Comparison of exercise and dobutamine echocardiography in the haemodynamic assessment of small size mechanical aortic valve prostheses

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Abstract

Objective: Doppler echocardiographic evaluation of prosthetic heart valve function is usually performed at rest although this situation is not representative of patients’ daily activities. Following aortic valve replacement, patients most likely to remain symptomatic are those with a small aortic root and dobutamine or exercise echocardiography has been proposed to elicit the presence of abnormal haemodynamics or persistently elevated transvalvular gradients in these patients. This study was carried out to compare dobutamine echocardiography with a symptom limited treadmill exercise echocardiography in patients following aortic valve replacement with a small size (19 mm) St. Jude Mechanical valve prosthesis. Methods: The study population consisted of ten unselected patients following aortic valve replacement. Dobutamine was infused intravenously starting at 5 µg/kg/min and increasing by 5 µg/kg/min at 15 min interval up to 20 µg/kg/min. Heart rate, blood pressure, cardiac output (CO), peak and mean gradients as well as effective orifice area (EOA) were measured. These parameters were also measured following a symptom limited treadmill exercise. Results: Dobutamine stress increased heart rate (HR) and CO by 50 and 74%, respectively (both *P* < 0.0002), and mean transvalvular gradient from 22 ± 4.1 mmHg at rest to 40.0 ± 10 mmHg at maximum stress (*P* < 0.001). With exercise, HR and CO increased by 48 and 70%, respectively while mean transvalvular gradient increased from 22 ± 3.1 mmHg at rest to 38.0 ± 6.4 mmHg (*P* < 0.0001). The maximum increase in HR, CO and mean transvalvular gradient with dobutamine and exercise were similar however. There was no significant change in the EOA with either dobutamine or exercise. Conclusion: The result suggests that both treadmill exercise and dobutamine stress echocardiography are equally effective for the hemodynamic evaluation of small aortic valve prosthesis.

Keywords: Exercise echocardiography; Dobutamine echocardiography; Small size aortic valve prosthesis

1. Introduction

The haemodynamic evaluation of mechanical aortic valve prosthesis is usually carried out using Doppler echocardiography performed at rest [1]. Occasionally, one may encounter patients who continue to remain symptomatic following aortic valve replacement and exercise echocardiography has been promoted to elicit a haemodynamic response that may unmask prosthetic valve dysfunction [2–4]. Exercise echocardiography, however, requires a considerable degree of patient cooperation and qualitatively adequate Doppler signals are difficult to obtain because of the exercise and wall motion related artefacts. Dobutamine echocardiography has been suggested as an alternative to exercise echocardiography especially in the elderly group of patients who are unable or unwilling to perform an exercise protocol [5–8]. So far, no study has yet been performed to compare the haemodynamic response of dobutamine with that of exercise. This study was undertaken to compare and characterise the haemodynamic and Doppler changes induced by dobutamine and a symptom limited treadmill exercise echocardiography in the same patient with a normally functioning small size mechanical aortic valve prosthesis.

2. Methods

2.1. Patient population

Ten patients [nine women, mean age 68 years (range 29–80)] who underwent isolated aortic valve replacement for aortic stenosis with a size 19 mm St. Jude mechanical valve at our institute were studied. All patients were in sinus...
rhythm and on no medication other than anticoagulation. There was no history of angina pectoris or myocardial infarction after the operation. In addition, normal coronary arteries had been documented in all subjects by pre-operative coronary angiography. The study protocol was approved by the United Bristol Healthcare Trust Ethics Committee, and written informed consent was obtained from all subjects.

2.2. Dobutamine stress protocol

The dobutamine stress protocol has been previously reported [5]. Patients underwent stress echocardiography after a 3-h fast of solids with fluid maintenance. Following a detailed history and physical examination to exclude the presence of any contraindication to stress testing [9], complete pre-stress two-dimensional echocardiography was performed in order to exclude prosthetic valve malfunction, other valvular disease, or severe left ventricular dysfunction. Apical four chamber views were then acquired from which baseline (rest) Doppler measurements of transvalvular flow were obtained.

