

Accuracy of Dobutamine Stress Echocardiography as A Predictor for Major Adverse Cardiovascular Events in Patients with Reduced Exercise Capacity Undergoing Major Non-Cardiac Surgery

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Received: 05 July 2020; Accepted: 02 August 2020

Citation: Shafy Tabl MA, NammourAY. Accuracy of Dobutamine Stress Echocardiography as A Predictor for Major Adverse Cardiovascular Events in Patients with Reduced Exercise Capacity Undergoing Major Non-Cardiac Surgery. *Cardiol Vasc Res.* 2020; 4(3): 1-5.

ABSTRACT

Background: Before major non cardiac surgeries, non-invasive functional testing widely indicated for evaluating patients with reduced exercise capacity.

Aim: To assess the accuracy of dobutamine stress echocardiography (DSE) for risk stratification prior to major non-cardiac surgeries.

Methods: Eighty patients hospitalized for major non-cardiac surgeries underwent DSE and were reviewed to determine major adverse cardiac events (MACE) up to 30 days post-discharge.

Results: Out of 80 DSE performed for preoperative risk stratification, 12.5% were positive and 87.5% were negative. Post-operative MACE in the DSE +ve group was 36% compared to 4% in the DSE-ve group ($OR = 14.8889$, $p = 0.002$). Based on the MACE rates, the overall sensitivity of DSE was 56%, specificity was 90%, and positive predictive value (PPV) was only 36% while negative predictive value (NPV) was 95%. The admission for ICU and total days of hospital stay post surgery was comparable in both groups ($p = 0.177$).

Conclusion: DSE for preoperative risk stratification had a high clinical utility in patients undergoing major non-cardiac surgery. In particular, a normal DSE had a high negative predictive value for post-operative MACE up to 30 days post discharge. Positive DSE did not correlate with the admission for ICU or total days of hospital stay post major non cardiac surgery.

Keywords

Dobutamine stress echocardiography, Major surgeries, Risk stratifications.

Introduction

Death and complication rates after major non cardiac surgeries are not rare, major morbidity complicates 3–16% of all inpatient surgical procedures in developed countries, with permanent disability or death rates of about 0.4–0.8%. Nearly half of the adverse events in these studies were identified as preventable

[1]. Annually about 10 million patients develop major adverse cardiac events (MACE) within 30 days post major surgeries [2]. Proper preoperative cardiovascular evaluation could minimize this risk and should assess the decision-making regarding risk reduction and optimal timing of surgery [3]. Previous guidelines recommended cardiac stress testing for patients with estimated preoperative risk of MACE >1% and poor exercise tolerance of less than four metabolic equivalents (METs) [4]. The role of DSE in preoperative risk assessment in patients undergoing non-cardiac surgery has been evaluated in several studies [5].

The definition of an abnormal stress echocardiogram in the majority of these studies was restricted to the presence of new wall motion abnormalities with stress or the presence of akinetic segments at baseline, indicative of MI. The results of the DSE were available to the managing clinicians and surgeons, which influenced preoperative management, including the preoperative use of diagnostic coronary angiography and coronary revascularization [6]. In 2003, Dhond MR, et al., assessed the predictive value of DSE in preoperative risk assessment for patients aged > 65 years. Their results showed negative predictive value of DSE equal 1% for non-fatal MI and cardiac death and 7.3% for re-hospitalization or a need for revascularization therapy [7]. In 2017, Gus Kathy et al. concluded that any negative DSE result had a high specificity (90%) and high NPV (96%) for inpatient preoperative MACE while any positive DSE result was associated with a significantly increased risk of MACE (OR 12.4, 95% CI 2.3–67, $P = 0.003$) [8].

The aim of this study was to assess the value of DSE in risk stratification for patients underwent major non cardiac surgeries with significant risk factors and reduced exercise capacity.

Methods

This observational study included 80 patients with documented reduced exercise capacity and multiple cardiac risk factors that underwent different major non cardiac surgeries in a private hospital in Benha from December 2019 to March 2020.

