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Dobutamine stress echocardiography for assessment of myocardial viability: impact of beta-blockade on exam accuracy

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Abstract. *Background and Objectives*: The impact of β-blockers on the assessment of viability with stress echocardiography has not been defined. The purpose of this study was to assess the impact of β-blocker intake status on the accuracy of dobutamine stress echocardiography (DSE) to detect myocardial viability in patients with ischaemic left ventricular dysfunction.

Methods: A retrospective study including 25 patients who underwent myocardial revascularization after a DSE showing regional wall motion abnormalities at rest. The performance of DSE was determined by analyzing each dysfunctional segment (total of 206 segments) at rest to assess viability and recovery after revascularization.

Results: DSE predicted viability in 78 (34%) dysfunctional segments. After revascularization, 134 (60%) dysfunctional segments improved resting function. The overall sensitivity was 52% and specificity was 83%. ß-blocker intake at increasing doses significantly decreased exam sensitivity for viability assessment (no intake: 77%; low-dose: 57%; high-dose: 40%; p=.001). The effect was more marked for akinetic segments (no intake: 80%; low-dose: 50%; high-dose: 10%; p=.006).

Conclusions: β-blocker medication has a negative impact on the diagnostic performance of DSE in assessing viability in patients with ischemic left ventricular dysfunction. This effect is dose-dependent. Tab. 4, Ref. 8, on-line full text (Free, PDF) www.cardiologyletters.sk

Keywords: stress echocardiography – viability – beta-blockers

Despite convincing evidence that β-blockers decrease the sensitivity of dobutamine stress echocardiography (DSE) to detect coronary artery disease (CAD), leading to a recommendation to withdraw β-blockers before performing a diagnostic DSE test (1), no recommendation exists regarding this practice for viability studies. It has been suggested that concurrent β-blockade may alter the DSE ability to detect dysfunctional myocardium viability (2). The purpose of this study was to assess the impact of β-blocker intake status on the accuracy

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of DSE to detect myocardial viability in patients with ischaemic left ventricular (LV) dysfunction.

Methods

Retrospective study of consecutive patients undergoing revascularization after performing DSE at our centre between 2016 and 2019. Inclusion criteria were CAD causing regional wall motion abnormalities (WMA) at rest in ≥ 3 LV segments. All patients underwent revascularization followed by echocardiography ≥3 months later. Exclusion criteria were concurrent significant valve disease and cardiac resynchronization device implantation or myocardial infarction during the study period. Patients were grouped according to ß-blocker intake status at the time of DSE (per patient records): no intake (naïve or ≥3-day suspension); low-dose (bisoprolol <5mg od or carvedilol <12.5 mg bid); high-dose (bisoprolol ≥5mg od or carvedilol ≥12.5 mg bid).

All patients underwent the routine institution protocol of incremental dobutamine infusion at 3-minute intervals – 10, 20, 30 and 40 mcg/Kg/minute, followed by a 0.5 m atropine bolus if ischemia assessment was needed and the heart rate was <85% the age predicted maximum value. Imaging was acquired using a Vivid E9 ultrasound machine (GE®). LV WMA were assessed by expert visual analysis in a standard 16 LV segmentation model. Evidence of wall thickening in a previously akinetic segment, or normalization of wall thickening in a previously hypokinetic segment, were considered the criteria for viability. The same criteria were used to define recovery of segmental WMA after revascularization. DSE performance was assessed by analysing each dysfunctional segment at rest for viability and recovery. Although not all patients underwent complete revascularization, only dysfunctional segments with target coronary lesion revascularization were included in the analysis.

Continuous variables were described as median (interquartile range) due to non-Gaussian distribution. Categorical data were expressed as proportions. The sensitivity, specificity, accuracy, positive and negative predictive values of DSE for viability detection were calculated using recovery of segmental WMA after revascularization as the benchmark. The sensitivity of the DSE was calculated using the following formula: 100 x (viable segments correctly identified by DSE/total number of viable segments). Specificity was calculated using the formula: 100 x (non-viable segments correctly identified by ESD/total number of non-viable segments). Accuracy was determined by 100 x (viable and non-viable segments correctly identified in the DSE / total number of segments). The $\chi 2$ test was used for comparison between proportions. A p value <.05 was considered significant.

