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ORIGINAL ARTICLE

Benefits of Cardiac Biomarkers and Stress ECG in Cardiac Risk Stratification of Patients Scheduled for Non-Cardiac Surgery

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Abstract

Background: ***Every year, millions of noncardiac surgeries occur, with 25% of patients aged 45 or older suffering from atherosclerosis-related cardiovascular disease and 45% experiencing hyperlipidemia and hypertension, all of which correlate with perioperative cardiovascular events.***

Aim and objectives: ***Evaluation of the ability of cardiac biomarkers and stress tests to estimate the risk of noncardiac operations.***

Subjects and methods: ***We performed this prospective observational research on 60 patients selected from the outpatient cardiovascular clinics of Al Azhar University Hospitals between February 2023 and December 2023. We divided them into survivors and deceased groups based on their respective outcomes.***

Result: ***Stress ECG showed positive findings in 75% of the patients, negative findings, and inadequate results in 6.7% of each, while 11.7% showed inconclusive results. Based on dobutamine stress echocardiography, 8.3% of the patients showed high function capacity, and 10% showed low function capacity. Regarding the outcome, 81.7% of the patients survived, and 18.3% died (60% of them died due to myocardial infarction, 30% of them died due to stroke, 10% of them died due to pulmonary embolism). There wasn't statistically significant variance among survived and non-survived subjects regarding stress ECG and dobutamine stress echocardiography.***

Conclusion: ***The cardiac biomarkers BNP and CK-MB have played a significant role in the cardiac risk stratification of cases scheduled for noncardiac surgery. There are no benefits to the stress ECG when used to compare patients' outcomes after noncardiac surgery.***

Keywords: Cardiac biomarkers; Stress ECG; Cardiac risk stratification; Patients scheduled; non-cardiac surgery

1. Introduction

The underlying pathophysiological causes of myocardial ischemia in noncardiac operations are correlated with either an imbalance between the supply and demand of oxygen or an existing flow.[1] Restricting the development of coronary stenosis or the rupture of weak atherosclerotic plaques, each of which increases the risk of a negative cardiac event in CAD patients. The surgical procedure's pro-inflammatory and hypercoagulable states, as well as the hemodynamic disturbances brought on by fluid changes and anesthesia, are all significant causes of perioperative myocardial ischemia. [2,3]

Biomarker-enhanced preoperative risk assessment may help patients make well-informed decisions when conservative therapy is also an option. [4]

Treatable compounds that become detectable in certain physiological situations, including ventricular failure or myocardial damage, are known as biomarkers.[5] Examples of these molecules are natriuretic peptides and troponins. Due to the inadequate sensitivity of early troponin assays, myocardial ischemia detection occurred later than expected. Acute coronary syndrome (ACS) specificity has decreased in current 4th and 5th-generation troponin assays, although sensitivity has clearly increased. Similarly, people have used natriuretic peptides to diagnose or predict heart failure. Examples of these peptides are the brain natriuretic peptide (BNP) and the inactive prohormone N-terminal pro-BNP (NT-proBNP). Despite the similarity between the two assays, the NT-proBNP assays demonstrate a slightly better capacity to forecast mortality or prehospitalization in heart failure cases. [6]

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The purpose of the present research was to evaluate the usefulness of stress electrocardiograms (ECGs) and cardiac biomarkers in the cardiac risk assessment of noncardiac surgery cases.

2. Patients and methods

This prospective observational research was performed on 60 patients selected from the outpatient cardiovascular clinics of Al Azhar University Hospitals from February 2023 until December 2023. We observed the patients under study for at least 6 months in the postoperative postoperative period. We divided them into survivors and deceased groups based on their respective outcomes. We collected the samples through a systematic random method.

Inclusion criteria: patients who undergo non-cardiac surgery (intermediate risk operations) (orthopedic, abdominal, thoracic, and endocrine surgery); patients who are more than fifty-five years old and have at least one of the selected cardiovascular risk factors (diabetes mellitus, smoking, hypertension, hyperlipidemia, or a positive family history of cardiac disease).

Exclusion criteria: patients who had more than one non-cardiac surgery.

Sample Size:

This research was performed in agreement with the findings of Marković et al.[7] We used Epi Info STATCALC to determine the sample size, considering the following assumptions: An eighty percent power confirms a two-sided confidence level of ninety-five percent. The calculated risk ratio's five percent error is 1.115%. The Epi-Info output ultimately yielded a maximum sample size of fifty-three. Consequently, we increased the sample size to sixty subjects to account for potential dropouts during the follow-up period.