Using a peripheral venous cannula, a graded infusion of dobutamine was administered intravenously starting at 5 μg/kg/min and increasing by 5 μg/kg/min at 15-min intervals up to 20 μg/kg/min. During the study, patients underwent continuous electrocardiographic monitoring, and blood pressure was recorded at 5-min intervals with an automated cuff. Criteria for stopping the dobutamine infusion included (1) hypotension (systolic blood pressure <100 mmHg), (2) dyspnea, or (3) significant ventricular or supraventricular arrhythmias. Repeat (stress) Doppler measurements were obtained before each incremental increase in the infusion rate. Following the completion of the final assessment at a dose of 20 μg/kg/min (maximum stress), dobutamine infusion was discontinued, and the patient was monitored for a minimum of 20 min, or until heart rate (HR) had returned to pre-stress values.

2.3. Exercise stress protocol

Following a period of acclimatisation to the treadmill machine, a symptom limited treadmill exercise test was carried out. The machine was set at stage 1, i.e. 2.7 km/h at 10° slope and the patient exercised until he/she were either short of breath or tired. Patients were then transferred to the examination couch as rapidly as possible and the echocardiogram performed. This stage is equivalent to a workload of 5 mets where 1 met = 3.5 l/kg/min of body weight. A formal Bruce protocol was not used because of the patient’s unfamiliarity with the machine and a standard protocol would have been too strenuous for the patients.

2.4. Doppler measurements and calculations

An experienced echocardiographer performed all tests. Echocardiography was carried out using an Aloka SSD-830 ultrasound system with a 2.5 MHz transducer (Aloka, Japan) with facilities for continuous-wave and pulsed-wave Doppler. Parasternal long-axis views were obtained and the early-systolic diameter (D) of the left ventricular outflow tract (LVOT) was measured just below the prosthetic valve using an inner-edge-to-inner-edge method. For each patient, an average of three diameter measurements was used. The LVOT cross-sectional area (CSA) was calculated as:

\[ \text{CSA} = \pi D^2 \quad (\text{cm}^2) \]

The pulsed-wave Doppler cursor was then placed in the LVOT immediately proximal to the aortic valve, and pulsed-Doppler flow velocity was recorded. Peak and mean velocities in the LVOT were then measured. Cardiac output (CO) was calculated as follows:

\[ \text{CO} = \text{VTI} \times \text{CSA} \times \text{HR} \quad (\text{L/min}) \]

where VTI is the velocity time integral in the LVOT, and HR in beats per min.

Flow velocity across the valve was obtained by means of continuous-wave Doppler after interrogation from multiple windows. Great care was taken to orientate the transducer so that the angle between the Doppler cursor and LVOT was as close to 0° as possible, and to obtain the highest possible velocity signal. Peak velocity was measured, averaging from three velocity envelopes, and mean velocity was calculated by online averaging of the instantaneous velocities measured throughout the velocity complexes. Measurements were made in triplicate in each stage to ensure reproducibility. The modified Bernoulli equation was used to calculate pressure drop (gradient) across the prosthesis as follows:

\[ \Delta P = 4(V_{CW}^2 - V_{PW}^2) \quad (\text{mmHg}) \]

where \( \Delta P \) is the pressure drop, and \( V_{CW} \) and \( V_{PW} \) are the velocities (peak or mean) across the valve (using continuous-wave Doppler) and in the LVOT (using pulsed-wave Doppler), respectively. The mean pressure drop was calculated by applying the modified Bernoulli equation at multiple instantaneous velocities measured throughout the velocity profile. The average of all such instantaneous pressure gradients represents the mean. In practice, this is done by online computer software during planimetry of the velocity waveform. Velocity ratio (VR), the ratio of mean subaortic to mean transaortic velocity, gives an approximate guide to orifice behaviour, independent of measurements of LVOT diameter [10]. The prosthetic valve effective orifice area (EOA) was calculated using the modified continuity equation as follows:

\[ \text{EOA} = \text{CSA} \times \text{VR} \quad (\text{cm}^2) \]

This simplified equation has shown an extremely good correlation with that of the original continuity equation [10].
2.5. Statistical analysis

Parameters were calculated for each patient at rest, maximum dobutamine infusion and maximum exercise and the data is presented as mean ± standard deviation. The effect of dobutamine and exercise on the mean resting Doppler measurements was compared using the paired Student’s t test. In addition, the extent of the difference between exercise and dobutamine were compared using a paired non-parametric test (Wilcoxon test). The comparative assessment of the two measurements was performed according to the method described by Bland and Altman [11]. A P value of <0.05 was considered significant. The statistical program Statview (SAS Institute, Inc, version 5.0, Cary, NC) was used to perform these analyses.

