Myocardial damage influences short- and mid-term survival after valve surgery: A prospective multicenter study

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Objective: Myocardial damage occurs after valve surgery, but its prognostic implication has not been evaluated. The aim of the present study was to assess the influence of myocardial damage on mortality and morbidity in patients undergoing aortic surgery (AVS) and mitral valve surgery (MVS).

Methods: In a prospective multicenter study from the cardiac surgery registry of the Puglia region, cardiac troponin I (cTnI) was measured immediately after and the morning after the intervention in consecutive patients undergoing AVS or MVS. The percentile ranks of the cTnI peak values within each center were analyzed.

Results: Of 965 patients (age, 67 ± 12 years; 45.5% women), 579 had undergone AVS and 386 MVS. cTnI release was significantly greater in the MVS group than in the AVS group and in the nonsurvivors than in the survivors in both groups. The cTnI cutoff with the greatest sensitivity and specificity (60th percentile for AVS and 91st for MVS) in predicting hospital mortality (2.6%) was also associated with a greater rate of postoperative complications and mortality within 3 months postoperatively (multivariate hazard ratio, 3.38; $P = .005$). Compared with the reference model, which included the multivariate predictors of hospital mortality (active endocarditis, New York Heart Association class III-IV, left ventricular ejection fraction $\leq 30\%$, and cardiopulmonary bypass duration), the addition of cTnI greater than the cutoffs showed significant improvement in model performance (likelihood ratio test, $P = .009$; net reclassification improvement, 0.751; $P < .001$; integrated discrimination improvement, 0.048; $P = .002$; c-index 0.832 vs 0.838).

Conclusions: An elevated postoperative cTnI level was an independent risk factor for mortality and morbidity. Measurement of the cTnI level improved the risk reclassification of patients undergoing AVS or MVS. (J Thorac Cardiovasc Surg 2014;148:2373-9)

See related commentary on page 2380.

Supplemental material is available online.

Cardiac surgery is invariably associated with a certain degree of myocardial damage. Although myocardial protection is accomplished through different types of

cardioplegic solutions during cardiac arrest, the markers of myocardial necrosis will be elevated after surgery compared with the preoperative values. The mechanisms leading to myocardial damage after cardiac operations are multifactorial and also depend on the type of surgery each patient has undergone. Most of the studies performed to date on this subject have focused on patients undergoing coronary artery bypass grafting (CABG),¹⁻³ with cardiac troponin I (cTnI) the most reliable marker to detect myocardial damage. These studies have invariably demonstrated that greater postoperative cTnI levels are associated with increased short- and mid-term mortality and a greater rate of postoperative complications after CABG surgery. However, the extent of myocardial damage differs according to the type of operation: mitral valve surgery (MVS) provokes greater cTnI postoperative values than aortic valve surgery (AVS) and CABG.⁴ The causes of myocardial damage will also differ according to the type of surgery. In CABG, coronary disease extension, recent myocardial infarction, incomplete revascularization, and early graft failure are possible causes. In valve surgery heart manipulation and incision, an iatrogenic coronary lesion and the efficacy of cardioplegia administration can lead to different degrees of cellular necrosis. From these observations, the extent and prognostic

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Abbreviations and Acronyms

AVS	= aortic valve surgery
CABG	= coronary artery bypass grafting
cTnI	= cardiac troponin I
MVS	= mitral valve surgery

implication of myocardial damage cannot be generalized; they should be assessed for each type of procedure. Few studies have considered myocardial damage after valve surgery,^{5,6} and its prognostic implications have not been clearly described. Therefore, the present study aimed to outline the pattern of myocardial damage in patients undergoing MVS or AVS without coronary stenosis and to assess its influence on short- and mid-term mortality and morbidity.

