Diagnosis of perioperative myocardial infarction after heart valve surgery with new cut-off point of high-sensitivity troponin T and new electrocardiogram or echocardiogram changes

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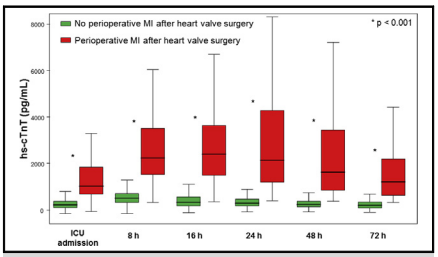
ABSTRACT

Objective: Criteria for diagnosing myocardial infarction (MI) after heart valve surgery are not collected in the Third Universal Definition of MI. We aimed to define cut-offs for high-sensitivity cardiac troponin T (hs-cTnT) and creatine kinase-MB (CK-MB) for the diagnosis of perioperative MI after heart valve surgery according to perioperative MI determined by new alterations in electrocardiogram (ECG) and/or transthoracic echocardiogram (TTE). Secondary endpoints were incidence of perioperative MI, postoperative complications, 30-day mortality, and 2-year survival.

Methods: Heart valve surgery was performed in 805 patients (June 2012-January 2016). hs-cTnT and CK-MB were measured at intensive care unit (ICU) admission and 8, 16, 24, 48, and 72 hours after surgery. Blind to outcomes, we analyzed ECGs and TTEs before and after surgery. Patients were divided into 2 groups: with ECG and/or TTE criteria after surgery (following the consensus statement) and without these changes. We conducted receiver operating characteristic analyses for hs-cTnT and CK-MB in the group with ECG and/or TTE criteria.

Results: ECG and/or TTE criteria were observed in 88 patients. Receiver operating characteristic analyses in this group showed hs-cTnT levels of 732.3 pg/mL at ICU admission; 1008 pg/mL at 8 hours, 1057 pg/mL at 16 hours, and 958.3 pg/mL at 24 hours after surgery ($P < .001$) and CK-MB levels of 26.78 mg/dL at ICU admission, 54.88 mg/dL at 8 hours, 38.98 mg/dL at 16 hours, and 18.4 mg/dL at 24 hours after surgery ($P < .001$).

Conclusions: Cut-offs for hs-cTnT and CK-MB to diagnose perioperative MI after heart valve surgery are well above upper reference limit. These findings update the Third Universal Definition providing cut-offs to diagnose perioperative MI after heart valve surgery. (J Thorac Cardiovasc Surg 2017;154:895-903)



High-sensitivity cardiac troponin T levels after heart valve surgery in patients with and without perioperative myocardial infarction.

Central Message

Cut-offs for high-sensitivity cardiac troponin and creatine kinase-MB to diagnose perioperative myocardial infarction after heart valve surgery are well above the upper reference limit, which update the definition of myocardial infarction, adding real cut-offs for biomarkers to electrocardiogram and transthoracic echocardiogram criteria.

Perspective

The findings of this study improve The Third Universal Definition of myocardial infarction, providing new cut-offs points for high-sensitivity cardiac troponin T and creatine kinase-MB above the upper reference limit, with the greatest sensitivity and specificity in patients with electrocardiogram and/or transthoracic echocardiogram criteria after heart valve surgery to diagnose perioperative myocardial infarction, thus allowing an early and comprehensive diagnosis to establish suitable treatment and decrease mortality.

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Abbreviations and Acronyms

AUC = area under receiver operating characteristic curve
CABG = coronary artery bypass grafting
CK-MB = creatine kinase-MB
CPB = cardiopulmonary bypass
ECG = electrocardiogram
hs-cTnT = high-sensitivity cardiac troponin T
ICU = intensive care unit
LBBB = left bundle branch block
MI = myocardial infarction
ROC = receiver operating characteristic
TTE = transthoracic echocardiogram
TUD = Third Universal Definition
URL = upper reference limit

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Open-heart surgery carries a well-established risk of perioperative acute myocardial infarction (MI).[1] The incidence of perioperative MI after coronary artery bypass grafting (CABG) is 5% to 10%, depending on the diagnostic criteria used.[2] Perioperative MI could not be only attributed to CABG; in fact, it also might be associated with isolated heart valve surgery, although this association is less common. McGregor and colleagues[3] reported an incidence of perioperative MI of 4% after heart valve surgery in 1984. Greaves and colleagues[4] conducted a study with 499 patients undergoing CABG in 1996 and reported an incidence of perioperative MI of 5%. Podgoreanu and colleagues[5] conducted a study in 2006 with 434 patients undergoing elective cardiac surgery and reported an incidence of perioperative MI of 12%. Perioperative MI after cardiac surgery is associated with high morbidity and hospital mortality[6] and an increased use of healthcare resources.[7]

