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Preoperative Longitudinal Left Ventricular Function by Tissue Doppler Echocardiography at Rest and During Exercise is Valuable in Timing of Aortic Valve Surgery in Male Aortic Regurgitation Patients

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Abstract

Aim: To evaluate if left ventricular (LV) systolic function by tissue Doppler Echocardiography (TDE) at rest and exercise preoperatively, could predict postoperative LV function and thereby be useful in timing of aortic valve surgery in patients with severe aortic regurgitation (AR).

Methods: In 29 patients (median 59 years, interquartile 39-64) echocardiography, TDE and radionuclide ventriculography were performed pre- and postoperatively, at rest and during supine bicycle exercise.

Results: Preoperative EF (ejection fraction) was 62%. Patients formed two groups with basal LV peak systolic velocity (PSV) 5.9 cm/s preoperatively as the cut-off value (Low and High PSV). Preoperatively, Low PSV had lower $PSV_{exercise}$, $EF_{exercise}$, atrioventricular plane displacement (AVPD) at rest and upon exercise than High PSV ($p<0.005$, $p<0.05$, $p<0.005$ and $p<0.05$). Postoperatively, Low PSV had smaller $AVPD_{rest}$, $AVPD_{exercise}$ and $PSV_{exercise}$ ($p<0.05$, $p<0.01$, $p<0.01$).

Conclusion: In chronic AR patients with EF and LV dimensions not fulfilling criteria for surgery according to guidelines, preoperative PSV and AVPD at rest and upon exercise detected postoperative LV dysfunction.

Key words

Aortic valve insufficiency

Left ventricular function

Cardiac surgery

Tissue Doppler Echocardiography

Exercise Echocardiography

Introduction

Symptoms and preoperative left ventricular (LV) systolic function are the main predictors of outcome and long-term survival after aortic valve replacement (AVR) in patients with severe aortic regurgitation (AR). Surgery is therefore currently recommended when left ventricular (LV) systolic dysfunction or symptoms evolve in AR patients. LV ejection fraction below 50% at rest, LV end-systolic dimension more than 55 mm or LV end-diastolic dimensions above 75 mm are the most used indicators for LV systolic dysfunction when planning surgery in asymptomatic patients. [1] However, these parameters have limitations in predicting early LV dysfunction.

It has been shown that LV systolic dysfunction can be identified before EF has declined in asymptomatic AR patients through examination of LV longitudinal motion.[2] The longitudinal contraction of the LV is performed by longitudinal myocardial fibres connected anatomically with the atrioventricular ring and located in the subendocardium.[3] The importance of these fibres for LV pump function was first described in the 1980s. [4, 5] Due to the volume overload associated with AR, these subendocardial cells are exposed early to stress that initiates a fibrotic process.[1] Clinically, this can be measured as a lowered atrioventricular plane displacement (AVPD) and interpreted as early myocardial dysfunction.

In the analysis of longitudinal myocardial function, tissue Doppler echocardiography (TDE) is a valuable technique. It can give information about regional, as well as global LV systolic and diastolic function through quantification of myocardial velocity.[5, 6] Colour TDE has also proven to be a feasible tool for quantitative assessment of LV response to supine exercise.[5, 7, 8]

Exercise echocardiography has been proposed as a non-invasive, safe and inexpensive method in regurgitant valvular lesions.[9] Moreover, LV systolic function on exercise has been suggested as an approach to find early signs of LV deterioration in AR patients.[10] A previous study has shown that preoperative exercise echocardiography is a better predictor of postoperative LV function than resting indices in AR patients.[11] It has also been found that LV long axis contraction at rest measured by TDE is reduced in AR patients with poor exercise response.[12, 13]

It is of utmost importance that AR patients are operated in time to prevent development of irreversible LV dysfunction. Conventional echocardiography at rest may be insufficient for the early detection of LV dysfunction in states of volume overload as in chronic AR. Our hypothesis is that colour tissue Doppler echocardiography and exercise data would provide precise and sensitive information of LV function in AR patients, and that these methods could be developed into clinically useful tools for better timing of surgery. There are limited data concerning TDE parameters at rest and exercise in AR patients pre- and postoperatively. Consequently, the aim of this study was to (i) explore the effects of aortic valve surgery on LV systolic function in chronic AR patients by TDE; (ii) assess potential TDE indicators for postoperative subnormal LV performance related to preoperative measures.

Methods

Patients

Patients with severe chronic AR referred for aortic valve surgery on fulfilment of criteria according to guidelines, were included in the study. [1] Diagnosis and severity of AR were determined based on an integrated echocardiographic evaluation, taking LV dimensions, vena contracta width, backflows in descending aorta and forward stroke volume into consideration.[14] Besides, the progression of severity or hemodynamic impairment, judged from progressive LV dilatation, indication of a declining LV function despite a normal EF, or the appearance of symptoms were regarded as additional indications for surgery.

Exclusion criteria were active endocarditis, previous heart surgery, aortic stenosis, concomitant valve disease or coronary artery disease. Twenty-nine male patients met the above criteria. These patients also participated in a radionuclide ventriculography study.[15]

The ethics committee of the Faculty of Health Sciences, University of Linköping approved the study. The patients received information and gave their informed consent before being enrolled into the study.