3. Results

Ten patients who underwent isolated aortic valve replacement using a size 19 mm St. Jude Medical prosthesis were studied. Mean body surface area was 1.68 ± 0.14 m². Patients underwent the dobutamine stress protocol 15.6 ± 6.3 months following aortic valve replacement. Eight patients were in NYHA class 1 and two patients were in NYHA class 2. The dobutamine infusion was well tolerated up to a maximum of 20 μg/kg/min in all patients. All patients had good left ventricular function and no impairment in regional myocardial contractility with dobutamine stress could be detected in any patient. All patients completed the symptom limited exercise protocol which was conducted 27.3 ± 7.3 months post-operatively in all the same patients.

Heart rate increased by 50% with dobutamine from a resting rate of 81 ± 20 beats/min to 121 ± 24 beats/min (P = 0.0002). At peak exercise, the increase in HR was 48% from a resting HR of 79 ± 8 beats/min to 117 ± 20 beats per min (P < 0.0001). The maximum increase in HR observed with dobutamine and exercise was similar, however (P = 0.68; value −0.41).

During dobutamine infusion, there was a small but significant decrease in mean blood pressure. Resting mean blood pressure of 112 ± 15 mmHg decreased to 101 ± 14 mmHg (P = 0.047). With exercise, however, there was a highly significant increase in mean blood pressure. Resting mean blood pressure of 99 ± 4.7 mmHg increased to 123 ± 12 mmHg with maximum exercise (P = 0.0001). When the mean blood pressure achieved during maximum exercise was compared with that achieved during maximum dobutamine infusion, there was a high significant increase with exercise (mean difference, 23.4 mmHg, P = 0.005).

The CO changed significantly with both dobutamine and exercise (Fig. 1). There was an increase in CO by 74% from 5.0 ± 1.9 L/min at rest to 8.7 ± 2.4 L/min with maximum dobutamine (P < 0.0001). Similarly with exercise, there was an increase in CO by 70% from 4.8 ± 0.8 L/min at rest to 8.2 ± 1.7 L/min with maximum exercise (P = 0.0001). The changes in CO with maximum dobutamine infusion and exercise were similar (P = 0.72, z value −0.36).

The changes in mean and peak gradients are illustrated in Figs. 2 and 3. The peak gradient with dobutamine increased from 39 ± 6.0 mmHg at rest to 77 ± 14 mmHg with maximum dobutamine (P < 0.001). With exercise, there was a similar and significant increase in peak gradient from a resting gradient of 39 ± 6.0 to 73 ± 10.0 mmHg (P < 0.001). Both of these increases in peak gradient were comparable, however (mean difference 3.8 mmHg, P = 0.15, z value −1.43).

The mean gradient at rest increased by 82% with dobutamine from a resting gradient of 22 ± 4.1 to 40 ± 10 mmHg (P < 0.001). With exercise, there was a 72% increase in mean gradient from 22 ± 3.1 to 38 ± 6.4 mmHg. Again, both increases were comparable (P = 0.54, z value −0.61).

It was possible to calculate the EOA for all ten patients receiving a size 19 mm St. Jude Medical prosthesis in the dobutamine arm of the study. There was no significant change in EOA with maximum dobutamine (rest 0.97 cm² versus 1.14 cm², P = 0.09; indexed EOA rest 0.58 ± 0.12 cm²/m² versus 0.68 ± 0.13 cm²/m², P = 0.10).

Fig. 1. Changes in cardiac output with dobutamine and exercise.
In the exercise group, it was not possible to detect an adequate pulse wave velocity trace adequate enough to allow planimetry in the LVOT in three patients. In the remaining seven patients, however, there was a non-significant increase in EOA with maximum exercise (0.95 cm² versus 1.18 cm², \( P = 0.07 \); indexed EOA at rest 0.57 ± 0.10 cm²/m² versus 0.70 ± 0.15 cm²/m², \( P = 0.11 \)).

4. Discussion

The St. Jude Medical mechanical valve has been in clinical use for more than 20 years showing good haemodynamic performance and satisfactory long-term durability in the aortic position [12]. The haemodynamic properties of small aortic valve, however, have been questioned particularly when implanted in a patient with a large body surface area because of residual high transvalvular gradient. It has thus been suggested that small size prosthesis should be avoided because unfavourable gradients may result thus placing persistently high demands on the left ventricle and hindering or delaying the regression of left ventricular hypertrophy [13].

