Safety and Feasibility of Dobutamine-Atropine Stress Echocardiography for the Diagnosis of Coronary Artery Disease in Diabetic Patients Unable to Perform an Exercise Stress Test

ABDOU ELHENDY, MD, PHD
RON T. VAN DOMBURG, MSC
DON POLDERMANS, MD, PHD
JEROEN J. BAX, MD, PHD
PETER R. NIEROP, MD
MARCEL L. GELEIJNSE, MD
JOS R.T.C. ROELANDT, MD, PHD

OBJECTIVE — Dobutamine stress testing is increasingly used for the diagnosis and functional evaluation of coronary artery disease. However, little is known about the safety and feasibility of this stress modality in diabetic patients.

RESEARCH DESIGN AND METHODS — We studied the impact of diabetes on hemodynamic profile and on the safety and feasibility of dobutamine (up to 40 $\mu g \cdot kg^{-1} \cdot min^{-1}$) and atropine (up to 1 mg) stress echocardiography for the diagnosis of coronary artery disease in 1,446 consecutive patients (aged 60 ± 12 years, 962 men) with limited exercise capacity and suspected myocardial ischemia. Of these, 184 patients were known to have IDDM or NIDDM. The test was considered feasible when 85% of the maximal heart rate and/or an ischemic end point (new or worsened wall motion abnormalities, ST segment depression, or angina) was achieved.

RESULTS — No myocardial infarction or death occurred during the test. There was no significant difference between diabetic and nondiabetic patients with regard to heart rate increase during dobutamine stress echocardiography (58 ± 25 vs. 61 ± 24 beats/min), peak rate pressure product (18,400 ± 3,135 vs. 18,048 ± 4454), or the prevalence of hypotension (systolic blood pressure drop of >40 mmHg) (7 vs. 5%), ventricular tachycardia (5.4 vs. 4.5%), and supraventricular tachycardia (3 vs. 4%) during the test. Dobutamine stress echocardiography was feasible in 92% of the diabetic patients and in 90% of the nondiabetic patients. Coronary angiography was performed in 55 diabetic and 240 nondiabetic patients. Sensitivity, specificity, and accuracy of dobutamine stress echocardiography for the diagnosis of coronary artery disease in diabetic patients were 81, 85, and 82%. Those in nondiabetic patients were 74, 87, and 77%, respectively (NS).

CONCLUSIONS — Dobutamine stress echocardiography is a feasible method for the diagnosis of coronary artery disease in patients with limited exercise capacity with a comparable safety, feasibility, and accuracy in diabetic and nondiabetic patients.

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Coronary artery disease is the leading cause of death in diabetic patients (1–3). The Framingham Study showed an increased incidence of myocardial infarction, angina, and sudden death in diabetic patients, particularly in women, and the risk was independent of the usual risk factors for coronary artery disease (3). Therefore, noninvasive diagnosis of coronary artery disease in diabetic patients is important for planning a management strategy and for the selection of patients for coronary angiography and possible revascularization. Exercise stress testing is the most common stress modality used for the noninvasive evaluation of coronary artery disease. However, exercise tolerance in diabetic patients may be impaired, particularly because of the higher prevalence of peripheral vascular disease. Dobutamine-atropine stress echocardiography (DSE) is an accurate and safe alternative method that is increasingly used for evaluation of coronary artery disease in patients unable to perform an adequate exercise test (4–7). The potential advantages of this technique in diabetic patients are the ability to define the early onset of myocardial ischemia in absence of symptoms due to autonomic neuropathy (8) and the ability to localize and quantify the amount of myocardial ischemia and the extent of coronary artery disease. Despite the established safety, feasibility, and accuracy of DSE for the diagnosis of coronary artery disease (9–13), these results have not been confirmed in diabetic patients. The presence of diabetic neuropathy can potentially alter the chronotropic and the inotropic response to dobutamine, and thereby reduce the ability of the test to induce myocardial ischemia or impair the compensatory mechanisms in response to dobutamine-induced hypotension, leading to a reduced feasibility of the test (8,14). Diabetic patients with clinical or subclinical autonomic neuropathy are at