Echocardiography

All patients were studied by the same investigator at rest and upon exercise two days before and six months after surgery. 2D echocardiography and colour TDE were obtained (GE vivid 5 or 7, GE Medical Systems, Wauwatosa, USA). The patients were examined in a semi-supine left lateral position on an Ergoselect 1200EL ergometer (Ergoline, Bitz, Germany). The exercise examination was sub maximal with a starting load at 50 W and an increase after 5 min to 100 W. To study a steady state physiology, echocardiographic and Colour TDE images were recorded after 5 minutes at the work load of 100W. Blood pressure and heart

rate were registered. Echocardiography and Colour TDE images were recorded during two RR intervals at rest and upon exercise at 100W.

Apical four and two chamber views by TDE were saved for off-line analysis using the EchoPac^{TM} system (GE vivid 5 or 7, GE Medical Systems, Wauwatosa, USA). All off-line analysis was performed by the same investigator. Myocardial velocity profile was obtained from basal segments of lateral, septal, inferior and anterior left ventricular walls at rest and during exercise at 100 W. The peak systolic velocity (PSV) was measured at the highest velocity recorded within the systolic interval on the ECG. Velocities recorded during isovolumetric contraction were excluded. From the four walls a mean PSV was calculated.

To evaluate global diastolic function, the early (e´) and atrial (a´) waves during diastole were identified in the myocardial velocity profiles. Due to difficulty in identifying and separating e´- and a´-waves on exercise these measurements were not included. The e´/a´-ratio was calculated.

Tissue tracking is a modality of colour TDE that visualizes the myocardium by a graded display of 7 colour bands where each colour represents a displacement distance. This gives the possibility of quickly and easily performing visual estimation of AVPD. By integrating the velocity signal at the junction of the valve and ventricular wall at four positions (septal, lateral anterior and inferior), the AVPD distance was measured as the distance between maximum and minimum value. A mean AVPD of the four sites was calculated.

From digitally stored images, the systolic AVPD was measured by M-mode echocardiography at the same four positions as with tissue tracking. The measurements were carried out as previously described by Carlhäll et al.[16] A mean systolic AVPD was calculated.

Radionuclide Ventriculography

Radionuclide ventriculography with multiple gated acquisition (MUGA) was performed two days before planned surgery and six months postoperatively. Using a General Electric XR/T gamma camera (General Electric Medical Systems, Milwaukee, USA), supine multigated blood pool imaging was first performed at rest and during exercise. The initial workload was 50 W, which was increased to 100W. Xeleris Functional Imaging Workstation, EF Analysis (General Electric Medical Systems, Milwaukee, USA) was used to measure EF.

Statistics

Data are expressed as medians (interquartile). Non-parametric analyses were used due to skewed data. Pre- and postoperative and rest and exercise data were compared by the Wilcoxon´s signed rank test. Mann-Whitney test was used to analyse differences between the High and Low PSV- groups. Correlation between measurements of preoperative longitudinal function and postoperative EF, LV dimensions and LV volumes were determined by Spearman's rho.

Missing data due to missing images were handled as true missing data, while missing values due to patients' incapability of performing exercise due to their heart condition were replaced with a "0" in the Wilcoxon´s matched pairs test and an approximated low value in the Mann-Whitney analysis, in order to preserve the information about the low performance group of patients. Bland-Altman analysis was used to evaluate the agreement between Tissue Tracking and M-mode.[17] To evaluate inter- and intraobserver variability, studies from 10 randomly selected patients were analysed pre- and postoperatively separately by two observers and re-measured by observer 1. Mean differences and reproducibility coefficient (1.96xSD) were calculated.

Data analysis was performed with SPSS 15.0 (SPSS Inc. Chicago, Illinois, USA). Significance was defined as $p \leq 0.05$.

Results

Baseline Characteristics

Clinical and echocardiographic features of the patients are summarized in table 1 and 2 respectively. The etiology of AR was cusp prolapse in nineteen patients, degenerative in six, dilatation in two and rheumatic in one patient. Sixteen patients had bicuspid aortic valves. Twenty seven patients underwent aortic valve replacement surgery and two had aortic valve reconstructive surgery. Three patients were not studied postoperatively, one due to postoperative complications, one who did not wish to be examined again and one who moved out of the country. At the MUGA and echocardiography examinations, two and four patients respectively were not able to perform the exercise part preoperatively. Because of missing images, 27 patients were analysed with colour TDE and 28 with M-mode preoperatively.

In table 3, results from peak systolic velocity (PSV), AVPD by tissue tracking (TT), AVPD from M-mode (MM), ejection fraction (EF) and diastolic parameters are presented.

Radionuclide Ejection Fraction and Echocardiographic LV Dimensions

Preoperatively, one patient had an EF at rest <50%. The EF change from rest to exercise, ΔEF, was negative in ten patients, i.e. they showed a falling EF upon exercise, which is considered to be an abnormal reaction. There was no significant increase of EF as a response to physical exercise for the whole patient population. Nine had a LVESD >50 mm and six had LVEDD >70 mm (table 2).

Postoperatively, the LV end-systolic and -diastolic diameters and volumes had diminished significantly (all $p < 0.01$, table 2). Moreover, ΔEF had increased ($p< 0.001$) but there were no changes in EF at rest and upon exercise compared to preoperatively (figure 1, table 3).

Preoperative Rest

The mean PSV of the four heart walls was close to a previously published value in healthy subjects in the same age range as our population (5.9±1.3 cm/s).[18] Among our patients, one half had a lower PSV than this value and the other half had a higher PSV. Thus, with the value 5.9 cm/s as the cut off point, the AR patients were divided into two groups; High PSV group (14 patients) and Low PSV group (13 patients). The two groups did not differ with respect to baseline and echocardiographical characteristics besides LV end systolic volume where the High PSV group had significantly lower volumes both before and after surgery (table 1 and 2, respectively). The High PSV group had greater MM-AVPD (p= 0.002) and TT-AVPD (p= 0.005) than the Low PSV group preoperatively (figure 1, table 3).

