

Dobutamine-Stress Echocardiography as a Predictor of Cardiac Function after Surgery for Aortic Valve Regurgitation with Poor Function

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ABSTRACT

Background: Patients with aortic valve regurgitation (AR) present at a late stage with impaired function. Some may not show improved function after surgery.

Aim of the work: To evaluate the functional outcome in patients with and without poor left ventricular (LV) function and to evaluate the role of dobutamine echocardiography in predicting persistent dysfunction after surgery.

Patients and Methods: Patients with severe AR (71) who underwent valve replacement (AVR) were divided into 2 groups based on the ejection fraction (EF); Group I: patients with EF <50% and Group II: patients with EF >50%. Group I was subdivided into 2 subgroups according to the response to dobutamine-stress echocardiography (DSE): Group Ia: patients whose EF increased to >50%, and Group Ib: patients whose EF remained <50%. Six months postoperatively, echocardiography was performed to assess the cardiac function and volumes.

Results: Seventy one patients were included in the study: 39(54.9%) in Group I, 32(45.1%) in Group II, 21(29.6%) in Group Ia and 18(25.4%) in Group Ib. Preoperative criteria was not significantly different between the 2 groups apart from the intensive care unit (ICU) stay which was longer in group I (p = 0.006). In group Ia, EF raised on DSE (p < 0.001) and after surgery (p < 0.001). In group II, EF showed significant change on DSE (p < 0.001), but not after surgery (p = 0.203).

Conclusions: Preoperative DSE can predict improvement of LV function after AVR in cases with severe AR with ventricular dysfunction.

Keywords: Dobutamine-stress echocardiography, Aortic regurgitation, Myocardial dysfunction.

INTRODUCTION

Aortic valve regurgitation (AR) is associated with left ventricular volume overload, which may lead eventually to severe dilatation of the left ventricle, which is usually associated with changes at the cellular level in the form of myocardial fibrosis and contractile dysfunction⁽¹⁾. Nuclear studies have revealed the presence of perfusion defects in cases with left ventricular dysfunction due to decreased coronary perfusion pressure, which is correlated well with the results of DSE test^(2,3).

The resulting dysfunction may persist after surgical correction of the valvular pathology. Hence, patients with chronic valvular lesions must be carefully assessed before surgery to predict such persistent dysfunction⁽⁴⁾.

It is reported that all cases who had their aortic valve replaced for regurgitation with good ventricular function showed good prognosis at a 10-year follow-up, while patients with ejection fraction below 30% showed persistent ventricular dysfunction after surgery^(5,6).

Symptoms do not necessarily reflect the degree of ventricular dysfunction. Patients with more manifesting symptoms (> Class II **New York Heart Association** (NYHA)) may show normal ventricular function, and on the other hand, ventricular function may be significantly impaired in patients with milder symptoms (< NYHA class II)⁽⁷⁾.

It is reported that preoperative left ventricular end-systolic volume (ESV) and dimensions are independent predictors for persistent dysfunction after operation. It would be more useful to depend on preoperative systolic wall stress and ejection fraction to predict ventricular dysfunction after surgery⁽⁸⁾.

This study aims to compare between the 6-month functional outcomes after aortic valve replacement in cases with and without poor ventricular function. Also, to evaluate the role of dobutamine echocardiography in predicting persistent dysfunction after surgery.

PATIENTS AND METHODS

This is a prospective comparative study that included cases with severe aortic regurgitation who underwent aortic valve replacement at Cardiothoracic Surgery Department at Mansoura University during the period from December 2017 to December 2019. All patients with severe aortic regurgitation who underwent aortic valve replacement were included in the study. Patients with less than severe AR, ischemic heart disease, hypertrophic cardiomyopathy, ventricular arrhythmia, or dobutamine hypersensitivity were excluded from the study.

A total of 71 patients were included in the study. Patients were divided into 2 groups based on the preoperative LV ejection fraction (LVEF): Group (I)

included patients with EF <50% and Group (II) included patients with EF >50%. Group I was subjected to Dobutamine- stress echocardiography and was further subdivided into two subgroups; group Ia included patients whose EF improved to >50%, and group Ib included whose EF was still <50% (little or no improvement). Six months after surgery, echocardiography was performed to assess the changes of the cardiac function.

