Heart Surgery Forum 2023; 26(3): E240–E248
doi: 10.1532/hsf.5471

Article

Perioperative Levels of Troponin and BNP and the Outcome after Coronary Artery Bypass Grafting

Ayman R. Abdelrehim[1,2,*], Faisal A. Alnasser[3], Fareed A. Alnozaha[3], Mohammadnizam S.H. Uddin[4], Hasan I. Sandogji[1], Hussain R. Aynusah[5], Asim S.S. Alluhaybi[5], Refal A. Alahmadi[5], Hussam M. Alahmadi[5], Wafaa M. Alharbi[6], Ahmed M. Shabaan[1,7]

[1]Cardiac Surgery Department, Madina Cardiac Center, 42364 Madina, Saudi Arabia
[2]Cardiothoracic Surgery Department Faculty of Medicine, Menoufia University, 32111 Menoufia, Egypt
[3]Cardiology Department, Madina Cardiac Center, 42364 Madina, Saudi Arabia
[4]Cardiac Anesthesia Department, Madina Cardiac Center, 42364 Madina, Saudi Arabia
[5]Research Department, Taibah University, 42364 Madina, Saudi Arabia
[6]Research Department, Madina Cardiac Center, 42364 Madina, Saudi Arabia
[7]Cardiothoracic Surgery Department Faculty of Medicine, 41522 Suez Canal University, Egypt
*Correspondence: ayman_elmeghawry@yahoo.com (Ayman R. Abdelrehim)

Submitted: 22 January 2023 Revised: 15 February 2023 Accepted: 27 February 2023 Published: 31 May 2023

Abstract

Background: The independent predictive values of troponin I (cTnI) and B-type natriuretic peptide (BNP) after coronary artery bypass grafting (CABG) have been reported in several studies. However, adjustment only has been limited to preoperative risk factors. **Aim**: This study was conducted to assess the independent values of postoperative cTnI and BNP to predict the outcome after CABG with adjustment for preoperative risk estimates and postoperative complications and to report risk stratification gains, when considering the European System for Cardiac Operative Risk Evaluation (EuroSCORE) combined with postoperative biomarkers. **Methods**: This retrospective cohort study included 282 consecutive patients undergoing CABG between January 2018 and December 2021. We evaluated the preoperative and postoperative cTnI and BNP, EuroSCORE, and postoperative complications. The composite endpoint was death or cardiac-related adverse events. **Results**: The AUROC for postoperative cTnI was significantly higher than that of BNP (0.777 *vs.* 0.625, p = 0.041). The optimal cut-off values to predict the composite outcome were >4830 (pg/mL) and >6.95 (ng/mL) for BNP and cTnI, respectively. Adjustment for relevant and significant perioperative factors showed that postoperative BNP and cTnI had a high discriminatory power (C-index = 0.773 and 0.895, respectively) for predicting major adverse events. **Conclusions**: Postoperative BNP and cTnI are independent predictors of death or major adverse events, following CABG, and can add to the predictive power of EuroSCORE II.

Keywords

atrial natriuretic peptide; cardiac troponin I; coronary artery bypass grafting; prognosis

Introduction

Coronary artery bypass grafting (CABG) has been reported as the most common cardiac surgery worldwide [1]. After surgery, patients may experience major adverse events and poor outcomes [2]. Early identification of patients at high risk of experiencing poor outcomes after cardiac surgery is crucial to perform prophylactic measures that may improve the patient outcome.

Several prognostic biomarkers have been assessed to predict the probability of poor outcomes in patients undergoing cardiac surgeries, including postoperative creatine kinase-MB, troponin levels [3] and B-type natriuretic peptide (BNP) [4]. In addition, surgical risk stratification models, such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE) [5,6], have been employed to estimate the preoperative risk/benefit assessments based on selected preoperative and intraoperative risk factors.

The BNP is produced by the atria and ventricles. The increased stress of the ventricular wall in cases of volume overload, pressure overload, or ischemia results in the release of BNP from myocytes into plasma [7]. Troponins are regulatory proteins present within cardiac myocytes and consist of three subunits: cardiac troponin I (cTnI), cardiac troponin T (cTnT), and cardiac troponin C (cTnC). Calcium binds to cardiac troponins, resulting in changes in the structure of the protein complex, which ultimately facilitates the binding of actin and myosin. While cTnT can be