Preoperative Exercise

Three patients could not perform the exercise examination due to cardiac symptoms. Upon exercise, the systolic function parameters PSV, TT-AVPD and MM-AVPD of the entire patient population increased from resting values (table 3).

Both the High and Low PSV groups could increase their PSV (p=0.01 and p= 0.006, respectively) and MM-AVPD (p=0.002 and p=0.01 respectively) on exercise, while no increase was seen in the Low PSV group for AVPD measured by Tissue Tracking (figure 1, table 3). The High PSV group reached significantly higher exercise values than did Low PSV (PSV p =0.004, TT-AVPD p =0.002, MM-AVPD p =0.029, table 3).

Postoperative Rest

Six months after surgery, PSV, TT-AVPD and MM-AVPD were significantly lower than before surgery for the whole patient cohort (table 3). However, when analysing the two patient groups, it was only the High PSV group that significantly decreased in all three parameters compared to preoperatively (PSV p =0.005, TT-AVPD p =0.008, MM-AVPD p

=0.02). At rest, the High PSV group still had longer TT-AVPD and MM-AVPD than the Low PSV but a difference between the two groups of patients regarding PSV could no longer be seen (table 3, figure 1).

Postoperative Exercise

Postoperatively, both groups increased their PSV, TT-AVPD and MM-AVPD in response to exercise (figure 1, table 3). The High PSV group attained significantly larger PSV, TT-AVPD and MM-AVPD than did Low PSV (figure 1, table 3).

Compared to exercise before surgery, the AVPD, but not PSV, was lower on exercise after surgery in the entire patient population (table 3).

High and Low PSV Group and EF

Before surgery, the High and Low PSV groups differed only in EF at exercise, where High PSV had a higher EF (p =0.043, figure 1). Both groups increased their ΔEF significantly after surgery compared to before (table 3). Moreover, the median ΔEF for High PSV was postoperatively equal to the often used limit for normal LV function (ΔEF>5%).

Prediction of Postoperative LV function

Correlation analysis between preoperative longitudinal LV function and postoperative LV function outcomes by conventional measures, such as LV dimensions and EF, showed stronger correlations when studying preoperative exercise variables than variables obtained at rest (table 4). The overall strongest correlation was found between the increase of AVPD from rest to exercise and indexed EDV at exercise (φ=-0.573, p =0.008).

Evaluation of Methods Measuring AVPD

The median values of AVPD measured by M-mode and Tissue Tracking are shown in Table 2. The variability of the two methods described by Bland-Altman analysis is presented in figure 2. The mean difference differed significantly from zero both at rest and exercise pre- and postoperatively. Despite a good correlation (preoperative rest r=0.84; exercise r= 0.70; postoperative rest r=0.60; exercise r=0.60) between the two methods they are not interchangeable due to this demonstrated variability.

Reproducibility of AVPD and PSV

The mean interobserver variability (±1.96 SD, the reproducibility coefficient) was, for the measurement of PSV at rest 0.1±0.7 cm/s, PSV during exercise 0.2±1.6 cm/s, TT-AVPD at rest 1.4±1.6 mm, TT-AVPD during exercise 0.7±1.2 mm, MM-AVPD at rest -0.4±2.4 mm and MM-AVPD during exercise 0.5±3.3 mm. There were also only small differences in the mean intraobserver variability in measurement of PSV at rest (-0.1±0.8 cm/s), PSV during exercise (-0.55±1.1 cm/s), TT-AVPD at rest (0.2±2.3 mm), TT-AVPD during exercise (-0.1±1.1 mm), MM-AVPD at rest (-0.2±1.8 mm) and MM-AVPD during exercise (-0.3±2.7 mm). Inter- and intraobserver variability for é was 0.1±0.7 cm/s and -0.2±1.4 cm/s respectively, and for á 0.0±0.4 cm/s and 0.0±0.5 cm/s respectively.

Left Ventricular Diastolic Function by TDE.

Atrial fibrillation was registered in three patients before surgery and in one patient at 6-month follow up (see table 1). The myocardial velocity of the é-wave was significantly higher in the High PSV-group than Low PSV, both pre- and postoperatively (p <0.001 and p =0.009, table 3). The é/á ratio was lower in the Low PSV-group as compared to High PSV group at follow up (p=0.025, table 3). Regarding á-wave velocity, no significant differences could be identified.

Discussion

In this study, we investigated global LV systolic function at rest and during exercise in patients with chronic severe AR before and after aortic valve surgery with the hypothesis that TDE can provide information about early LV dysfunction in these patients. Our main findings were (i) despite an EF at rest above the criteria for surgery, AR patients had a lower AVPD at rest and lowered PSV upon exercise preoperatively as compared to previously published values in healthy subjects.[7, 18, 19] (ii) Postoperatively, patients in the High PSV group had a larger AVPD and PSV than the Low PSV group, although there were no significant differences in LV dimensions or EF.