Criteria for diagnosing perioperative MI after heart valve surgery are controversial and are not collected in the Third Universal Definition (TUD) of MI.[8,9] High-sensitivity cardiac troponin T (hs-cTnT) is a reliable biomarker with high sensitivity and high negative predictive value in detecting myocardial necrosis.[9] CK-MB is a traditional biomarker that is relatively sensitive, but its specificity is affected by the presence of this marker in skeletal muscle.[10] For that reason, cardiac troponins have been recommended by the TUD of MI as the preferred biomarkers for diagnosing MI after CABG.[8] The TUD of MI in 2012 defined MI after CABG (type 5) as requiring 2 criteria: (1) increase in cardiac biomarkers (with troponins preferred) >10 times 99% upper reference limit (URL) from a normal preoperative level; and (2) new pathological Q-waves or new left bundle branch block (LBBB) and/or imaging or angiographic evidence of new occlusion of native vessels or grafts, new regional wall motion abnormality, or loss of viable myocardium.[8] There are no studies, however, that support that the increase of hs-cTnT must be >10 times URL to diagnose perioperative MI after heart valve surgery, and it is not collected in the TUD of MI.[8] This contributes to the great variability in the incidence of perioperative MI after heart valve surgery and also to the underdiagnosis.

There are not any clinical trials that support the value of hs-cTnT >10 times 99% URL to diagnose perioperative MI after heart valve surgery. This cut-off point, suggested by The TUD of MI, has been chosen arbitrarily.[8] For that reason, we aimed to define the real cut-off for hs-cTnT and CK-MB above URL to diagnose perioperative MI after heart valve surgery, according to perioperative MI defined by new ECG and/or TTE changes. Secondary endpoints included determining the incidence, main complications, and 30-day mortality rate of perioperative MI after heart valve surgery.

METHODS

Hospital Setting and Study Population

This was a prospective, observational study (n = 805) carried out at the Hospital Clínico Universitario, a tertiary-level medical center with 800 beds in Valladolid, Spain. The Department of Cardiac Surgery annually performs approximately 550 open-heart surgeries with cardiopulmonary bypass (CPB) in adult patients. Two operating rooms were used routinely. There was an intensive care unit (ICU) with 10 beds dedicated exclusively to the postoperative care of patients who had undergone cardiac surgery.

A total of 805 consecutive patients who underwent heart valve surgery with CPB without other concomitant cardiac surgery were included prospectively from June 2012 to January 2016 and follow-up continued until June 2016. Two patients died in the operating room. This study was performed according to the provisions of the Declaration of Helsinki, and the study protocol was approved by the institutional ethics committee and the hospital's research commission. Written informed consent was obtained from all patients (ClinicalTrials.Gov identifier: NCT02518282).

The surgical and anesthetic techniques and the treatment the patient received in the ICU did not differ from ordinary procedures. Electrocardiograms (ECGs) were performed before and after surgery every 24 hours. Transthoracic echocardiograms (TTEs) were performed before and 24 to 48 hours after surgery. Cardiologist reading ECGs and TTEs were blinded to the outcomes.

Study Design and Data Collection

The target population consisted of patients who underwent heart valve surgery with CPB. Major exclusion criteria included patients younger than 18 years, recent medical history of coronary artery disease, CABG, heart transplantation, and patients with preoperative paced rhythms or LBBB. Patients included were divided into 2 groups after heart valve surgery: (1) patients with new Q-waves or LBBB in the ECG and/or imaging

TABLE 1. Demographic and clinical characteristics of the group of patients with ECG and/or TTE criteria and the group without ECG and/or TTE criteria

Preoperative characteristics	Group with ECG and/or TTE criteria (n = 88)	Group without ECG and/or TTE criteria (n = 715)	*P* value
Age, y	68.5 ± 9.3	69.4 ± 9.5	.404
Sex, male	50 (56.8%)	366 (51.2%)	.319
Functional classification (NYHA)			
I-II	65 (73.9%)	496 (69.4%)	.386
III-IV	23 (26.1%)	219 (30.6%)	
Ejection fraction, %	59.3 ± 6.3	60.4 ± 6.9	.150
Arterial hypertension	77 (87.5%)	631 (88.3%)	.837
Dyslipidemia	64 (72.7%)	528 (73.8%)	.822
Diabetes mellitus type 2	19 (21.6%)	143 (20%)	.726
Smoker	29 (33%)	203 (28.4%)	.373
Previous stroke	5 (5.7%)	33 (4.6%)	.657
Peripheral arterial disease	2 (2.3%)	20 (2.8%)	.776
Chronic obstructive pulmonary disease	6 (6.8%)	58 (8.1%)	.672
Chronic renal failure	10 (11.4%)	36 (5%)	.016*
Previous coronary artery disease	8 (9.1%)	50 (7%)	.473
Previous heart valve surgery	12 (13.8%)	84 (11.7%)	.606
Atrial fibrillation	40 (45.5%)	253 (35.4%)	.064
EuroSCORE II, %	1.78 ± 0.79	1.75 ± 0.77	.736