Occasionally one may encounter patients who continue to remain symptomatic following aortic valve replacement and exercise echocardiography has been proposed as a means of unmasking sub-optimal valvular function. Exercise, however, requires a considerable degree of patient co-operation and qualitatively adequate Doppler signals are difficult to obtain because of the exercise and wall motion related artefacts. We have recently reported the utility of dobutamine echocardiography in the assessment of a number of small size aortic prosthesis [5–8]. With this approach, changes in transprosthetic gradients can be continuously documented while CO is manipulated by increasing doses of dobutamine. While the physiological alterations induced by dobutamine and exercise are probably dissimilar, the net effect of a change in flow across the valve orifice with a resultant change in gradients are comparable [14].

While dobutamine and exercise echocardiography are used interchangeably in the investigations of persistent symptoms following aortic valve replacement, these two investigations have not been compared in this surgical group of patients. Accordingly 10 patients who had a size 19 mm St. Jude mechanical aortic prosthesis were chosen and studied.

Both dobutamine and exercise resulted in a similar and comparable increase in HR. In the study by Zabolgoitia et al. [14], the increase in HR observed was much greater as dobutamine was used in doses of up to 40 μg/kg/min. It is unlikely that such HRs are ever achieved in this elderly subgroup of patients. One advantage of such high doses, however, is the observance of systolic anterior motion of the mitral valve and the assessment of regional wall motion.
abnormality, which may alert the clinician to other mechanisms resulting in persistence of symptoms or delaying symptomatic recovery.

The change in blood pressure observed with dobutamine and exercise were quite contrasting. Dobutamine resulted in a significant decrease in mean blood pressure through changes in peripheral vascular resistance. It has been suggested that such changes in peripheral vascular resistance may affect valve function independently in ways that are not fully understood [15]. Exercise resulted in a marked increase in both systolic and mean blood pressure through mechanisms, which are quite complex but thought to involve a massive sympathetic discharge. The difference in blood pressure observed between the two stress modalities may also be exaggerated by the somewhat higher and lower baseline value, respectively, prior to the dobutamine and exercise protocol. It should be stressed that dobutamine at a dose of 20 μg/kg/min in this study is comparable to a symptom limited treadmill exercise as both these techniques achieve similar increases in CO. A higher dose of dobutamine only results in a greater degree of tachycardia without a significant increase in CO [14] and is unlikely to mimic the physiological state of exercise.

It is of interest to note that changes in mean gradient, peak gradient and EOA are quite similar with both dobutamine and exercise. It should be noted, however, that the patients were mainly in NYHA Class I (eight out of 10) with good left ventricular function. The response of patients with impaired left ventricle, prosthetic valve stenosis or pathologic regurgitation to either dobutamine or exercise echocardiography requires further investigation.

In this comparative study, there was a delay of approximately 12 months between the two methods of stress testing. It may well be argued that during this time, favourable ventricular remodelling as a result of sustained relief of outflow obstruction may have occurred thus hindering a true comparison between the methods as suggested. While this is possible, it should be noted that with near normalisation of systolic load following valve replacement, there is a rapid rate of reduction in myocyte hypertrophy and left ventricular (LV) mass (~35%) within a few weeks [16]. In addition, while ventricular remodelling can persist for up to 10 years following aortic valve replacement, after an intermediate period of 1.6 years, the rate of regression of LV mass is very much decreased [17]. Thus, in the time frame during which our study was conducted (15.6 ± 6.3 and 27.3 ± 7.3 months post-operatively), it is unlikely that the delay may have significantly influenced the results of the comparison. This is borne out by our comparison of interventricular septal and posterior left ventricular wall thickness measured in the parasternal long axis view. In all patients at both time intervals, these measurements were less than 11 mm and in addition, there was no difference between these measurements as a result of the exercise study being conducted 11.7 months after the dobutamine protocol. Furthermore, the exercise protocol was undertaken only when patients had recovered from surgery and were confident enough to undertake this, which was usually later than the dobutamine protocol.

5. Study limitations

One of the major limitations of continuous-wave Doppler assessment of pressure gradients is its overestimation, which is invariably observed in bi-leaflet prosthesis as a result of downstream pressure recovery. Since the rest and stress (dobutamine and exercise) echocardiographic assessment of the prosthesis are both subject to the same limitation, the ensuing intraindividual comparison that follows is statistically valid.

6. Conclusion

While there is yet no ideal Doppler echocardiographic stress test for patients with prosthetic valves, exercise testing seems to be the most physiological approach. Occasionally, however, we encounter the patient who is either unwilling or unable to conduct an exercise protocol and dobutamine echocardiography may be a useful alternative yielding results similar to those obtained with exercise.

References