With AVR the intention should be to operate before irreversible damage to the myocardium has occurred. Although there is no universally accepted definition of postoperative LV dysfunction, it can hardly be questioned that the ultimate goal would be to strive for a LV function as near the generally accepted characteristics of normality in healthy individuals as possible. Colour TDE and thus PSV have been proposed to be a technique that is useful in finding early myocardial dysfunction at rest in AR patients.[12, 13] In our study, patients had a lowered PSV and AVPD preoperatively despite an EF at rest >50% and LV dimensions not indicating surgery according to guidelines. This supports the results by Sokmen et al where longitudinal function was lowered in AR patients in spite of an EF >50%.[2] The subendocardial, longitudinally oriented cardiomyocytes are exposed to shear stress at an early stage of the volume overload in AR. As a response a fibrotic process in the endocardium starts, resulting in a decreased longitudinal motion of the LV.[1, 3] Therefore, a normal EF but a decreased longitudinal motion measured by AVPD or PSV will be seen in AR patients as early signs of LV systolic dysfunction.[12] Vinereanu et al showed that a decreased myocardial velocity is associated with a smaller change in EF as a response to exercise in patients with

severe chronic AR.[12] An increase of more than 5% in EF upon exercise has in earlier studies been defined as a normal LV response to exercise in AR patients.[20] In this study, the patients in the High PSV group had a median ΔEF of 5% and showed a normal EF-reaction on exercise postoperatively, while patients in the Low PSV group did not. This suggests that TDE variables measured preoperatively at rest can identify persisting disturbances of the LV function of AR patients and might be useful in guiding to optimal timing of surgery.

PSV and AVPD as Early Indicators of LV Dysfunction

EF, known as both a pre- and afterload dependent parameter, reflects to a substantial extent volume changes more than the contractile function of the LV ventricle. [21, 22] Borer et al have previously concluded that a load independent method that is better able to measure contractility would predict development of symptoms and LV dysfunction in AR in a better way than EF does.[10] There are diverging opinions about the load independency of TDE.[23, 24] In our study, we observed a marked decrease in PSV and AVPD postoperatively, especially in the High PSV group. This could be explained through stroke volume having a significant impact on LV longitudinal velocities.[25] With a decline in stroke volume, a decline in myocardial wall movements also occurs. The demand on a large stroke volume, together with the LV dilatation associated with AR, would result in a higher PSV and a larger AVPD in a LV with normal myocardial function. An early sign of LV dysfunction would then be a drop from supernormal to subnormal values. One half of the included patients in our study had a PSV above earlier published normal values and the other half had lower values. However, almost all patients had decreased AVPD at rest and decreased PSV upon exercise compared to reference values.[7, 19] Decreased AVPD at rest or upon exercise and decreased PSV on exercise could therefore represent an even earlier sign of myocardial dysfunction.

AVPD by M-mode and Tissue Tracking

AVPD is a widely used method for identification of global and regional myocardial function in ischemic heart disease and heart failure. With Tissue Tracking, it is possible to better visualize the different phases of AVPD in the setting of poor 2D image quality, for example in exercise echocardiography.[26] In this study, we used two methods to register the excursion of the AV-plane: M-mode and Tissue Tracking. With Bland Altman analysis it was demonstrated that these two methods were not interchangeable. These results were expected since we measured only the systolic displacement by M-mode but on the other hand included both systolic and diastolic displacement when measuring AVPD by TDE.

Exercise Echocardiography

In this study, almost none of our AR patients had a PSV on exercise that was concordant with previously published values in healthy subjects.[7] Also, the strongest correlations with common postoperative LV function outcomes were found with preoperative exercise variables measuring longitudinal LV function. This suggests that an early latent myocardial dysfunction could be unmasked in these patients by exercise echocardiography. In healthy subjects, TDE parameters increase significantly between rest and exercise.[7, 8] In our study, the increase was often significant but nevertheless smaller than in healthy subjects.[7]

Pioneer studies by Bonow et al in the early 1980-ies showed that preoperative EF exercise response was not of prognostic importance for postoperative survival in AR patients.[27] Today survival has improved, which has shifted the interest towards preserving postoperative LV function. Exercise echocardiography has been proposed as being a feasible method for optimising the timing of surgery.[10, 11] However, measurement of EF is a highly observer dependent technique and in connection with exercise echocardiography, it can be challenging to identify the whole of the endocardial border.[28] TDE is proposed to be a less operator

dependent method in exercise testing and has shown to be reliable and reproducible for assessing longitudinal shortening during exercise echocardiography.[7, 8]

Diastolic Function

In our study, the e´-velocity was significantly higher in the High PSV group both pre- and postoperatively. A higher e´-wave in healthy controls than among AR patients has been reported earlier. [29] Moreover, at follow up the é/á was higher in the High PSV group than in the Low PSV group. Together this could be interpreted as higher probability for improved LV diastolic function in patients with preoperative high PSV.

Clinical Implication

Currently timing of valve surgery remains a matter of debate. A future vision is to identify reliable and simple measurements to unmask early deterioration of LV systolic function in AR patients. This study demonstrates that TDE measurements at rest and upon exercise can detect subnormal systolic velocities when EF is still >50%, and thereby the method may offer a sensitive tool to be used in improving timing of surgery in AR patients. Myocardial velocity has been proposed as a method for early identification of left ventricular dysfunction.[2] This, together with our results, suggests that when EF is still >50% in an AR patient but AVPD and PSV declining, more frequent echocardiographic controls might be in place and after integration with other parameters surgery might be considered.

Limitations

Data are missing due to overlying pulmonary tissue, as has been reported in earlier studies.[8] Especially in the anterior and lateral walls, echocardiographic images of dissatisfactory

quality have been regarded as missing data. Missing data in these cases have been replaced by the mean values.

