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Incidence and Significance of Profound Hypotension during Dobutamine Stress Echocardiography

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Summary

Background: Mild hypotension (drops of systolic blood pressure of ≥ 20 mmHg) occurs in 14–38% of dobutamine stress echo (DSE) and carries a good prognosis for subsequent cardiac events. The incidence and significance of more profound hypotension (PH) (≥ 50mmHg) is unknown.

Hypothesis: The aim of the study was to determine the incidence of PH during DSE and its prognosis for subsequent cardiac events.

Methods: We reviewed 617 DSE performed at our institution between 1992 and 1996 and identified two DSE subgroups. The first group (PH group) consisted of all patients with PH during DSE. A second group was selected with baseline characteristics similar to the PH group but without PH during DSE (non-PH group). Follow-up was by a physician chart review and direct telephone contact. Cardiac event rates were determined for hard [myocardial infarction (MI), or cardiac death] and soft (angina, congestive heart failure, coronary angioplasty, or coronary bypass surgery) events occurring after the DSE.

Results: Of the 617 DSE performed, 16 (3%) patients developed PH (PH group) during DSE, with 13 showing no inducible ischemia. The hard and soft cardiac event rate in this 13 PH group was 46% (mean follow-up of 28.7 ± 18 months). Of the non-PH group, 32 patients had a negative DSE with a coronary event rate of 12.5%. Profound hypotension correlated with a significantly higher cardiac event rate ($p < 0.02$).

Conclusions: The incidence of PH during DSE is low (3%) and appears to predict a worse prognosis for subsequent cardiac events.

Key words: hypotension, dobutamine stress echo, incidence, prognosis

Introduction

Dobutamine stress echocardiography (DSE) has been shown to be a safe and accurate tool in the risk stratification of patients with known or suspected coronary heart disease or in the risk stratification of patients post myocardial infarction.[1–9] The presence of a vasodepressor response [defined as a drop in systolic blood pressure (SBP) of ≥ 20 mmHg occurring during the procedure] has been reported to be in the range of 14–38% and has not been shown to be a marker for the presence of significant coronary artery disease.[7] None of these studies has looked at the subset of patients who experience an exaggerated form of the vasodepressor response with falls in systolic pressures of ≥ 50 mmHg.

We reviewed this subset of patients to determine the incidence and prognosis for subsequent cardiac events.

Methods

We reviewed all DSE performed at our institution from May 1992 to December 1996. A normal response to dobutamine was defined as a progressive increase in myocardial wall motion and/or thickening with an increasing dose of dobutamine. An abnormal response (positive test) was defined as a new or worsening wall motion/thickening abnormality with an increasing dose of dobutamine. A nondiagnostic test was defined as failure to obtain adequate images or failure to reach 85% of predicted maximal heart rate (PMHR). Negative tests were defined as those having no new or worsening wall motion/thickening abnormality following either a normal resting echo or an abnormal segmental resting echo. Profound hypotension was defined as a drop of 50 mmHg in SBP from the peak blood pressure recorded during the infusion protocol.

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Patient Population

Patients were referred for DSE based on a physicians evaluation and assessment of their medical problem. Most were referred to evaluate chest pain or for preoperative assessment of cardiac risk.

Dobutamine Stress Echocardiography

Echocardiographic images were obtained using a Hewlett-Packard (HP) 2500 echo machine with digital acquisition and storage of 16 sequential images (Tomtec). Patients were examined transthoracically in the left lateral decubitus position by an experienced echocardiographer and had fasted prior to the examination. Dobutamine infusion was started at 5 μg/kg/min and increased by 5 μg/kg/min increments at 2-min intervals to a minimum of 30 μg/kg/min and a maximum of 55 μg/kg/min or until the patient's heart rate reached 85% of PMHR. During 1993, the maximum dose of dobutamine was set at 40 μg/kg/min. Atropine sulfate was used to increase heart rate further if the 85% PMHR had not been reached using dobutamine alone. Continuous three-lead electrocardiographic (ECG) recordings were maintained and 12-lead ECGs were performed every min during the examination. Blood pressure was monitored at 2-min intervals using a Dynamap blood pressure measuring cuff. If and when hypotension developed, blood pressure was confirmed by manual measurement.

Echocardiographic images were obtained continuously during the test and were recorded on S-VHS video. Echocardiographic images were recorded at baseline, 20 μg/kg/min, peak dose, and recovery. Separate images were stored for the parasternal long and short axes as well as two- and four-chamber apical views. Following the procedure, images were displayed using a quad screen with simultaneous display of images. The test was stopped if the patient reached 30 μg/kg/min of dobutamine and 85% of the PMHR, if new wall motion/thickening abnormalities occurred, if significant side effects developed (including dizziness or altered consciousness felt secondary to hypotension), or if ECG demonstrated new or significant ST-segment elevation or the appearance of an arrhythmia.