Dobutamine-stress echocardiography

The test was conducted in a left lateral position with ECG monitored and recorded. Then, dobutamine was infused at an initial dose of 5 mcg/kg/min increased every 3 min to 10 mcg/kg/min, then to 15 mcg/kg/min then to 20 mcg/kg/min. Echocardiographic measurements were obtained at this stage.

The surgical technique

All cases were performed by the same surgical team using the standard procedure. On supine position, general anesthesia was induced, central intravascular lines were placed followed by median sternotomy and heparin was given at a dose of 3 mg/kg body weight targeting Activated Clotting Time (ACT) more than 400 seconds then cardiopulmonary bypass (CPB) was initiated.

After cooling down to 32°C, aortic cross clamping was placed followed by oblique incomplete aortotomy of the ascending aorta, then cardioplegia was infused sequentially into both coronary arteries at a total dose of 20 ml/kg. The native aortic valve was resected, and the prosthetic valve was implanted and fixed down by interrupted mattress sutures.

Removal of the aortic clamping was done after closure of the aortotomy incision and careful de-airing. Patient was then rewarmed and weaned off CPB. Wound was then closed in layers after placing the necessary drains.

Ethical Consideration

This work was carried out following The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans and has been approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Mansoura University, Egypt. All patients provided informed written consents before enrollment. The study was conducted after approval of the IRB of and patients provided consents.

Statistical analysis

Categorical variables were expressed as numbers and percentages were used to express categorical variables, while mean and median were used to express continuous variables. Paired (t) test, Chi square and independent t-test were used to compare variables. P value of 0.05 or less was required to be considered significant. Statistical Package for the Social Sciences (SPSS release 22, Chicago, IL) was used for the analysis.

RESULTS

A total of 71 patients were included in the study: 39 patients in group I (54.9%) and 32 patients in group II (45.1%). Group Ia included 21 patients (29.6%) and group Ib included 18 patients (25.4%).

Table (1): Comparison of group I and group II regarding demographic characteristics and operative details.

Variables		Group I (n= 39)	Group II (n= 32)	P
Age (Year)		34.59 ± 7.184	33.53 ± 8.621	0.574
Gender	Male	32 (82.1%)	22 (68.8%)	0.191
	Female	7 (17.9%)	10 (31.3%)	
NYHA	II	22 (56.4%)	24 (75.0%)	0.103
	III	17 (43.6%)	8 (25.0%)	
DM		2 (5.1%)	0 (0.0%)	0.498
HTN		1 (2.6%)	4 (12.5%)	0.167
Ring	Fibrotic ring	26 (66.7%)	18 (56.3%)	0.688
	Mild calcification	12 (30.8%)	13 (40.6%)	
	Severe calcification	1 (2.6%)	1 (3.1%)	
Valve	21 mm	10 (25.6%)	6 (18.8%)	0.688
	23 mm	11 (28.2%)	13 (40.6%)	
	25 mm	14 (35.9%)	9 (28.1%)	
	27 mm	4 (10.3%)	4 (12.5%)	
Bypass time (min)		50.13 ± 14.577	51.09 ± 13.839	0.777
Cross clamp time (min)		39.62 ± 14.929	40.47 ± 14.445	0.809
Ventilation time (hour)		9.46 ± 3.755	10.81 ± 3.297	0.116
ICU stay (hour)		49.54 ± 14.871	40.50 ± 10.884	0.006

DM: Diabetes Mellitus, HTN: Hypertension, ICU: Intensive care unit, NYHA: New York Heart Association

The mean age of the patients was 34.59 and 33.53 years in groups I and II respectively. Males represented 82.1% and 68.8% of cases in both groups respectively. The rest of the demographic and operative data were not significantly different between the two groups apart from the duration of the ICU stay, which was significantly prolonged in the first group (49.54 vs 40.50 hours for group II, $p = 0.006$). These data are illustrated at **Table (1)**. **Table (2)** compares echocardiographic parameters between the groups I and II.