After preparing patients for non-cardiac surgery, we exposed all cases to the following: Complete history, including name, age, parity, place of residence, type of work, and any unique medically significant habits—smoking in particular. Complaint and length of time, examination of the patient's current complaint, medication sensitivity history, past medical history, list of prior surgeries, and family history, physical examinations to exclude systemic illnesses, vital signs (temperature, blood pressure, respiratory rate, heart rate), and signs of cyanosis, pallor, lymph node enlargement, and jaundice.

Investigational studies:

Cardiac biomarkers

Seven days before the planned surgery, we collected a blood sample from the antecubital vein into serum Vacutainer containers without any additives. We separated the serum by centrifugation and then frozen it at -70 degrees Celsius until analysis. We conducted analyses after collecting all the samples. The kit we used in ProBNP is an ELISA kit that uses the sandwich-ELISA principle with a detection range of 120–1000 pg/ml and a sensitivity of 90 pg/ml. The kit we used in CKMB is the CKMB ELISA kit, which uses the sandwich-ELISA principle with a detection range of 7.813-500 ng/ml and a sensitivity of 4.6 ng/ml. The kit we used for high-sensitivity cardiac troponin (Hs-cTn) is the procaine high-sensitivity cardiac troponin I ELISA kit. The detection sensitivity is 0.001 ng/mL. We measured the optical density of the DIAREADER Elx800G (DIALAB, Austria) after implementing the manufacturers' recommended protocol. We then constructed a standard curve from the parametric logistic curve and presented the results.

Stress Testing by Treadmill:

Treadmill protocol: We used electrocardiography (ECG) for treadmill cycling exercise. We quantified exercise capacity in estimated metabolic equivalents of tasks (METs). 1 MET is equal to 3.5 mL/min/kg of body weight and represents the resting volume of oxygen consumption per minute (VO2) for a 70-kg, 40-year-old male. We followed the standard Bruce protocol, designating stage 1 as a starting point of 1.7 mph at a ten percent grade (5 METs). Stage 2 was a 12-percent grade at 2.5 mph (7 METs). At a grade of fourteen percent, Stage 3 reached 3.4 mph (9 METs). This protocol involved three-minute intervals to permit the achievement of a steady state prior to increasing the burden.[8,9] The modified Bruce protocol consisted of two three-minute preparation phases. One was at a velocity of 1.7 mph with a grade of zero percent, and the other was at 1.7 mph with a grade of five percent. This protocol was administered to elderly patients and cases with cardiac disease-related exercise limitations.

Causes of termination of exercise stress ECG:

The guidelines of the American College of Cardiology (ACC) and the American Heart Association (AHA) also specify the indications for ceasing exercise testing. We discontinued exercise stress testing for the following reasons: if a person has moderate to severe angina, increasing neurological symptoms, signs of poor blood flow, fatigue, shortness of breath, wheezing, increasing chest pain, hypertension (SBP of 250 mm Hg or DBP exceeding 115 mm Hg, or both), and the patient's desire to stop.

Interpretation of test findings:

We used the classic criteria for the visual interpretation of positive stress test findings, which include:

J point depression of at least 0.1 mV (1 mm) and ST-segment slope of±1 mV/sec over the course of three beats.

Dobutamine echocardiography:

A 2-D echocardiogram was conducted in the

left lateral decubitus position, adhering to the guidelines of the American Society of Echocardiography (ASE).[10] We utilized Harmonic Imaging (HDI 5000, Philips Medical Systems, Eindhoven, Netherlands) for this purpose. We administered dobutamine peripherally to patients deemed unsuitable for exercise testing. We raised the dosage in three-minute intervals, starting at ten mg/kg/min and gradually increasing it to forty mg/kg/min. We introduced atropine in four divided doses of 0.3 milligrams, with a maximum dose of 1.2 milligrams when no endpoint was achieved.

End-points were detected under the following conditions:

Achieving eighty-five percent of the age-predicted target heart rate, onset of severe ischemia (extensive wall motion abnormality, severe angina), or reaching the peak dosage (40 mg/kg/min of dobutamine IV or 1.2 mg of atropine IV).

Technique:

The patient was in the left decubitus position.[11] To enhance sound wave transmission, we applied a gel-like substance to the patient's chest, then placed the transducer (a handheld device) on the patient's chest wall.

