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Usefulness of postoperative high-sensitive troponin T measurement and implications for defining type 5 infarction

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Abstract

Background and aim of the study: Guidelines indicate for type 5 myocardial infarction (MI) that postoperative troponin need not be exclusively ischemic but may also be caused by epicardial injury. Complexity arises from the introduction of high-sensitive troponin. This study attempts to contribute to the understanding of postoperative high-sensitive cardiac troponin T (hs-cTnT) increase.

Methods: The median enzyme increase of different cardiac operations was compared. Linear regression analyses were used to determine correlations between enzyme rise and independent parameters. Receiver-operating characteristics (ROC) served to evaluate the discriminatory power of enzyme rise in detecting ischemia and to determine possible thresholds.

Results: Among 400 patients, 2.8% had intervention-related ischemia analogous to type 5 MI definition. The median postoperative hs-cTnT/creatine kinase myocardial band (CK-MB) increase varied according to types of surgery, with highest increase after mitral valve and lowest after off-pump coronary surgery. After ruling out patients with preoperatively elevated hs-cTnT, regression analysis confirmed Maze procedure ($p < .001$), intra-pericardial defibrillation ($p = .002$), emergency intervention ($p = .01$), blood transfusions ($p = .02$), and cardiopulmonary bypass time ($p = .03$) as significant factors associated with hs-cTnT increase. In addition, CK-MB increase was associated with mortality ($p = .002$).

ROC confirmed good discriminatory power for hs-cTnT and CK-MB with ischemia-indicating thresholds of 1705.5 ng/L (hs-cTnT) and 113 U/L (CK-MB) considering different types of operations.

Conclusions: The Influence of the type of surgery and intervention-related parameters on hs-cTnT increase was confirmed. Potential thresholds indicating perioperative ischemia appear to be significantly elevated for high sensitive markers.

KEYWORDS
cardiovascular pathology, cardiovascular research, coronary artery disease, valve repair/replacement

1 | INTRODUCTION

The European society of cardiology (ESC) state that "for the detection of type 5 myocardial infarction (MI), a specific cut-off value for all procedures and all cardiac troponin (cTn) assays is difficult to define." According to them, coronary artery bypass grafting (CABG)-related MI is defined by an increase of cTn more than 10 times the 99th percentile upper reference limit (URL) during the first 48 h after surgery (in patients with normal baseline cTn) with one of the following: (1). Development of new Q waves (the authors explicitly include ECG changes in the form of ST-segment elevation with reciprocal depression and new-onset left bundle branch block), (2) angiographic documented graft or coronary occlusion, (3) imaging evidence of loss of viable myocardium or regional wall motion abnormality.[1] The authors point out the existing complexity of type 5 MI diagnosis: "Postoperatively observed ST-segment deviations and T-wave changes as well as isolated cTn elevations indicate direct procedural epicardial injury rather than myocardial ischemia."[1]

The introduction of high-sensitive cTn assays has led to additional ambiguity. Several assays exist for the detection of two different regulatory proteins of the tropomyosin complex based on high-affinity antibodies specific for troponin T or I. An increase in sensitivity of the corresponding tests is usually accompanied by a loss of specificity, despite improved analytical performance. Accordingly, it appears difficult to classify postoperative high-sensitive cTn values with regard to the clinical course.

The aim of this study, intentionally including different cardiac surgeries, is to investigate the postoperative increase in high-sensitive cardiac troponin T (hs-cTnT) in relation to the type of operation and to pre- and procedural factors. These data are analyzed with consideration of adverse postoperative events, with emphasis on the detection of myocardial ischemia.

Because there are no general guidelines or thresholds for acceptable enzyme elevations after various cardiac surgical procedures, analysis and discussion are performed with reference to the ESC criteria of type 5 MI (a comparative analysis considering only CABG patients is provided as a supplement). Furthermore, an attempt is made to determine possible postoperative enzyme thresholds indicative of surgically induced myocardial ischemia.

2 | MATERIALS AND METHODS

The institutional review board ensured ethics approval in accordance with international recommendations. According to the decision of the Ethics Committee, (protocol number 2016-01884) patient consent was waived.

Patients were operated by two surgeons in 2016/2017. All major cardiac interventions, except surgery for terminal heart failure (assist devices, transplantation) or acute aortic disease (dissection), were included. Follow-up focused on 30 days after surgery and documented adverse events: Mortality, type 5 MI (which requires a significant hs-cTnT increase by analogy with ESC guidelines, although the threshold needs to be further defined), stroke, changes in ventricular function, and new ECG modifications.