Data are expressed as median ± standard deviation, absolute rate, and percentage. Statistical significance was defined as $P < .05$. *ECG*, Electrocardiogram; *TTE*, transthoracic echocardiogram; *NYHA*, New York Heart Association; *EuroSCORE*, European System for Cardiac Operative Risk Evaluation. *Statistical significance.

evidence of new wall motion abnormality by TTE after surgery (ECG and/or TTE criteria); and (2) patients without these changes. An experienced cardiologist, blinded to outcomes, analyzed ECG and TTE before and after heart valve surgery. Blood samples, for the measurements of hs-cTnT and creatine kinase-MB (CK-MB), were taken by qualified personnel at ICU admission and 8, 16, 24, 48, and 72 hours after surgery. Several parameters were recorded preoperatively, intraoperatively, and in the ICU (Tables 1-3).

Study Endpoints

Primary endpoints were cut-off values to diagnose perioperative MI. Secondary endpoints included the incidence, postoperative complications, 30-day mortality rate, and survival at 2 years.

Analytical Characteristics of hs-cTnT and CK-MB Levels

The Elecsys hs-cTnT assay (Roche, Indianapolis, Ind), which is guideline compliant (American College of Cardiology/European Society of Cardiology and National Academy of Clinical Biochemistry/American Association for Clinical Chemistry), was introduced in July 2010. This test has a limit of detection of 3 pg/mL. The 99th percentile URL of this assay is 14 pg/mL.[11] Preoperative and postoperative troponin assay used at our hospital was the same hs-cTnT.

The CK-MB was assayed with an enzymatic assay (Elecsys; Roche), with a measuring range of 0.1 to 5 mg/dL, defined by the lower detection limit and the maximum of the master curve. A normal value at our laboratory was defined as <5 mg/dL.[12]

TABLE 2. Intraoperative and postoperative characteristics in the group of patients with ECG and/or TTE criteria and the group without ECG and/or TTE criteria

Intraoperative and postoperative characteristics	Patients with ECG and/or TTE criteria (n = 88)	Patients without ECG and/or TTE criteria (n = 715)	*P* value
Surgical procedure			
Mitral surgery	20 (22.7%)	150 (21%)	.705
Aortic surgery	22 (25%)	369 (51.6%)	<.001*
Mitral + aortic surgery	22 (25%)	95 (13.3%)	.003*
Mitral + tricuspid surgery	17 (19.3%)	71 (9.9%)	.008*
Mitral + aortic + tricuspid surgery	6 (6.8%)	18 (2.5%)	.025*
Tricuspid surgery	1 (1.1%)	12 (1.7%)	.704
Intraoperative characteristics			
Time of CPB, min	140.1 ± 51.3	99.2 ± 28.3	<.001*
Time of aortic crossclamp, min	100.8 ± 39.3	73.7 ± 23.9	<.001*
Defibrillation	26 (29.5%)	149 (20.8%)	.062
Postoperative characteristics			
Time of mechanical ventilation, h	52.4 ± 106.3	12.8 ± 33.5	<.001*
Complications after surgery	50 (56.8%)	171 (23.9%)	<.001*

Data are expressed as median ± standard deviation, absolute rate, and percentage. Statistical significance was defined as $P < .05$. *ECG*, Electrocardiogram; *TTE*, transthoracic echocardiogram; *CPB*, cardiopulmonary bypass. *Statistical significance.

TABLE 3. Complications after heart valve surgery in the group of patients with ECG and/or TTE criteria and the group without ECG and/or TTE criteria

Postoperative complications	Group with ECG and/or TTE criteria (n = 88)	Group without ECG and/or TTE criteria (n = 715)	*P* value
Complications	50 (56.8%)	171 (23.9%)	<.001*
Acute kidney injury 2 (AKIN 2)	48 (54.5%)	189 (26.5%)	<.001*
Stroke	1 (1.1%)	7 (1%)	.888
Pneumonia	3 (3.4%)	16 (2.2%)	.495
Cardiogenic shock	16 (18.2%)	2 (0.3%)	<.001*
Mediastinal bleeding > 1000 mL	3 (3.4%)	6 (0.8%)	.031*
Pneumothorax	0 (0%)	7 (1%)	.351
Septic shock	1 (1.1%)	11 (1.5%)	.769
Cardiac tamponade	0 (0%)	13 (1.8%)	.202
Multiorgan failure	1 (1.1%)	1 (0.1%)	.077
Redo surgery for bleeding < 24 h	1 (6.3%)	15 (2.1%)	.542
IABP	6 (6.8%)	2 (0.3%)	<.001*
ECMO	2 (2.3%)	0 (0%)	<.001*
Cardiac arrest	2 (2.3%)	2 (0.3%)	.012*
Altered tissue perfusion	25 (28.4%)	124 (17.4%)	.012*
In-hospital mortality	16 (18.2%)	19 (2.7%)	<.001*
Mortality at 30 d	13 (14.8%)	16 (2.2%)	<.001*

Data are expressed as absolute rate and percentage. Statistical significance was defined as $P < .05$. *ECG*, Electrocardiogram; *TTE*, transthoracic echocardiogram; *IABP*, intra-aortic balloon pump; *ECMO*, extracorporeal membrane oxygenation. *Statistical significance.