The incidence and prevalence of chronic AR are higher in men. Due to this fact our sample only included men though female gender was not an exclusion criterion. However, the homogeneity of the population limits generalization to a mixed gender population.[30]

Conclusion

LV dysfunction can be detected by preoperative PSV and AVPD analysis at rest and upon exercise in chronic AR patients with EF not fulfilling the criteria for surgery according to present recommendations. High preoperative PSV can predict higher AVPD and PSV postoperatively. Therefore, we propose TDE at rest and on exercise as a valuable complement in preoperative screening when evaluating the optimal timing of AR surgery.

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Legends

Figure 1 Left ventricular function in aortic regurgitation patients measured as peak systolic velocity (PSV), atrioventricular plane displacement (AVPD) and ejection fraction (EF) pre- and postoperatively. The patients are divided into two groups according to their preoperative PSV: High PSV (grey) respectively Low PSV (white) group. Boxes present median and 25th-75th percentile values. Significant differences between Low vs. High PSV group are presented as actual p-values.

Figure 2 Bland-Altman plots of atrioventricular plane displacement (AVPD) by Tissue Tracking (TT) vs. M-mode (MM) in aortic regurgitation patients, at rest and upon exercise presented in the Low and High PSV groups (unfilled and filled symbols, respectively). (TT+MM)/2 were used to calculate the average AVPD presented on the x-axis. On the y-axis the absolute difference between TT and MM is displayed. Horizontal lines indicate mean differences between the two methods and dashed horizontal lines represent 2 SDs of the mean. $P < 0.05$ indicates significant difference between the methods. R represents correlation between TT-AVPD and MM-AVPD, r = Spearman´s rho correlation coefficient. PSV= peak systolic velocity

Table 1. Preoperative baseline characteristics of all patients and subgroups with low and high peak systolic velocity (PSV).

Variable	All patients (n=29)	Low PSV (n= 13)	High PSV (n=14)	*p**
Age (years)	53 (39-64)	56 (49-67)	44 (37-59)	0.08
Length (cm)	178 (174-182)	178 (172-180)	180 (175-186)	0.13
Weight (kg)	84 (75-95)	82 (75-95)	88 (75-97)	0.52
Body mass index (kg/m2)	27 (25-30)	26 (24-31)	27 (26-29)	0.76
Body surface area (m2)	2.0 (1.9-2.1)	2.0 (1.9-2.1)	2.0 (1.9-2.2)	0.55
NYHA class (n)				
I	13	5	7	-
II	10	4	5	-
III	5	3	2	-
IV	1	1	0	-
Cardiac rhythm AF/Sinus (n)	3/25	1/11	2/12	0.98
Diabetes (n)	1	0	1	0.76
Angina (n)	3	2	1	0.72
Hypertension (n)	4	1	3	0.55
Medication (n)				
ACE inhibitors	14	7	5	0.51
B-blocker	12	5	6	0.51
Ca-antagonists	5	2	2	1.00
Digoxin	1	1	0	0.74
Diuretics	6	5	0	0.10

*Low vs. High PSV group. AF = Atrial fibrillation

Table 2. Exercise and two-dimensional echocardiography characteristics of all patients and groups with low and high peak systolic velocity (PSV).

Variable		All patients (n=29)	Low PSV (n=13)	High PSV (n=14)	$p^{\S}$
Heart rate (bpm)					
Preop	Rest	67 (57-73)	62 (56-70)	66 (59-74)	0.43
	Exercise	108 (102-118) †††	114 (105-125) ††	104 (101-115) ††	0.19
Postop	Rest	62 (60-73)	61 (50-80)	62 (60-69)	0.69
	Exercise	104 (92-123) †††	104 (90-124) ††	104 (95-117) ††	0.81
Systolic Blood Pressure (mmHg)					
Preop	Rest	140 (130-150)	138 (126-175)	140 (135-148)	1.00
	Exercise	178 (164-210) †††	200 (155-210) †	175 (163-198) ††	0.57
Postop	Rest	138 (116-145)	130 (114-149)	140 (118-148)	0.61
	Exercise	175 (161-189) †††*	173 (163-185) ††	175 (158-188) ††	0.98
Diastolic Blood Pressure (mmHg)					
Preop	Rest	70 (60-80)	60 (55-81)	70 (65-80)	0.36
Postop	Rest	80 (70-90)	88 (70-90)	80 (70-84)	0.50
Indexed LV End-diastolic volume (ml/m^2)					
Preop	Rest	90 (78-110)	94 (77-114)	87 (78-98)	0.41
	Exercise	76 (68-99) ††	77 (74-110) †	75 (68-89) †	0.33
Postop	Rest	56 (45-70))***	59 (45-81)**	49 (44-69)**	0.61
	Exercise	58 (47-67)***	60 (45-69)**	55 (48-62)**	0.73
Indexed LV End-systolic volume (ml/m^2)					
Preop	Rest	39 (33-55)	41 (31-63)	37 (33-50)	0.83
	Exercise	35 (29-51)	43 (32-61)	33 (27-42)	0.12

Postop	Rest	23 (19-33)***	28 (20-38)*	33 (18-32)**	0.36
	Exercise	22 (16-34) ***	24 (15-37)*	22 (17-30)**	0.78
Indexed LV End-diastolic diameter (mm/m^2)					
Preop	Rest	33 (32-35)	35 (31-37)	33 (32-34)	0.23
Postop	Rest	27 (25-30)***	28 (25-31)**	27 (24-28) **	0.41
Indexed LV End-systolic diameter (mm/m^2)					
Preop	Rest	24 (22-26)	26 (22-29)	23 (20-24)	0.04
Postop	Rest	19 (18-24)***	23 (19-25)	18 (17-21)**	0.04
Indexed LV mass (g/m^2)					
Preop		213 (179-254)	216 (166-259)	211 (176-254)	0.70
Postop		146 (130-172)***	156 (126-256)*	141 (125-170)**	0.40

Values expressed as median (25th-75th percentile) or number (n). NYHA = New York Heart Association, LV = left ventricle. Preoperative vs. postoperative *p< 0.05, ** p<0.01, *** p<0.001. Rest vs. exercise † p<0.05 †† p< 0.01 ††† p<0.001. §Low vs. High PSV group.