From the Thoraxcenter, University Hospital Rotterdam-Dijkzigt, Erasmus University, Rotterdam, the Netherlands.
Address correspondence to Abdou Elhendy, MD, PhD, Thoraxcenter, Ba 300, Dr Molewaterplein 40, 3015 GD Rotterdam, the Netherlands.
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Abbreviations: DSE, dobutamine-atropine stress echocardiography; OR, odds ratio.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

higher risk of ventricular arrhythmias and sudden death (15). Therefore, the safety of administration of a high dose of an arrhythmogenic drug like dobutamine should be evaluated, particularly knowing that a large number of patients subjected to this test have left-ventricular dysfunction that may provide a substrate for arrhythmias (16). We have recently shown that hypertensive patients are more likely to develop dobutamine-induced hypotension (13), and therefore, the propensity to develop hypotension in diabetic patients may also be increased because of the higher prevalence of hypertension in diabetic patients. Another confounding characteristic of diabetic patients is the occurrence of left-ventricular dysfunction in the absence of significant coronary artery disease (17), which may complicate echocardiographic interpretation of wall motion abnormalities during the test. The aim of this study is to evaluate the safety, feasibility, and hemodynamic response to dobutamine-atropine stress testing in diabetic patients with suspected myocardial ischemia who are unable to perform exercise stress testing.

RESEARCH DESIGN AND METHODS

Patient population

The study population comprised 1,446 consecutive patients with limited exercise capacity who had been referred to our imaging laboratory for evaluation of myocardial ischemia by DSE. Of these patients, 184 had an established diagnosis of diabetes according to World Health Organization criteria (18) (group 1). There were 40 patients with IDDM and 144 patients with NIDDM. Group 2 comprised 1,262 nondiabetic patients. Contraindications for DSE were severe heart failure, significant valvular heart disease, severe hypertension (blood pressure $\geq$180/110), hypotension (blood pressure $<$90/60), and unstable chest pain. Mean age was 60 ± 12 years (962 men). All patients gave a verbal informed consent to undergo the study. The Hospital's ethical committee approved the use of DSE for evaluation of patients with known or suspected coronary artery disease.

Dobutamine stress test

Dobutamine was infused through an antecubital vein starting at a dose of 5 μg · kg^{-1} · min^{-1} followed by 10 μg · kg^{-1} · min^{-1} (3-min stages), increasing by 10 μg · kg^{-1} · min^{-1} every 3 min to a maximum of 40 μg · kg^{-1} · min^{-1}. Atropine (up to 1 mg) was given to patients not achieving 85% of age-predicted maximal heart rate, and dobutamine infusion was continued (19). The electrocardiogram was monitored throughout dobutamine infusion and recorded each minute. Cuff blood pressure was measured at rest, every 3 min during stress, and at maximal stress. The test was interrupted if severe chest pain, ST-segment depression $>$2 mm, significant ventricular or supraventricular arrhythmia, hypertension (blood pressure $\geq$240/120), systolic blood pressure fall $>$40 mmHg, or any intolerable side effect regarded as being due to dobutamine occurred during the test. Metoprolol (1–5 mg) was available and was used intravenously to reverse the effects of dobutamine if they did not revert quickly. The test was considered feasible if the patient could achieve 85% of the maximal heart rate predicted for age and/or when an ischemic end point (angina, ST-segment depression, new or worsened wall motion abnormalities) was reached.