Other parameters that could have an impact on enzyme elevation were also considered: Demographics and risk factors, that is, preoperative MI, European System for Surgical Cardiac Risk Evaluation (EuroSCORE II), renal function, and so forth, direct surgery-related factors, that is, type of cardioplegia, cross-clamp and cardiopulmonary bypass time, blood transfusions, intra-pericardial defibrillation, and so forth, and type of surgery.

Cardiac enzymes, that is, hs-cTnT and creatine kinase myocardial band (CK-MB), were recorded before and 1, 6, 12, 24 to at least 48 h after surgery. The hs-cTnT assay used (Elecsys Troponin T high sensitive by Roche) has the following specifications: 99th percentile URL is 14 nanogram per liter (ng/L) with a precision value (coefficient of variation ≤10%) of 13 ng/L, a limit of detection at 5 ng/L, and a blank at 3 ng/L.[2] CK-MB was measured in international units and its concentration expressed in units per liter (U/L).

Pre- and postoperative echocardiography was performed in all patients, with a focus on new ventricular dysfunction (considered significant if it had worsened by at least one grade according to the EuroSCORE classification) or new regional wall motion abnormalities attributable to coronary perfusion territories.[3]

2.1 | Type 5 MI

All patients with new ECG changes (according to the type 5 MI criteria mentioned above) not directly related to surgical technique and/or with echocardiographic criteria, and concomitant elevated postoperative hs-cTnT and CK-MB, were identified.

2.2 | Thresholds for type 5 MI

Receiver-operating characteristics (ROC), respectively, the area under the ROC curves (AUROC) were determined to investigate the discriminatory power of postoperative enzyme increase to identify ischemic events. The coordinates of the ROC curves were used to define potential thresholds that were as specific as possible (while maintaining high sensitivity) for ischemic events (closest point to the upper left corner).

2.3 | Determination of other non-type 5 MI-related factors influencing cardiac enzyme increase

Median postoperative hs-cTnT, respectively, CK-MB release was compared, depending on the type of surgery, to detect possible significant *differences*. To identify possible *correlations* between enzyme increase and independent parameters, linear regression analyses were performed, which also allowed comparison between hs-cTnT and CK-MB. Binary-coded thresholds for the hs-cTnT, respectively, for the combination of hs-cTnT and CK-MB, were *correlated* with binary-coded independent factors in logistic regression analyses.

2.4 | Statistical analysis

The SPSS 27.0 software package for Windows (SPSS Inc.) was used. Categorical variables are presented as numbers and proportions (%). Nonnormally distributed variables (Kolmogorov–Smirnov/Shapiro–Wilk test) are described by their median and interquartile range (IQR).

To identify significant *differences* in hs-cTnT increase, according to the type of surgery, the nonparametric Kruskal–Wallis test was used (significant at a *p* value of less than 0.05). If group differences were significant, their effect size was determined by calculating the correlation coefficient, the strength of which was determined following the definition of Cohen et al.[4] Linear regression analysis was used to identify *correlations* between enzyme release and potential cofactors. Logistic regression analysis was used to analyze *correlations* between hs-cTnT/CK-MB thresholds and binary coded parameters.

The authors had full access to the data and take responsibility for its integrity.

3 | RESULTS

Four hundred patients were prospectively enrolled during the 2-year study period. Demographic data, comorbidities, and risk profiles are presented in Table 1. All patients had 30 days follow-up. Mortality rate was 1.8% (*n* = 7; three deaths were cardiac-related), stroke rate was 3.3% (*n* = 13).

3.1 | Type of surgery and technical aspects (Table 1)

One hundred and sixty-eight patients (42%) underwent CABG, performed on-pump in 30% (*n* = 120) and off-pump in 12% (*n* = 48). One hundred and one patients (25%) had an isolated aortic valve replacement (AVR), 50 (13%) had combined surgery (AVR + CABG), and 56 (14%) had some form of mitral valve surgery (MVR). The remaining 25 patients (6%; Others) had surgery on the ascending aorta. Cold blood cardioplegia was predominantly used for myocardial protection (68%; *n* = 271). Surgical parameters included blood transfusions in 4.5% (*n* = 18), intra-pericardial defibrillations in 8% (*n* = 31), septal myectomies in 18% (*n* = 70, all in combination with AVR/AVR + CABG), maze procedures in 1% (*n* = 4), and left atrial appendage closure in 7% (*n* = 28) of all patients.