Statistical Analysis

Continuous and categorical variables are presented as mean ± standard deviation or median (25th-75th interquartile range) and n (%), respectively. The assumption of normality in quantitative variables was checked by analyzing skewness and kurtosis and Kolmogorov-Smirnov test. Student *t* test and the Fisher exact test for 2 groups or analysis of variance and χ^2 for 3 or more groups were used for univariate analyses.

Receiver operating characteristic (ROC) analysis was used to assess postoperative hs-cTnT and CK-MB levels in the group of patients with ECG and/or TTE criteria after heart valve surgery. The cut-off for hs-cTnT and CK-MB were estimated with the greatest Youden index ([sensitivity + specificity] − 1). The area under receiver operating characteristic curve (AUC) and corresponding 95% confidence intervals and *P* values were calculated with the Wald Test for pairwise comparison with chance.

Kaplan-Meier curves and log-rank test were performed for longitudinal survival (secondary analysis). Statistical significance was set at the .05 level for all comparisons. All analyses were conducted with the statistical package SPSS, version 23.0 (IBM Corp, Armonk, NY).

RESULTS

A total of 805 patients who underwent heart valve surgery from June 2012 to January 2016 were enrolled in the study. Two patients died in the operating room. New Q-waves or new LBBB on ECG and/or new regional wall motion on TTE (ECG and/or TTE criteria) were documented in 88 patients (10.9%): 69 patients with ECG criteria; 78 patients with TTE criteria; and 59 patients with ECG and TTE criteria. There was no patient with an uninterpretable postoperative ECG.

Demographic and Clinical Characteristics

In the group with ECG and/or TTE criteria, there were 88 patients (Table 1), 50 men (56.8%) and 38 women (43.2%). Mean age was 68.5 ± 9.3 years. Ten patients had chronic renal failure (11.4% vs 5%, $P < .016$). Mean ejection fraction was 59.3± 6.3% and mean European System for Cardiac Operative Risk Evaluation II calculated was 1.78± 0.79%, without statistical significance.

Intraoperative and Postoperative Characteristics

In the group with ECG and/or TTE criteria (Table 2), we observed that more patients underwent aortic valve surgery and multiple valve surgery with statistically significant results; prolonged CPB time ($P < .001$); prolonged aortic cross-clamp time ($P < .001$); more frequency of complications in the postoperative period ($P < .001$); and prolonged intubation and invasive mechanical ventilation ($P < .001$).[13]

Levels of hs-cTnT and CK-MB after Heart Valve Surgery

We observed an enzymatic curve of hs-cTnT with an increase after heart valve surgery in both groups of patients and a peak value at 16 hours (median = 2569 pg/mL) after surgery followed by a decrease. hs-cTnT values were significantly greater in the group with ECG and/or TTE criteria likewise in the other group in every moment ($P < .001$) (Figures 1 and 2).

In the enzymatic curve of CK-MB, there was an increase after heart valve surgery in both groups from ICU admission with a peak value at 8 hours after surgery (group with ECG and/or TTE criteria with a median = 83.2 mg/dL and group without ECG and/or TTE criteria with a median = 27.1 mg/dL). CK-MB values were greater in the group with