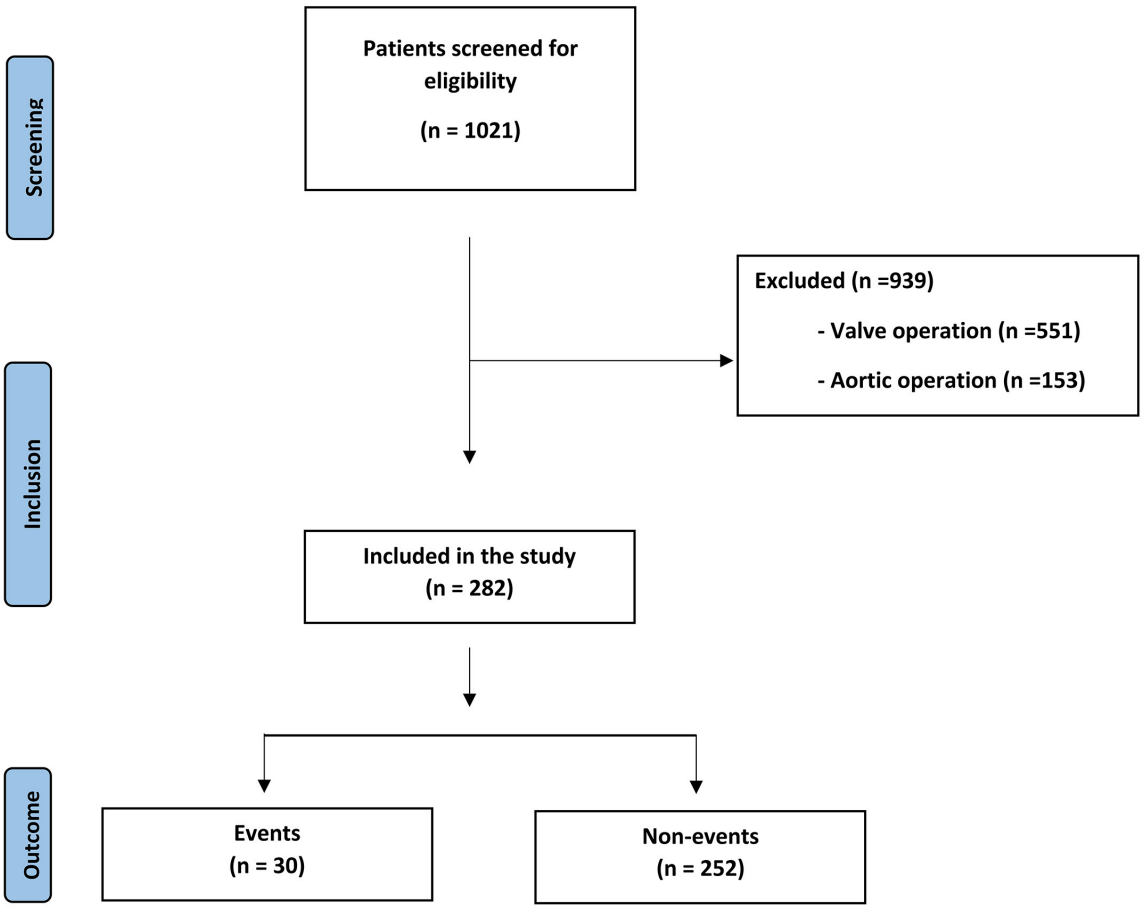

Fig. 1. Patient selection flow chart.

found in other body cells (e.g., skeletal muscles) besides cardiac myocytes [8], cTnI exclusively is found in myocardial cells. Injured cardiac myocytes release unbound cytoplasmic troponin, and its plasma level increases 4–6 h post-injury, reaching the peak 12–24 h post-injury. A second peak occurs 2–4 days post-injury [9].

Elevated concentrations of BNP [10,11] and cardiac troponins [12–14], during the early postoperative period following CABG, significantly have been associated with the occurrence of post-discharge major adverse events and mortality.

To improve the predictive performance of the currently used risk stratification models, previous studies assessed the addition of biomarkers, such as troponin and BNP to EuroSCORE [15].

However, most studies that assessed prognostic biomarkers or models for predicting short- and long-term outcomes, following CABG, did not consider the potential influence of perioperative risk factors or complications [16,17]. Hence, there still is a gap in knowledge regarding the prognostic value of these biomarkers and risk stratification models after adjusting for relevant perioperative factors.

Therefore, the present study was conducted to assess the independent value of postoperative cTnI and BNP to predict the outcome after CABG with adjustment for preoperative risk estimates and postoperative complications and to report risk stratification gains, when considering EuroSCORE combined with postoperative biomarkers.

Patients and Methods

Study design and settings: This retrospective cohort study enrolled patients who underwent CABG at Madinah Cardiac Centre MCC Hospital during the period from January 2018 to December 2021. The protocol of the study was approved by the Research Ethics Committee of General Directorate of Health Affairs in Madinah National Registration Number (IRB22-107). Confidentiality of the participants' data was ensured by keeping the data sheets anonymous after assigning a code number specific to each patient, which was known only by the investigators.

Eligibility criteria: This study included all patients who underwent CABG surgery only, during the period from January 2018 to December 2021. Patients were excluded if they underwent combined intervention (e.g., valvular replacement and aortic surgery), the measurements of the biomarkers were unavailable or loss of follow up.

Table 1. Baseline and preoperative characteristics of the studied patients.

Baseline and preoperative characteristics		Total (n = 282)	Non-events (n = 252)	Events (n = 30)	*p*-value
Age	Mean ± SD	60.0 ± 8.9	59.8 ± 8.9	61.8 ± 9.4	0.256 t
	Min–Max	39.0–81.0	39.0–81.0	40.0–78.0	
Gender	Female	27 (9.6%)	23 (9.1%)	4 (13.3%)	0.507 X^2
	Male	255 (90.4%)	229 (90.9%)	26 (86.7%)	
BMI	Mean ± SD	28.5 ± 3.5	28.5 ± 3.3	29.0 ± 4.6	0.378 t
	Min–Max	20.0–44.7	20.0–44.7	24.0–44.0	
Surgical status	Elective	238 (84.4%)	217 (86.1%)	21 (70.0%)	0.031* X^2
	Urgent	44 (15.6%)	35 (13.9%)	9 (30.0%)	
Dyspnea	1	91 (32.3%)	85 (33.7%)	6 (20.0%)	0.209 X^2
	2	78 (27.7%)	68 (27.0%)	10 (33.3%)	
	3	100 (35.5%)	88 (34.9%)	12 (40.0%)	
	4	13 (4.6%)	11 (4.4%)	2 (6.7%)	
Medical history	CHF	78 (27.7%)	66 (26.2%)	12 (40.0%)	0.131 X^2
	IABP	43 (15.2%)	32 (12.7%)	11 (36.7%)	0.002* X^2
	Smoking	148 (52.5%)	134 (53.2%)	14 (46.7%)	0.564 X^2
	Dyslipidaemia	138 (48.9%)	124 (49.2%)	14 (46.7%)	0.793 X^2
	Diabetes	203 (72.0%)	178 (70.6%)	25 (83.3%)	0.143 X^2
	Hypertension	198 (70.2%)	178 (70.6%)	20 (66.7%)	0.653 X^2
	Hypothyroidism	23 (8.2%)	20 (7.9%)	3 (10.0%)	0.722 X^2
	Recent CVA	14 (5.0%)	11 (4.4%)	3 (10.0%)	0.177 X^2
	PVD	23 (8.2%)	15 (6.0%)	8 (26.7%)	0.001* X^2
	COPD	13 (4.6%)	12 (4.8%)	1 (3.3%)	1.000 X^2
	Unstable Angina	126 (44.7%)	112 (44.4%)	14 (46.7%)	0.817 X^2
	Recent MI	171 (60.6%)	148 (58.7%)	23 (76.7%)	0.057 X^2
Serum creatinine	Median [IQR]	90.0 [80.0–106.0]	89.2 [79.5–105.0]	97.0 [85.0–137.0]	0.055 Z
	Min–Max	51.0–471.0	51.0–471.0	67.0–201.0	
Preoperative ejection fraction, %	Mean ± SD	44.3 ± 9.5	45.3 ± 9.0	35.6 ± 9.3	<0.001* t
	Min–Max	20.0–65.0	20.0–65.0	25.0–55.0	
EuroSCORE II	Median [IQR]	1.89 [1.20–2.16]	1.87 [1.15–2.13]	2.17 [1.50–2.82]	0.002* t
	Min–Max	0.80–4.21	0.80–3.67	0.93–4.21	
Preoperative BNP (pg/mL)	Median [IQR]	258.0 [111.0–520.0]	241.0 [99.0–489.0]	439.7 [269.0–696.0]	0.001* Z
	Min–Max	12.6–1360.0	12.6–1360.0	107.0–1341.1	
Preoperative cTnI (ng/mL)	Median [IQR]	0.52 [0.04–2.13]	0.45 [0.04–1.60]	5.75 [0.44–9.20]	<0.001* Z
	Min–Max	0.01–50.00	0.01–50.00	0.01–35.77	