Immediately after DSE, the echocardiographic images were reviewed by two experienced cardiologists.

Follow-Up

Follow-up consisted of a detailed questionnaire compiled by a physician chart review (100% follow-up) and direct telephone contact with the patients. If no direct telephone contact could be made, then the last date that the patient was seen in the cardiology clinic was used as the follow-up date. Cardiac events were defined as either hard or soft. Hard cardiac events were defined as MI or death attributable to a cardiac cause. Diagnosis of an MI was based on a typical history, characteristic ECG changes, and two sequential serum creatine kinase (MB fractions) of twice normal. Cardiac death was defined as death occurring within 24 h of a known cardiac event where no other obvious cause could be determined. Soft cardiac events were defined as emergency room visits/hospitalizations for angina/chest pain or congestive heart failure and coronary artery revascularization with either bypass surgery or angioplasty. The questionnaire also assessed patient risk factors. Patients were defined as having hypertension if they were taking antihypertensive medication or had been diagnosed as having hypertension by a physician. The patient was defined as having insulin-dependent and noninsulin-dependent diabetes mellitus if the patient was taking insulin or oral hypoglycemic agents. Hyperlipidemia was established if a patient had a fasting total cholesterol above 200 mg/dl or was taking cholesterol-lowering agents. A positive family history was defined as being a factor if a first-degree relative had documented coronary artery disease under the age of 60 years. Patients were considered smokers if they were currently smokers or had been in the 6 months prior to DSE. All results of patient characteristics and DSE data were logged into a computer database (Microsoft Windows 95, Access).

Statistical Analysis

Age and risk factor profiles were analyzed using the Student's *t*-test. The categorical demographic and cardiac variables were analyzed using Fisher's exact test, as were post-DSE events. Statistical significance was taken as a p value of < 0.05.

Results

In the time period evaluated, 617 patients were referred for DSE, of whom 16 (2.6%) had profound hypotension. The mean SBP reduction was 62 ± 17 (range 50–96). The average dobutamine dose was 41 ± 6 μg/kg/min. The non-PH group was selected to have a similar risk factor profile (and, as far as possible, baseline characteristics) to the PH group. It was taken from the total non-PH group (200 patients) and did not differ significantly in event rates from the larger group over the follow-up time.

Using the methods outlined, follow-up was obtained in 100% of DSEs performed with a mean follow-up time of 28.7 ± 18 months in the PH group and 36.9 ± 18 months in the non-PH group ($p = 0.16$).

Patient characteristics are shown in Table I. The PH group consisted of 8 men and 8 women with a mean age of 64 ± 9 years and an average risk factor profile of 3.1 ± 1.2 risk factors, and the non-PH group of 14 men and 18 women with a mean age of 57 ± 12.1 ($p = 0.04$) and a risk factor profile of 3.0 ± 1.1 [p = not significant (NS)]. Apart from age, which was significantly higher in the PH group, there were no significant differences in patient characteristics between the two groups.

Dobutamine Echo Results

PH group: Three patients had echocardiographic criteria positive for ischemia, and of these one had a subsequent cardiac event (bypass surgery).

TABLE I Patient demographics for PH and non-PH groups

Patient demographics	PH group n = 16 (%)	Non-PH group n = 32 (%)	p Value
Male	8 (50)	14 (43.4)	NS
Hypertension	6 (37.5)	21 (65.6)	NS
IDDM	1 (6.3)	4 (12.5)	NS
NIDDM	4 (25)	9 (28.1)	NS
Smoking	7 (43.8)	11 (34.4)	NS
Family history	6 (37.5)	7 (21.9)	NS
Prior MI	6 (37.5)	4 (12.5)	NS
Prior CABG	2 (12.5)	1 (3.1)	NS
Prior PTCA	0 (0)	2 (6.2)	NS
Prior angina	9 (56.3)	13 (40.6)	NS
Prior CHF	1 (6.3)	1 (3.1)	NS

Abbreviations: PH = profound hypotension, IDDM = insulin-dependent diabetes mellitus, NIDDM = non-insulin-dependent diabetes mellitus, MI = myocardial infarction, CABG = coronary artery bypass grafting, PTCA = percutaneous transluminal coronary angioplasty, CHF = congestive heart failure, NS = not significant.

