients undergoing AVR with larger size prosthesis, suggesting that prosthesis-patient mismatch is not an issue of clinical relevance (5-7).

During DSE, two patients in our series developed significant dynamic subvalvular obstruction without clinical symptoms. This phenomenon has been observed in patients with proven or suspected coronary artery disease, or in patients undergoing mitral valve repair. The encountered mechanisms of the dynamic subvalvular obstruction are the increased myocardial contractility, decreased venous return to the LV, mitral valve systolic anterior motion, cavity squeezing or peculiar characteristics of the LV geometry. The abnormal intraventricular gradients and velocities occurs in 14% of patients at rest after AVR, similar to our series, and can be provoked or worsened by ventricular unloading or inotropic stimulation (44), however under stress such phenomenon has been identified in almost 60% of patients undergoing AVR with SJSD-19 or SJMHP-19 (37).

The DVI which gives an approximate guide to orifice

Table nr. 1 Demographic Data

Variables	Nr (%)
Females	18(%)
Mean age (years)	69.75±7.4
Mean height (cm)	159±6.7
Mean weight (kg)	65.7±16
Mean Body Surface Area (sq.m)	1.67±0.2
Mean Body Mass Index (kg/sq.m)	26.05±5.2
Diabetes	5(%)
Insulin therapy	1(%)
Hypercholesterolemia	4(%)
Ischemic heart disease	4(%)
Hypertension	10(%)
Hypothyroidism	2(%)
Smoking history	6(%)
Cerebrovascular disease	4(%)
Previous Transitory ischemic arrest episodes	2(%)
Previous carotid endarterectomy	1(%)
Previous peptic ulcer	1(%)
Peripheric vascular disease	2(%)
Atrial fibrillation	1(%)
Acute myocardial infarction	2(%)
Chronic obstructive pulmonary disease	5(%)
Mean New York Heart Association Functional class	2.75±0.86
Mean Canadian Cardiovascular Class	1.63±0.72
Left ventricular ejection fraction<35%	1(%)
Mitral valve disease	5(%)

behavior, independently of the LVOT diameter measurement. Low DVI values are associated with higher TPG, lower EOA and greater LVMi (12). Low DVI has been attributed also to aortic prothesis obstruction due to pannus formation or restricted leaflet openings (45). In our series of patients the mean DVI at rest was similar to larger size prosthesis (46). The DVI remained relatively unchanged (slightly increased) during DSE similarly to the EOA and the EOA_i. Based in such outcome, we may hypothesize that the increased transprothesis velocities and gradients during DSE in our series are strictly related to the increased CO and transprothesis flow and not due to patient-prothesis mismatch.

Study limitations: 1) The small cohort of patients undergoing AVR with a SJMR-17. 2) Another limitation is the older age of patients undergoing AVR with a SJMR-17. These patients have reduced daily physical activities and as consequence might be "false" asymptomatic. 3) One of the major limitations of the continuous –wave Doppler is the possibility of overestimation of valvular flow velocity and pressure gradients and underestimation of the valve area by the continuity equation, as a consequence of pressure-recovery phenomenon. Since the rest and dobutamine prosthetic assessment are both subject to the same limitation, the ensuing intraindividual comparison that follows is statistically valid.

We may conclude that the SJMR-17 might be employed with satisfactory postoperative clinical and hemodynamic outcome in patients with small aortic annulus, especially in elderly patients, as an alternative to other valves' choice or alternative surgical strategies such as annulus enlargement.