Stress echocardiography

Echocardiographic images were acquired at rest and during stress and recovery. The echocardiograms were recorded on video tapes and were also digitized on optical disk and displayed side-by-side in quad-screen format (Vingmed-CFM 800; Vingmed Sound A/S, Horten, Norway) to facilitate the comparison of rest and stress images. The left ventricular wall was divided into 16 segments and scored using a four-point scale, where 1 = normal, 2 = hypokinesis, 3 = akinesis, and 4 = dyskinesis. Wall motion score index was derived by dividing the sum of individual scores for the 16 segments by 16 (19). The interpretation of images was performed by two experienced observers without knowledge of the patients' clinical data. In case of disagreement, a majority decision was achieved by a third observer. In our laboratory, the inter- and intraobserver agreements for DSE assessment are 92 and 94%, respectively (20). Ischemia was defined as new or worsening wall motion abnormalities. As we have previously concluded (21), ischemia was not considered when akinetic segments at rest became dyskinetic during stress without improvement at low-dose dobutamine (5–10 μg · kg^{-1} · min^{-1}).

Coronary angiography

Coronary angiography was performed within 3 months from DSE in 295 patients. Lesions were quantified as previously described (22). Significant coronary artery disease was defined as a diameter stenosis $\geq$50% in $\geq$1 major epicardial arteries. Coronary arteries were assigned to myocardial segments as previously described (7). The peri-infarction zone was defined as myocardial segments in the distribution of infarct-related artery (6).

Statistical analysis

Unless specified, data are presented as mean values ± SD. The χ^2 test was used to compare differences between proportions. The Student's *t* test was used for analysis of continuous data. Stepwise logistic regression models were fitted to identify independent predictors of hypotension. The difference in risk was expressed as an odds ratio (OR) with the corresponding 95% CI. Differences were considered significant if the null hypothesis could be rejected at the 0.05 probability level. Sensitivity, specificity, and accuracy of DSE for the diagnosis of significant coronary artery disease were derived according to standard definitions and were presented with the corresponding 95% CI.

RESULTS

Clinical characteristics

Patient characteristics, medications, and indications of stress testing in both groups are presented in Table 1. Patients of group 1 had a higher prevalence of a history of hypertension, myocardial infarction, and congestive heart failure and were receiving diuretics and angiotensin-converting enzyme inhibitors more commonly than patients of group 2. Among the 144 patients with NIDDM, 24 (17%) were not receiving antidiabetic medication, 80 (56%) were receiving oral antidiabetic drugs, and 40 (28%) were receiving insulin (in 32 patients as monotherapy and in 8 patients combined with oral antidiabetic drugs).

Symptoms and hemodynamic response

There was no death or myocardial infarction during or shortly (24 h) after the test. Systolic blood pressure and heart rate increased significantly from rest to peak stress (133 ± 25 [range 90–180] vs. 135 ± 30 [60–280] mmHg, $P < 0.00005$, and 73 ± 14 [41–130] vs. 133 ± 16 [64–212] beats/min, $P < 0.00001$), whereas diastolic blood pressure decreased significantly (76 ± 13 [45–110] vs. 71 ± 16 [35–130] mmHg, $P <$

Table 1—*Clinical features of diabetic (group 1) and nondiabetic (group 2) patients undergoing DSE*

	Group 1	Group 2	*P* value
n	184	1,262	—
Clinical features			
Age (years)	60 ± 10	60 ± 12	1
Males	118 (64)	844 (67)	0.5
Previous myocardial infarction	110 (60)	641 (49)	<0.01
History of heart failure	41 (22)	183 (15)	<0.01
History of hypertension	89 (48)	467 (37)	<0.005
Medications			
β-blockers	58 (32)	444 (35)	0.3
Calcium channel blockers	74 (40)	445 (35)	0.2
Nitrates	76 (41)	458 (36)	0.2
ACE inhibitors	84 (46)	408 (32)	<0.0005
Diuretics	60 (33)	280 (22)	<0.005
Indications for stress testing			
Typical chest pain	60 (33)	401 (32)	0.8
Atypical chest pain	46 (25)	367 (29)	0.3
Exertional dyspnea or fatigue	17 (9)	125 (10)	0.8
Assessment after myocardial infarction or revascularization	61 (33)	369 (29)	0.3

Data are means ± SD or *n* (%).