3.2 | Type 5 MI

Eighteen patients met the criteria for perioperative MI. Of these, seven already had significant enzyme elevation preoperatively, indicating ongoing infarction. This left 11 patients to whom definite perioperative ischemia could be assigned, corresponding to a perioperative MI rate of 2.8% (3.2% of those without preoperatively elevated hs-cTnT).

3.3 | Hs-cTnT/CK-MB increase depending on type of surgery

The median hs-cTnT release was 769 ng/: (IQR: 483–1306 ng/L). The median CK-MB release was 50 UL (IQR: 37–71 U/L). The Kruskal–Wallis test showed significant *differences* in hs-cTnT release depending on the type of surgery, with the AVR-CABG and MVR groups having the highest median values. The strongest significance was found in the pairwise comparison of off-pump CABG with AVR-CABG or with MVR (Table 2). Comparatively, the median CK-MB increase was also dependent on the type of surgery, with the MVR group consistently having the highest median rank (Table 2).

3.4 | Hs-cTnT/CK-MB thresholds (Arrows in Figure 1A,B)

The AUROC confirmed good discriminatory power of more than 95% for both hs-cTnT ($p < .001$, 95% CI: 92%–99%) and CK-MB ($p < .001$, 95% CI: 93%–99%) to identify patients with type 5 MI. The threshold was 1705.5 ng/L for hs-cTnT with 100% sensitivity and (1–0.12) 88% specificity, and 113 U/L for CK-MB with 91% sensitivity and (1–0.07) 93% specificity.

A corresponding CABG subgroup analysis was discarded because of the small number of events with definite perioperative ischemia (Table S1A).

3.5 | Associated factors

- *Linear regression of all patients* revealed a significant, positive *correlation of increased hs-cTnT* with type 5 MI, Maze procedure, cardiopulmonary bypass time, emergency intervention, perioperative blood transfusion, and intrapericardial defibrillation. In contrast, creatinine clearance and increasing age were inversely correlated (Tables 1A and S2).
- (In the *CABG subgroup*, a positive *correlation* was found for high risk and emergency interventions, mortality and cardiopulmonary bypass time (Tables S1A,B)].
- *Correlations for CK-MB increase* were somewhat similar, although creatinine clearance, emergency intervention, and blood transfusion had no effect. Moreover, the strongest correlation was for cardiopulmonary bypass time, and notably, increased CK-MB release was associated with mortality (Tables 1A and S2).
- (Also in the *CABG group, correlation concerning CK-MB* were initially similar to that of hs-cTnT. However, after exclusion of patients with preoperatively elevated cardiac enzymes, elevated

TABLE 1 Regression analysis

	All patients ($n = 400$)					Patients without preoperative hs-cTnT ↑ ($n = 349$)				
		(A) Linear		(B) Logistic (thresholds)			(A) Linear		(B) Logistic (thresholds)	
		hs-cTnT ↑	CK-MB ↑	hs-cTnT ≥ 1705.5 ng/L	hs-cTnT ≥ 1705 ng/L + CK-MB ≥ 113 U/L		hs-cTnT ↑	CK-MB ↑	hs-cTnT ≥ 1705.5 ng/L	hs-cTnT ≥ 1705 ng/L + CK-MB ≥ 113 U/L
Continuous	Median (IQR)	*p*				Median (IQR)	*p*			
Age (years)	**71 (64; 77)**	**.03**	**.03**			**71 (63; 77)**	**.03**	**.049**		
Weight (kg)	**78 (70; 89)**	.17	.77			**78 (69; 90)**	.07	.66		
Body surface (m^2)	**1.9 (1.76; 2.05)**	.16	.5			**1.9 (1.75, 2.05)**	.12	.44		
EuroSCORE II (%)	**1.83 (1.12; 3.29)**	.26	.08			**1.71 (1.09; 2.97)**	.11	.07		
Preoperative creatinine clearance (ml/min)	**72 (57; 93)**	.08	.99			**73 (57; 94)**	.08	.86		
Postoperative creatinine clearance (ml/min)	**67 (49; 87)**	**.04**	.09			**68 (50; 89)**	.34	.12		
LVEF (%)										
Preoperative	**60 (50; 61)**	.3	.2			**60 (50; 62)**	.57	.3		
Postoperative	**55 (46; 60)**	.89	.39			**55 (49; 60)**	.93	.25		
Cardiopulmonary bypass time (min)	**96 (70; 126)**	**.01**	**.01**			**95 (70; 125)**	**.03**	**.03**		
Cross clamping time (min)	**76 (54; 100)**	.23	.68			**74 (55; 99)**	.71	.7		
Binary coded	No (%)	*p*				No (%)	*p*			
Gender/risk										
♂/♀	**292 (73)/108 (27)**	.35	.36	.46	.35	**246 (71)/103 (29)**	.47	.51	.58	.88
High risk (EuroSCORE II ≥7%)	**37 (9)**	.06	.07	.09	.44	**24 (7)**	.07	.23	.26	.17
Acute MI (≤7 days prior surgery)	**45**	.76	.71	.99	.99					
Impaired renal function										
Clearance <50 ml/min) preoperative	**53 (13)**	.95	.48	.4	.15	**45 (13)**	.49	.29	.22	.73
Clearance < 50 ml/min) postoperative	**97 (24)**	.61	.77	**.04**	**.004**	**82 (24)**	.93	.6	.16	.26
Emergency	**35 (9)**	**<.001**	.3	**.005**	.12	**12 (3)**	**.01**	.14	.2	.69
Procedure related										