Results

The characteristics of the 25 included patients are summarized in **Table 1**. At the time of DSE, 4 (16%) patients were not taking ß-blocker, 10 (40%) were on low-dose and 11 (44%) were on high-dose ß-blocker. All

Table 1 Clinical characteristics of study patients

Medical History	
Hypertension	23 (92%)
Dyslipidaemia	22 (88%)
Diabetes	14 (56%)
Obesity	6 (24%)
Prior myocardial infarction	11 (44%)
Medical therapy	
β-blocker	23 (92%)
ACEi	25 (100%)
Spironolactone	8 (32%)
Statin	25 (100%)
Antiplatelet/Anticoagulant	25 (100%)
Baseline Echocardiogram	
LV Volume [ml/m^{2,} median (IQR)]	61 (39)
LVEF [%, median (IQR)]	42 (15)
Coronary arteries narrowed >50% [N, median (IQR)]	2 (1)
Revascularization	
Time to revascularization [months, median (IQR)]	3.9 (6.3)
PCI	15 (60%)
CABG	10 (40%)
Complete revascularization	16 (64%)
Echocardiography after revascularization	
Time to echocardiography [months, median (IQR)]	8.9 (6.3)
LV Volume [ml/m^{2,} median (IQR)]	57 (40)
LVEF [%, median (IQR)]	46 (16)

Data shown as N (%) except where otherwise noted. ACEi – angiotensin-converting enzyme inhibitors; CABG – coronary artery bypass graft; IQR – interquartile range; LV – left ventricle; EF – ejection fraction; PCI – percutaneous coronary intervention.

patients completed the full DSE protocol. No significant adverse events occurred. Of 400 segments analyzed, 232 (58%) had baseline WMA. Target coronary lesion revascularization was performed in 206 (89%) dysfunctional segments, which were included in the final analysis. Fifty-nine (29%) were akinetic.

DSE predicted viability in 78 (38%) dysfunctional segments, including 18 akinetic segments (31%). After revascularization, 64 (82%) segments improved contractility, including 13 previously akinetic segments. Fourteen segments that DSE predicted viability did not improve. Among 128 (62%) segments that were not predicted to be viable by DSE, 60 (47%) showed improvement after undergoing revascularization. Thus, among 206 revascularized dysfunctional segments, 124 (60%) dysfunctional and 39 (66%) akinetic segments improved resting function (**Table 2**). The overall sensitivity was 52% and specificity was 83%. Overall accuracy was 64%.

The number of viable segments with improved motion abnormalities after revascularization for each ß-blocker intake group is shown in **Table 3** [viable segments identified in DSE that improved after revascularization (n=64/124) – no intake: 10/13; low-dose: 31/54; high--dose: 23/57].

ß-blocker intake at increasing doses significantly decreased exam sensitivity for viability assessment (no intake: 77%; low-dose: 57%; high-dose: 40%; p=.001). This effect was more marked for akinetic segments (no intake: 80%; low-dose: 50%; high-dose: 10%; p=.006). The overall accuracy for detection viable dysfunctional segments was not impacted by ß-blocker intake (p=.201), but was significantly reduced for akinetic segments (no intake: 85%; low-dose: 52%; high-dose: 27%; p=.005).

There were no statistically significant differences in the specificity, sensitivity and accuracy of DSE for predicting viability according to the myocardial wall assessed – anterior, inferior, septal and lateral (**Table 4**). Moreover, there were no differences in test accuracy among the different myocardial walls assessed in each ß-blocker group.

Table 2 Diagnostic accuracy of DSE for predicting improvement of segmental wall motion abnormalities according to β-blocker intake status

	Sensivity	Specificity	PPV	NPV	Accuracy
Dysfunctional segments (n=206)	52% (64/124)	83% (68/82)	82% (64/78)	53% (68/128)	64% (132/206)
No intake (n=26)	77% (10/13)	85% (11/13)	83% (10/12)	79% (11/14)	81% (21/26)
Low-dose (n=87)	57%(31/54)	70% (23/33)	76% (31/41)	50% (23/46)	62% (54/87)
High-dose (n=93)	40% (23/57)	94% (34/36)	92% (23/25)	50% (34/68)	61% (57/93)
p value	.001	.065	.294	.224	.201
Akinetic segments (n=59)	33% (13/39)	75% (15/20)	72% (13/18)	37% (15/41)	47% (28/59)
No intake (n=13)	80% (4/5)	88% (7/8)	80% (4/5)	88% (7/8)	85% (11/13)
Low-dose (n=21)	50% (7/14)	57% (4/7)	70% (7/10)	36% (4/11)	52% (11/21)
High-dose (n=25)	10% (2/20)	80% (4/5)	67% (2/3)	18% (4/22)	27% (6/25)
p value	.006	.401	.895	.001	.005