0.00005). Atropine was administered in 649 patients (45%), and the mean dose was similar in both groups (0.60 ± 0.29 vs. 0.60 ± 0.28 mg). Atropine induced a significant comparable increase of heart rate in both groups (Table 2). Heart rate, systolic and diastolic blood pressures, and rate pressure product were higher in group 1 at rest and similar for both groups at peak stress. The prevalence of symptoms and arrhythmias was similar in both groups (Table 3). There was no significant difference between the two groups with regard to percentage of patients reaching the target heart rate or the prevalence of various types of arrhythmias (Table 3). Ventricular tachycardia was terminated in all cases spontaneously by stopping dobutamine infusion or administration of metoprolol. Systolic blood pressure drops of >40 mmHg occurred in 71 patients (5%) during stress. Multivariate analysis identified baseline systolic blood pressure >140 mmHg (OR 7.2, 95% CI 3.5–16), older age (OR 1.03, 95% CI 1.02–1.09), and medication with calcium channel blockers (OR 1.8, 95% CI 1.2–3.4) as independent predictors of hypotension. Hypotension was the reason for test termination in only 30 of the 71 patients who developed hypotension. Reasons for termination of the test are shown in Table 4. The test was considered feasible (achievement of 85% of maximal heart rate and/or an ischemic end point) in 169 patients in group 1 (92%) and in 1,142 patients in group 2 (90%) ($P = 0.8$).

Stress echocardiography

Wall motion abnormalities were present at rest in 125 patients in group 1 (68%) and in 724 patients in group 2 (57%) ($P < 0.01$). Ischemia was detected in 63 patients in group 1 (34%) and in 426 patients in group 2 (34%), whereas 45 patients in group 1 (24%) and 421 patients in group 2 (33%) had normal wall motion at rest and during stress ($P < 0.05$). Wall motion score index increased from rest to stress in group 1 (1.49 ± 0.49 vs. 1.53 ± 0.25, $P < 0.001$) and in group 2 (1.37 ± 0.46 vs. 1.41 ± 0.51, $P < 0.0001$). Wall motion score index was higher in group 1 than in group 2 at rest ($P < 0.005$) and at stress ($P < 0.01$).

Accuracy of dobutamine stress echocardiography for the diagnosis of coronary artery disease

Coronary angiography was performed in 295 patients within 3 months of DSE (55 patients in group 1 and 240 patients in group 2). Significant coronary artery disease was detected in 228 patients (42 patients in group 1 and 186 patients in group 2), while 67 patients (13 patients in group 1 and 54 patients in group 2) had a normal coronary angiogram or nonsignificant lesions. Tables 5 and 6 demonstrate the accuracy of DSE in both groups for the diagnosis of significant coronary artery disease on the basis of ischemia in patients with and without previous myocardial infarction. Sensitivity, specificity, and accuracy were fairly comparable in both groups.

Table 2—*Hemodynamic data of diabetic (group 1) and nondiabetic (group 2) patients undergoing DSE*

	Group 1	Group 2	*P* value
n	184	1,262	—
Hemodynamic and stress test variables			
Heart rate at rest (beats/min)	76 ± 14	72 ± 14	<0.0001
Heart rate at peak stress (beats/min)	134 ± 17	133 ± 16	0.3
Systolic blood pressure at rest (mmHg)	137 ± 26	132 ± 22	<0.01
Systolic blood pressure at peak stress (mmHg)	137 ± 30	135 ± 29	0.6
Diastolic blood pressure at rest (mmHg)	77 ± 13	75 ± 13	0.06
Diastolic blood pressure at peak stress (mmHg)	70 ± 15	71 ± 16	0.4
Rate pressure product at rest	10,507 ± 3,135	9,521 ± 2,412	<0.00001
Rate pressure product at peak stress	18,400 ± 3,135	18,048 ± 4,454	0.3
Heart rate before atropine* (beats/min)	112 ± 23	111 ± 23	0.5
Heart rate after atropine* (beats/min)	136 ± 19	134 ± 18	0.3
Systolic blood pressure before atropine* (mmHg)	131 ± 28	131 ± 25	1
Systolic blood pressure after atropine* (mmHg)	134 ± 25	131 ± 28	0.3
Systolic blood pressure drop >20 mmHg	38 (21)	225 (18)	0.4
Systolic blood pressure drop >40 mmHg	12 (7)	59 (5)	0.3
Maximal dobutamine dose ($\mu g \cdot kg^{-1} \cdot min^{-1}$)	36.5 ± 7.2	37 ± 6.4	0.4
Atropine given	87 (47)	562 (45)	0.5
ST-segment depression	36 (20)	172 (14)	<0.05