Table nr.2 Intraoperative and early postoperative data

Variables	Nr (%)
Bicuspid aortic valve	9(%)
Mean cardiopulmonary bypass time	89±25
Mean aortic cross-clamping time	71±19
Annulus enlargement	1(%)
Mitral valve replacement	5(%)
Mechanical mitral valve prosthesis	4(%)
Number	25.8± 1.1
Coronary artery bypass grafting	4(%)
Total grafts	10
Left internal mammary arteries employed	4
Postoperative Outcome	
Mean mechanical ventilation (hours)	9.8±3.5
Mean Intensive Care Unit stay (days)	1.94±2.2
Reoperation for bleeding	1(%)
Blood used	6(%)
Low cardiac output	2(%)
Ventricular arrhythmias	3(%)
Permanent ventricular pacing	1(%)
Multi organ failure	1(%)
Coagulopathy	1(%)
Hospital death	1(%)
Follow-up (months)	18.7±9.2
Patients-prostheses missmatch	9(%)
Mean NYHA FC class	1.3±0.6
Mean INR	2.8±1.2
Mean LDH	510±63
Mean Hgb (g/dl)	12±1.3
Serum Haptoglobin (g/l)	2±1.2
Reticulocyte fraction (%)	0.9±0.4

Legend: *Nyha fc class- new york heart association functional class; ldh- lactic dehydrogenase*

Table nr.3 Formula for calculating hemodynamic parameters

Mean TPG = 4* [(MeanVAV)2-(MeanVLVOT)2]
Peak TPG = 4* [(PeakVAV)2-(PeakVLVOT)2]
EOA = 0.785 * (LVOTd)2 * (LVOT TVI) / (AV TVI)
BSA = (Wt0.425 * Ht0.725) * 0.007184
EOAi = EOA / BSA
LVM = 0.00083 * [(IVST+ PWT + LVEDD)3 – LVEDD3] + 0.6
LVMi = LVM /BSA
CO = 0.785 * (LVOTd)2 * (LVOT TVI) * HR
DVI = VLVOT / VAV
LVMi reduction = Preoperative LVMi – Postoperative LVMi

Legend: *TPG-Transprothesic gradient;LVOT-Left ventricular outflow tract; AV-Aortic Valve* V_{AV}*-Transaortic velocity flow;* V_{LVOT}*–Velocity flow in the LVOT; EOA-Effective orifice area; eoai-Indexed Effective Orifice Area; lvotd-Diameter of the LVOT; LVOT TVI- LVOT Time velocity interval; AV TVI – Aortic valve time velocity interval; BSA-Body Surface Area; Wt-Weight; Ht-Height; LVM-Left Ventricular Mass, lvmi-Indexed Left Ventricular Mass; IVS-Interventricular septal thickness, PW-Posterior wall of the left ventricle thickness; LVEDD-Left Ventricular End-Diastolic Diameter; Hr-Heart Rate; DVI-Doppler Velocity Index.*

Table nr.4 Preoperative versus postoperative echocardiographic data at six months after surgery

Variables	Preoperative (n=19)	Postoperative (n=19)	p-value
Diameter of the ascending aorta (mm) (Dao)	28.75±1.66	28.36±3.4	0.68
Diameter of the left atrium (mm) (DLA)	41.5±7.4	43.5±7.5	0.44
End-diastolic right ventricle diameter (mm)	19±2.2	20.1±4. 2	0.35
End-diastolic LV diameter (mm)	46.5±3	48±4.3	0.25
End-systolic LV diameter (mm)	26±4.4	25±2.5	0.42
End-diastolic IVST (mm)	14±1.2	12±1.7	0.001
End-systolic IVST (mm)	19±0.7	18.2±3.2	0.32
End-diastolic PWT (mm)	12±1.4	11.5±1.2	0.27
End-systolic PWT (mm)	21±1.5	19.2±2	0.006
DLA/Dao	1.35±0.24	1.56±0.32	0.038
End-diastolic IVST/PWT	1.2±0.18	1.07±0.11	0.016
Shortening Fraction (%)	46.18±7	46.2±5.3	0.99
End-diastolic left ventricle volume (ml)	96.25±32.5	95.17±14.1	0.9
End-systolic left ventricle volume (ml)	40.75±13.86	37.1±6.4	0.33
Index End-diastolic LV volume (ml/m2)	59.58±17.12	59.179.3	0.93
LVEDD/LVEDVi (mm x m2/ml)	0.81±0.11	0.99±0.27	0.015
Index End-systolic LV volume (ml/m2)	25.17±7.1	23.17±3.9	0.32
Left ventricular ejection fraction (%)	54.7±7.4	55.2±9	0.86
VmaxE (cm/s)	119±30	139±37	not measured
VmaxA (cm/s	106±25	147±43	not measured
Mitral valve regurgitation grade	2.06±1.2	1.07±0.6	0.006
Peak pulmonary artery pressure (mmHg)	52±18	32±10.3	0.0001
Left ventricular mass (gm)	258±40	*191±22.6	0.000007
Left ventricular mass index (gm/m2)	157±26	*114.5±10	0.00002
Left ventricular mass index reduction (gm/m2)	43±19		
Left ventricular outflow diameter (mm)	18±1,3	18.3±1.05	0.47
Prosthesis hemodynamic evaluation			
TVIAO	-	608±92.6	
V1LVOT	-	1.43±0.36	
P1LVOT	-	5.13±2.7	
TVILVOT	-	321±74	
Peak transvalvular gradient (mmHg)	116±38.7	29±6.8	0.00001
Mean transvalvular gradient (mmHg)	66±12.7	17.5±4.5	0.00001
Aortic valve regurgitation grade	1.7±0.7	0.73±0.46	0.001