Standard Views: To obtain various echocardiographic views, we positioned the transducer on specific areas of the chest.

The following were the standard views typically acquired: parasternal long-axis view, parasternal short-axis view, and apical four-chamber view.

Image Optimization: To improve image quality, we adjusted the transducer position and angulation, and we asked the patient to take deep breaths or hold their breath momentarily to reduce interference from respiratory motion.

Image Acquisition: We captured images in real-time. We also used doppler ultrasound to evaluate blood flow velocities and assess valve function.

Image Analysis and Interpretation: We analyzed the obtained echocardiographic images. We evaluated the images for abnormalities in chamber size, wall thickness, valve function, and myocardial function.

Ethical Consideration

Participants provide private information. Every study report or publication included a list of study participants' names. Prior to their admission, the participants received disclosure of the trial's aim, design, and risk-benefit analysis. Informed consent was obtained.

Statistical Analysis

We analyzed the recorded data using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). We expressed the quantitative data as the mean and standard deviation (SD). We expressed qualitative data in terms of frequency and percentage.

The following tests were done:

We used an independent-sample t-test of significance to compare two means.

We used a chi-square (x2) test of significance to compare the proportions between two qualitative parameters.

The confidence interval was set to 95 percent, and the margin of error accepted was set to five percent. The p-value was considered significant for the following reasons: Probability (P-value) P-value <0.05 was considered significant; P-value <0.001 was considered highly significant; and P-value >0.05 was considered insignificant.

3. Results

The mean age was 71.25 ± 6.65, regarding comorbidity majority of patients had Hypertension (78.3%), regarding cardiac risk, majority of patients had dyspnea level NYHA II-IV (78.3%), regarding Medications majority of patients took ACEI (56.7%), regarding Type of surgery majority of patients had Abdominal surgery (30%), regarding Clinical presentation majority of patients had Enlarged LNs (56.7%) (Table 1).

Table 1. Demographic and clinical data of the studied patients. (n=49)

VARIABLES		MEAN±SD / FREQUENCY
AGE (YEARS)	Mean±SD (range)	71.25 ± 6.65 (57 – 85)
SEX	Male	31 (51.7%)
	Female	29 (48.3%)
BMI (KG/M2)	Mean±SD (range)	24.95 ± 0.686 (23.5 – 26.4)
ASSOCIATED COMORBIDITIES	Smoking	8 (13.3%)
	Hypertension	47 (78.3%)
	Diabetes mellitus type II	16 (26.7%)
	Diabetes mellitus type I	5 (8.3%)
	Dyslipidemia	9 (15%)
CARDIAC RISK	CAD	19 (31.7%)
	Atrial fibrillation	7 (11.7%)
	NYHA II-IV	47 (78.3%)
MEDICATIONS	Aspirin	18 (30%)
	β-blockers	32 (53.3%)
	ACEI	34 (56.7%)
	Diuretics	11 (18.3%)
	Nitrates	5 (8.3%)
	OAT	6 (10%)
	Clopidogrel	13 (21.7%)
TYPE OF SURGERY	Abdominal surgery	18 (30%)
	Endocrine surgery	14 (23.3%)
	Orthopedic surgery	16 (26.7%)
	Thoracic surgery	12 (20%)
CLINICAL PRESENTATION	Pallor	30(50%)
	Cyanosis	12(20%)
	Jaundice	18(30%)
	Enlarged LNs	34(56.7%)
HEART RATE (BEAT/MIN)	Mean±SD (range)	80.17 ± 9.04 (57 – 100)
RESPIRATORY RATE (CYCLE/MIN)	Mean±SD (range)	14.02 ± 0.911 (12-16)
TEMPERATURE (ºC)	Mean±SD (range)	36.97 ± 0.231 (36.5 - 37.4)
SBP REST (MM HG)	Mean±SD (range)	120.02 ± 4.51 (111 –

		130)
DBP REST (MM HG)	Mean±SD (range)	80.22 ± 2.29 (74 – 85)
HEMOGLOBIN (G/DL)	Mean±SD (range)	11.91 ± 0.518 (10.5 – 13.1)
CK-MB (NG/ML)	Mean±SD (range)	1.24 ± 0.119 (1 – 1.25)
BNP (PG/ML)	Mean±SD (range)	126.75 ± 54.44 (23.2 – 243)
HS-CTN (NG/ML)	Mean±SD (range)	0.0238 ± 0.008 (0.01 – 0.04)

BMI: body mass index, CAD: coronary artery disease, ACEI: angiotensin converting enzyme inhibitor, OAT: oral anticoagulant therapy, HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, CK-MB: creatine kinase-MB, BNP: Brain natriuretic peptide, Hs-cTn: high-sensitivity cardiac troponin.