Baseline demographic data collected as age, gender, risk factors as diabetes, hypertension, smoking or hypercholesterolemia. Special concern was done to perform a detailed analysis of functional status. Prior research has shown a correlation between a patient's functional capacity and cardiovascular outcome post major non cardiac surgeries.

The study included only patients who were able to perform activities of daily living, such as clothing, bathing, and feeding themselves who diagnosed to have low functional capacity at a level less than 4 METS. Conversely, patients who are able to walk up 1 to 2 flights of stairs without stopping, walk on level ground at 4 miles per hour, or perform moderate household activities such as vacuuming were excluded and were considered to be at lower risk for preoperative cardiovascular complications.

Also, patients with recent history of significant arrhythmias (including atrial arrhythmias with rapid ventricular response), severe hypertension, or known severe valvular disease were excluded. Minor or intermediate risk surgeries were excluded from this study. Major operation type was reported according to Detsky Modified criteria [9]. MACE was defined as mortality due to cardiovascular causes, non-fatal STEMI, stroke, acute heart failure or non-fatal ventricular arrhythmia [10].

DSE procedure protocol:

Echocardiographic images were obtained using a Philips HD7XE digital echo machine with programmed acquisition and storage. DSE were reported by one expert echo cardiologists working for

DSE more than 20 years. Dobutamine infusion was started at 5 $\mu\text{g/kg/min}$ increased gradually at 3-min intervals to a maximum of 40 $\mu\text{g/kg/min}$ until the patient achieved 85% PMHR. Atropine was given in 0.2 mg boluses up to a maximal dose of 1.8 mg to increase heart rate further if 85% PMHR had not been reached. Blood pressure was documented every 3 min during the test. ECG images were obtained intermittently. ECG images were recorded at baseline, low dose (5 $\mu\text{g/kg/min}$), pre-peak (70% of PMHR), peak dose ($\geq 85\%$ PMHR) and recovery. Separate images were obtained from parasternal long and short axis as well as apical four-chambers, apical two-chambers, apical long axis and apical short axis. Following the procedure, images were displayed using a quad screen with simultaneous display of images. The test end points defined as: reaching 40 $\mu\text{g/kg/min}$ of dobutamine and $\geq 85\%$ PMHR, new wall motion abnormalities, new or significant ST segment deviation, and significant side effects developed (e.g. typical chest pain, limiting dyspnoea, sustained ventricular arrhythmias, marked hypotension or hypertension). A normal response to dobutamine was defined as a progressive increase in myocardial wall thickening and/or wall excursion with an increasing dose of dobutamine. An abnormal response was defined as a new or worsening segmental wall motion abnormality with an increasing dose of dobutamine. A non-diagnostic test was defined as a failure to achieve adequate images or a failure to achieve 85% of age predicted maximum heart rate (APMHR) [11].

Statistical methods

$P < 0.05$ was considered significant. Categorical variables are presented as n (%) while continuous variables are expressed as mean \pm standard deviation. Odd ratio was used in comparison between variables.

Ethical considerations

This work was approved by the local ethics committee and consent was obtained prior to the study.

Results

The study included 80 patients underwent major non-cardiac surgery; DSE was performed for all participants. Majority of them had a negative DSE (70 patients) while positive DSE results were recorded among only 12.5% of study population (10 patients).

The majority of study populations were elderly males above 65 years old. Male gender represented (87.5%) of study population (OR=0.0769, $p = 0.001$) while elderly patients > 65 years old represented (72.5%) (OR=1.6000, $p = 0.5729$).

The majority of patients with positive DSE had previous coronary artery diseases (CAD) (80%) while only 37.1% of patients with negative DSE had previous CAD (OR =6.7692, $p = 0.02$). 20% of patients with positive DSE had chronic kidney diseases (CKD) while only 2% of patients with negative DSE had CKD (OR=8.5000, $p = 0.045$). Otherwise, there were no significant differences between the two groups as regard congestive heart failure, stroke or major risk factors. All demographic characteristics of the study population represented in Table 1.