Legend: *LVOT-Left ventricular outflow tract; AV-Aortic Valve; LV-Left Ventricle; V_{AV}-Transaortic velocity flow; V_{LVOT}–Velocity flow in the LVOT; EOA-Effective orifice area; EOAi-Indexed Effective Orifice Area; LVOTd-Diameter of the LVOT; LVOT TVI- LVOT Time velocity interval; AV TVI – Aortic valve time velocity interval; BSA-Body Surface Area; Wt-Weight; Ht-Height; LVM-Left Ventricular Mass, LVMi-Indexed Left Ventricular Mass; IVST-Interventricular septal thickness, PWT-Posterior wall of the left ventricle thickness; LVEDD-Left Ventricular End-Diastolic Diameter; Hr-Heart Rate; DVI-Doppler Velocity Index. LVEDVi-Indexed Left ventricular End-Diastolic Volume*

Table nr.5 Postoperative echocardiographic data at rest and under stress at follow-up

Variables	at rest (n=19)	under stress (n=19)	p-value
Effective Orifice Area	1.26±0.3	1.33±0.34	0.53
Indexed Effective Orifice Area	0.76±0.20	0.78±0.18	0.76
Maximal gradient	34.3±9.9	73.8±17.7	0.0001
Mean gradient	18.3±5.3	37±10.7	0.0001
Doppler Velocity Index	0.48±0.14	0.5±0.14	0.68
Left Ventricular Ejection Fraction (%)	58.4±8	68±9.9	0.004
Cardiac Output	4.7±1.6	8±2	0.0001
Heart rate	64.5±10	100.6±28	0.001
Systolic pressure	139±23	152±26	0.13
Diastolic pressure	77±10.6	77±12.5	1.0
Double Product	8978±2184	15225±5147	0.0008
Maximal velocity	1.45±0.27	2.22±0.28	0.00003
Mean velocity	1.01±0.2	1.58±0.22	0.000004

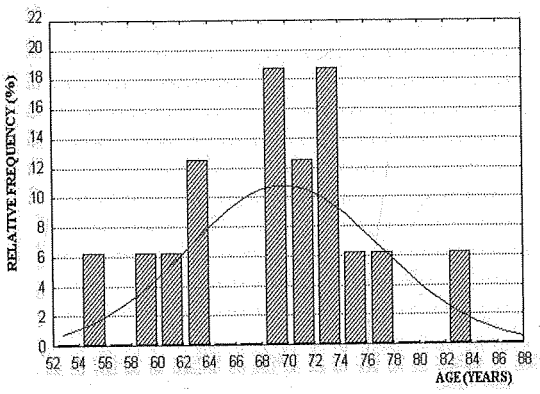
Table nr.6 Predictors for higher postoperative trans-prosthesis gradient at rest and under stress