BMI, body mass index; BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; CHF, congestive heart failure; IABP, intra-aortic balloon pump; CVA, cerebrovascular accident; PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; IQR, interquartile range (25th–75th percentiles); n, number; Max, maximum; Min, minimum; SD, standard deviation; t, independent samples *T*-test; X^2, Pearson's Chi-square/Fisher's exact tests; Z, Mann-Whitney test; * significant at $p < 0.05$.

Analysis of cardiac biomarkers: The levels of BNP and cTnI were available for the included patients, both preoperatively and the peak postoperative level. The peak postoperative levels were obtained on postoperative days 2 for BNP and day 3 for cTnI.

Clinical endpoint: The primary endpoint was the composite outcome of all-cause mortality or the development of major adverse events after surgery, including myocardial infarction, need for subsequent cardiac intervention, congestive heart failure requiring hospitalization, revascularization, and cerebrovascular accidents.

Statistical analysis: Statistical analysis was performed using the Statistical Package for Social Sciences (IBM SPSS Statistics), version 26 for Windows (IBM Corp., Armonk, NY, USA).

The categorical variables (e.g., gender and urgency of surgery) were summarized as counts and percentages. The association of major adverse events with categorical variables were assessed using Pearson's Chi-Square test for independence of observation, Chi-Square test for trend, and Fisher's exact test.

The Shapiro-Wilk test was performed to determine the distribution of continuous numerical variables. Numerical variables that followed the normal distribution (e.g., age and ejection fraction) were summarized as the mean and standard deviation (SD) and compared between the groups

Table 2. Operative details and postoperative data of the studied patients.

Operative & postoperative data		Total (n = 282)	Non-events (n = 252)	Events (n = 30)	*p*-value
Grafts/Patient	1	7 (2.5%)	7 (2.8%)	0 (0.0%)	0.027* X^2
	2	105 (37.2%)	99 (39.3%)	6 (20.0%)	
	3	138 (48.9%)	119 (47.2%)	19 (63.3%)	
	4	32 (11.3%)	27 (10.7%)	5 (16.7%)	
Bypass time, min	Median [IQR]	92.0 [75.0–110.0]	90.0 [74.0–110.0]	111.0 [90.0–138.0]	<0.001* Z
	Min–Max	37.0–230.0	37.0–206.0	38.0–230.0	
C-clamp time, min	Median [IQR]	44.0 [25.0–59.0]	44.0 [25.5–59.0]	43.0 [25.0–60.0]	0.905 Z
	Min–Max	10.0–193.0	10.0–138.0	15.0–193.0	
Postoperative ejection fraction, %	Mean ± SD	45.7 ± 8.5	46.7 ± 7.8	37.0 ± 9.5	<0.001* t
	Min–Max	20.0–65.0	20.0–65.0	20.0–50.0	
Ventilation, day	Median [IQR]	4.0 [3.0–5.0]	3.0 [3.0–5.0]	5.0 [4.0–7.0]	<0.001* Z
	Min–Max	1.0–77.0	1.0–33.0	2.0–77.0	
Postoperative dyspnea	0	2 (0.7%)	2 (0.8%)	0 (0.0%)	<0.001* X^2
	1	197 (70.1%)	186 (73.8%)	11 (37.9%)	
	2	63 (22.4%)	54 (21.4%)	9 (31.0%)	
	3	19 (6.8%)	10 (4.0%)	9 (31.0%)	
Peak postoperative BNP (pg/mL)	0	2310.0 [1113.0–4480.0]	2110.0 [1050.0–4340.0]	2750.0 [1640.0–6092.0]	0.025* Z
	Min–Max	2.6–14988.0	2.6–14600.0	247.0–14988.0	
Peak postoperative cTnI (ng/mL)	Median [IQR]	1.13 [0.35–4.00]	1.01 [0.32–3.00]	8.04 [2.17–9.41]	<0.001* Z
	Min–Max	0.01–32.87	0.01–9.41	0.07 – 32.87	
Postoperative complications	Pneumonia	16 (5.7%)	12 (4.8%)	4 (13.3%)	0.175 X^2
	Sepsis	11 (3.9%)	8 (3.2%)	3 (10.0%)	0.100 X^2
	CVA	8 (2.8%)	6 (2.4%)	2 (6.7%)	0.205 X^2
	Renal impairment	39 (13.8%)	26 (10.3%)	13 (43.3%)	<0.001* X^2
	Dialysis/UltraFiltration	14 (5.0%)	8 (3.2%)	6 (20.0%)	0.001* X^2
	Low cardiac output	54 (19.1%)	37 (14.7%)	17 (56.7%)	<0.001* X^2
	Cardiac arrest	11 (3.9%)	8 (3.2%)	3 (10.0%)	0.100 X^2
	Atrial fibrillation	39 (13.8%)	29 (11.5%)	10 (33.3%)	0.003* X^2
	Ventricular fibrillation	17 (6.0%)	11 (4.4%)	6 (20.0%)	0.005* X^2
	Deep sternal wound infection	53 (18.8%)	44 (17.5%)	9 (30.0%)	0.097 X^2
Hospital stay, day	Median [IQR]	9.0 [7.0–12.0]	9.0 [7.0–12.0]	12.5 [11.0–17.0]	<0.001* Z
	Min–Max	5.0–77.0	5.0–70.0	6.0–77.0	
Follow up, month	Median [IQR]	21.0 [17.0–28.0]	21.0 [17.0–27.0]	22.0 [17.0–42.1]	0.241 Z
	Min–Max	3.0–52.0	3.0–52.0	12.0–51.0	

BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; CVA, cerebrovascular accident; IQR, interquartile range (25th–75th percentiles); n, number; Max, maximum; Min, minimum; SD, standard deviation; t, independent samples *T*-test; X^2, Pearson's Chi-square/Fisher's exact tests; Z, Mann-Whitney test; *significant at $p < 0.05$.

using the independent sample *t*-test. Numerical variables that did not follow the normal distribution were summarized as the median and interquartile range (IQR, expressed as 25th–75th percentiles) and comparisons between the groups were done using the Mann-Whitney test.

Receiver operating characteristics (ROC) curve analysis was performed to assess the predictive performance of the studied biomarkers and identify the optimal cutoff point. The cutoff points of the studied markers were then used to assess the impact of the levels of the biomarkers on the time to death in Kaplan-Meier curves and in further logistic regression models to predict the composite outcome.

Binomial logistic regression analysis was conducted to assess the additive effect of the biomarkers on EuroSCORE II with adjustment for perioperative relevant factors with a *p*-value in the univariate analysis <0.1. We excluded from the models the factors that were used for calculating the EuroSCORE II (e.g., the urgency of surgery and ejection fraction). For each model, the c-index was calculated to assess its predictive performance and the information criterion (AIC) to assess the model fit. A *p*-value < 0.05 was adopted to indicate statistical significance.

Results

During the study duration, 1021 patients underwent adult cardiac operations and were screened for eligibility. We excluded 939 patients (551 patients underwent valve operation and 153 underwent aortic operation). The re-

maining 282 patients were included in the present study (Fig. 1). The duration of follow up after surgery varied from 3 months to 52 months, with a median [IQR] duration of 21 [17–28] months. During the follow up, 30 (10.6%) patients had major adverse events, including mortality in five (1.8%) cases, stroke in two (0.7%) cases, revascularization in four (1.4%), and rehospitalization for MI or heart failure in 19 (6.7%) cases.

Patients were categorized, according to their outcome into two groups: the non-events group ($n = 252$) and events group ($n = 30$). Table 1 compares the baseline and preoperative data of the patients in both groups (Table 1). The two groups were comparable, regarding age, gender distribution, body mass index (BMI), smoking, dyspnea status, medical history of DM, hypertension, dyslipidemia, hypothyroidism, COPD, recent CVA, and MI, and serum creatinine level (all $p > 0.05$). The occurrence of adverse events was significantly associated with the urgency of surgery ($p = 0.031$), IABP ($p = 0.002$), and PVD ($p = 0.001$). Moreover, the events group showed significantly lower preoperative EF ($p < 0.001$) as well as higher preoperative EuroSCORE II ($p = 0.002$), BNP ($p = 0.001$), and cTnI ($p < 0.001$) compared with the non-events group.

Regarding the operative and postoperative data of the studied patients, the events group was significantly associated with a higher number of grafts ($p = 0.027$), a longer BP time ($p < 0.001$), lower postoperative EF ($p < 0.001$), longer duration of ventilation ($p < 0.001$), and more severe grades of dyspnea ($p < 0.001$). In addition, the events group showed a significantly higher percentage of some postoperative complications including renal impairment ($p < 0.001$), need for dialysis ($p = 0.001$), low cardiac output ($p < 0.001$), atrial fibrillation ($p = 0.003$), and ventricular fibrillation ($p = 0.005$). The length of hospital stay was significantly longer in the events group ($p < 0.001$). The peak postoperative BNP and cTnI levels were significantly higher in the events group compared with the non-events group ($p = 0.025$ and $p < 0.001$, respectively). There was no significant difference in the duration of follow up between the two groups ($p = 0.241$) (Table 2).

Analysis of the ROC curve was performed to assess the predictive performance of postoperative peak BNP and cTnI and identify an optimal cutoff value (Fig. 2, Table 3). The area under the ROC curve (AUROC) for cTnI was significantly higher than that of BNP (0.777 *vs.* 0.625, $p = 0.041$). The optimal cutoff values to predict events were >4830 (pg/mL) and >6.95 (ng/mL) for BNP and cTnI, respectively.

Kaplan-Meier curves were constructed to assess the impact of peak postoperative BNP and cTnI (using the identified cutoff values) on the time-to-death occurrence (Figs. 3,4 and Table 4). The log rank test showed a lack of significant difference between the biomarkers groups of the cutoff values ($p > 0.05$).