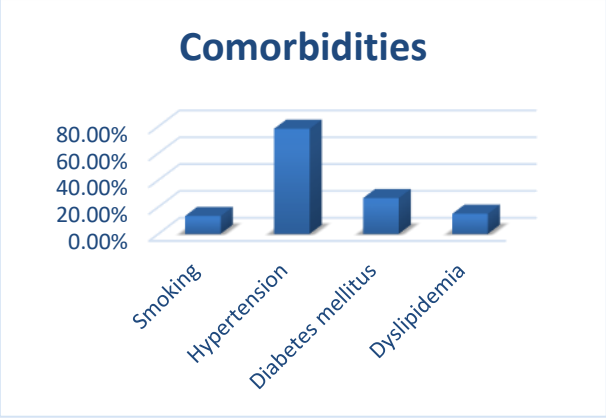


Figure 1. showing 13.3% of the patients were smoking, 26.7% were diabetic patients; 5 of them were type 1, 15% were dyslipidemic and 78.3% were hypertensive.

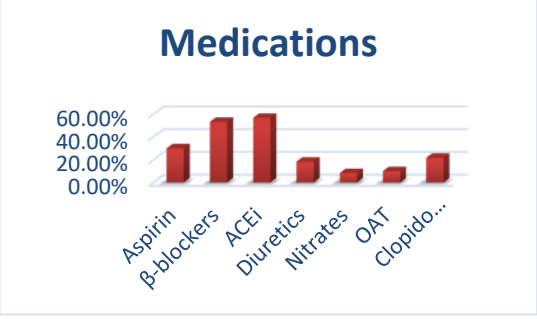


Figure 2. showing that 30% of the patients were on aspirin, 53.3% were BB, 56.7% were ACEi, 18.3% were diuretics, 8.3% were on nitrates, 10% were OAT, and 21.7% on Clopidogrel.

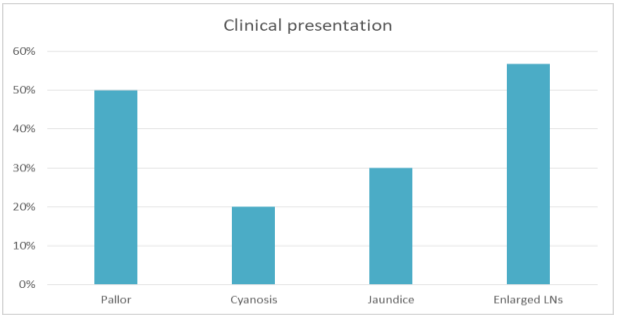


Figure 3. showing that 50% of the patients presented with pallor, 20% presented with cyanosis, 30% presented with jaundice, and 56.7% showed enlarged lymph nodes.

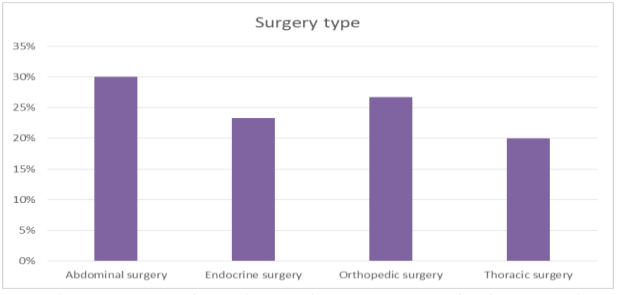


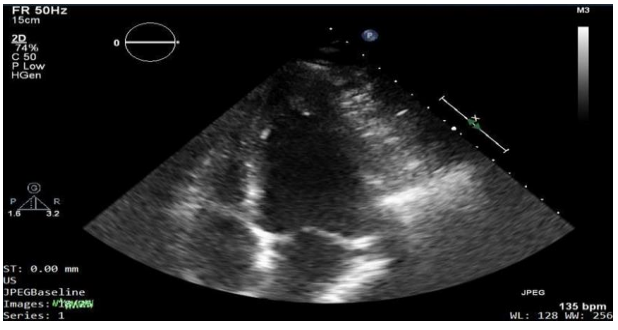
Figure 4. showing that 30% of the patients underwent abdominal surgery, 23.3% underwent endocrine surgery, 26.7% underwent orthopedic surgery, and 20% underwent thoracic surgery.

