ORIGINAL ARTICLE

Accelerated dobutamine stress testing: Feasibility and safety in patients with moderate aortic stenosis

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KEYWORDS
Dobutamine stress echocardiography; Moderate aortic stenosis; Accelerated protocol; Safety

Abstract Objective: A continuous infusion of a single high dose of dobutamine was suggested as a simple protocol of dobutamine stress echocardiography (DSE). The present study explores the feasibility and safety of an accelerated DSE protocol in patients with calcific moderate valvular aortic stenosis undergoing DSE for evaluation of suspected coronary artery disease.

Methods: Eligible patients (n = 100) were prospectively enrolled. They were randomly assigned to undergo either the accelerated (group A, 50 patients) or the conventional protocol (group B, 50 patients). Group A received a continuous infusion of 40 µg/kg/min ± 1–2 mg atropine. Patients were monitored for adverse drug effects. Test duration was recorded. Patients with positive stress results underwent coronary angiography (CA).

Results: Mean age of the study cohort was 62.29 ± 9.8 years, 62 (62%) being males. Mean pressure gradient across the aortic valve was recorded (group A: 32.2 mmHg and group B: 31.16 mmHg, P < 0.05). Group B showed a longer mean test duration (17.9 ± 2.3 vs. 8.9 ± 1.9 min, P < 0.001) and higher mean weight-adjusted cumulative dobutamine dose (385 ± 115 vs. 350 ± 110.24 µg/kg, P < 0.05). The two groups received a similar total dose of atropine. Group A patients showed significantly lower incidence of extra-systoles, non-sustained ventricular tachycardia and severe hypotension (P < 0.05). CA results yielded almost similar diagnostic outcomes in both groups.

Conclusion: In patients with calcific moderate aortic stenosis undergoing DSE; adopting the described accelerated protocol is associated with shorter test duration, lower weight-adjusted cumulative dobutamine dose for target heart rate achievement and fewer adverse effects, while maintaining a comparable diagnostic value.

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1. Introduction

Dobutamine stress echocardiography (DSE) is widely used for the diagnosis of coronary artery disease (CAD). Data regarding the diagnosis of CAD in patients with moderately elevated maximal gradient across the stenosed aortic valve (AV) are limited. However, the diagnostic value of DSE for the diagnosis of CAD in patients with stenosed AV is high.\(^1\) Safety of
DSE for ischemia detection has been extensively evaluated. The most frequent side effects are hypotension and arrhythmia. Currently, in patients with suspected or known CAD, most laboratories use stepwise increments of dobutamine at three-minute intervals, which had evolved from the commonly used exercise treadmill protocols. However, steady-state dobutamine levels during dobutamine infusion are not obtained for up to ten minutes. Consequently, the full effect of any infusion rate of dobutamine is not obtained before the dobutamine dose had advanced to the next level and plasma dobutamine concentrations increase rapidly and nonlinearly during the test. Shortening the time of infusion of dobutamine would increase the feasibility and the cost effectiveness of DSE. Therefore, a continuous infusion of a single high dose of dobutamine has been suggested as a simple and effective protocol of DSE. It is worth mentioning that an “accelerated” diprydilinfusion protocol had been already used and validated in a large study.

The current study prospectively sought to explore the feasibility and safety of infusion of a fixed high dose of dobutamine i.e. accelerated DSE protocol in achieving the target heart rate compared to the conventional DSE protocol, in a series of patients suffering from calcific moderate valvular aortic stenosis, being evaluated for suspected CAD.