TABLE 1 (Continued)

	All patients (n = 400)					Patients without preoperative hs-cTnT ↑ (n = 349)				
		(A) Linear		(B) Logistic (thresholds)			(A) Linear		(B) Logistic (thresholds)	
		hs-cTnT ↑	CK-MB ↑	hs-cTnT ≥ 1705.5 ng/L	hs-cTnT ≥ 1705 ng/L + CK-MB ≥ 113 U/L		hs-cTnT ↑	CK-MB ↑	hs-cTnT ≥ 1705.5 ng/L	hs-cTnT ≥ 1705 ng/L + CK-MB ≥ 113 U/L
Cardioplegia										
Cold blood	**271 (68)**	.78	.56	.68	.97	**240 (69)**	.81	.32	.99	1
Crystalloid	**81 (20)**	.59	.79	.52	.87	**71 (20)**	.7	.43	.99	1
Transfusion	**18 (4.5)**	**.008**	.07	.34	**.02**	**10 (3)**	**.02**	.07	.89	.2
Defibrillation	**31 (8)**	**.03**	**.02**	**<.001**	**.001**	**30 (9)**	**.002**	**.01**	**<.001**	**<.001**
Operative techniques										
CABG										
Off-pump	**48 (12)**	.77	.81			**36 (11)**	.76	.34		
On-pump	**120 (30)**	.22	.24	.85	.87	**94 (27)**	.05	.26	.99	1
AVR	**101 (25)**	.19	.42	.77	.33	**101 (29)**	.13	.13	.98	1
AVR + CABG	**50 (13)**	.28	.96	.25	.13	**43 (12)**	.15	.22	.99	1
MVR	**56 (14)**	.49	.77	.19	.05	**53 (15)**	.45	.63	.99	1
Others	**25 (6)**	.7	.4	.53	.99	**22 (6)**	.1	.05	.99	1
Myectomy	**70 (18)**	.36	.85	.29	.39	**68 (20)**	.52	.88	.32	.05
Left appendage closure	**28 (7)**	.52	.45	.2	.43	**27 (8)**	.22	.35	.11	.21
Maze procedure	**4 (1)**	**<.001**	**<.001**	**001**	.08	**4 (1.1)**	**<.001**	**<.001**	.99	.99
Single mammary	**145 (36)**	.42	.92	.45	.08	**115 (27)**	.08	.43	.09	.57
Double mammary	**71 (18)**	.41	.93	.98	.09	**55 (16)**	.14	.77	.42	.99
Outcome (30 days)										
Mortality	**7 (1.8)**	.3	**<.001**	**.03**	.42	**7 (2)**	.5	**.002**	.05	.53
Type 5 MI	**11 (2.8)**	**<.001**	**<.001**	.11	.3	**11 (3.2)**	**<.001**	**<.001**	**<.001**	.09
Stroke	**13 (3.3)**	.68	.47	.33	.93	**11 (3)**	.65	.61	.36	.65
LVEF										
Increase	**32 (8)**	.68	.77	.5	.69	**23 (7)**	.88	.99	.58	.5
Decrease	**24 (6)**	.12	.2	.09	.33	**18 (5)**	.62	.43	.99	.99
New wall motion ↓	**38 (10)**	.51	.34	.42	.16	**26 (7)**	.05	.37	.99	.99