METHODS**Study Population**

This was a prospective cohort study in which consecutive adult patients who had undergone isolated AVS or MVS in the Puglia region from January 1, 2011 to June 30, 2013 were considered. Pre-, intra-, and postoperative information were gathered prospectively from the Puglia Regional Adult Cardiac Surgery Registry, which includes the 7 adult cardiac surgery centers in Puglia: University of Bari–Policlinico Hospital (coordinating center), Anthea Hospital (Bari, Italy), Santa Maria Hospital (Bari), Villa Bianca Hospital (Bari), Villa Verde Hospital (Taranto, Italy), Vito Fazzi Hospital (Lecce, Italy), and Città di Lecce Hospital (Lecce). Health regional agency personnel guaranteed the data accuracy and performed the quality control procedures. All cases performed in each center were checked by operating room documents to ensure that all patients who had undergone heart surgery had been included in the registry. “Cleaning” consisted of minimizing the amount of missing data through interactions with the hospitals, and auditing consisted of inspection of the data in the hospital medical records. Hospital mortality risk prediction was performed for each patient using the EuroSCORE II model.⁷ The postoperative cTnI values were included in the data set with the specific aim of conducting prospective studies on myocardial damage during cardiac surgery. Of the 7 cardiac surgery units in the region, 2 were excluded from the analysis because of systematic missing values for the postoperative myocardial injury biomarkers. The primary outcome was hospital mortality, defined as death occurring at any point after surgery during the hospital period in which the operation had been performed. The secondary endpoints were the incidence of postoperative complications and mid-term mortality, evaluated as death occurring within 3 months after surgery. Deaths occurring after hospital discharge for patients resident in Puglia who had undergone surgery before December 2012 were identified by a link to the regional health information system. The study was conducted in accordance with the Declaration of Helsinki. The institutional review board policy determined that the research did not require informed consent.

cTnI Analysis

Blood samples for the determination of the cTnI level were collected at intensive care unit acceptance and serially thereafter at 7 AM every day of the intensive care unit stay. The assays included Troponin I STAT (Roche Diagnostics, Basel, Switzerland), AxSYM Troponin-I (Abbott Diagnostics, Abbot Park, Ill), and Dimension EXL (Siemens Healthcare Diagnostics, Malvern, Pa); for 2 centers, the assay used was Dimension RxL (Siemens Healthcare Diagnostics). The cTnI threshold among the centers for the diagnosis of myocardial necrosis ranged from 0.056 to 0.40 ng/mL.

Statistical Analysis

The categorical variables are expressed as percentages and continuous variables as the mean $\pm$ standard deviation or median and interquartile range. Univariate logistic regression analyses were used to assess the association of baseline variables with the primary outcome. Odds ratios (OR) are given with the 95% confidence intervals (CIs). The baseline characteristics associated with mortality on univariate analyses with $P < .05$ were retained for possible inclusion in the final model. To avoid multicollinearity, the redundant variables were removed from the multivariate logistic regression models, keeping the variable with the stronger individual effect size. Because the absolute concentrations of cTnI and the 99th percentile concentrations are currently not comparable among manufacturers,⁸⁻¹⁰ the postoperative cTnI peak values were transformed into percentile ranks for each patient within each center. Using ranking removed the differences in the assay used without removing the relative differences among the patients within each clinic. For each clinic, the distribution varied uniformly from 0 to 100. A greater cTnI release from each center had a percentile rank close to 100, and a lower release had a percentile rank close to 0. The ranked data of the centers were combined for the global analysis, and the groups were compared using the Wilcoxon rank sum test. Multivariate regression analysis was applied to evaluate the associations between the operative variables and the percentile ranked cTnI peak values. Receiver operating characteristics curves were constructed, and the optimal cutoff points were obtained according to the greatest sum of sensitivity and specificity. To address the question whether the cTnI level has incremental prognostic utility, we, first, developed a predictive model incorporating the clinical variables only (the reference model). Next, we added cTnI to the reference model. Models with and without cTnI were compared using a likelihood ratio test. Discrimination was assessed using the c-statistic,¹¹ and the Akaike information criterion was calculated.¹² The goodness-of-fit for the logistic model was evaluated using the Nagelkerke likelihood ratio-based R^2 measure. The effect of adding cTnI to the reference model on risk classification was evaluated using the category-free net reclassification improvement and the integrated discrimination improvement.^{13,14} The Cox proportional hazards model was used to assess the associations of variables with mid-term mortality during the first 3 months after surgery. The hazard ratios are given with their 95% CIs. The event-free curves were determined using Kaplan-Meier analyses stratified by the cTnI cutoff level, and the comparison was made using the log-rank test. The postoperative complications were compared using the χ^2 test. The analyses were made using STATA software, version 12 (StataCorp, College Station, Tex).