2. Materials and methods

2.1. Study design and data collection

A total number of 100 consecutive patients suffering from calcific moderate valvular aortic stenosis were prospectively enrolled in the present study. They were referred to the stress echocardiography lab in the Cardiology department of Ain Shams University (Cairo, Egypt) in the period between February 2011 and August 2013. Patients were considered eligible for inclusion if they exhibit normal resting left ventricle ejection fraction (LVEF%) and suffer from symptoms suggestive of myocardial ischemia, requiring evaluation by DSE. Exclusion criteria included; prior history of unstable angina or myocardial infarction (MI), previous percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) surgery, other etiologies of aortic stenosis or significant aortic regurgitation, presence of other significant valvular disease, congenital heart disease or any myocardial disease apart from ischemia. Also, patients with contraindications to dobutamine infusion (for example; with a history of complex ventricular arrhythmias or uncontrolled hypertension with blood pressure > 180/110 mmHg), with contraindications to atropine intake (for example; with a history of narrow-angle glaucoma or obstructive uropathy) and patients with limited life expectancy due to coexistent disease (for example; malignancy), were excluded. After enrollment, patients were randomly assigned in 1:1 fashion to undergo either; accelerated DSE protocol (group A) or conventional DSE protocol (group B) according to a computer-generated random series of numbers. Randomization was performed by block randomization (blocks of 10 patients). All included patients were subjected to detailed history taking including drug-intake, continuous electrocardiogram (ECG) monitoring, in addition to baseline transthoracic echocardiogram (TTE) assessment before stress testing. All included patients stopped beta blocker and calcium antagonist therapies 48 h before stress testing, while nitrate therapy was stopped 24 h before it. Before inclusion, informed written consent was obtained from each patient and the study protocol was reviewed and approved by our local institutional human research committee; as it conforms to the ethical guidelines of the 1975 Declaration of Helsinki, as revised in 2008.

2.2. Definition of risk factors of coronary artery disease

The presence of hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg, previously recorded by repeated non-invasive office measurements, which led to life-style modification and/or intake of antihypertensive drug therapy. The presence of diabetes mellitus was defined as fasting plasma glucose ≥ 126 mg/dl and/orput 2 h post-glucose load ≥ 200 mg/dl, or specific anti-diabetic drug therapy intake. Dyslipidemia was defined as LDL cholesterol > 100 mg/dl, and/or serum triglycerides > 150 mg/dl, and/or HDL cholesterol < 40 mg/dl (< 50 mg/dl in women).

2.3. Baseline echocardiographic assessment

Assessment of regional and global LV systolic functions was performed in all patients by TTE using a General Electric Vivid 7 cardiac ultrasound machine (General Electric, Horten, Norway), equipped with harmonic imaging capabilities. A 2.5 MHz phased array probe was used to obtain standard 2D, M-mode and Doppler images. Patients were examined in the left lateral recumbent position using standard parasternal and apical views. Images were digitized in cine-loop format, and saved for subsequent playback and analysis. Views were analyzed by a single echocardiographer blinded to the study protocol, employing the software program of the echocardiography machine. All patients suffered from calcific moderate valvular aortic stenosis defined echocardiographically by having aortic valve area of 1–1.5 cm² (measured using continuity equation) and recorded mean pressure gradient (PG) of 25–40 mmHg (across the valve). Regional wall motion was assessed according to the standard 17-segment model as recommended by the American Society of Echocardiography. That was achieved through visual assessment for each segment individually, considering both endocardial excursion and systolic thickening. Each segment was graded according to the semi-quantitative scoring system described by Knudsen et al. Segments with poorly-defined endocardial borders for 50% or more of their length were considered non-visualized and assigned a score of 0. Wall thickening was assessed at a distance of at least 1 cm from the adjacent segment, to minimize the effect of tethering.

2.4. Dobutamine stress echocardiography protocols

Once eligible, patients were randomly assigned to undergo one of the following two DSE protocols:

2.4.1. Accelerated DSE protocol (group A, 50 patients)

Dobutamine (Dobutamine MYLAN®, MYLAN S.A.S, France) was administered by intravenous (IV) infusion using a high fixed dose from the start (40 μg/kg/min). Infusion duration was assigned to be 10 min. In patients not achieving
85% of age predicted maximum heart rate (APMHR), a dose of 1.0 mg of IV atropine was administered, followed by another similar dose after 1 min, if needed. Test was terminated upon reaching any of the test end-points.

2.4.2. Conventional DSE protocol (group B, 50 patients)

Dobutamine was administered by IV infusion starting at a dose of 5 μg/kg/min and raised incrementally every three minutes up to a maximum of 40 μg/kg/min or until a study end-point was reached. In patients not achieving 85% of their APMHR at the end of the final stage, IV atropine was administered in 0.25–0.5 mg increments at one-minute intervals up to a maximum dose of 2.0 mg, while dobutamine infusion was continued.