Table 1: Patient characteristics.

	DSE positive (n = 10)	DSE negative (n = 70)	Odd ratio	p value
Mean age	72.6 ± 6.4	70.5 ± 8.0	-	0.43
Male gender	5 (50%)	65 (92.8%)	0.0769	0.0011
Elderly (above 65 years)	8 (80%)	50 (71.4%)	1.6000	0.5729
CAD	8 (80%)	26 (37.1%)	6.7692	0.0210
CKD	2 (20%)	2 (2.8%)	8.5000	0.0450
CHF	1 (9.1%)	5 (7.4%)	1.4444	0.7495
Stroke	0 (0)	9 (13.2%)	0.3083	0.4293
Hypertension	10 (90.9%)	52 (76.5%)	3.4000	0.4127
Smoking	5 (50%)	28 (40 %)	1.5000	0.5497
Dyslipidemia	10 (90.9%)	51 (75.0%)	7.9515	0.1589
diabetes	4 (40%)	28 (40 %)	1.0000	1.0000
Mean of BMI	29.7 ± 6.1	33.4 ± 8.9	-	0.18

CAD: Coronary Artery Disease; CKD: Chronic Kidney Disease; CHF: Congestive Heart Failure; BMI: Body Mass Index.

The majority of study populations were on antiplatelet therapy (ADP receptor blockers and/or acetyl salicylic acid (71.2%), statins (75%) and either an Angiotensin Converting Enzyme inhibitor (ACEI) or an Angiotensin II Receptor Blockers (ARB) (70%).

There were no significant differences between the two groups as regard type of medications. 50% of DSE +ve group were diabetics on insulin therapy versus only 14.2% of DSE -ve group (OR = 6.000, $p = 0.01$). All patient medications prior to surgery were reported in Table 2.

As regards type of major non cardiac surgery, (55%) of patients in study population underwent orthopedic operations, (27.5%) underwent gastric, small bowel or colonic surgeries, and while only (10%) underwent neurosurgical procedures or gynecologic malignancies, no vascular or emergencies surgeries, no reconstructive, exploratory or transplant surgeries. There were no significant differences between the two groups as regard type of surgery (Table 2).

Table 2: Patient medications and type of major surgery.

	DSE positive (n = 10)	DSE negative (n = 70)	Odd ratio	p value
Antiplatelets	10 (100%)	47 (67.1%)	10.3895	0.111
Statins	10 (100%)	50 (71.4%)	8.5248	0.1452
ACEI/ARB	10 (100%)	46 (65.7%)	11.0645	0.101
Diuretic	5 (50%)	24 (34.2%)	1.9167	0.3392
Beta blocker	5 (50%)	26 (37.1%)	1.6923	0.4385
Oral hypoglycaemic agents	3 (33%)	24 (34.2%)	0.8214	0.7889
Insulin	5 (50%)	10 (14.2%)	6.000	0.01
Orthopedic surgery	5 (50%)	39 (55.7%)	0.7949	0.7344
Gastroenterology surgery	2 (20%)	20 (28.5 %)	0.7500	0.7294
neurosurgery	2 (20%)	6 (8.5%)	2.6667	0.2750
Gynecological surgeries	1 (10%)	5 (7.1%)	1.4444	0.7495

ACEI: Angiotensin-Converting Enzyme Inhibitor; ARB: Angiotensin-II Receptor Blocker; DSE: Dobutamine Stress Echocardiography.

The indication for ICU admission, the duration of ICU stays and total days in hospital were comparable in both groups ($p = 0.1778$, 0.75 & 0.38). There were significantly more positive troponin results in the DSE +ve group (45%) vs (11%) (OR = 7.7500, $p = 0.01$) (Table 3).

Table 3: ICU and troponin profile during index admission.