PPV – Positive predictive value; NPV – negative predictive value

Table 3 Description of the viable and non-viable segments identified by DSE according to the β-blocker intake status

	Improved segments* (total)	Viable segments in DSE that improved with R	Non-viable segments in DSE that improved with R	Non-improved segments (total)	Non-viable segments in DSE without improvement with R	Viable segments in DSE without improvement with R
Dysfunctional segments (n=206)	124/206	64/124	60/124	82/206	68/82	14/82
No intake (n=26)	13/124	10/64	3/60	13/82	11/82	2/82
Low-dose (n=87)	54/124	31/64	23/60	33/82	23/82	10/82
High-dose (n=93)	57/124	23/64	34/60	36/82	34/82	2/82

DSE – Dobutamine stress echocardiography; R – revascularization

* total number of segments that improved after revascularization

Table 4 Description of specificity, sensitivity and accuracy according to myocardial walls

	Anterior wall	Inferior wall	Septal wall	Lateral wall	p value
Sensivity					
No intake (n=13)	33% (1/3)	100 % (2/2)	100% (5/5)	67% (2/3)	NA
Low-dose (n=54)	63% (5/8)	83% (5/6)	46% (6/13)	56% (15/27)	.485
High-dose (n=57)	43% (6/14)	50% (3/6)	53% (8/15)	27% (6/22)	.410
Overall (n=124)	48% (12/25)	71% (10/14)	58% (19/33)	44% (23/52)	.268
Specificity					
No intake (n=13)	0% (0/0)	25% (1/4)	100% (1/1)	0% (0/8)	NA
Low-dose (n=33)	17% (1/6)	33% (3/9)	11% (1/9)	56% (5/9)	.183
High-dose (n=36)	0% (0/3)	11% (1/9)	9% (1/11)	0% (0/13)	.630
Overall (n=82)	11% (1/9)	23% (5/22)	14% (3/21)	17% (5/30)	.840
Accuracy					
No intake (n=26)	33% (1/3)	83% (5/6)	83% (5/6)	91% (10/11)	.163
Low-dose (n=87)	71% (10/14)	73% (11/15)	64% (14/22)	53% (19/36)	.445
High-dose (n=93)	53% (9/17)	73% (11/15)	69% (18/26)	54% (19/35)	.418
Overall (n=206)	59% (20/34)	75% (27/36)	69% (37/54)	59% (48/82)	.280

NA: not applicable – Statistical analysis is not possible in this subgroup due to the small sample size (n)

Discussion

In this retrospective study of patients with hibernated myocardium undergoing revascularization, ß-blockers at incremental doses had a progressive impact in the sensitivity of DSE to predict recovery of dysfunctional segments. There is a physiological rationale, since ß-blockers exert opposite effects on the same ß1 adrenergic receptor, thus attenuating the response to dobutamine. A lower sensitivity for akinetic than for hypokinetic segments has been previously reported, suggesting that some akinetic segments may have exhausted coronary flow reserve and cannot respond to dobutamine despite the presence of myocardial viability (3). Our results suggest that this effect could be aggravated by ß-blocker intake.

Previous studies have reported for DSE a mean sensitivity of 76% and specificity of 81% for evaluating viability (4). However, in most studies, ß-blockers were either stopped before DSE: a small portion of patients were taking ß-blockers or the status was not reported. Very few studies have evaluated the impact of ß-blockers on DSE performance for detection of myocardial viability, with mixed results (5-8), suggesting that further investigation is needed, preferably with a prospective study comparing ß-blocker withdrawal and maintenance prior to DSE.

Our study has some limitations. First, due to the retrospective nature, sample heterogeneity could be an important bias. Second, small sample size may impact the results. However, the number of dysfunctional segments was enough to provide significant results. Third, interobserver agreement was not confirmed. Fourth, incomplete revascularization may have influenced recovery in potentially viable segments. Finally, viable segments may have been underestimated due to the timing of evaluation of recovery.

Conclusion

Our findings suggest that ß-blocker intake significantly reduces DSE sensitivity for detection of viable myocardium in patients with ischaemic LV dysfunction. There is a rationale for ß-blocker withdrawal before DSE. Further studies are needed to confirm the efficacy and safety of this practice.

Conflicts of interests: There are no conflicts of interests.

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