2.5. Test termination end-points

End-points for terminating the test included: attainment of the maximum dose of dobutamine and/or atropine; achievement of target heart rate (>85% of APMHR); echocardiographic detection of wall motion abnormality not present at baseline or worsening of previously existing wall motion abnormality; symptoms judged to be unacceptable by the attending cardiologist; serious arrhythmia detected by ECG monitoring, ST segment elevation >0.1 mV at 80 ms from the J point, systolic blood pressure >200 mmHg or diastolic blood pressure >110 mmHg or a decrease in systolic blood pressure >30 mmHg from the baseline.23 Standard views were recorded at the baseline, at the end of each stage of dobutamine infusion, as well as during recovery. Visual assessment of wall motion and systolic thickening was performed as mentioned before. The test was considered positive upon detecting wall motion abnormality not present at the baseline, or worsening of previously existing wall motion abnormality in two contiguous LV segments belonging to the same blood supply territory.

2.6. Patients’ monitoring

All patients had continuous heart rate, ECG and pulse oximetry monitoring. All patients were subjected to heart rate, non-invasive blood pressure and 12-lead ECG recordings at baseline, every three minutes and during recovery. Patients were asked at the end of the test regarding any symptoms or adverse drug reactions. Test duration was recorded from the onset of dobutamine infusion, till the end of the recovery period. The point of time or the dose of dobutamine infusion at which the test was terminated was recorded for each patient in group A and group B, respectively. Moreover, the amount of administered IV atropine was quantified for each patient.

2.7. Coronary angiography

All patients with positive DSE test results (in both groups) underwent coronary angiography (femoral artery access using Seldinger’s technique) within 2 weeks after stress testing. Subsequently, coronary revascularization modalities were individually tailored. Coronary angiographic data were interpreted by an independent interventionalist, blinded to the results of DSE test. Number of patients showing significant coronary stenosis (epicardial vessels of at least 2.5 mm diameter showing ≥70% diameter reduction) was recorded in both groups in order to detect the positive predictive value (PPV) of each test protocol.

2.8. Statistics

All continuous variables were statistically described in terms of mean ± standard deviation (±SD). Categorical variables were described with absolute and relative (percentage) frequencies. Comparison of continuous variables between the study groups was done using Student t-test. For comparing categorical data, Pearson Chi square and Fisher exact tests were performed. P values were used to describe significance. All statistical calculations were done using Statistical Package for Social Sciences (SPSS for Windows) software (version 15.0, SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Baseline clinical characteristics

A total of 100 consecutive patients suffering from calcific moderate valvular aortic stenosis were prospectively enrolled in the current study, which comprises 50 patients randomly assigned to undergo the accelerated DSE protocol (group A), and 50 others randomly assigned to undergo the conventional DSE protocol (group B). The mean age of the whole study cohort was 62.29 ± 9.8 years, 62 (62%) being male patients. The two groups were matched regarding age, gender, risk factors of CAD and resting LV EF%. Table 1 shows baseline clinical characteristics of the two study groups. No statistically significant difference was recorded between both groups concerning aortic valve area and mean PG across AV both at rest and at peak stress. Moreover, there was no recorded significant rise in mean PG across AV in both groups. These data are shown in Table 2.

3.2. Test protocol data

Patients belonging to group B had longer mean test duration (17.9 ± 2.3 min vs. 8.9 ± 1.9 min, P < 0.001). All patients achieved their target heart rate. Accelerated dobutamine infusion offered a rapid increase in heart rate (13.7 ± 5.2 vs. 6.3 ± 2.3 beats/min, P < 0.001). Regarding group B, five (10%) patients achieved it at a dobutamine infusion rate of 30 μg/kg/min, while the remaining 45 (90%) patients achieved it at a dobutamine infusion rate of 40 μg/kg/min ± IV atropine. Meanwhile, in group A, 40 (80%) patients achieved their target heart rate before the end of the assigned duration (ten minutes) of dobutamine fixed dose infusion (40 μg/kg/min), 7 (14%) patients achieved it after receiving 1.0 mg of IV atropine and 3 (6%) patients achieved it after receiving 2.0 mg of IV atropine. The mean weight-adjusted cumulative dose of dobutamine used was recorded to be 350 ± 110.24 μg/kg among group A patients, while it was recorded to be 385 ± 115 μg/kg among group B (P < 0.05). No significant difference was seen between both groups regarding mean IV atropine dose administered. Analysis of intra-observer variability revealed a close correlation between repeated measurements of regional wall motion by the single operator, with a correlation coefficient r = 0.94.
3.3. Hemodynamic data during test protocols

Table 3 shows hemodynamic data recorded at rest and peak stress (point of time at which the test was terminated due to reaching any of the test end-points). No significant difference was recorded regarding mean heart rate, systolic and diastolic blood pressure at baseline and at peak stress upon comparing both groups.