	DSE positive (n = 10)	DSE negative (n = 70)	Odd ratio	P value
ICU admission	6 (60%)	26 (37.1%)	2.5385	0.1778
Troponin positive	5 (50%)	8 (11.4%)	7.7500	0.0054
Troponin negative	3 (30%)	20 (28.5%)	1.0714	0.9256
Duration of ICU stay (days)	3.3 ± 0.7	3.2 ± 1.6	-	0.75
Total duration of stay (days)	9.5 ± 5	7.4 ± 8	-	0.38

There were significantly more patients with MACE in the DSE + ve group (36.4%) vs (4.4%) (OR = 14.8889, $p = 0.002$). This was mainly derived from higher non-fatal STEMI rates in the DSE + ve group (36.4%) vs (1.5%) (OR = 46.00, $p = 0.0014$). Other MACE as congestive cardiac failure or ventricular arrhythmias was comparable in both groups (9%) vs (4.4%) (OR = 2.4815, $p = 0.4518$). There were no deaths, or a need for further coronary intervention post operatively in both groups.

Table 4: MACE event rates.

Event rates	DSE +ve (n = 10)	DSE -ve (n = 70)	Odd ratio	P value
Total MACE	4 (40%)	3 (4.28%)	14.8889	0.002
Non-fatal STEMI	4 (40%)	1 (1.42%)	46.0000	0.0014
Congestive Cardiac Failure	1 (10%)	3 (4.28%)	2.4815	0.4518
Ventricular arrhythmias	1 (10%)	3 (4.28 %)	2.4815	0.4518
Further coronary intervention	0	0	-	-
Cardiac mortality	0	0	-	-

MACE: Major Adverse Cardiovascular Events; STEMI: ST Segment Elevation Myocardial Infarction.

Based on the above MACE rates, the overall sensitivity of DSE was 56%. Specificity was 90% for overall MACE. The positive predictive value (PPV) was only 36% for overall MACE while the negative predictive value (NPV) was 95%.

Diagnostic accuracy of DSE for predicting perioperative MACE is shown in Figure 1.

Discussion

American Society of Echocardiography Appropriateness guidelines in 2011 indicated noninvasive stress testing for patients with elevated risk and poor (<4 METs) or unknown functional capacity prior to major surgeries to assess for myocardial ischemia if it will change management (Class IIb, Level of Evidence: B).

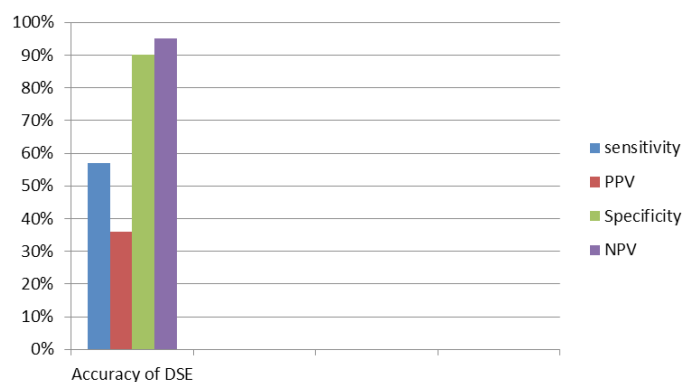


Figure 1: Diagnostic accuracy of DSE for predicting preoperative MACE.

While, noninvasive stress testing is not recommended prior to low or intermediate-risk surgery or for patients who have no cardiac risk factors (Class III, Level of Evidence: C). the type of stress test performed depends upon the individual patient and the data needed to provide optimal care. In patients in whom left ventricular function is in question or presence or severity of valvular disease is a concern, stress echocardiography provides reliable, cost-effective information [4].

In correlation with ACC/AHA 2014 guidelines, this study included 80 patients with known poor functional capacity (<4 METs) and multiple risk factors. 77% were hypertensives, 76% had dyslipidemia, 40% were diabetics majority of them on insulin therapy, 72.5% were elderly, 57% had known CVD. All patients underwent high risk major non cardiac surgeries based on Detsky Modified criteria. Majority of patients underwent orthopedic operations (55%), gastric, small bowel or colonic surgeries (27.5%), neurosurgical procedures or gynecologic malignancies (10%), no vascular surgeries.