(Continues)

TABLE 1 (Continued)

	All patients ($n = 400$)					Patients without preoperative hs-cTnT ↑ ($n = 349$)				
		(A) Linear		(B) Logistic (thresholds)			(A) Linear		(B) Logistic (thresholds)	
		hs-cTnT ↑	CK-MB ↑	hs-cTnT ≥ 1705.5 ng/L	hs-cTnT ≥ 1705 ng/L + CK-MB ≥ 113 U/L		hs-cTnT ↑	CK-MB ↑	hs-cTnT ≥ 1705.5 ng/L	hs-cTnT ≥ 1705 ng/L + CK-MB ≥ 113 U/L
ECG (LBBB, Q wave)	**12 (3)**	.78	.09	.66	.66	**6 (1.7)**	.79	.26	.99	.99
Atrial fibrillation	**78 (20)**	.59	.82	.17	.1	**63 (18)**	.82	.86	.15	.06

Note: Bold values indicate statistically significant results.

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass graft; CK-MB, creatine kinase myocardial band; MI, myocardial infarction; MVR, mitral valve replacement; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; *similar to the off-pump CABG group.

TABLE 2 Median enzyme increase depending on surgery

Type of intervention	No (%)	Median (IQR = Q3–Q1)	Mean rank	Kruskal–Wallis test asymptotic significance	Pairwise comparisons	Effect size/correlation coefficient r
(3A) hs-cTnT: all patients						
					Off-pump - on-pump: $p < .001$	.4
					Off-CABG - AVR: $p < .001$	.4
					Off-CABG - AVR/CABG: $p < .001$	**.7**
					Off-CABG - MVR: $p < .001$	**.7**
CABG						
Off-pump	48 (12)	328 (201–594)	101		Off-CABG - others: $p < .001$	.4
On-pump	120 (30)	776 (533–148)	203		On-CABG - AVR: $p = .38$	
Isolated AVR	101 (25)	728 (460–1173)	189		On-CABG - AVR/CABG: $p = .007$	0.2
AVR + CABG	50 (13)	1220 (710–1947)	255	$p < .0001$	On-CABG - MVR: $p = .008$	.2
MVR	56 (14)	1078 (642–2103)	253		On-CABG - others: $p = .91$	
Others	25 (6)	838 (482–1368)	200		AVR - AVR/CABG: $p = .001$	.3
					AVR - MVR: $p = .001$	.3

TABLE 2 (Continued)

Type of intervention	No (%)	Median (IQR = Q3–Q1)	Mean rank	Kruskal–Wallis test asymptotic significance	Pairwise comparisons	Effect size/correlation coefficient *r*
Total	400	769 (483–1306)			AVR - others: $p = .68$	
					AVR/CABG - MVR: $p = .92$	
					AVR/CABG - others: $p = .05$	
					MVR- others: $p = .06$	
(3B) hs-cTnT: without preoperative hs-cTnT↑						
					Off-CABG - on-CABG: $p < .001$	.5
					Off-CABG - AVR: $p < .001$	.5
					Off-CABG - AVR/CABG: $p < .001$	**.8**
					Off-CABG - MVR: $p < .001$	**.8**
CABG						
Off-pump	36 (10)	272 (159–407)	60		Off-CABG - others: $p < .001$	.5
On-pump	94 (27)	742 (501–1034)	169		On-CABG - AVR: $p = .78$	
Isolated AVR	101(29)	728 (460–1173)	174		On-CABG - AVR/CABG: $p = .004$	.25
AVR + CABG	43 (12)	1019 (687–1870)	223	$p < .0001$	On-CABG - MVR: $p = .001$	.3
MVR	53 (15)	1077 (625–2152)	229		On-CABG - others: $p = .99$	
Others	22 (6)	671 (474–1364)	170		AVR - AVR/CABG: $p = .007$	.2
					AVR - MVR: $p = .001$	.3
Total	349	746 (464–1188)			AVR - others: $p = .87$	
					AVR/CABG - MVR: $p = .75$	
					AVR/CABG - others: $p = .04$	.2
					MVR - others: $p = .02$	.3
(4A) CK-MB: all patients						
					Off-CABG - on-CABG: $p < .001$	.5
					Off-CABG - AVR: $p < .001$	.4
					Off-CABG - AVR/CABG: $p < .001$	**.7**
					Off-CABG - MVR: $p < .001$	**.9**
CABG						
Off-pump	48 (12)	27 (21–33)	79		Off-CABG - others: $p < .001$	.4