Table (2): Comparison of group I and group II regarding studied ECHO parameters.

Variables		Group I (n= 39)	Group II (n= 32)	P
Rest	ESVi	120.85 ± 35.220	57.31 ± 16.009	< 0.001
	EDVi	196.49 ± 56.433	143.09 ± 47.836	< 0.001
	EF	40.64 ± 6.276	60.81 ± 6.698	< 0.001
	SVi	50.33 ± 7.318	74.34 ± 4.539	< 0.001
Dobutamine	ESVi	103.51 ± 40.380	61.50 ± 17.126	< 0.001
	EDVi	194.46 ± 52.225	149.19 ± 50.269	< 0.001
	EF	52.05 ± 8.482	65.38 ± 7.504	< 0.001
	SVi	62.79 ± 6.388	81.75 ± 4.412	< 0.001
Postoperative	ESVi	72.03 ± 28.521	33.66 ± 10.748	< 0.001
	EDVi	125.23 ± 39.267	72.47 ± 26.349	< 0.001
	EF	46.41 ± 8.958	61.56 ± 6.420	< 0.001
	SVi	41.95 ± 5.568	38.84 ± 3.693	0.192

ESVi: indexed end-systolic volume, EDVi: indexed end-diastolic volume, EF: ejection fraction, SV: Stroke volume

In group I, when comparing dobutamine to rest echocardiography findings, both EF and SV showed a significant increase, EDVi did not show a significant change. After surgery, all echocardiographic parameters decreased significantly compared to rest values but in favor of a significant increase of EF ($p < 0.001$). In group II, EF was not significantly changed ($p = 0.128$) after surgery. **Table (3)** illustrates these data.

Table (3): Within-group comparison of the echocardiographic parameters of dobutamine-stress and postoperative values compared to resting values.

Group I (n= 39)			
	Dobutamine	Rest	p
ESVi	103.51 ± 40.380	120.85 ± 35.220	< 0.001
EDVi	194.46 ± 52.225	196.49 ± 56.433	0.104
EF	52.05 ± 8.482	40.64 ± 6.276	< 0.001
SVi	62.79 ± 6.388	50.33 ± 7.318	< 0.001
	Postoperative	Rest	p
ESVi	72.03 ± 28.521	120.85 ± 35.220	< 0.001
EDVi	125.23 ± 39.267	196.49 ± 56.433	< 0.001
EF	46.41 ± 8.958	40.64 ± 6.276	< 0.001
SVi	41.95 ± 5.568	50.33 ± 7.318	< 0.001
Group II (n= 32)			
	Dobutamine	Rest	p
ESVi	61.50 ± 17.126	57.31 ± 16.009	< 0.001
EDVi	149.19 ± 50.269	143.09 ± 47.836	< 0.001
EF	65.38 ± 7.504	60.81 ± 6.698	< 0.001
SVi	81.75 ± 4.412	74.34 ± 4.539	< 0.001
	Postoperative	Rest	p
ESVi	33.66 ± 10.748	57.31 ± 16.009	< 0.001
EDVi	72.47 ± 26.349	143.09 ± 47.836	< 0.001
EF	61.56 ± 6.420	60.81 ± 6.698	0.203
SVi	38.84 ± 3.693	74.34 ± 4.539	< 0.001

ESVi: indexed end-systolic volume, EDVi: indexed end-diastolic volume, EF: ejection fraction, SV: Stroke volume

When group I was subdivided into two subgroups, no significant difference was detected between the two subgroups regarding demographic or operative characteristics. **Table (4)** compares the different echocardiographic parameters between groups Ia and Ib.

Table (4): Comparison of group Ia and group Ib regarding studied ECHO parameters.