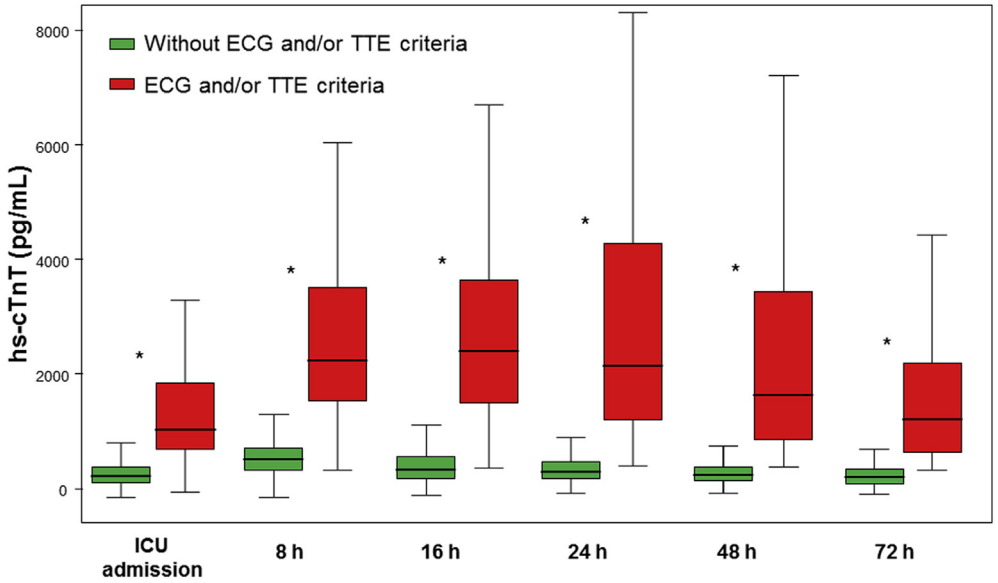

FIGURE 1. Box plot of hs-cTnT levels at ICU admission, at 8, 16, 24, 48 and 72 hours after heart valve surgery in the group of patients with and without ECG and/or TTE criteria. The data are expressed as median (25th-75th interquartile range). *Statistically significant differences ($P < .001$). *hs-cTnT*, High-sensitivity cardiac troponin; *ECG*, electrocardiogram; *TTE*, transthoracic echocardiogram; *ICU*, intensive care unit.

ECG and/or TTE criteria than in the other group in every moment ($P < .001$).

ROC analyses were performed for hs-cTnT and CK-MB with estimation of the AUC and its 95% confidence interval in both groups of patients. Cut-off points for hs-cTnT and CK-MB in the group with ECG and/or TTE criteria were established by analyzing ROC curves, choosing values with the greatest sensitivity and specificity.

It was documented a hs-cTnT level of 732.3 pg/mL at ICU admission, 1008 pg/mL at 8 hours, 1057 pg/mL at 16 hours, and 958.3 pg/mL at 24 hours after surgery ($P < .001$) (Figure 3). ROC analysis showed a CK-MB level of 26.78 mg/dL at ICU admission, 54.88 mg/dL at 8 hours, 38.98 mg/dL at 16 hours, and 18.4 mg/dL at 24 hours after surgery ($P < .001$) (Figure 4). hs-cTnT and CK-MB values were chosen with the greatest sensitivity and specificity and the largest AUC.

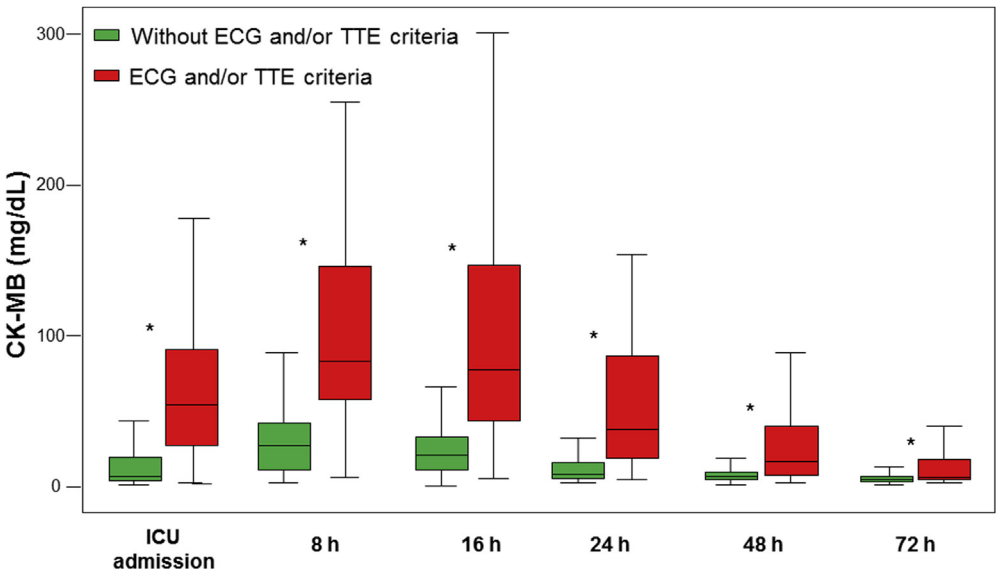

FIGURE 2. Box plot of CK-MB levels at ICU admission, at 8, 16, 24, 48, and 72 hours after heart valve surgery in the group of patients with and without ECG and/or TTE criteria. The data are expressed as median (25th-75th interquartile range). *Statistically significant differences ($P < .001$). *CK-MB*, Creatine kinase-MB; *ECG*, electrocardiogram; *TTE*, transthoracic echocardiogram; *ICU*, intensive care unit.