In order to assess the effect of adding the studied biomarkers to EuroSCORE II, we first carried out univariate binomial logistic regression analysis for each parameter (models 1–3) (Table 5). Then, we attempted to combine

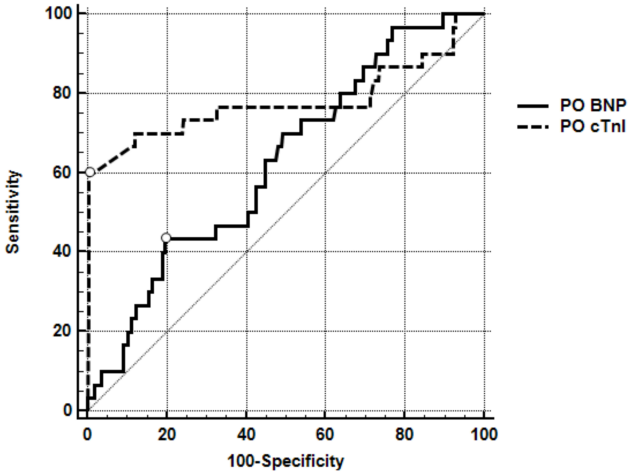

Fig. 2. Receiver operating characteristics curve for postoperative BNP and cTnI as predictors of outcome. BNP, B-type natriuretic peptide; cTnI, cardiac troponin I.

Table 3. Predictive performance of postoperative BNP and cTnI in the studied patients (ROC curve analysis).

	Postoperative BNP	Postoperative cTnI
AUROC	0.625	0.777
SE	0.052	0.064
95% CI	0.523–0.727	0.651–0.904
p-value (AUROC = 0.5)	0.016*	<0.001*
Youden index J	0.2381	0.5960
Cut-off value	>4830	>6.95
Sensitivity (%)	43.3	60.0
Specificity (%)	80.5	99.6

BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; ROC, receiver operating characteristics; AUROC, area under the ROC curve; CI, confidence interval of AUROC; SE, standard error of AUROC.

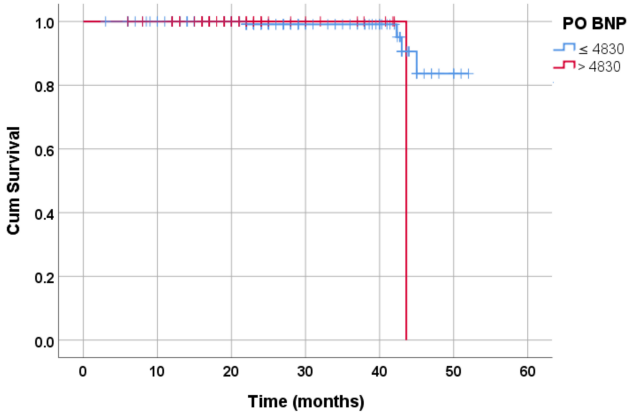

Fig. 3. Kaplan-Meier curve for overall survival according to postoperative BNP groups. BNP, B-type natriuretic peptide.

Table 4. Mean time to death (month) according to the levels of postoperative BNP and cTnI.

Groups	Mean	SE	95% CI	1-year OS% (SE)	3-year OS% (SE)	5-year OS% (SE)	*p*-value
Postoperative BNP ≤4830	50.45	0.74	49.00–51.89	100 (0)	99.1 (0.9)	83.6 (8.6)	0.195
Postoperative BNP >4830	43.60	0.00	43.60–43.60	100 (0)	100 (0)	100 (0)	
Postoperative cTnI ≤6.95	50.70	0.74	49.24–52.15	100 (0)	99.2 (0.8)	87.0 (8.2)	0.175
Postoperative cTnI >6.95	47.66	1.77	44.19–51.13	100 (0)	100 (0)	53.3 (24.8)	
Overall	50.10	0.79	48.56–51.65	100 (0)	99.2 (0.7)	79.1 (9.3)	

BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; CI, confidence interval; SE, standard error; *significant at $p < 0.05$.

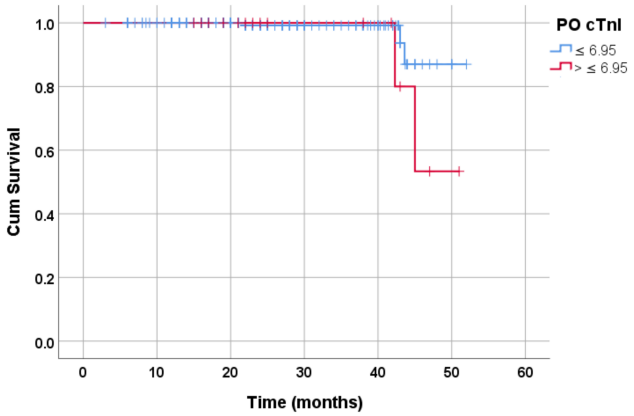

Fig. 4. Kaplan-Meier curve for overall survival according to postoperative cTnI groups. cTnI, cardiac troponin I.

each biomarker with EuroSCORE II separately (Table 5, models 4 and 5). Lastly, we created two models (Table 5, models 6 and 7) that each included one biomarker with the EuroSCORE II plus adjusting for preoperative, operative, and postoperative relevant data that were significant on univariate analysis in Tables 1,2. Models 6 and 7 showed that both postoperative BNP (OR: 2.63, 95% CI: 1.03 to 6.73, $p = 0.044$) and cTnI (OR: 446.62, 95% CI: 40.41 to 4935.66, $p < 0.001$) independently were associated with the outcome. Model 7 showed the largest C-index among the created models (C-index = 0. 896), indicating higher discriminatory power in predicting major adverse events. Moreover, model 7 offered the best fit as a multivariate model as observed by having the AIC of 110.439.