Variables	β	ERR.STD. Di β	B	ERR.STD. Di B	T(1)	P-Level
Basal						
PWTED	-0.4	0.0023	-2.16	0.02	-105	0.0061
EOAi at rest	-1.53	0.003	-0.42	0.0007	-606	0.0011
LVMIpostoperative	-1.15	0.0033	-0.33	0.0009	-349	0.002
BSA	-0.044	0.0013	-1.41	0.041	-34.3	0.019
Under stress						
Dobutamine EOAi	-0.62	0.0073	-0.37	0.0043	-85.8	0.0074
Age	0.85	0.0043	1.58	0.008	198.5	0.0032
LVMIpostoperative	-0.57	0.0042	-0.63	0.0046	-137	0.0046
LVMIpreoperative	0.15	0.007	0.06	0.0028 2	22	0.029
EOAi at rest	-0.21	0.0062	-8.14	0.24	-34.1	0.019
M-TPG at rest	0.083	0.006	0.18	0.013	13,75	0.046

Legend: *M-TPG-Mean transprothesic Gradient; icle; EOAi-Indexed Effective Orifice Area; BSA-Body Surface Area; LVMi-Indexed Left Ventricular Mass; PWTED-Posterior wall of the left ventricle thickness*

ISSN 2304-2354
Number 2, Volume 44, 2013

Figure nr.1 A. Age distribution; B. Weight distribution, C. Body surface area distribution



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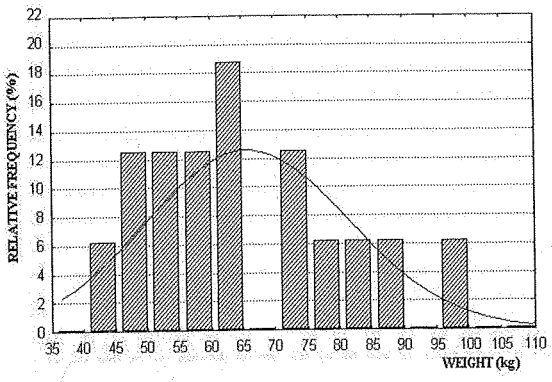

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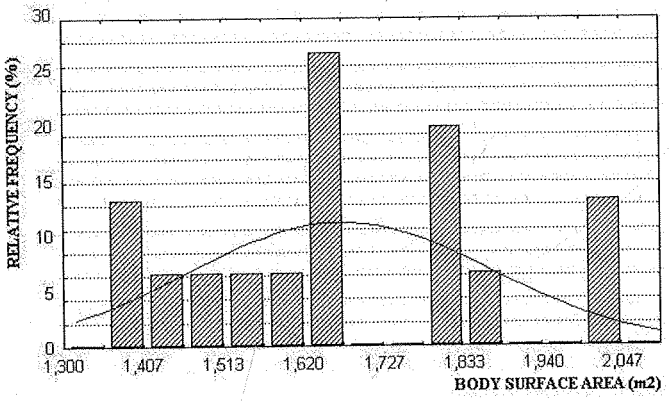
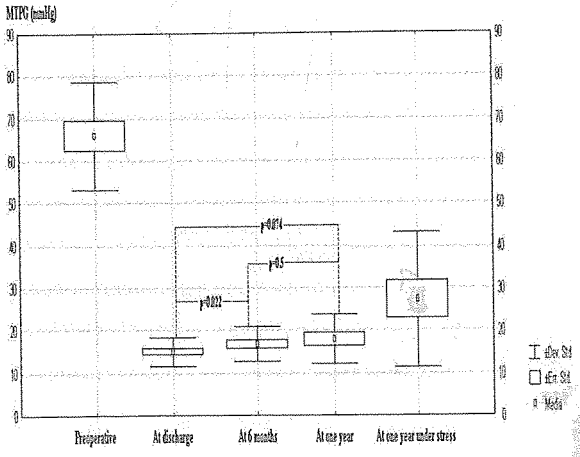


C.