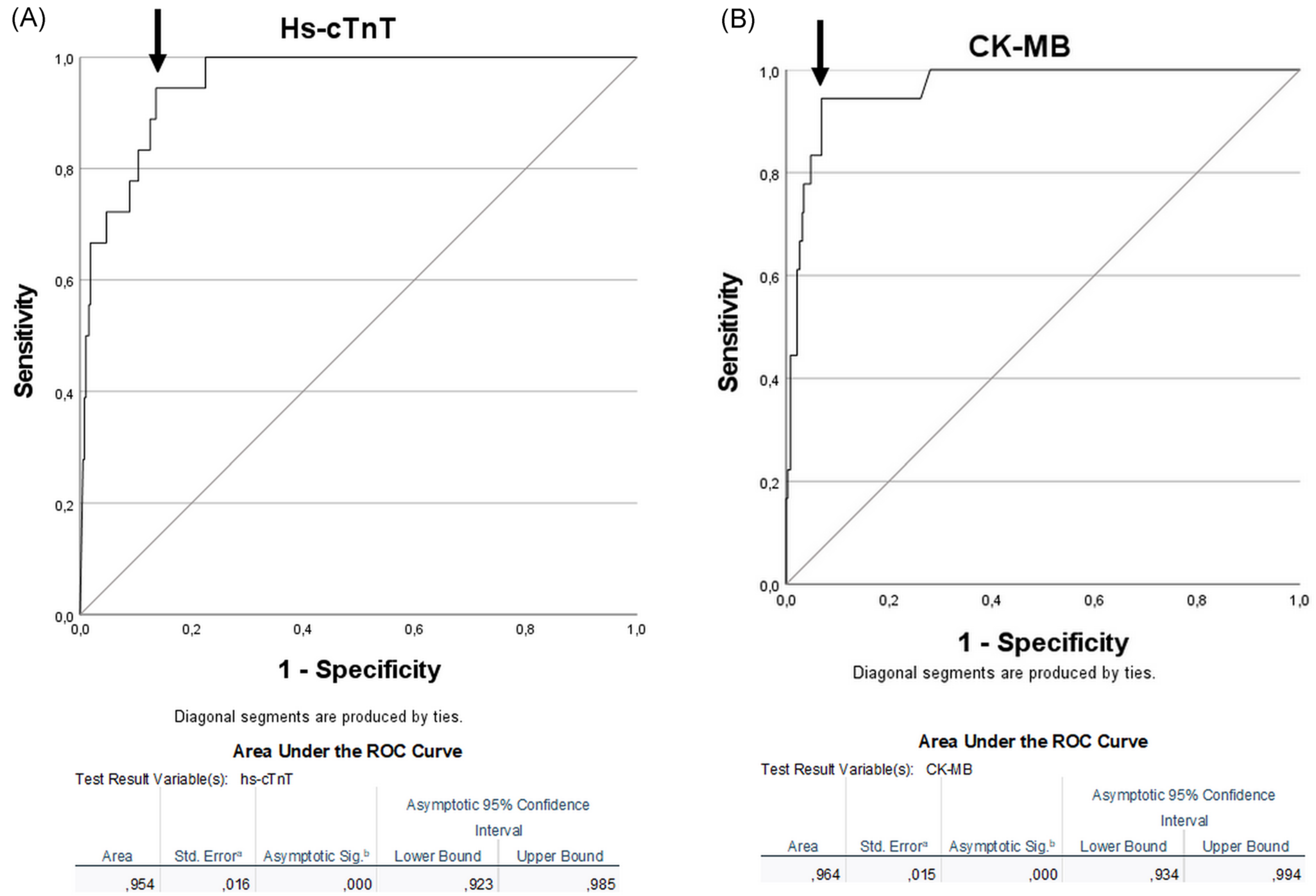
(Continues)

TABLE 2 (Continued)