Variables		Group Ia (n= 21)	Group Ib (n= 18)	p
Rest	ESVi	102.81 ± 31.152	141.89 ± 27.574	< 0.001
	EDVi	164.14 ± 43.548	234.22 ± 45.691	< 0.001
	EF	42.81 ± 5.335	38.11 ± 6.480	0.018
	SVi	40.14 ± 3.762	63.56 ± 5.375	< 0.001
Dobutamine	ESVi	87.52 ± 45.236	122.17 ± 23.520	0.006
	EDVi	161.90 ± 45.149	225.44 ± 42.555	< 0.001
	EF	57.14 ± 6.872	40.44 ± 8.926	0.012
	SVi	68.19 ± 5.643	66.33 ± 3.235	0.953
Post-operative	ESVi	95.10 ± 16.568	131.28 ± 20.790	< 0.001
	EDVi	100.71 ± 29.355	153.83 ± 28.706	< 0.001
	EF	51.57 ± 6.867	40.39 ± 7.253	< 0.001
	SVi	41.67 ± 4.844	42.44 ± 5.039	0.767

Data is expressed as mean and standard deviation. 95% CI: 95% confidence interval of the mean difference between both groups. P is significant when < 0.05.

Table (5): Within-subject comparison of group Ia and group Ib regarding studied ECHO parameters compared to resting value.

Group Ia (n= 21)			
	Dobutamine	Rest	p
ESVi	87.52 ± 45.236	102.81 ± 31.152	< 0.001
EDVi	161.90 ± 45.149	164.14 ± 43.548	0.0762
EF	57.14 ± 6.872	42.81 ± 5.335	< 0.001
SVi	68.19 ± 5.643	40.14 ± 3.762	< 0.001
	Postoperative	Rest	p
ESVi	95.10 ± 16.568	102.81 ± 31.152	0.032
EDVi	100.71 ± 29.355	164.14 ± 43.548	< 0.001
EF	51.57 ± 6.867	42.81 ± 5.335	< 0.001
SVi	41.67 ± 4.844	40.14 ± 3.762	0.430
Group Ib (n= 18)			
	Dobutamine	Rest	p
ESVi	122.17 ± 23.520	141.89 ± 27.574	< 0.001
EDVi	225.44 ± 42.555	234.22 ± 45.691	0.036
EF	41.44 ± 8.926	38.11 ± 6.480	0.128
SVi	66.33 ± 3.235	63.56 ± 5.375	0.094
	Postoperative	Rest	P
ESVi	131.28 ± 20.790	141.89 ± 27.574	< 0.001
EDVi	153.83 ± 28.706	234.22 ± 45.691	< 0.001
EF	40.39 ± 7.253	38.11 ± 6.480	0.110
SVi	67.42 ± 5.039	63.56 ± 5.375	0.081

In group Ia, dobutamine echocardiographic findings showed an insignificant change compared to the rest values except for iEDV (p = 0.0762). After surgery, all echo parameters changed significantly apart from the SV (p = 0.430). In group Ib, dobutamine-stress readings significantly changed compared to the rest values, apart from EF and SVi (p = 0.128, p = 0.094 respectively). After operation, ESVi and EDVi were reduced significantly compared to the rest values, while EF and SVi did not show significant changes (p = 0.110, p = 0.081 respectively). **Table (5)** illustrates these data.

DISCUSSION

Chronic regurgitation of the aortic valve is naturally characterized by prolonged reservation of the systolic function of the LV, progression of asymptomatic patients with severe degree of regurgitation to valve replacement is estimated to be 3% annually⁽⁹⁾. Replacement or repair of the aortic valve would reverse the myocardial dysfunction in its early stage. Surgery is performed in symptomatic patients with moderate/severe aortic regurgitation, or asymptomatic patients with myocardial dysfunction. Detection of residual myocardial reserve in this subgroup of patients is important in predicting the postoperative outcome. The excessive preload reduction after valve replacement in aortic regurgitation explains the improved ventricular function in early and late follow-up⁽¹⁰⁾.

Practically, dobutamine improves the systolic function of the myocardium due to enhanced contractility which explains the decrease of the ESV, however, dobutamine may have a lesser effect on the EDV that may be attributed to the increased heart rate, which shortens the diastolic time and hence the regurgitant volume and as a sequence of reduced ESV as well. Cardiac stress testing can unmask the myocardial dysfunction in asymptomatic patients and assess the degree of reversibility of this dysfunction, which has a significant mortality benefit from early intervention compared to delayed surgery⁽¹¹⁾.