Table 3. Myocardial velocity, atrioventricular plane displacement (AVPD) and ejection fraction (EF) pre- and postoperatively, at rest and on exercise in aortic regurgitation (AR) patients.

Method	**All patients**			**Low peak systolic velocity (Low-PSV)**		**High Peak Systolic velocity (High-PSV)**		***P*-value (Low vs. High)**	
n=Number of patients									
rest/exercise	**preop**	**postop**	**p-value**	**preop**	**postop**	**preop**	**postop**	**preop**	**postop**
Peak Systolic Velocity	*n = 27/23*	*n=26/26*							
rest (cm/s)	6.1 (5.3-7.3)	5.4 (5.1-6.3)	0.026	5.3 (4.7-5.5)	5.3 (4.6-5.7)	7.2 (6.4-7.7)	6.0 (5.1-6.7) ††	X	0.107
exercise (cm/s)	8.3 (7.4-9.9) §§§	7.7 (6.4-8.9) §§§	0.819	7.5 (6.7-7.9) §§	6.3 (6.1-7.6) §§	9.6 (8.3-10.1) §	8.4 (7.3-9.7) §§	0.004	0.009
Δ (cm/s)	2.2 (1.4-2.8)	1.8 (1.0-3.0)	0.115	2.1 (1.7-2.7)	1.1 (0.7-2.7)	2.2 (1.2-3.0)	2.5 (1.7-3.3)	0.976	0.149
Tissue Tracking AVPD	*n = 27/23*	*n = 26/26*							
rest (mm)	13.0 (10.7-14.6)	11.6 (9.3-12.4)	0.004	10.7 (9.8-12.5)	9.4 (8.4-11.7)	14.1 (14.4-15.6)	12.2 (11.4-13.2) ††	0.002	0.003
exercise (mm)	15.7 (12.3-17.3) §	13.7 (10.9-15.5) §§§	0.028	12.3 (10.7-12.5)	11.0 (10.1-12.9)§	17.0 (16.3-18.6) §	15.4 (14.1-16.4) §§§	0.002	<0.001
Δ (mm)	2.1 (-0.2-3.3)	2.3 (0.5-3.8)	0.061	0.5 (-0.3-3.3)	1.6 (0.0-2.3)	2.5 (0.7-3.4)	3.1 (1.7-4.0)	0.343	0.029
M-mode AVPD	*n = 28/28*	*n = 26/26*							
rest (mm)	11.8 (10.5-13.5)	10.3 (8.6-11.1)	0.001	10.5 (9.9-11.8)	9.8 (7.8-10.4) †	13.1 (10.9-13.9)	10.8 (9.3-12.8) †	0.005	0.038
exercise (mm)	14.8 (11.5-16.0) §§§	12.4 (10.7-14.0) §§§	0.009	11.5 (10.8-15.3) §	10.8 (9.8-12.3) §§	15.5 (14.2-17.4) §§	13.6 (12.3-15.2) §§	0.029	0.006
Δ (mm)	2.0 (0.8-3.9)	2.6 (1.3-4.3)	0.872	1.5 (0.1-3.8)	1.3 (0.4-4.3)	2.8 (1.3-3.9)	2.9 (1.9-4.4)	0.223	0.183

Ejection fraction (EF)	*n = 29/27*	*n =26/26*							
rest (%)	62 (56-68)	60 (54-67)	0.269	61 (57-63)	59 (54-66)	65 (56-68)	60 (54-68)	0.302	0.647
exercise (%)	62 (57-71)	65 (55-70)	0.059	58 (54-63)	61 (55-72)	70 (61-71)	67 (54-80) §§	0.043	0.267
ΔEF (%)	3 (-5-5)	4 (-1-7)	<0.001	-3 (-7.-4)	3 (-3-4)†	3.5 (1-5)	5 (3-9)††	0.077	0.085
Diastolic velocity	*n = 26/24(é/á)*	*n = 25/25(é/á)*							
e´-wave velocity (cm/s)	5.1 (4.4-7.3)	5.6 (3.6-7.5)	0.549	4.5 (3.8-5.1)	3.6 (3.0-5.2)	6.8 (5.1-8.1)	6.6 (5.3-7.9)	<0.001	0.009
a´-wave velocity(cm/s)	5.6 (4.6-6.8)	5.6 (4.1-6.9)	0.058	5.5 (4.4-6.3)	4.7 (3.4-6.7)	6.3 (5.1-7.4)	5.7 (4.3-6.9)	0.198	0.546
e´/a´-wave (cm/s)	1.1 (0.7-1.4)	1.1 (0.8-2.0)	0.548	1.1 (0.7-1.2)	0.8 (0.6-1.5)	1.2 (0.9-1.7)	1.5 (1.1-2.3)	0.114	0.025