Figure nr.2 A. Mean transprothesis gradient measurement in different time points. B.Comparison between the preoperative and postoperative values of the indexed left ventricular mass. C & D. Effective orifice area and indexed orifice area of the aortic valve after replacement at basal and stress conditions



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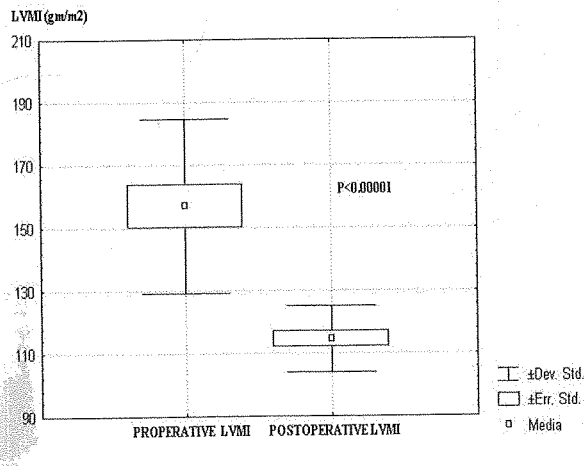

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ISSN 2304-2354
Number 2, Volume 44, 2013

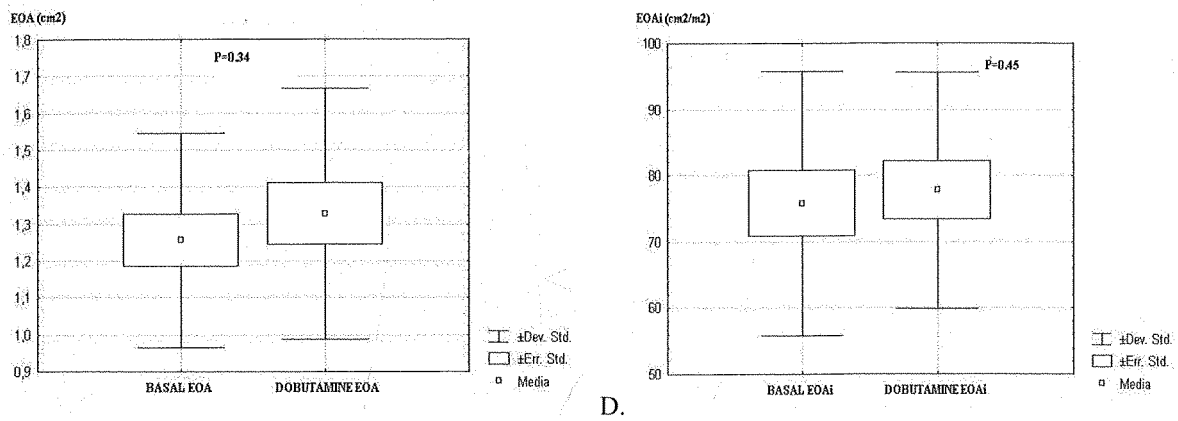
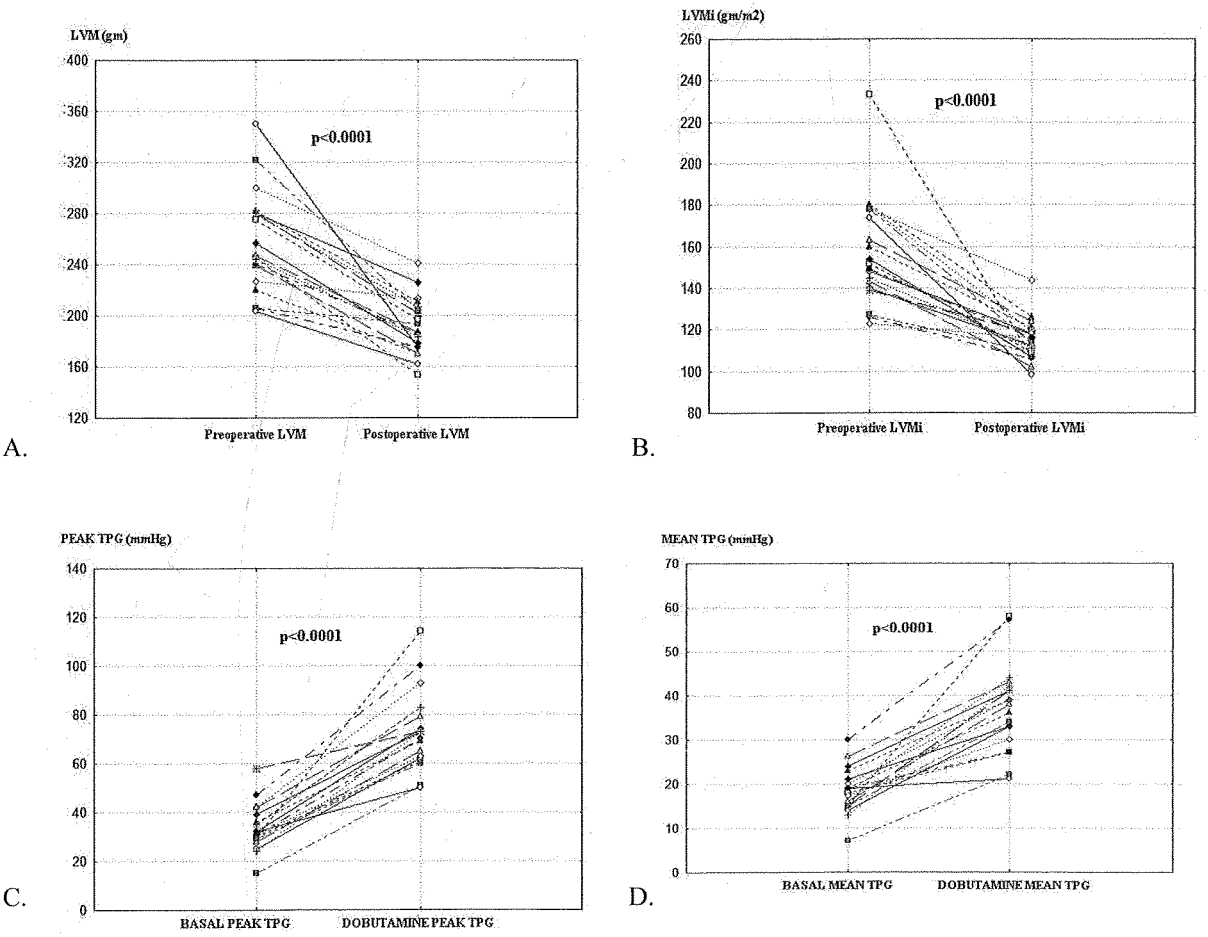
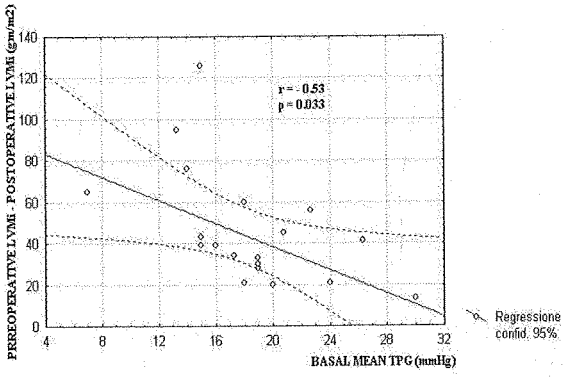


Figure nr.3 A &B Left ventricular mass and indexed left ventricular mass reduction for each patient. D&C Peak and mean transprothesic gradients for each patient at basal and under stress conditions



ISSN 2304-2354
Number 2, Volume 44, 2013

Figure nr.4 a. Correlation between the basal mean transprothesic gradients and indexed left ventricular mass reduction. b & c. Correlations between the postoperative indexed left ventricular mass and the mean transprothesic gradient at basal and stress conditions.