3.4. Safety of DSE protocols

The conventional DSE protocol revealed positive results for coronary ischemia in 43 (86%) patients and negative results in seven (14%) patients. The accelerated DSE protocol showed positive results in 44 (88%) patients and negative results in six (12%) patients. Reported complications from the two DSE test protocols are summarized in Table 4. Mild hypotension was defined by a drop in systolic and/or diastolic blood pressure by ≤20 mmHg, while severe hypotension was defined by a drop in systolic and/or diastolic blood pressure by >20 mmHg. Hypertension was defined by an increase in systolic and/or diastolic blood pressure by >20 mmHg. Patients belonging to group B showed a statistically significant higher incidence of ventricular extra-systoles, atrial extra-systoles, non-sustained ventricular tachycardia, nausea, headache and severe hypotension (P < 0.05). The same group of patients showed higher incidence of atrial fibrillation (Af), supraventricular tachycardia (SVT), symptomatic bradycardia, chest pain and hypertension, yet did not reach statistical significance. There were no recorded cases of sustained ventricular tachycardia, ventricular fibrillation, syncope or death in both groups, during or immediately after the test.

Table 1 Baseline characteristics of the two study groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (No. = 50)</th>
<th>Group B (No. = 50)</th>
<th>*P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>63.4 ± 9.4</td>
<td>61.18 ± 10.2</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Males</td>
<td>30 (60)</td>
<td>32 (64)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>27 (54)</td>
<td>25 (50)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29 (58)</td>
<td>30 (60)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>18 (36)</td>
<td>16 (32)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Smoking</td>
<td>14 (28)</td>
<td>12 (24)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>7 (14)</td>
<td>8 (16)</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

Table 2 Echocardiographic data of the two study groups at rest and at peak stress.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (No. = 50)</th>
<th>Group B (No. = 50)</th>
<th>*P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>55.5 ± 3.4</td>
<td>57 ± 3.2</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean PG across AV (mmHg)</td>
<td>32.2 ± 2.5</td>
<td>31.16 ± 3.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>AV area (cm²)</td>
<td>1.33 ± 0.14</td>
<td>1.34 ± 0.12</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>50.3 ± 4.6</td>
<td>51.4 ± 5.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean PG across AV (mmHg)</td>
<td>31.6 ± 3.3</td>
<td>31.2 ± 4.3</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>AV area (cm²)</td>
<td>1.33 ± 0.16</td>
<td>1.34 ± 0.13</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>At peak stress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV EF (%)</td>
<td>50.3 ± 4.6</td>
<td>51.4 ± 5.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Mean PG across AV (mmHg)</td>
<td>31.6 ± 3.3</td>
<td>31.2 ± 4.3</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>AV area (cm²)</td>
<td>1.33 ± 0.16</td>
<td>1.34 ± 0.13</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

Table 3 Hemodynamic data of the two study groups at rest and at peak stress.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (No. = 50)</th>
<th>Group B (No. = 50)</th>
<th>*P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>127.4 ± 5.2</td>
<td>126 ± 6</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>78.3 ± 5.3</td>
<td>77.4 ± 6.7</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>75.3 ± 4.3</td>
<td>78.36 ± 5.8</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>At peak stress</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>150 ± 8.4</td>
<td>153.4 ± 9.2</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>95.4 ± 6.4</td>
<td>97.5 ± 8.9</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>140 ± 7.2</td>
<td>139.18 ± 8.3</td>
<td>&gt; 0.05</td>
</tr>
</tbody>
</table>

BP: blood pressure, bpm: beat per minute.
All variables are presented as mean ± SD.
P value > 0.05 = non-significant.
* Student t-test.
Accelerated dobutamine infusion in patients with aortic stenosis

3.5. Coronary angiographic data

All patients with positive stress test results underwent coronary angiography. Regarding the conventional DSE protocol, 36 patients showed angiographically significant coronary stenosis with a PPV of 83.7%. Meanwhile, 37 patients belonging to accelerated DSE protocol group; showed significant coronary stenosis, mounting to a comparable PPV i.e. 84% (P value > 0.05).