The results of 80 DSE showed significant correlation between positive results and MACE (36.4% in DSE +ve group vs only 4.4% in DSE -ve group) (Odd ratio = 14.8889, $p = 0.002$). This significant correlation was mainly derived from higher rates of non-fatal STEMI (36.4% vs 1.5%) (Odd ratio = 46.00, $p = 0.0014$). Other MACE as congestive cardiac failure or ventricular arrhythmias was comparable in both groups (9% vs 4.4%) (Odd ratio = 2.4815, $p = 0.4518$). In correlation, there were significantly more positive troponin results in the DSE +ve group (45%) vs (11%) (Odd ratio = 7.7500, $p = 0.01$) (Table 3). Acute myocardial ischaemia post major non cardiac surgeries represent one of common cardiovascular complications post major non cardiac surgeries which caused by unfavorable imbalance between myocardial oxygen supply and demand and reflecting the continuous stress of major surgery in the setting of limited coronary or myocardial structural reserve [12].

This study found that a negative DSE result had a high specificity (90%) and high NPV (95%) for inpatient preoperative MACE. Therefore, a negative DSE study provides reassurance that the patient is at low risk of significant preoperative cardiac complications. In correlation to our results, Kathy G et al. 2017

concluded that DSE had a higher diagnostic accuracy if only the hard-cardiac events were taken into account (non-fatal STEMI, acute heart failure or ventricular arrhythmias) (specificity 90% and NPV 98%) [8].

The low sensitivity (57%) and PPV (33%) are more difficult to interpret given patients with a positive DSE result were either medically or surgically treated for CAD prior to elective surgery, thereby lowering their risk of preoperative MACE (Figure 1). In contrast to our results, the meta-analysis of Nguyen P et al. in 2013 included 1877 patients underwent major vascular surgery and found a higher sensitivity of DSE (85%) for predicting preoperative cardiac deaths and non-fatal MI [13]. This contrast in diagnostic accuracy could be explained with the higher incidence of CAD in vascular patients who enrolled in this meta-analysis in comparison to our patient cohort, which comprised a general surgical patient population.

In current study, positive DSE did not correlate with the indication for ICU, the duration of ICU admission or total days of hospital stay post major non cardiac surgeries, all of three parameters were comparable in both groups ($p = 0.1778, 0.75$ & 0.38) Table 3.

Indication for ICU and prolonged hospital stay can be theoretically predicted via functional status of the patient before surgery and presence of risk factors. Patients with preoperative reduced functional capacity and history of known CVD or multiple risk factors could be at increased risk of ICU admission post-surgery [14]. Many preoperative risk scores can help distinguish which patients are most likely to experience poor post-operative outcomes. The Revised Cardiac Risk Index (RCRI) is a simple tool that has been validated to assess this risk. Patients having 2 or more risk factors have elevated cardiovascular risk post-surgery [15]. None of these scoring systems alone is generally sufficient to provide adequate information regarding the need for ICU admission and the duration of hospital stay post-surgery [16]. For our knowledge, no RCT directly tested the correlation between DSE, indication for ICU admission and the duration of hospital stay post major non cardiac surgeries.

Finally, DSE had a high clinical utility for the preoperative risk stratification of patients with multiple cardiac risk factors and reduced exercise capacity. Significant positive correlation was found between positive DSE results and risk for MACE mainly derived by non-fatal STEMI. In particular, a normal DSE has a high NPV for preoperative MACE. Negative DSE could safely rule out any risk for MACE during hospitalization and up to 30 days after discharge. DSE had limited predictive value for ICU admission and over all hospital stay post major non cardiac surgery.

Limitations

This study has several limitations. First, it was an observational study. Second, this study involved a limited number of patients and low event rates. Third, vascular surgery was not included.

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