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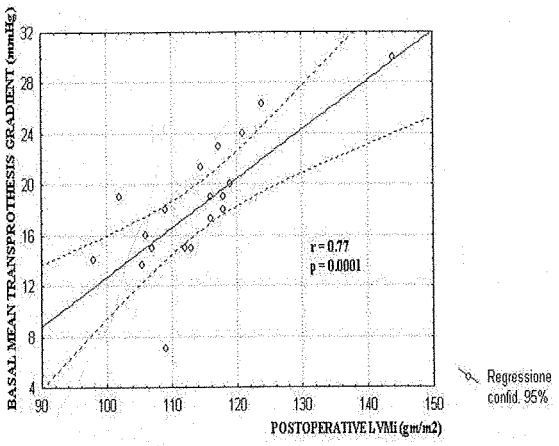

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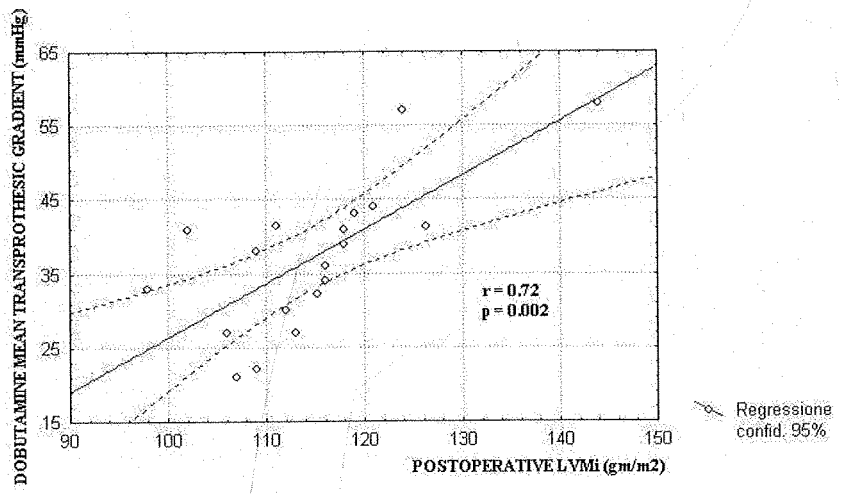
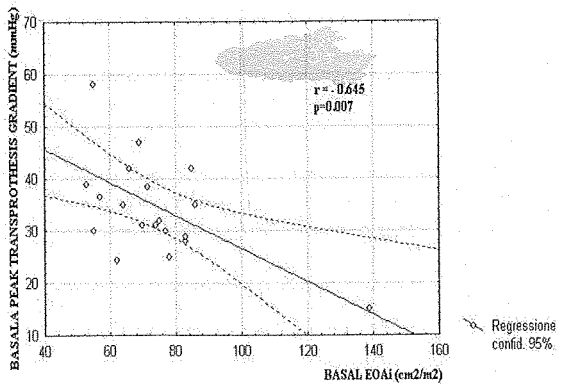


C.

Figure nr.5 A&B Correlations between the indexed orifice area of the aortic valve after replacement in basal conditions and peak and mean transprothesis gradients. C&D. Correlations between the indexed orifice area of the aortic valve after replacement under stress and peak and mean transprothesis gradients



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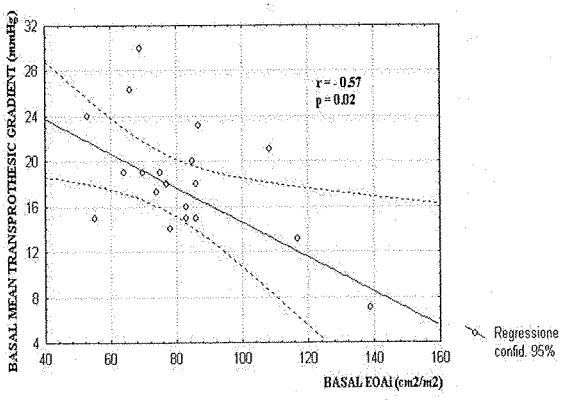