Values expressed as median (25^{th}-75^{th} percentiles). Δ = the increase from rest to exercise. AVPD = Atrioventricular plane displacement. e´ = early diastolic wave. a´= atrial diastolic wave. Low and High PSV; patients with preoperative peak systolic velocity <5.9 cm/s and >5.9 cm/s respectively. x: not analysed since subgroups was defined on basis of PSV at rest. Rest-exercise § $p < 0.05$, §§ $p < 0.01$, §§§ $p < 0.001$. † Rest-rest, exercise-exercise $p < 0.05$, †† $p < 0.01$, ††† $p < 0.001$

Table 4 Correlation between preoperative longitudinal LVF and postoperative LVF outcome

	Variable	φ *	*p*		**Variable**	φ *	*p*		**Variable**	φ *	*p*
	EF at rest postop				*EF at exercise*				*Δ EF*		
Rest	**AVPD(TT)**	0.413	0.040	**Rest**	**AVPD (TT)**	0.477	0.016	**Rest**	**PSV**	0.280	0.194
Ex/Δ	**PSV**	0.356	0.080	**Ex/Δ**	**ΔAVPD(MM)**	0.560	0.003	**Ex/Δ**	**PSV**	0.454	0.023
	Indexed ESV at rest				*Indexed EDV at rest*				*Indexed ESD at rest*		
Rest	**AVPD (TT)**	-0.232	0.275	**Rest**	**AVPD (MM)**	-0.058	0.788	**Rest**	**AVPD (MM)**	-0.503	0.014
Ex/Δ	**AVPD (MM)**	-0.535	0.008	**Ex/Δ**	**ΔAVPD (MM)**	-0.529	0.009	**Ex/Δ**	**AVPD (MM)**	-0.391	0.065
	Indexed ESV at exercise				*Indexed EDV at exercise*				*Indexed EDD at rest*		
Rest	**AVPD (TT)**	-0.161	0.451	**Rest**	**AVPD (TT)**	-0.096	0.663	**Rest**	**AVPD (MM)**	-0.523	0.010
Ex/Δ	**ΔPSV**	-0.499	0.025	**Ex/Δ**	**ΔAVPD (TT)**	-0.573	0.008	**Ex/Δ**	**AVPD (MM)**	-0.339	0.114

Postoperative LV function outcome measurements marked by italics. The bold variables represent the preoperative longitudinal LV function measurements with highest correlation coefficient to respective LV function outcome. Ex; exercise, LV; Left ventricular, PSV; Peak systolic velocity, AVPD; Atrioventricular plane displacement, TT; Tissue Tracking, MM; M-mode, Δ; change from rest to exercise. *Spearman´s rho correlation coefficient.

Figure 1

Figure 1. Left Ventricular Function in Aortic Regurgitation Patients Pre- and Postoperatively