Majority of patients had Positive Stress ECG (75%), majority of patients had High function capacity regarding Dobutamine Echocardiography and majority of patients were Survived regarding outcome (81.7%) (Table 2).

Table 2. Stress ECG, dobutamine echocardiography findings and outcome distribution among the studied patients

VARIABLES		MEAN±SD / FREQUENCY
STRESS ECG (N=49)	Positive	45 (75%)
	Negative	4 (6.7%)
	Inadequate	4 (6.7%)
	Inconclusive	7 (11.7%)
DOBUTAMINE ECHOCARDIOGRAPHY (N=11)	High function capacity	5 (45.5%)
	Low function capacity	6 (54.5%)
OUTCOME (N=49)	Survivor	49 (81.7%)
	Deceased	11 (18.3%)

ECG; electrocardiogram



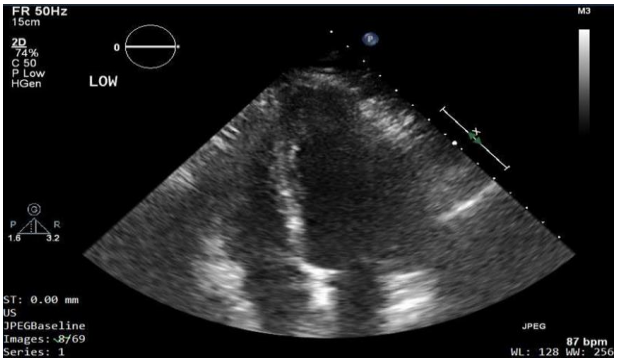


Figure 5. this is a selected case of high functional capacity Dobutamine echocardiography

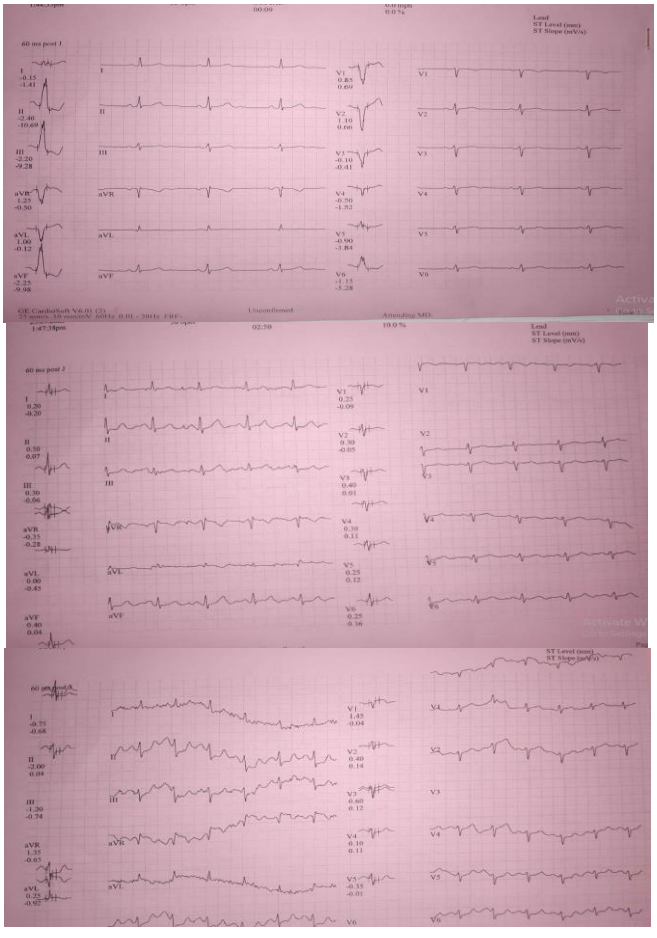


Figure 6. this is a selected case of positive stress ECG

There was statistically insignificant difference between survived and non-survived subjects regarding age, HR, temperature, SBP, and DBP. Non-survived subjects have statistically significant higher Hb, BNP, CK-MB level, Dyspnea level (NYHA II-IV) and clopidogrel use compared to survived subjects as demonstrated in Table 3.