Type of intervention	No (%)	Median (IQR = Q3–Q1)	Mean rank	Kruskal–Wallis test asymptotic significance	Pairwise comparisons	Effect size/correlation coefficient *r*
On-pump	120 (30)	51 (40–65)	197		On-CABG - AVR: $p = .62$	
Isolated AVR	101 (25)	48 (38–65)	190		On-CABG - AVR/CABG: $p = .02$	.2
AVR + CABG	50 (13)	61 (46–86)	242	$p < .0001$	On-CABG - MVR: $p < .001$	.3
MVR	56 (14)	78 (58–114)	282		On- CABG - others: $p = .83$	
Others	25 (6)	49 (34–79)	192		AVR - AVR/CABG: $p = .008$	.2
					AVR - MVR: $p < .001$	.4
Total	400	50 (37–71)			AVR - others: $p = .93$	
					AVR/CABG - MVR: 0.08	
					AVR/CABG - others: 0.08	
					MVR- others: 0.001	.4
(4B) CK-MB: without preoperative hs-cTnT↑						
					Off-CABG - on-CABG: $p < .001$	.4
					Off-CABG - AVR: $p < .001$	.5
					Off-CABG - AVR/CABG: $p < .001$	**.7**
CABG					Off-CABG - MVR: $p < .001$	**.9**
Off-pump	36 (10)	272 (159–407)	57		Off-CABG - others: $p < .001$	.4
On-pump	94 (27)	742 (501–1034)	164		On-CABG - AVR: $p = .77$	
Isolated AVR	101(29)	728 (460–1173)	168		On-CABG - AVR/CABG: $p = .01$	.2
AVR + CABG	43 (12)	1019 (687–1870)	210	$p < .0001$	On-CABG - MVR: $p < .001$	.4
MVR	53 (15)	1077 (625–2152)	247		On-CABG - others: $p = .76$	
Others	22 (6)	671 (474–1364)	157		AVR - AVR/CABG: $p = .02$	.2
					AVR - MVR: $p < .001$	.4
Total	349	746 (464–1188)			AVR - others: $p = .63$	
					AVR/CABG - MVR: 0.07	
					AVR/CABG - others: 0.04	.2
					MVR - others: <0.001	.4

Note: Bold values indicate statistically significant results.

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass graft; CK-MB, creatine kinase myocardial band; MVR, mitral valve replacement.



Area Under the ROC Curve

Test Result Variable(s): hs-cTnT

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,954	,016	,000	,923	,985

Area Under the ROC Curve

Test Result Variable(s): CK-MB

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
,964	,015	,000	,934	,994

FIGURE 1 (A) Receiver-operating characteristics of hs-cTnT increase indicating ischemic events. (B) Receiver-operating characteristics of creatine kinase myocardial band increase indicating ischemic events

CK-MB was exclusively associated with ischemic events (Table S1A,B)].

- *In logistic regression*, intrapericardial defibrillation, emergency intervention, maze procedure, mortality, and renal insufficiency were positively *correlated with hs-cTnT* threshold, whereas the *combination of hs-cTnT and CK-MB threshold* was correlated with intra-pericardial defibrillation, renal insufficiency, and blood transfusions (Table 1B).
- After screening *patients with preoperatively elevated hs-cTnT*, intrapericardial defibrillation remained as an independent parameter associated with the thresholds (Table 2B).

4 | CONCLUSIONS

The present study is an attempt to provide an analytical overview of postoperative cardiac enzyme release considering various influencing factors in cardiac surgery. We deliberately did not select patients but considered different operations including additional procedure-related factors to cover a representative spectrum. One problem of postoperative troponin release is its multifactorial origin. Therefore, the systematic classification remains a challenge. It is a difference whether the operative trauma is limited to epicardial regions (as in CABG) or whether opening of the heart cavities is necessary (as in MVR). Comparison of median postoperative hs-cTnT (and of CK-MB) shows an increase depending on the type and complexity of surgery. This was described for non-high-sensitive troponin by Landoni et al., who showed that "different operations were associated with a different release of … biomarkers," with the highest troponin release after MVR, analogous to results presented here.[5]

To complicate matters, other factors influence troponin increase. Studies in nonsurgical patients have shown that the utility of the marker for the diagnosis of acute coronary syndrome in the presence of renal insufficiency is limited.[6,7] In the surgical patients studied here, there was also some association in this regard. In addition, the maze procedure, emergency intervention, blood transfusion, cardiopulmonary bypass time, and intrapericardial defibrillation (and correspondingly for the CABG subgroup, high-risk patients in addition to emergency intervention and prolonged cardiopulmonary bypass time) were identified as independent parameters affecting hs-cTnT release.