Data are means ± SD or *n* (%). *Data are taken only from patients who received atropine.

Table 3—*Symptoms and arrhythmias in diabetic (group 1) and nondiabetic (group 2) patients during dobutamine-atropine stress echocardiography*

	Group 1	Group 2	*P* value
n	184	1,262	—
Symptoms/arrhythmias			
Nausea	7 (4)	58 (5)	0.6
Flushing	0 (0)	11 (0.9)	0.2
Dizziness	5 (3)	36 (3)	0.9
Anxiety	3 (2)	27 (2)	0.7
Chills	7 (4)	48 (4)	1
Headache	4 (2)	57 (5)	0.1
Symptomatic hypotension	1 (0.5)	17 (1)	0.4
Typical angina	48 (26)	307 (24)	0.6
Premature atrial contractions	13 (7)	90 (7)	0.9
Premature ventricular contractions	63 (34)	397 (31)	0.4
Supraventricular tachycardia	5 (3)	51 (4)	0.4
Atrial fibrillation	2 (1)	17 (1)	0.8
Ventricular tachycardia <10 beats	8 (4)	48 (4)	0.7
Ventricular tachycardia ≥10 beats	2 (1)	9 (0.07)	0.6

Data are *n* (%).

CONCLUSIONS — To our knowledge, this is the first study to evaluate the impact of diabetes on the safety, feasibility, and diagnostic accuracy of DSE in a large series of patients. Our study demonstrates that DSE is a feasible and safe method for evaluation of coronary artery disease in diabetic patients with suspected myocardial ischemia and limited exercise capacity. No myocardial infarction or death occurred during the test. Despite the fact that diabetic patients had more severe left-ventricular dysfunction at rest, the feasibility and safety profile were similar in diabetic and nondiabetic patients. Ventricular tachycardia was terminated in all cases spontaneously by stopping dobutamine infusion or administration of metoprolol. Minor side effects, including chills, dizziness, flushing, headache, nausea, and anxiety, were common and occurred in 18% of the entire population. However, these symptoms were usually well tolerated and were the reason for termination of the test in a minority of patients (0.07%). The prevalence of these side effects was similar in diabetic and nondiabetic patients.

Hemodynamic response of diabetic patients to dobutamine

Heart rate increased significantly and equally in patients with and without diabetes, and there was no significant difference between the two groups with regard to age, sex, or the maximal dobutamine dose. This implies that the chronotropic response to high-dose dobutamine is not impaired in diabetic patients. Borow et al. (23) have previously reported that in normotensive young adults with diabetes and no evidence of coronary artery disease, the contractile response to low-dose dobutamine infusion ($5\ \mu g \cdot kg^{-1} \cdot min^{-1}$) was similar to that of normal subjects despite the occurrence of ejection fraction drop during exercise in 45% of diabetic patients. Despite the reported parasympathetic dysfunction in diabetic patients (16), atropine induced a similar increase of heart rate in diabetic and nondiabetic patients in our study, denoting the feasibility of the administration of this parasympatholytic agent in achieving a significant increase of heart rate in diabetic patients with inadequate chronotropic response to high-dose dobutamine. There was a modest but significant increase of systolic blood pressure in nondiabetic patients from rest to peak stress, whereas this failed to increase in diabetic patients. This may be explained by the higher baseline systolic blood pressure and the higher frequency of medication with angiotensin-converting enzyme inhibitors in diabetic patients. Both factors have been implicated in impairment of blood pressure response to dobutamine (13,24). Peak systolic blood pressure and rate pressure product were similar in patients with and without diabetes, denoting the achievement of a similar hemodynamic stress required to provoke myocardial ischemia. The prevalence of symptomatic and asymptomatic hypotension was similar in diabetic and nondiabetic patients. Independent predictors of hypotension were medication with calcium antagonists, baseline systolic blood pressure ≥140 mmHg, and older age, which are in accordance with previous studies (13).