4. Discussion

Currently, DSE is widely approved for detection of CAD, for risk stratification after MI and for prediction of peri-operative and late cardiac events in patients scheduled for major surgery. However, in addition to being time consuming, DSE had often been limited by patient intolerance; chiefly related to drug adverse effects and test duration. Furthermore, heart rate response might be inadequate in elderly patients and in patients receiving beta-blocker therapy. In this case, larger doses of dobutamine and longer test durations are needed, besides the addition of atropine to achieve the targeted heart rate. In turn, this would further increase patients’ intolerance. The author tested the hypothesis that administration of a high fixed dose of dobutamine during DSE would reduce dobutamine weight-adjusted cumulative dose and test duration, and consequently improve tolerance of patients suffering from moderate aortic stenosis, being subjected to DSE. Moreover, this protocol can be adopted yielding a final diagnostic outcome that is comparable to that obtained using the conventional protocol.

4.1. Mechanisms of drug action

At low doses (up to 10 µg/kg/min), dobutamine induces a marked inotropic effect, probably mediated by a combined beta 1 and alpha 1 adrenoreceptor stimulation, augmenting myocardial contractility without a significant increase in heart rate. At higher doses of dobutamine infusion (20–40 µg/kg/min), heart rate progressively increases through its action on beta 2 adrenoreceptors. Systemic blood pressure modestly increases as a result of an increase of the cardiac output, and a decrease of the systemic vascular resistance; the alpha 1 adrenoreceptor-mediated vasoconstricting effect is balanced by the beta 2 adrenoreceptor-mediated vasodilator effect. Consequently upon these hemodynamic changes; myocardial oxygen demand increases. Yet, in myocardial segments supplied by a coronary artery with significant stenosis, this increased demand cannot be met with a parallel increase of myocardial blood flow. Hence, regional myocardial ischemia develops, and manifests as regional wall motion abnormalities; detected by 2D echocardiography. Atropine, instead, acts as reversible competitive antagonist to acetylcholine action at muscarinic receptors in the sino-atrial node, resulting in a positive chronotropic effect. Indirectly, an inotropic effect would also be expected through the force-frequency relationship; probably mediated by increased availability of cytosolic calcium for actin–myosin interaction.

4.2. Consequences of accelerated dobutamine infusion

The current study results showed that accelerated dobutamine IV infusion significantly decreased the test duration by about 50%, yielding almost similar percentage of positive results suggesting myocardial ischemia, when compared against the conventional DSE protocol. Also, this was achieved using a lower weight-adjusted cumulative dobutamine dose, hence, yielding a similar diagnostic outcome at a lower level of myocardial ischemia. This adds to the safety profile of the accelerated protocol. This might be due to modest increase of coronary blood flow with higher doses of dobutamine infusion; balancing myocardial oxygen demand and delaying the appearance of myocardial wall motion abnormalities. It is worth mentioning that mean PG across AV was recorded to be almost similar in both groups at rest and at peak dose of dobutamine infusion with no significant rise. This is probably due to a large number of patients showing positive results suggesting myocardial ischemia. Effect of increased heart rate is balanced by

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### Table 4 Adverse outcomes among the two study groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A (No. = 50)</th>
<th>Group B (No. = 50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arrhythmias</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular extrasystoles</td>
<td>4 (8)</td>
<td>15 (30)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Atrial extrasystoles</td>
<td>4 (8)</td>
<td>10 (20)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0 (0)</td>
<td>3 (6)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Non sustained VT</td>
<td>0 (0)</td>
<td>5 (10)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sustained VT</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>VT</td>
<td>0 (0)</td>
<td>2 (4)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Vf</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Bradycardia</td>
<td>1 (2)</td>
<td>4 (8)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2 (4)</td>
<td>5 (10)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Mild hypotension</td>
<td>3 (6)</td>
<td>7 (14)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Severe hypotension</td>
<td>1 (2)</td>
<td>6 (12)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>5 (10)</td>
<td>9 (18)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Nausea</td>
<td>4 (8)</td>
<td>12 (24)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (2)</td>
<td>6 (12)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

VT: ventricular tachycardia, SVT: supraventricular tachycardia, Vf: ventricular fibrillation. All variables are presented as number (percentage).

P value > 0.05 = non-significant.

P value < 0.05 = significant.