In what is, to our knowledge, the only analysis of postoperative hs-cTnT, the authors found that isolated hs-cTnT raise was not related to mortality.[8] In contrast, if ECG and/or echocardiographic criteria were present, hs-cTnT elevation above 10 times the URL (>140 ng/L) was associated with increased 30-day and 1.8-year follow-up mortality, thus apparently confirming guidelines. Strikingly, the authors state "the level of postoperative hs-cTnT >140 ng/L was found in 90% of all patients…" which is consistent with the results presented here when considering only the CABG group (in 91.6% hs-cTnT was above 140 ng/L).[8] This leads to the question of the usefulness of hs-cTnT determination when a possible threshold for intervention-related ischemia is exceeded and the diagnosis is thus essentially based on ECG and/or echocardiographic findings. A fundamental problem also arises with regard to a precise threshold definition of the type 5 MI-indicating troponin increase, which should be redefined specifically for "high-sensitive" assays.

Another analysis of troponin T measurements in 847 CABG patients concluded that although only 2% had ECG changes after surgery (comparable to the incidence recorded here), "… troponin T concentrations… (are) … almost universally elevated and are determined by numerous factors…"[9] The latter included prolonged cardiopulmonary bypass time and intraoperative defibrillation, both of which were associated with increased, whereas higher glomerular filtration rate and off-pump were associated with decreased troponin.[9] Januzzi noted, in one of the first reviews of troponin testing after cardiac surgery, that: "… biomarker(s)… could lead to an inordinate percentage of patients diagnosed with 'acute MI'… (with) … a sensitivity of 100% … observed for post-CABG MI … associated with a specificity of 4.2% and an alarmingly high misclassification rate…"[10]

The use of high-sensitive troponin assays has done little to change this. An even higher overall postoperative rise in these markers may further limit their specificity. Therefore, it seems important to include in addition to hs-cTnT, CK-MB and, of course, in accordance with guidelines, any ECG changes and/or regional wall motion abnormalities. Pointing this out is of current importance, especially in view of reinterpretation attempts, as occurred in a therapy optimization study, in which, deviating from the guidelines, the isolated postoperative troponin rise with a new low-threshold definition served as the sole assessment criterion of type 5 MI.[11]

With regard to a generally applicable hs-cTnT threshold definition, a binding statement based on the results presented here seems difficult. The calculated high hs-cTnT cutoff of 1075.5 ng/L (>120 URL) results from the patients evaluated here. With an AUROC of more than 95%, the model has a good discriminatory predictive value in the classification chosen herein for type 5 MI. However, only 11 patients with clearly detectable perioperative infarction events constitute the type 5 MI group thus defined, and a corresponding CABG subgroup analysis was not possible because of the extremely small number of perioperative ischemic events. On the other hand, the calculated concomitant CK-MB increase with its type 5 MI-indicating threshold seems to allow some comparability with the results of previous analyses.[12,13] Furthermore, comparison of the markers shows that CK-MB is slightly inferior to hs-cTnT in terms of sensitivity but has higher specificity and, according to regression analysis, probably allows a greater focus on exclusively myocardial ischemic events.

A major limitation arises from the study design, namely to analyze the increase in cardiac enzymes after different surgical procedures. This limits both comparability with previous studies and transferability to type 5 MI guideline criteria.

5 | NEVERTHELESS, THE FOLLOWING FINDINGS CAN BE SUMMARIZED

- The identification of distinct ischemic perioperative events seems possible in other (than CABG) cardiac surgical procedures in analogy to type 5 MI criteria.
- In the vast majority, hs-cTnT thresholds analogue to type 5 MI definition (140 ng/L) are far exceeded. This is also true when considering the CABG group separately.
- In a single further study analyzing the hs-cTnT increase after CABG, nearly identical results were obtained regarding the high overall number of exceedances of guideline-conform type 5 MI thresholds.
- The hs-cTnT increase is strongly multifactorially influenced, with data presented here essentially pointing to an association with emergency and high-risk surgery, intrapericardial defibrillation, renal insufficiency, and type and duration of surgery.

This may stimulate a discussion on a possible redefinition of current thresholds for high-sensitive troponin markers. However, larger prospective (multicenter) studies are needed for further evaluation.

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CONFLICT OF INTEREST

The authors declare that there are no conflict of interests.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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