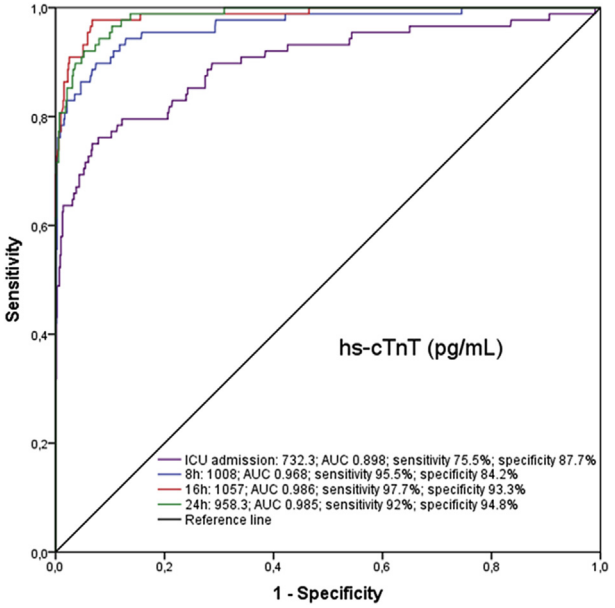

FIGURE 3. Receiver operating characteristic curves of postoperative hs-cTnT levels in the group of patients with and without ECG and/or TTE criteria at ICU admission, at 8, 16, and 24 hours after heart valve surgery. *hs-cTnT*, High-sensitivity cardiac troponin; *ICU*, intensive care unit; *AUC*, area under receiver operating characteristic curve.

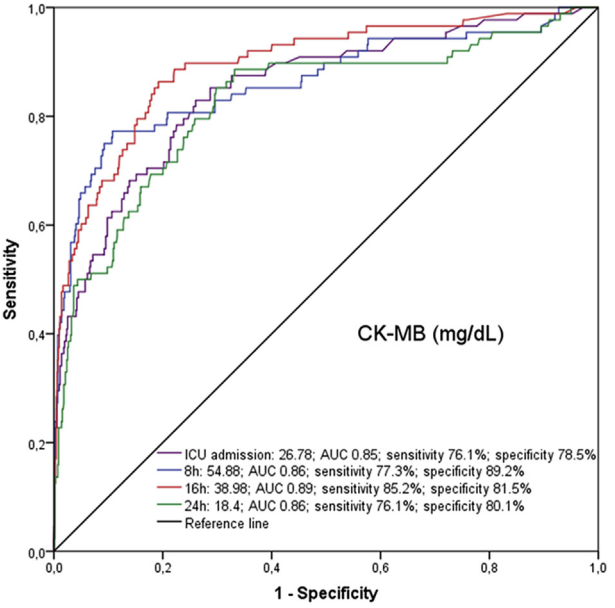

FIGURE 4. Receiver operating characteristic curves of postoperative CK-MB levels in the group of patients with and without ECG and/or TTE criteria at ICU admission, at 8, 16, and 24 hours after heart valve surgery. *CK-MB*, Creatine kinase-MB; *ICU*, intensive care unit; *AUC*, area under receiver operating characteristic curve.

Postoperative Characteristics

Patients with enzymatic curves of hs-cTnT and CK-MB suggestive of myocardial necrosis and ECG and/or TTE criteria after heart valve surgery were identified as patients with perioperative MI. The stay in ICU was longer in patients with ECG and/or TTE criteria ($P < .001$), and the stay in hospital was also longer in the same group of patients ($P = .002$). Postoperative complications are shown in Table 3. Complications were documented in 56.8% of patients in the group with ECG and/or TTE criteria ($P < .001$). Main complications in patients after heart valve surgery in the group of patients with ECG and/or TTE criteria were (1) acute kidney injury 2; (2) cardiogenic shock; (3) excessive mediastinal bleeding (>1000 mL); (4) patients requiring intra-aortic balloon pump; and (5) cardiac arrest (Table 3).

Mortality and Survival

In-hospital mortality and 30-day mortality were greater in the group of patients with perioperative MI after heart valve surgery ($P < .001$) (Table 1). Kaplan-Meier survival curves at 2 years in both groups of patients are shown in Figure 5.

DISCUSSION

There are several novel findings of this study. (1) In patients with perioperative MI after heart valve surgery, there is an enzymatic curve of hs-cTnT with a peak value of 2569 pg/mL (median) at 16 hours after surgery and an enzymatic curve of CK-MB with a peak value of 83.2 mg/dL reached at 8 hours after surgery. (2) Cut-off points of hs-cTnT were 732.3 pg/mL at ICU admission, 1008 pg/mL at 8 hours, 1057 pg/mL at 16 hours, and 958.3 pg/mL at 24 hours after surgery; cut-off points of CK-MB were 26.78 mg/dL at ICU admission, 54.88 mg/dL at 8 hours, 38.98 mg/dL at 16 hours, and 18.4 mg/dL at 24 hours after surgery. (3) The incidence of perioperative MI after heart valve surgery