Of the 13 patients whose tests were negative for inducible ischemia, there were seven subsequent events. There were two perioperative myocardial infarctions within 6 months of DSE, three patients were admitted with typical angina pain, one was admitted with congestive heart failure, and one had coronary bypass surgery. Of the three patients admitted with angina, two were found to have triple-vessel coronary artery disease (one had bypass surgery during the follow-up period and the other was awaiting bypass surgery), while the third had a normal persantine thallium study. The seven events occurred in a subset of patients with a mean risk factor profile of 3.6, mean age of 59 years, but with an 80% prevalence of prior myocardial infarction. Non-PH group: All patients in this group had negative DSE results. There were four cardiac events in the non-PH group, two patients being admitted with angina and two with congestive heart failure (Table II).

All patients in the PH group had cavity obliteration on DSE compared with none in the non-PH group ($p < 0.05$). Comparison of cardiac event rates of the 13 negative DSE in the PH group with the 32 negative DSE in the non-PH group was performed using Fisher's exact test. It showed that the presence of PH in a negative DSE is associated with a statistically significant increase in the incidence of subsequent cardiac events ($p < 0.02$).

TABLE II Cardiac events occurring in the PH versus non-PH group

Cardiac events	PH group		Non-PH group (n = 32)
	Positive DSE (n = 3)	Negative DSE (n = 13)	
Myocardial infarction	0	2	0
Coronary bypass surgery	1	1	0
Angioplasty	0	0	0
Angina	0	3	2
Congestive heart failure	0	1	2

Abbreviation: PH = profound hypotension.

Discussion

The occurrence of hypotension during exercise stress testing has been shown to be associated with the presence of significant coronary artery disease and subsequent coronary events.[9] Several authors have investigated the same phenomenon during DSE testing with the conclusion that hypotension does not carry a poor prognosis for subsequent cardiac events in this setting.[7, 8] The various studies looking at the vasodepressor response during DSE have differed in their definitions as to what constitutes a vasodepressor response. Their definitions have been a drop in SBP in the range of 10–20 mmHg occurring during the test. The incidence of this response has ranged from 14–38%.[7, 8] Our definition of a drop of ≥ 50 mmHg represents, to our knowledge, a much larger drop in SBP than was considered in any of the studies published to date. We found a very high incidence of subsequent hard and soft coronary events occurring after a large drop in SBP, despite the DSE demonstrating no new or worsening wall motion/thickening abnormalities.

There are several possible explanations for the increased event rate we observed. First, the high event rates following negative DSE may be related to the presence of "physiologically" silent lesions that gradually progressed over the time course of our study. The hard events that occurred in our PH group were in the first 6 months, which makes progression of a silent lesion unlikely. Certainly the patients in our study who developed hypotension during the DSE constituted a high-risk group by traditional risk factor analysis. Nevertheless, they still had a significantly higher incidence of coronary events when compared with patients in the non-PH group. A second possible explanation is the finding by Marshall *et al.* that cavity obliteration occurring during DSE may actually mask wall motion abnormalities.[10] Their study involved comparison of DSE with cavity obliteration and thallium perfusion imaging. Since cavity obliteration was almost universally present in our PH population, it raises the possibility that the cavity obliteration was masking wall motion abnormalities that would otherwise have been detectable.

The exact mechanism of hypotension during DSE still remains unclear. Most of the available studies have postulated that hypotension is secondary to excessive activation of cardiac mechanoreceptors leading to reflex hypotension via the vasodepressor response. Activation of the vasodepressor reflex is not the only postulated mechanism for hypotension. A small study by Tanimoto *et al.*[11] looking at hypotension during DSE in patients with angiographically documented coronary artery disease postulated five mechanisms: (1) an inadequate increase in cardiac output due to impaired systolic reserve (n = 5), (2) a marked prolongation of the isovolumic relaxation time (n = 2) due to myocardial ischemia and therefore reduced

left ventricular filling, (3) a marked isolated reduction in systemic vascular resistance (n = 1), (4) a decrease in cardiac output associated with cavity obliteration and reflex bradycardia (n = 2), and (5) a combination of the above. Marcovitz *et al.*[7] and Heinle *et al.*[12] showed that hypertension (a factor related to the development of diastolic dysfunction), or a history of it, was significantly associated with a vasodepressor response. In our study, the patients with PH did not have a significantly higher incidence of hypertension than those in the non-PH group. We postulate that the universal cavity obliteration in our PH group not only activated cardiac mechanoreceptors with the development of reflex hypotension, but also caused masking of wall motion abnormalities that would otherwise have been detected. The increased incidence of cardiac events may be related to this masking effect seen with cavity obliteration.

Thus, it would appear that patients with severe hypotension during DSE constitute a higher risk group irrespective of the wall motion result of the DSE. Therefore, these patients should undergo further risk stratification irrespective of the DSE wall motion result.

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