Comparison with previous studies

Bates et al. (25) studied 53 patients with IDDM by DSE before kidney and/or pancreatic transplantation. During a follow up period of 418 ± 269 days, cardiac event rates were 54% among patients with abnormal DSE and 6% among those with normal DSE by retrospective analysis. The dobutamine stress test was terminated prematurely because of hypotension in one patient and nausea in another. The incidence of arrhythmias during the test was not reported. In our study, the prevalence of different types of arrhythmias during dobutamine stress testing was similar in diabetic and nondiabetic

Table 4—*Reasons for termination of dobutamine stress testing in diabetic (group 1) and nondiabetic (group 2) patients*

	Group 1	Group 2	*P* value
n	184	1,262	—
Reasons for test termination			
85% of maximal heart rate	148 (80)	1,028 (81)	0.7
Maximal dose	11 (6)	99 (8)	0.4
Angina	14 (7)	59 (5)	0.09
ST changes	1 (0.5)	15 (1)	0.4
Arrhythmias	5 (3)	20 (2)	0.3
Hypertension	1(0.5)	1 (0.01)	0.1
Hypotension	3 (1.7)	27 (2.1)	0.7
Dyspnea	0 (0)	3 (0.2)	0.5
Chills, flushing, anxiety, dizziness	1 (0.05)	10 (0.07)	0.7

Data are *n* (%).

Table 5—*Accuracy of ischemic pattern at dobutamine stress echocardiography for the diagnosis of significant coronary artery stenosis in diabetic (group 1) and nondiabetic (group 2) patients without previous myocardial infarction*

Diagnostic parameters	Group 1	Number of patients	Group 2	Number of patients	*P* value
Overall diagnosis (all patients)					
Sensitivity	77 (58–95)	10/13	73 (61–85)	24/33	0.8
Specificity	86 (70–101)	6/7	86 (77–95)	19/22	1
Accuracy	80 (62–98)	16/20	78 (67–89)	43/55	0.9
Sensitivity in patients with single-vessel disease	67 (41–92)	4/6	67 (52–81)	12/18	1
Sensitivity in patients with multivessel disease	86 (67–104)	6/7	80 (67–93)	12/15	0.8
Diagnosis of multivessel disease by multivessel ischemic pattern					
Sensitivity	57 (35–79)	4/7	53 (40–67)	8/15	0.9
Specificity	85 (69–100)	11/13	90 (82–98)	36/40	0.6
Accuracy	75 (56–94)	15/20	80 (69–91)	44/55	0.6

Data are % (95% CI) or *n*.

patients. The overall prevalence of supraventricular tachycardia (including atrial fibrillation) (4.8%) and ventricular tachycardia (4.8%) in our study is consistent with that reported by Mertes et al. (9) (4.1% and 4.2% respectively). Arrhythmias were the reason for termination of the test in 2% of patients in our study, which is comparable to the findings of Mertes et al. (2.1%). There was no difference between diabetic and nondiabetic patients regarding the feasibility of dobutamine stress testing. Overall feasibility (91%) is comparable to that reported by Poldermans et al. (11) (98%), Cornel et al. (10) (97%), and Picano et al. (12) (88%).