Discussion

There is a need to identify high-risk patients, who may develop major adverse events after undergoing CABG to initiate prompt therapeutic interventions. Although several studies assessed the predictive performance of postoperative BNP and cTnI in patients following CABG surgery, limited data is available, regarding the additive value of these biomarkers when combined with EuroSCORE and/or when the perioperative factors are adjusted for.

The present study aimed to assess the independent value of postoperative cTnI and BNP to predict the outcome after CABG with adjustment for preoperative risk estimates and postoperative complications and to report risk stratification gains when considering the EuroSCORE combined with postoperative biomarkers. We preferred to assess cTnI rather than cTnT as cTnI is specific for myocardial injury, while cTnT is released also upon injury to some non-cardiac tissues [8].

The postoperative peak cTnI showed a significantly higher predictive performance than that of peak postoperative BNP (0.777 *vs.* 0. 625, $p = 0.041$). The optimal cutoff values to predict the composite outcome in our sample were >4830 (pg/mL) and >6.95 (ng/mL) for BNP and cTnI, respectively. These findings were confirmed by the results of logistic regression analysis, which showed that the peak postoperative levels of BNP (OR: 2.63, 95% CI: 1.03 to 6.73, $p = 0.044$) and cTnI (OR: 446.62, 95% CI: 40.41 to 4935.66, $p < 0.001$) were independent prognostic factors for the composite outcome. Previous studies support our results regarding postoperative BNP and cTnI as predictors of major adverse outcomes [11,18,19], though the studies varied in their definitions of the composite outcome.

However, we found that the peak postoperative levels of both biomarkers showed no significant impact on the time to death and overall survival in the studied patients. In line with our findings, Fox *et al.* [10] found that the peak postoperative BNP did not predict mortality after CABG surgery (HR = 1.62, 95% CI = 0.71–3.68, $p = 0.25$). These findings contradict the results of previous studies, which reported that postoperative BNP [19–21] and cardiac troponins [18,22–24] were significant independent predictors of perioperative myocardial infarction as well as short- and long-term all-cause mortality. The rate of mortality was relatively lower in our sample than in the other studies, which may be partially explained by the exclusion of patients undergoing other concomitant cardiac surgeries besides CABG. Consequently, the impact of elevated biomarkers levels on the time to death and overall survival was not significant. In addition, variations in the characteristics of populations, blood sample timing, and the used laboratory assays can contribute to the differences in findings across the studies.

Regarding the additive effect of the studied biomarkers on EuroSCORE II in the present study, both markers showed improved predictive performance as indicated by the c-index of the models, which was evident also in adjust-

Table 5. Logistic regression models for predicting MACE in patients after coronary artery bypass grafting.

Models	Independent variables	*p*-value	OR	95% CI of OR	C-index	AIC
Univariate models						
Model 1	EuroSCORE II	0.002*	2.27	1.33–3.85	0.660	185.923
Model 2	Postoperative BNP >4830	0.004*	3.15	1.44–6.92	0.617	194.914
Model 3	Postoperative cTnI >6.95	0.005*	18.00	2.40–134.83	0.798	109.373
Multivariate models						
Model 4	EuroSCORE II	0.011*	2.01	1.17–3.46	0.662	187.526
	Postoperative BNP >4830	0.025*	2.55	1.13–5.78		
Model 5	EuroSCORE II	0.954	1.03	0.45–2.35	0.802	111.370
	Postoperative cTnI >6.95	<0.001*	370.29	42.40–3234.13		
Model 6	EuroSCORE II	0.442	1.29	0.68–2.43	0.773	177.220
	Postoperative BNP >4830	0.044*	2.63	1.03–6.73		
	PVD	0.157	2.40	0.71–8.07		
	Grafts	0.006*	1.02	1.01–1.03		
	Bypass time, min	0.589	0.83	0.41–1.65		
	Postop Renal impairment	0.043*	2.97	1.03–8.53		
	Deep sternal wound infection	0.236	1.85	0.67–5.10		
Model 7	EuroSCORE II	0.408	0.658	0.244–1.775	0.896	110.439
	Postoperative cTnI >6.95	<0.001*	446.62	40.41–4935.66		
	PVD	0.167	3.11	0.62–15.49		
	Grafts	0.566	1.01	0.99–1.03		
	Bypass time, min	0.836	1.11	0.42–2.89		
	Postop Renal impairment	0.021*	5.34	1.29–22.19		
	Deep sternal wound infection	0.925	1.07	0.24–4.74		

BNP, B-type natriuretic peptide; cTnI, cardiac troponin I; IABP, intra-aortic balloon pump; PVD, peripheral vascular disease; AIC, Akaike information criterion; CI, confidence interval of odds ratio; OR, odds ratio; *significant at $p < 0.05$.

ing for the relevant potentially significant perioperative factors. We did not include some postoperative cardiac complications (e.g., low cardiac output, arrest, arrhythmias) in the models as these complications will mostly be reflected in the levels of the studied biomarkers.

Few studies have assessed the additive value of postoperative BNP and/or cardiac troponin to EuroSCORE as predictors of major adverse events after CABG [11,15,19,20,25]. Still, fewer studies have adjusted for relevant postoperative complications in assessing the prognostic models with the biomarkers [15,19].

Fellahi *et al.* [11] conducted their study on 224 patients who underwent cardiac surgery and were followed for 12 months after surgery. They defined the outcome (major adverse cardiac events [MACE]) as malignant ventricular arrhythmia, myocardial infarction, congestive heart failure, the need for myocardial revascularization, and/or death from a cardiac cause within 12 months after surgery. A multivariate analysis that included EuroSCORE revealed that elevated levels of C-reactive protein (>180 mg/L, OR: 2.14 [95% CI: 1.03–4.49], $p = 0.043$), cTnI (>3.5 ng/mL, OR: 2.37 [95% CI: 1.25–5.64], $p = 0.011$), and BNP (>880 pg/mL, OR: 2.65 [95% CI: 1.16–4.85], $p = 0.018$) independently predicted the outcome.