* Pearson Chi-Square and Fisher exact tests.
weakened myocardial contraction, mounting to almost neutral effect on the mean pressure gradient across the AV.

4.3. Safety of accelerated DSE protocol

Although, an almost similar percentage of patients showed positive results for myocardial ischemia in both groups, patients undergoing the conventional DSE protocol showed a higher incidence of adverse effects including arrhythmias; pointing to the arrhythmogenic potential of higher doses of dobutamine. Interestingly, all episodes of non-sustained ventricular tachycardia were recorded in the conventional DSE group. Furthermore, they were all recorded in the recovery period. This highlights the importance of this period that requires continuous monitoring.

4.4. Comparison with other studies

Previous studies had reported the feasibility, tolerability and safety of using the accelerated DSE protocols. Burger et al. reported a significant decrease in test protocol time and weight-adjusted cumulative dobutamine dose upon adopting the use of the accelerated protocol. However, their study protocol did not include a conventional DSE arm and about 30% of the included patients did not reach their APMHR. This might be explained by lower IV atropine dose used per patient in comparison with the present study. Most of the previous studies addressing the safety issue of adopting the accelerated DSE protocol did not demonstrate a significant decline in the incidence of adverse drug effects in comparison to the conventional DSE protocol. However, the present study demonstrated it significantly. This might be due to the higher number of patients showing positive results for ischemia in the current study. Moreover, the selected population in the present study is considered to be relatively risky for adverse effects of dobutamine and it seemed that they benefited more from the accelerated protocol. To the best of the author’s knowledge, the current study presents the first original research work evaluating the feasibility and safety of using the described accelerated DSE protocol in evaluation of suspected CAD in patients with valvular aortic stenosis. Finally, the fairly high rates of positive test results in the conventional DSE group (86%) and accelerated DSE group (88%) are more or less in agreement with the sensitivity rates reported in validated articles in the literature which described a sensitivity range of 74–86%.

4.5. Clinical implications

Patients with moderate valvular aortic stenosis might suffer from a wide range of symptoms including exertional shortness of breath, angina, dizziness or even, syncope. This population of patients is much more susceptible to procedural complications of DSE protocols, primarily due to adverse drug reactions (dobutamine and atropine). The performance of DSE with a significantly lower cumulative dose of dobutamine, shorter test duration, with almost the same total dose of atropine and with an essentially lower side-effect profile, would be an appealing option. All these advantages were clearly offered by the accelerated DSE protocol, as shown in the present study. Generally speaking, owing to its time-saving advantage, the accelerated protocol could be of special importance in busy stress echocardiography labs receiving a large number of patients regularly. Hence, at least from the ‘safety’ point of view, the author hypothesizes that adopting the accelerated DSE protocol as the protocol of choice in patients with calcific moderate valvular aortic stenosis undergoing DSE for evaluation of suspected CAD, should be encouraged.

4.6. Limitations of the study

The data presented in our study only apply for patients defined by inclusion and exclusion criteria. This is a single-center study with a relatively small sample size of the cohort, a fact that makes it difficult to generalize our results to all patients with aortic stenosis, undergoing DSE. This study included patients with calcific moderate valvular aortic stenosis. Other studies are needed to evaluate patients with more severe valvular aortic stenosis of other etiologies for the same purpose. Furthermore, test duration was calculated from the onset of dobutamine infusion till the end of the recovery time, which might be difficult to demarcate in some cases. However, being subjective in nature, it is difficult to delineate precisely the end of recovery time. Another limitation is lack of quantitative methods of measuring systolic LV wall thickening. Instead, the echocardiographer adopted visual assessment only. Finally, the diagnostic accuracy of the two protocols of stress testing was compared in terms of positive predictive value only, since patients with negative stress test results did not undergo coronary angiography. Further studies comparing sensitivity, specificity and negative predictive value of both protocols are needed.

4.7. Conclusion

In patients suffering from calcific moderate valvular aortic stenosis undergoing DSE; adopting the described accelerated protocol is associated with shorter test duration, lower weight-adjusted cumulative dobutamine dose for target heart rate achievement and consequently fewer adverse effects. Furthermore, these advantages could be obtained, while maintaining a diagnostic value for CAD that is comparable to that obtained by the conventional DSE protocol.

Conflict of interest

None declared.

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References

Accelerated dobutamine infusion in patients with aortic stenosis