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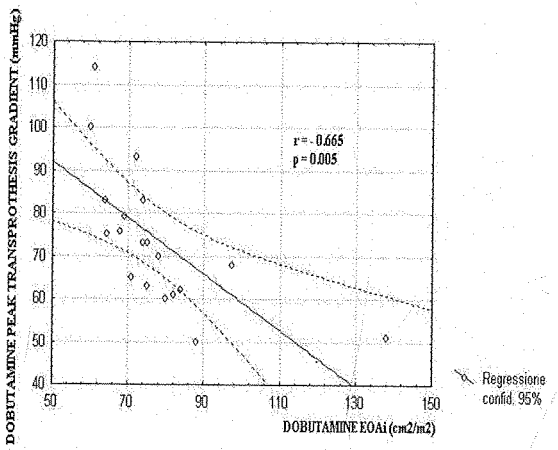

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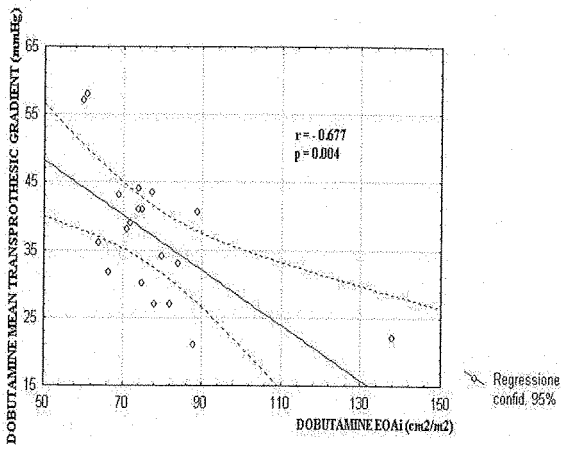
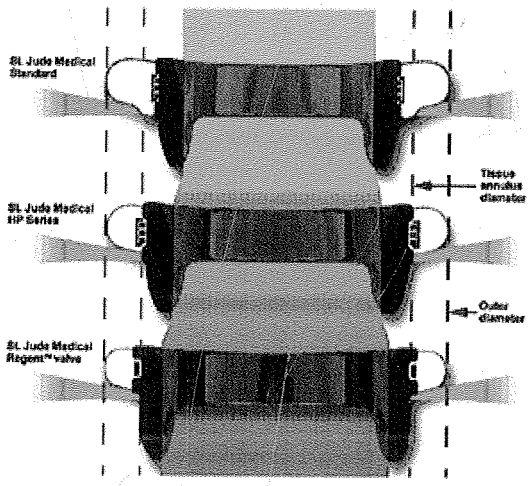


D.

Figure nr.6 A.Cross-sectional view of different st Jude medical mechanical heart valves. B.Sewing cuff options of the sjm regent^{tm} heart valves with the the flex cuff^{tm} configuration



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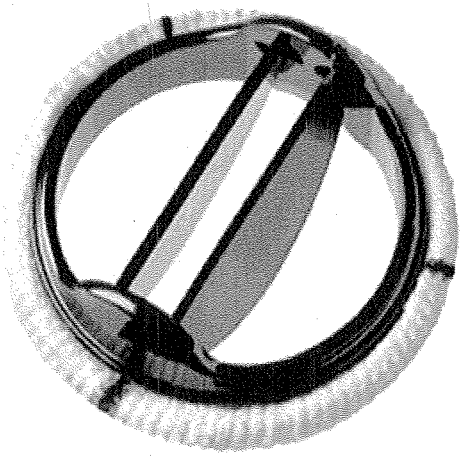

B.

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