Table 3. comparison of clinical and laboratory data in relation to outcome

VARIABLES		SURVIVOR	DECEASED	INDEPENDENT STUDENT T TEST/CHI SQUARE TEST	
		n=49	n=11	t/x2	P-value
AGE (YEARS)	Mean±SD	70.33 ± 6.6	75.36 ± 5.43	2.36	0.022
SEX	Male	25 (51%)	6 (54.5%)	0.045	0.833
	Female	24 (49%)	5 (45.5%)		
BMI (KG/M2)	Mean±SD	24.98 ± 0.727	24.81 ± 0.468	0.742	0.461
ASSOCIATED COMORBIDITIES	Smoking	8(16.3%)	0(0%)	2.100	0.150
	Hypertension	39(79.6%)	8(72.7%)	0.249	0.617
	Diabetes mellitus	15(30.6%)	1(9.1%)	2.130	0.145
	Dyslipidemia	9(18.4%)	0(0%)	2.380	0.123
CARDIAC RISK	CAD	14(28.6%)	5(45.5%)	1.180	0.227
	Atrial fibrillation	6(12.2%)	1(9.1%)	0.087	0.768
	NYHA II-IV	36(73.5%)	11(100%)	6.020	0.014
MEDICATIONS	Aspirin	13(26.5%)	5(45.5%)	1.530	0.216
	β-blockers	26(53.1%)	6(54.5%)	0.008	0.929
	ACEi	28(57.1%)	6(54.5%)	0.025	0.875
	Diuretics	8(16.3%)	3(27.3%)	0.719	0.396
	Nitrates	5(10.2%)	0(0%)	1.220	0.268
	OAT	5(10.2%)	1(9.1%)	0.012	0.911
	Clopidogrel	8(16.3%)	5(45.5%)	4.500	0.034
HEART RATE (BEAT/MIN)	Mean±SD (range)	78.9 ± 8.79	85.82 ± 8.27	2.380	0.020
RESPIRATORY RATE (CYCLE/MIN)	Mean±SD	13.92 ± 0.886	14.45 ± 0.934	1.800	0.078
TEMPERATURE (ºC)	Mean±SD	36.94 ± 0.224	37.14 ± 0.196	2.720	0.009
SBP (MM HG)	Mean±SD	119.43 ± 4.27	122.64 ± 4.84	2.200	0.032
DBP (MM HG)	Mean±SD	79.92 ± 2.28	81.55 ± 1.86	2.200	0.032
HEMOGLOBIN (G/DL)	Mean±SD	11.8 ± 0.465	12.42 ± 0.44	4.100	<0.001
CK-MB (NG/ML)	Mean±SD	1.22 ± 0.115	1.31 ± 0.114	2.370	0.021
BNP (PG/ML)	Mean±SD	117.88 ± 52.56	166.27 ± 46.1	2.820	0.007
HS-CTN (NG/ML)	Mean±SD	0.0229 ± 0.008	0.028 ± 0.009	1.980	0.052

There was no statistically significant difference between survived and non-survived subjects regarding Stress ECG and Dobutamine echocardiography as demonstrated in Table 4.

Table 4. Stress ECG and Dobutamin echocardiography among the studied groups according to survival rate

VARIABLE	SURVIVOR (N=49)		DECEASED (N=11)		CHI SQUARE TEST	
	N	%	N	%	x^2	P-value
STRESS ECG (N=49)						
POSITIVE	37	75.5%	8	72.7%	3.66	0.300
NEGATIVE	4	8.2%	0	--		
INADEQUATE	2	4.1%	2	18.2%		
INCONCLUSIVE	6	12.2%	1	9.15		
DOBUTAMINE ECHOCARDIOGRAPHY (N=11)	Survivor (n=8)		Deceased (n=3)		x^2	P-value
HIGH FUNCTION CAPACITY	5	62.5%	0	0%	3.437	0.064
LOW FUNCTION CAPACITY	3	37.5%	3	27.3%		

4. Discussion

Our study identified a total of thirty-one males and twenty-nine females as cases, with an average age of 71.25 years and a body mass index of 24.95 kg/m2.

Heinisch et al.,[12] whose objective was to compare the accuracy of four distinct cardiac risk indices presently employed in the prediction of perioperative cardiac complications, obtained results consistent with our own. A cardiologist assessed all 141 cases participating in this investigation, including those undergoing noncardiac surgical procedures. The age group (mean±SD) was determined to be 30-89 years (65±12 years).