Lurati Buse *et al.* [20] assessed cTnT in 741 patients, who underwent on-pump cardiac surgery. The composite endpoint was all-cause mortality or any major adverse cardiac event (myocardial infarction, need for subsequent surgical or percutaneous coronary intervention, and congestive heart failure requiring hospitalization) at 12 months. Multivariate analysis included continuous cTnT and the continuous logistic EuroSCORE, and it revealed that a 0.1 μg/L increase in cTnT was significantly and independently associated with the composite endpoint (OR: 1.03, 95% CI: 1.02–1.04). The AUC for the model as a predictor of the composite endpoint was 0.72, which was significantly higher than that of EuroSCORE alone (AUC = 0.64, $p < 0.001$).

Petäjä *et al.* [25] studied high-sensitivity troponin T (Hs-cTnT) in 648 patients undergoing CABG and other cardiac surgeries. The studied endpoints included 180-day mortality, 961-day mortality, and any major adverse event within 30 days (including any cardiac or neurological complication in the ICU, renal complication within 5 days, death, or ICU readmission). They found that cTnT measurements combined with EuroSCORE improved the prediction of the 30-day major adverse events (AUROC: 0.728 *vs.* 0.750) and the 180-day mortality (AUROC: 0.788 *vs.* 0.807) in CABG patients.

Lurati Buse *et al*. [15] enrolled 1559 patients undergoing on-pump cardiac surgery. The primary endpoint was the composite outcome of all-cause mortality or the occurrence of non-fatal MACE within 1 year after surgery (including myocardial infarction, cardiac arrest, need for subsequent surgical or percutaneous coronary intervention, and congestive heart failure requiring hospitalization). They found a significant association of the elevated postoperative BNP and cTnT levels with the composite outcome. The significant association persisted after adjustment of the preoperative and postoperative confounders and improved risk stratification by EuroSCORE.

Mauermann *et al*. [26] assessed HS cTnT in 1155 patients undergoing on-pump cardiac surgery as a predictor of 30-day all-cause mortality as well as 30-day MACE. The predefined MACE included acute coronary syndrome, cardiac arrest, congestive heart failure requiring rehospitalization, and coronary revascularization by either percutaneous coronary intervention or surgery. They found that adding HS cTnT to EuroSCORE II significantly increased the AUROC of predicting 30-day mortality from 0.816 to 0.870. Moreover, HS cTnT predicted mortality within 12 months and the 30-day MACE. In another study on 1199 patients, Mauermann *et al*. [19] assessed the addition of postoperative BNP to EuroSCORE with adjustment for intraoperative factors. They reported an improved prediction of 12-month MACE (which was defined as non-fatal cardiac arrest, myocardial infarction, and congestive heart failure).

The present study possesses several points of strength. First, measurements of postoperative BNP and cTnI were available for all included patients. Second, the extended follow-up period ($\geq$17 months in 75% and $\geq$28 months in 25% of patients) allowed for the assessment of the predictive models for long-term outcomes. Third, we employed cTnI, which is more specific than the cTnT used in some previous studies. Fourth, we adjusted for the postoperative complications in the predictive models, which were overlooked in most previous studies. Postoperative complications are bound to increase the concentrations of BNP and cTnI. The persistence of the significance of the biomarkers' effects after adjusting for the postoperative complications allowed for the estimation of the biomarkers' additive values.

Meanwhile, our study was prone to some limitations. As the study design was retrospective, the recording of some studied outcomes may be missing from the patients' files. Also, differences in the used laboratory assay for the same biomarker may have occurred.

Conclusions

Both postoperative BNP and cTnI added significantly to the prognostic value of EuroSCORE II in predicting long-term major adverse outcomes, even when relevant perioperative confounders and complications were adjusted for. The predictive performance of the model combining cTnI and EuroSCORE II is better than that of the EuroSCORE II + BNP model. The two biomarkers have several advantages, being non-invasive and easily obtained. Their use in combination with EuroSCORE II will allow for early identification of patients at high risk of long-term mortality and/or major adverse events after undergoing CABG.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

ARA, FaiAA and FarAA designed and gave the main idea of research study. MSHU, HIS, HRA, ASSA and RAA performed the research and collected the data. HMA, WMA, and AMS analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the Research Ethics Committee of the General Directorate of Health Affairs in Madinah National Registration Number (IRB22-107), confidentiality of the participants' data was ensured by keeping the data sheets anonymous after assigning a code number specific to each patient, which is known only by the investigators.

Acknowledgment

Not applicable.

Funding

This research received no external funding.

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Bachar BJ, Manna B. Coronary Artery Bypass Graft. StatPearls Publishing: Treasure Island (FL). 2023.

[2] Reiche S, Mpanya D, Vanderdonck K, Mogaladi S, Motshabi-Chakane P, Tsabedze N. Perioperative outcomes of coronary artery bypass graft surgery in Johannesburg, South Africa. Journal of Cardiothoracic Surgery. 2021; 16: 7.

[3] Saraiya NR, Sun LS, Jonassen AE, Pesce MA, Queagebeur JM. Serum cardiac troponin-I elevation in neonatal cardiac surgery is lesion-dependent. Journal of Cardiothoracic and Vascular Anesthesia. 2005; 19: 620–625.

[4] Fox AA, Marcantonio ER, Collard CD, Thoma M, Perry TE, Shernan SK, *et al*. Increased peak postoperative B-type natriuretic peptide predicts decreased longer-term physical function after primary coronary artery bypass graft surgery. Anesthesiology. 2011; 114: 807–816.

[5] Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). European Journal of Cardio-Thoracic Surgery. 1999; 16: 9–13.