Dobutamine-stress echocardiography is now widely available, cheap, safe and easily applicable, and at the same time is more preferred to the exercise-stress test since it avoids the pulmonary and physical limitations. It was also reported that DSE was able to reduce both ESV and EDV for >25 % which was not achieved in the physical exercise testing⁽³⁾.

Many parameters were investigated in order to predict the postoperative systolic function in patients with severe aortic regurgitation, **Gouda et al.**⁽¹²⁾ used the early diastolic driving force (DF), global longitudinal strain (GLS) and ejection fraction (EF) parameters in their study, which revealed strong relation to the postoperative function, however, they stated that LVEF would be inaccurate in detecting the subtle changes in myocardial function since it is augmented by the degree of EDV.

In our study, mean EDVi dropped after replacement of the aortic valve significantly decreased from 196.5 to 125.2 ml/m² for group I, and from 143.1 to 72.5 ml/m² ($p < 0.001$ for both groups), with statistically significant improvement of EF for group I (46.41 ± 8.96 to 40.64 ± 6.28 , $p = < 0.001$), but not for group II (61.56 ± 6.42 to 60.81 ± 6.69 , $p = 0.128$) since this group had already better LV function before surgery. **Bonow et al.**⁽¹⁰⁾ reported significant reduction of the EDV and wall stress, and improvement of EF between preoperative and early postoperative readings ($p < 0.001$), but only EF continued to show

improvement between early and late postoperative follow-up which may be attributed to insidious improvement of ESV over time.

Our results showed that group Ia, which demonstrated improved LV EF on dobutamine-stress test ($p < 0.001$), also showed a statistically significant increase of the EF between the preoperative and postoperative readings ($p < 0.001$), while group Ib did not show a significant change of EF for either dobutamine-stress ($p = 0.128$) or postoperative ($p = 0.102$) readings compared to the preoperative data. Similar findings were reported by **Abo El-Fotoh et al.**⁽⁴⁾ who stated that dobutamine-stress testing is a good predictor of postoperative LV function in this group of patients.

Espinola-Zavaleta et al.⁽¹³⁾ studied a total of 11 patients with aortic regurgitation and decreased systolic function. Although dobutamine caused a significant elevation of EF from 37 ± 9 up to $43 \pm 12\%$, both systolic wall stress and systolic pulmonary pressure did not show significant changes. One patient who showed no response to dobutamine test had passed away. It was concluded that in cases with aortic regurgitation and decreased EF, dobutamine-stress echocardiography is a good indicator for the contractile reserve.

El-Fiky et al.⁽⁸⁾ reported that EF was significantly increased in the group with better systolic response to dobutamine-stress test (62.43 vs. 8% increase in the other group, $p = 0.001$). Moreover, ESV showed a more significant improvement in the same group (43 vs. 29% decrease in group Ib, $p = 0.036$). However, EDV changes did not differ significantly between the two groups ($p > 0.05$).

Tam et al.⁽¹⁴⁾ stated that dobutamine-stress EF before operation is highly predictive of postoperative EF, which predicts the clinical outcome of patients following aortic valve replacement for aortic regurgitation. They also reported that dobutamine-stress echocardiography high-lightens the small changes in LV size and function between cases with and without complete recovery after valve replacement which may predict the LV function behavior after surgery.

Barbosa et al.⁽¹⁵⁾ investigated the relation between the preoperative EF to the postoperative events, death or need for surgery, in patients with severe aortic regurgitation, the authors stated that percent of increase in EF on low-dobutamine doses did not correlate with the postoperative events. We did not have mortality in our group of patients, so we could not correlate death to any preoperative parameter.

CONCLUSIONS

Preoperative dobutamine-stress echocardiography is a significant predictor for left ventricular systolic function after aortic valve replacement in cases with severe aortic valve regurgitation associated with left ventricular dysfunction.

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