Furthermore, our findings agree with those of Smilowitz et al.,[13] whose objective was to assess patterns of atherosclerotic cardiovascular disease (ASCVD) and cardiovascular risk factors at the national level among cases undergoing noncardiac operations. It was determined that the mean age of the cases in 2012–2013 was 65.75±11.82.

In our study, we found that regarding history taking, 13.3% of the patients were smokers, 26.7% were diabetic type II patients, 8.3% were type 1, 15% were dyslipidemic, and 78.3% were hypertensive.

Also, our findings align with those of Smilowitz et al.,[13] who discovered that 62.8% were hypertensive, 36.6% were dyslipidemic, and 27.4% were diabetic patients.

In our study, we found that 30% of the patients were on aspirin, 53.3% were on BB, 56.7% were on ACEi, 18.3% were on diuretics, 8.3% were on nitrates, 10% were on OAT, and 21.7% were on Clopidogrel,

In accordance with our findings, Ollila et al.[14] found that 48% of the patients were on acetylsalicylic acid (aspirin), 63.0% were on beta blockers, and 17.8% were on Clopidogrel.

In our study, we found that mean hemoglobin was 11.91±0.518 g/dl, mean creatinine was 1.02±0.087 mg/dl, mean CK-MB was 1.24±0.119 ng/ml, mean CK-MB was 126.75±54.44 pg/ml, and mean Hs-ctn was 0.024±0.008 ng/ml.

As well, our results are consistent with those of Ollila et al.,[14] who found that Hb 126 [108–145] g/L and creatinine 84 [64–125] μmol L-1.

Spence et al.[15] determined the frequency and duration of mortality as well as its correlation with perioperative complications. Our findings are consistent with theirs. We conducted a prospective cohort study to examine cases aged forty-five and older. The results revealed that 17.5 percent of the cases received a thoracic operation, while twelve percent received orthopedic operations.

Stress ECG showed positive findings in 75% of the patients, negative findings and inadequate results in 6.7% of each, and 11.7% showed inconclusive results. Based on dobutamine stress echocardiography, 8.3% of the patients showed high function capacity, and 10% showed low function capacity. Regarding the outcome, 81.7% of the patients survived, and 18.3% died.

Our results are consistent with Machado et al.[16] who aimed to compare the prediction of 30-day mortality after noncardiac surgery using continuous postoperative hs-cTnT levels to the use of the overall URL and age- and sex-specific URLs. They found that the mean HR was 76.5 beats per minute, the mean SBP was 130 mmHg, and the mean DBP was 77.5 mmHg. In our study, we found that mean hemoglobin was 11.91 ± 0.518 g/dl, mean creatinine was 1.02 ± 0.087 mg/dl, mean CK-MB was 1.24 ± 0.119 ng/ml, mean CK-MB was 126.75 ± 54.44 pg/ml, and mean Hs-ctn was 0.024 ± 0.008 ng/ml.

In our study, we found that 75% of the patients showed positive findings, 6.7% showed negative findings, 6.7% showed inadequate results, and 11.7% showed inconclusive results. Our results are consistent with Marcus et al.,[17] who aimed to explore the incidence of pre and new postprocedural ECG pathologies in an intermediate-high-risk population undergoing noncardiac surgery. This study was conducted on 217 patients, and they found that Preoperative pathologic ECG changes were recorded in 62.2% of the patients.

In our study, we found that 8.3% of the patients showed high function capacity, and 10% showed low function capacity. Our results are consistent with those of Das et al.[18] who aimed to evaluate the incremental value of dobutamine stress echocardiography (DSE) for the assessment of cardiac risk before nonvascular surgery. This study was conducted on 303 men and 227 women who underwent DSE before nonvascular surgery, and they found that dobutamine stress echocardiography identified 60% of patients as low (no ischemia), 32% as intermediate (ischemic threshold 60% or more) and 8% as high risk.

Recommendations: Cardiac biomarkers such as BNP and CK-MB could be used to strategize the cardiac risk of patients scheduled for noncardiac surgery.

4. Conclusion

According to our study, cardiac biomarkers such as BNP and CK-MB have played a major role in the cardiac risk stratification of patients scheduled for noncardiac surgery. There are no benefits to the stress ECG when used to compare patients' outcomes after noncardiac surgery.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article

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Conflicts of interest

There are no conflicts of interest.

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