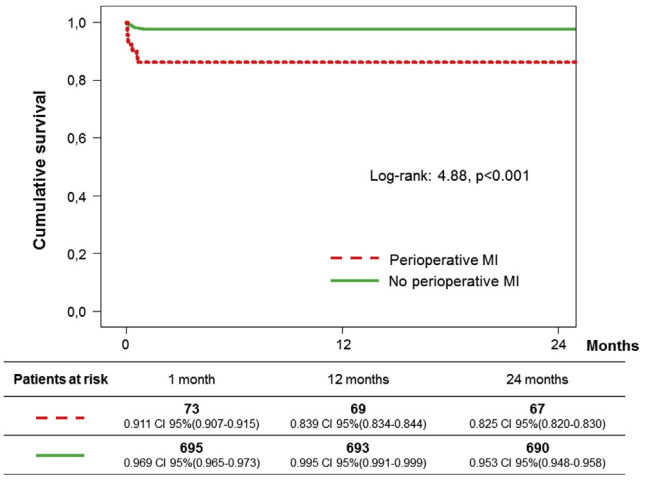

FIGURE 5. Kaplan-Meier survival curves at 2 years in the group of patients with and without ECG and/or TTE criteria. *CI*, Confidence interval; *MI*, myocardial infarction.

was 10.9%. (4) We found CPB time and renal chronic disease to be factors associated with perioperative MI after heart valve surgery. (5) In-hospital mortality in patients with perioperative MI after heart valve surgery was 18.2%, 30-day mortality was 14%, and 2-year mortality was 19.3%.

In spontaneous MI, serum levels of hs-cTnT increase within 3 to 12 hours from the onset of symptoms, peak at 16 to 24 hours, and return to baseline over 5 to 10 days after.[14] In the same way, CK-MB levels increase within 3 to 12 hours of onset of symptoms, reach peak values within 16 to 24 hours, and return to baseline after 46 to 72 hours.[14] Our study patients with perioperative MI after heart valve surgery showed similar enzymatic curves of hs-cTnT and CK-MB with peak values reached at similar times as described in literature for spontaneous MI.[14]

In the 2007 guidelines, the biomarker cut-off point for the Universal Definition of MI associated with CABG (type 5), was 5 times the URL.[15] In the 2012 guidelines, the biomarker cut-off point increased to 10 times the URL arbitrarily.[8] There are no studies with hs-cTnT and CK-MB in patients underwent isolated heart valve surgery. In our study, cut-off points for hs-cTnT and CK-MB at ICU admission, 8, 16, and 24 hours are much greater than the cut-off point described arbitrarily by The TUD of MI.[8] Perioperative MI is often an outcome in clinical trials in cardiac surgery, and the confusion regarding appropriate definitions is also a concern for such studies.

Criteria for diagnosing MI after cardiac surgery are open to discussion because chest pain is relieved by analgesics in these patients. To diagnose perioperative MI appropriately requires a stable baseline of hs-cTnT before heart valve surgery can be performed because if patients have elevated increasing hs-cTnT levels, it is not possible to distinguish accurately from a recent index MI.[16] Accordingly, we excluded patients with recent medical history of coronary artery disease. All patients included in our study had normal stable baseline hs-cTnT and CK-MB values.

Whitlock and colleagues[17] conducted a study with 7505 patients who underwent cardiac surgery whose objective was to assess the effects of steroids in patients at high risk of morbidity and mortality undergoing CPB. They established a postoperative CK-MB threshold to diagnose early myocardial injury. They used CK-MB instead of troponin because there were both non–high-sensitive and high-sensitive troponin assays for both troponin T and I assays and some centers did not have access to troponin.

There are no previous studies conducted in patients underwent isolated heart valve surgery with dual elevation of hs-cTnT and CK-MB plus ECG and/or TTE criteria for the diagnosis of perioperative MI. Consequently, we compare our results with studies conducted in patients who underwent CABG.[9,18] Omar and colleagues[18] conducted a study with 413 patients who underwent cardiac surgery. They found a cut-off point for hs-cTnT of 3466 ng/L in the first 24 hours, which could be diagnostic of perioperative MI after cardiac surgery following criteria as suggested in the TUD of MI.[8] This high cut-off point may be because most of the patients included underwent CABG (84%), and they included urgent surgeries and patients with recent MI. Not all the patients had a TTE after surgery to identify new regional wall motion.[18] In our study, ROC analyses reported a cut-off point for hs-cTnT of 1057 pg/mL at 16 hours and a cut-off point for CK-MB of 54.88 mg/dL at 8 hours after heart valve surgery, with the greatest sensitivity and specificity for the diagnosis of perioperative MI in patients who showed ECG and/or TTE criteria.[8]

Wang and colleagues[9] conducted a study with 818 patients who underwent CABG. hs-cTnT was measured 12 to 24 hours after CABG. Patients with increasing baseline or missing troponins were excluded. Fourteen percent of patients had perioperative MI, as defined by the dual criteria (elevation of hs-cTnT plus ECG and/or TTE criteria), and this finding was more prognostic of mortality than a single criterion.[9] Our results show that dual criteria are more specific for the diagnosis of perioperative MI after heart valve surgery. In the current study, 88 patients fulfilled the diagnostic ECG and/or TTE criteria described in the TUD of MI for MI type 5 (associated with CABG).[8]

Several studies on myocardial ischemia in the perioperative period of cardiac surgery have been conducted. The reported incidence of perioperative MI after CABG by the Society of Thoracic Surgeons database varies widely with an average of 3.9%.[19] There are few large series in which the incidence of perioperative MI is established clearly after heart valve surgery. These studies are old and retrospective, so the incidence of perioperative MI may be underdiagnosed. In the early 1980s, the incidence of perioperative MI after aortic valve replacement reported was 4% to 26% and after mitral valve replacement was 0% to 13%.[20,21] Javierre and colleagues[1] conducted a study with 2038 patients (1271 underwent valve surgery, 614 underwent CABG, and 153 underwent both types of surgery). They found that the incidence of perioperative MI was significantly lower in the valve surgery group (5.4%) than in the CABG group (14.6%). They did not use the Universal Definition to diagnose MI after cardiac surgery; for that reason, their results may be different from ours.