Accuracy of dobutamine stress echocardiography in diabetic and nondiabetic patients

To our knowledge, this is the first study that compares the diagnostic accuracy of DSE in diabetic and nondiabetic patients. Sensitivity, specificity, and accuracy were fairly comparable in both groups for the overall diagnosis of coronary artery disease, single-vessel disease, and multivessel disease, identification of multivessel disease on the basis of inducible ischemia in >1 vascular territory, and in the diagnosis of infarct-related and remote coronary artery stenosis. Therefore, the diagnostic accuracy of DSE was not limited in diabetic patients, despite the more severe baseline left-ventricular dysfunction. In the study by Bates et al. (25), 17 diabetic patients underwent coronary angiography. DSE had a sensitivity of 90% (9 of 10 patients) and a specificity of 86% (6 of 7 patients). However, the number of patients in that study was small, and the coronary angiogram was performed late after DSE in some patients (up to 557 days).

Limitations of the study

Diabetic and nondiabetic patients were not comparable with regards to clinical characteristics (hypertension, medications, and

Table 6—*Accuracy of ischemic pattern at dobutamine stress echocardiography for the diagnosis of significant coronary artery stenosis in diabetic (group 1) and nondiabetic (group 2) patients with previous myocardial infarction*

Diagnostic parameters	Group 1	Number of patients	Group 2	Number of patients	*P* value
Overall diagnosis (all patients)					
Sensitivity	83 (70–95)	24/29	74 (67–80)	113/153	0.3
Specificity	83 (71–96)	5/6	88 (83–92)	28/32	0.8
Accuracy	83 (70–95)	29/35	76 (70–83)	141/185	0.4
Sensitivity in patients with single-vessel disease	60 (31–89)	3/5	61 (50–71)	34/56	1
Sensitivity in patients with multivessel disease	88 (76–99)	21/24	81 (75–88)	79/97	0.5
Diagnosis of multivessel disease by multivessel ischemic pattern					
Sensitivity	50 (39–61)	12/24	49 (42–57)	48/97	1
Specificity	82 (69–95)	9/11	91 (87–95)	80/88	0.3
Accuracy	60 (44–76)	21/35	69 (62–76)	128/185	0.3
Infarct-related artery					
Sensitivity	71 (56–86)	22/31	61 (54–68)	93/152	0.3
Specificity	75 (61–89)	3/4	85 (80–90)	28/33	0.6
Accuracy	71 (56–86)	25/35	65 (58–72)	121/185	0.5
Remote coronary artery					
Sensitivity	72 (57–87)	18/25	67 (60–74)	70/104	0.7
Specificity	90(80–100)	9/10	89 (84–93)	72/81	0.9
Accuracy	77 (63–91)	27/35	77 (70–83)	142/185	1

Data are % (95% CI) or *n*.

baseline left-ventricular function). However, the safety profile was similar in diabetic and nondiabetic patients despite the more severe left ventricular dysfunction and the higher prevalence of hypertension in diabetic patients. We did not study the autonomic function in diabetic patients, and therefore, we were not able to assess the correlation between the autonomic function and safety of the test. Coronary angiography was performed only in 295 patients (20%). However, this is one of the largest studies correlating the findings at DSE with coronary angiography. Finally, the results of the test were available for the treating physicians with possible referral bias for coronary angiography, a factor that may reduce the specificity of the test by referring more patients with a positive rather than a negative test for angiography. However, specificity in nondiabetic patients is unlikely to be underestimated compared with that in diabetic patients because the latter have an established risk factor for coronary artery disease and a possibly higher rate of referral of patients with a positive test for coronary angiography.

Clinical implications and conclusions

It is concluded that DSE is a safe and feasible method for evaluation of coronary artery disease with a comparable chronotropic response, safety, feasibility, and diagnostic accuracy in diabetic and nondiabetic patients.

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