[6] Nashef SAM, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, *et al*. EuroSCORE II. European Journal of Cardio-Thoracic Surgery. 2012; 41: 734–745.

[7] Omran F, Kyrou I, Osman F, Lim VG, Randeva HS, Chatha K. Cardiovascular Biomarkers: Lessons of the Past and Prospects for the Future. International Journal of Molecular Sciences. 2022; 23: 5680.

[8] Stark M, Kerndt CC, Sharma S. Troponin. StatPearls Publishing: Treasure Island (FL). 2022.

[9] Wolfe Barry JA, Barth JH, Howell SJ. Cardiac troponins: their use and relevance in anaesthesia and critical care medicine. Continuing Education in Anaesthesia Critical Care & Pain. 2008; 8: 62–66.

[10] Fox AA, Muehlschlegel JD, Body SC, Shernan SK, Liu KY, Perry TE, *et al*. Comparison of the utility of preoperative versus postoperative B-type natriuretic peptide for predicting hospital length of stay and mortality after primary coronary artery bypass grafting. Anesthesiology. 2010; 112: 842–851.

[11] Fellahi JL, Hanouz JL, Le Manach Y, Gué X, Monier E, Guillou L, *et al*. Simultaneous measurement of cardiac troponin I, B-type natriuretic peptide, and C-reactive protein for the prediction of long-term cardiac outcome after cardiac surgery. Anesthesiology. 2009; 111: 250–257.

[12] Ma QL, Wang HJ, Shi MN, An JH, Ma J, Yu D, *et al*. Serum troponin I concentrations assessed 18-24 hours after coronary artery bypass grafting are significant predictors of early patient prognosis. European Review for Medical and Pharmacological Sciences. 2016; 20: 4129–4135.

[13] Devereaux PJ, Lamy A, Chan MTV, Allard RV, Lomivorotov VV, Landoni G, *et al*. High-Sensitivity Troponin I after Cardiac Surgery and 30-Day Mortality. The New England Journal of Medicine. 2022; 386: 827–836.

[14] Søraas CL, Friis C, Engebretsen KVT, Sandvik L, Kjeldsen SE, Tønnessen T. Troponin T is a better predictor than creatine kinase-MB of long-term mortality after coronary artery bypass graft surgery. American Heart Journal. 2012; 164: 779–785.

[15] Lurati Buse GAL, Bolliger D, Seeberger E, Kasper J, Grapow M, Koller MT, *et al*. Troponin T and B-type natriuretic peptide after on-pump cardiac surgery: prognostic impact on 12-month mortality and major cardiac events after adjustment for postoperative complications. Circulation. 2014; 130: 948–957.

[16] Kubota H, Miyata H, Motomura N, Ono M, Takamoto S, Harii K, *et al*. Deep sternal wound infection after cardiac surgery. Journal of Cardiothoracic Surgery. 2013; 8: 132.

[17] Tolpin DA, Collard CD, Lee VV, Virani SS, Allison PM, Elayda MA, *et al*. Subclinical changes in serum creatinine and mortality after coronary artery bypass grafting. The Journal of Thoracic and Cardiovascular Surgery. 2012; 143: 682–688.e1.

[18] Nesher N, Alghamdi AA, Singh SK, Sever JY, Christakis GT, Goldman BS, *et al*. Troponin after cardiac surgery: a predictor or a phenomenon? The Annals of Thoracic Surgery. 2008; 85: 1348–1354.

[19] Mauermann E, Bolliger D, Fassl J, Grapow M, Seeberger EE, Seeberger MD, *et al*. Absolute Postoperative B-Type Natriuretic Peptide Concentrations, but Not Their General Trend, Are Associated With 12-Month, All-Cause Mortality After On-Pump Cardiac Surgery. Anesthesia and Analgesia. 2017; 125: 753–761.

[20] Lurati Buse GA, Koller MT, Grapow M, Brüni CM, Kasper J, Seeberger MD, *et al*. 12-month outcome after cardiac surgery: prediction by troponin T in combination with the European system for cardiac operative risk evaluation. The Annals of Thoracic Surgery. 2009; 88: 1806–1812.

[21] Fox AA, Nascimben L, Body SC, Collard CD, Mitani AA, Liu KY, *et al*. Increased perioperative b-type natriuretic peptide associates with heart failure hospitalization or heart failure death after coronary artery bypass graft surgery. Anesthesiology. 2013; 119: 284–294.

[22] Adabag AS, Rector T, Mithani S, Harmala J, Ward HB, Kelly RF, *et al*. Prognostic significance of elevated cardiac troponin I after heart surgery. The Annals of Thoracic Surgery. 2007; 83: 1744–1750.

[23] Croal BL, Hillis GS, Gibson PH, Fazal MT, El-Shafei H, Gibson G, *et al*. Relationship between postoperative cardiac troponin I levels and outcome of cardiac surgery. Circulation. 2006; 114: 1468–1475.

[24] Lurati Buse GA, Koller MT, Grapow M, Bolliger D, Seeberger M, Filipovic M. The prognostic value of troponin release after adult cardiac surgery - a meta-analysis. European Journal of Cardio-Thoracic Surgery. 2010; 37: 399–406

[25] Petäjä L, Røsjø H, Mildh L, Suojaranta-Ylinen R, Kaukonen KM, Jokinen JJ, *et al*. Predictive value of high-sensitivity troponin T in addition to EuroSCORE II in cardiac surgery. Interactive Cardiovascular and Thoracic Surgery. 2016; 23: 133–141.

[26] Mauermann E, Bolliger D, Fassl J, Grapow M, Seeberger EE, Seeberger MD, *et al*. Postoperative High-Sensitivity Troponin and Its Association With 30-Day and 12-Month, All-Cause Mortality in Patients Undergoing On-Pump Cardiac Surgery. Anesthesia and Analgesia. 2017; 125: 1110–1117.