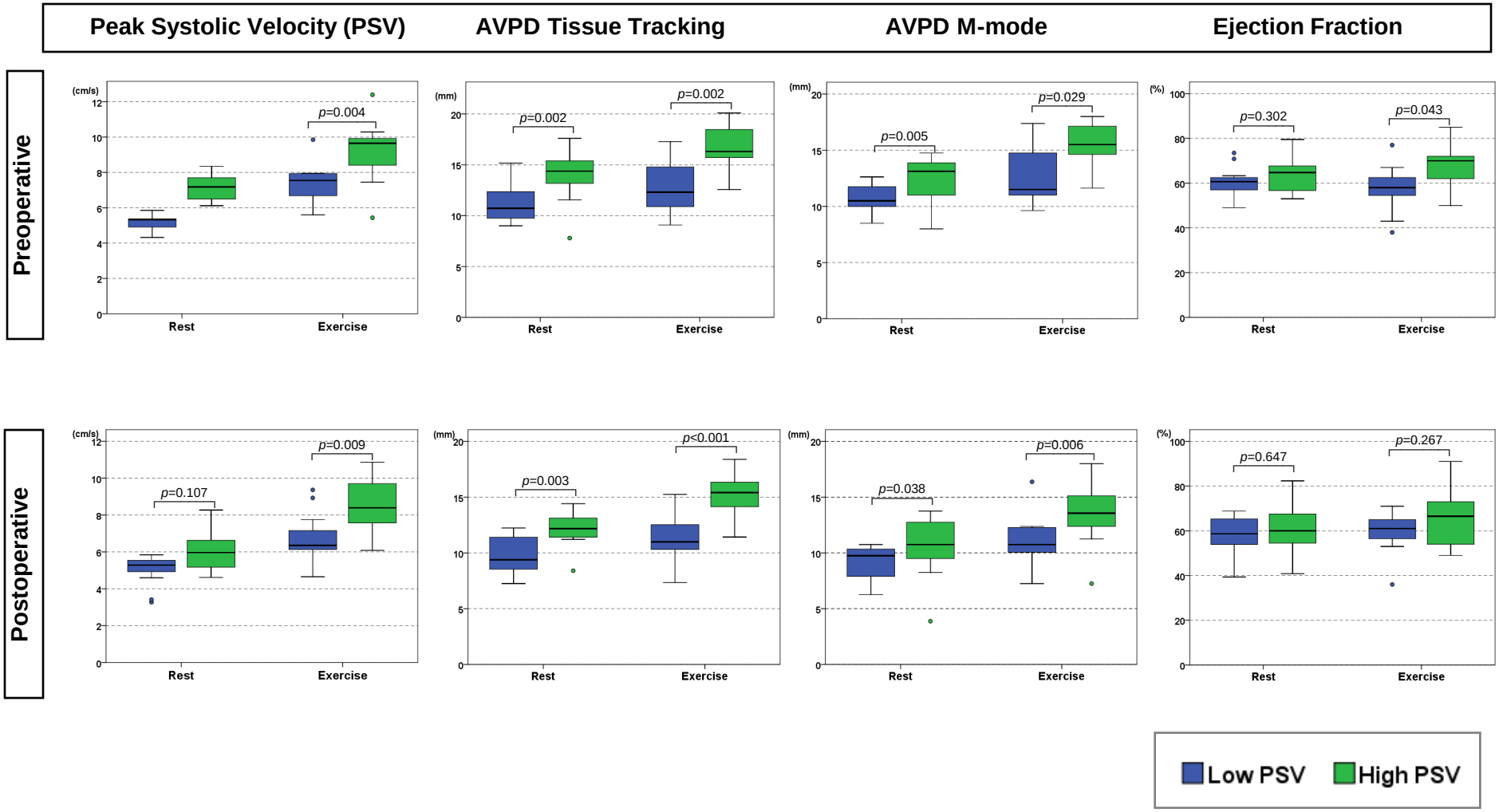
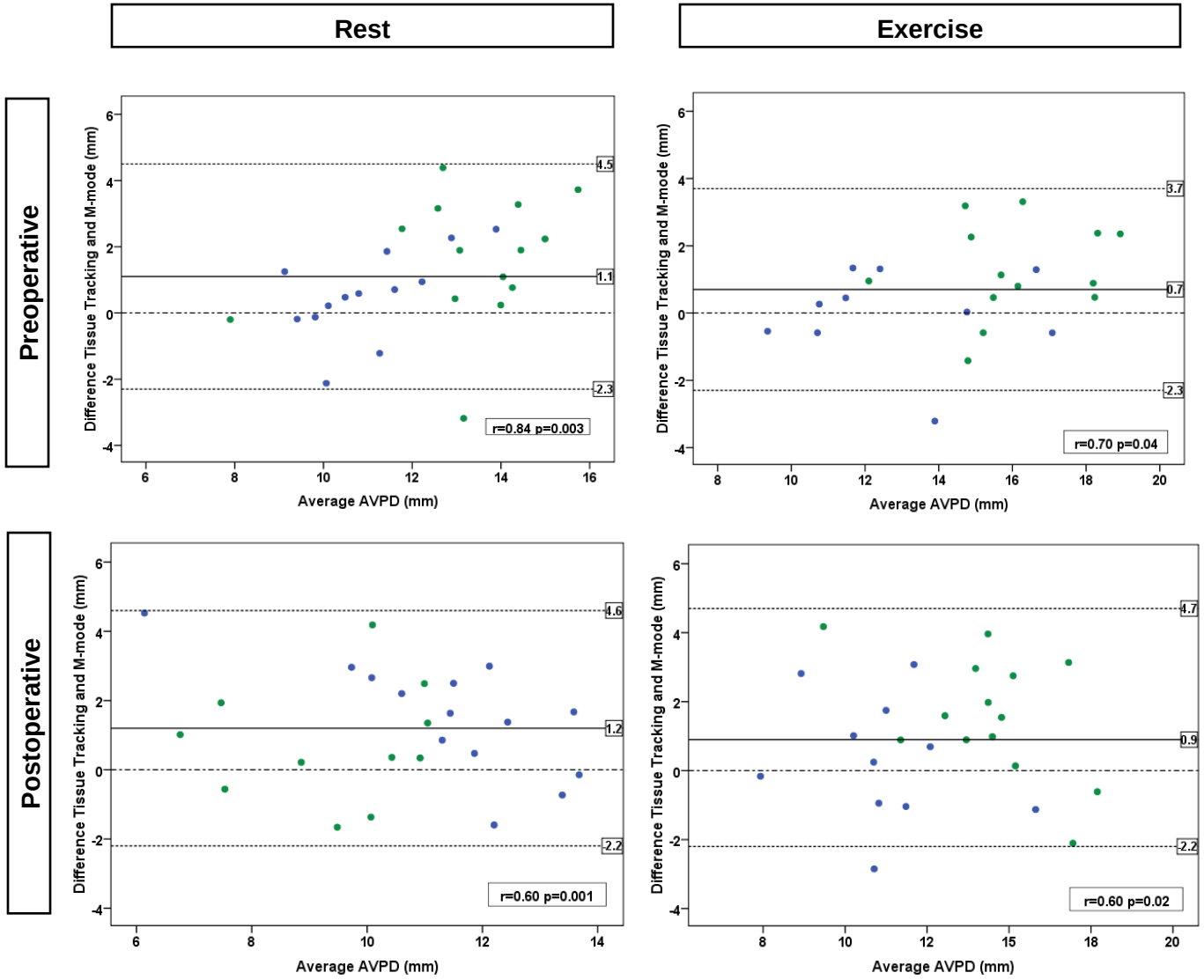


Figure 2.


Rest
Exercise
Preoperative
Postoperative
Difference Tissue Tracking and M-mode (mm)
Average AVPD (mm)
4.5
1.1
-2.3
r=0.84 p=0.003
3.7
0.7
-2.3
r=0.70 p=0.04
4.6
1.2
-2.2
r=0.60 p=0.001
4.7
0.9
-2.2
r=0.60 p=0.02