In their study of 818 patients who underwent CABG, Wang and colleagues[9] found an incidence of perioperative MI of 14% when using criteria suggested by the TUD of MI. In our study, 88 patients developed perioperative MI after heart valve surgery, which shows an incidence of 10.9%. These differences can be due to the probability of graft occlusion in patients who underwent CABG. Regarding results of the current study, surgeries in which more than one valve is treated have a greater incidence of

VIDEO 1. Dr Cubero-Gallego's comment about the importance of the diagnosis of perioperative myocardial infarction after heart valve surgery. Video available at: http://www.jtcvsonline.org/article/S0022-5223(17)30224-6/addons.

perioperative MI than surgeries where only one valve is operated.

CK-MB has been a widely used biomarker, and the elevation above URL was the standard for MI diagnosis in the past.[10] CK-MB has showed to be inferior to troponins in predicting adverse cardiovascular outcomes.[12,22] In our study, we observed that dual biomarker elevation (hs-cTnT and CK-MB) in patients with ECG and/or TTE criteria after heart valve surgery is more specific to diagnose perioperative MI (Video 1).

Associated Factors With Perioperative MI

Several factors may provide some insights into the mechanism of perioperative MI after heart valve surgery: (1) direct trauma of the myocardium by sutures; (2) inadequate intraoperative cardioprotection; (3) microvascular embolisms related to reperfusion; and (4) myocardial damage by the release of oxygen-free radicals.[23] Onorati and colleagues[24] conducted a study with 776 patients who underwent CABG, and they found the following to be independent predictors of perioperative MI at multivariate analysis: European System for Cardiac Operative Risk Evaluation >6, unstable angina, aortic crossclamp time >90 minutes, CPB time >180 minutes, incomplete revascularization, and intraoperative intra-aortic balloon pump. In their study, Wang and colleagues[9] found unstable angina and CPB time as independent predictors of perioperative MI after CABG. In the same way, we have identified in our study CPB time and chronic renal disease as associated factors with perioperative MI after heart valve surgery.

CPB time is an independent risk factor of morbidity and mortality in cardiac surgery.[25] In our study population, patients who developed perioperative MI after heart valve surgery had longer CPB time than patients without perioperative MI, which is consistent with previous studies.[25]

Patients with chronic renal disease have a greater risk of cardiovascular complications. In patients undergoing surgery, decreased renal function was associated with greater cardiac morbidity and mortality.[26,27] In our study, 10 (11.4%) patients from 88 with ECG and/or TTE criteria and 36 (5%) patients from 715 without ECG and/or TTE criteria had chronic kidney disease. All the patients included in our study, however, had normal stable baseline hs-cTnT and CK-MB before cardiac surgery. Abbas and colleagues[28] conducted a study with 222 patients with chronic kidney disease, and they observed that cTnT was increased above the 99th percentile URL in 43% of patients. The cause and the significance of increased cardiac troponin concentrations in patients with renal insufficiency in the absence of acute coronary disease are controversial.[28]

Mortality

The 30-day mortality reported by the Society of Thoracic Surgeons of isolated valve surgery in 2008 was 3.4%.[29,30] The 30-day mortality of heart valve surgery in Spain in 2011 was 4.97%.[31] Similarly in our study, from a total of 805 patients, 37 died during hospitalization.[32] This finding shows an incidence of mortality in patients underwent heart valve surgery of 4.6%. The 30-day mortality rate in patients with perioperative MI after heart valve surgery with CPB was 18.2%. At 2 years of follow-up, a significantly decreased survival was observed in patients with perioperative MI after heart valve surgery.

Implications

This finding improves the TUD of MI, providing a new cut-off point of hs-cTnT and CK-MB above URL, with the greatest sensitivity and specificity in patients with ECG and/or TTE criteria after heart valve surgery to diagnose perioperative MI.[8]

Study Limitations

This is a study from one center. In our opinion, it would be advisable to combine the efforts of several centers and compare their results with ours to conduct an external validation of the study.

CONCLUSIONS

The cut-offs for hs-cTnT and CK-MB to diagnose perioperative MI after heart valve surgery are well above URL. These findings update the definition of MI providing cut-offs of biomarkers to diagnose perioperative MI after heart valve surgery and improving The TUD of MI.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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