RESULTS

Of 1006 isolated AVS or MVS performed in the 5 participating centers, 965 (95.9%) were included in the analysis, and 41 (4.1%) were excluded (37 because of missing postoperative cTnI values and 4 because the patient died in the operating room). AVS included 5 repairs and 574 replacements. MVS included 201 repairs and 185 replacements. The centers performed 92 to 365 procedures. The patient characteristics are listed in Table 1 according to the main outcome. Compared with the survivors, those who died (11 patients after AVS and 14 after MVS) more frequently had preoperative renal failure requiring dialysis, previous cardiac surgery, active endocarditis, critical preoperative state, diabetes requiring insulin, advanced New York Heart Association class, poor left ventricular ejection fraction, severe pulmonary hypertension, nonelective operations, and longer bypass and crossclamp

TABLE 1. Baseline characteristics and univariate predictors of in-hospital mortality

Variable	All (n = 965)	Survivors (n = 940)	Nonsurvivors (n = 25)	OR* (95% CI)	P value
Age (y)	67 ± 12	67 ± 12	70 ± 9	1.02 (0.99-1.06)	.197
Female gender	45.5	45.5	44.0	0.94 (0.42-2.09)	.879
Renal impairment					
Creatinine clearance 50-85 mL/min	47.6	47.6	48.0	1.80 (0.63-5.17)	.272
Creatinine clearance <50 mL/min	16.0	15.7	24.0	2.72 (0.82-9.07)	.102
Dialysis	1.1	1.0	8.0	14.93 (2.55-87.53)	.003
Extracardiac arteriopathy	6.0	6.0	8.0	1.37 (0.32-5.97)	.673
Neurologic dysfunction	3.7	3.6	8.0	2.32 (0.52-10.23)	.267
Previous cardiac surgery	9.8	9.1	36.0	5.59 (2.40-13.02)	<.001
Bronchodilators or steroids for lung disease	5.2	5.1	8.0	1.62 (0.37-7.06)	.523
Active endocarditis	4.2	3.5	32.0	12.93 (5.21-32.11)	<.001
Critical preoperative state	0.7	0.5	8.0	16.26 (3.00-88.23)	.001
Diabetes on insulin	5.8	5.5	16.0	3.25 (1.08-9.82)	.036
NYHA class III-IV	55.5	54.7	88.0	6.08 (1.81-20.45)	.004
Left ventricular ejection fraction					
31%-50%	25.3	25.1	32.0	1.94 (0.78-4.80)	.153
≤30%	2.4	1.9	20.0	15.88 (5.06-49.82)	<.001
Recent myocardial infarction within 90 d	1.6	1.5	4.0	2.76 (0.35-21.82)	.337
Systolic pulmonary artery pressure					
31-55 mm Hg	25.8	25.9	24.0	1.19 (0.45-3.16)	.729
>55 mm Hg	8.0	7.6	24.0	4.07 (1.50-11.04)	.006
Nonelective operation	3.6	3.0	28.0	12.67 (4.9-32.77)	<.001
Operative details					
Bypass time (min)	100 ± 40	99 ± 38	146 ± 72	1.19 (1.11-1.26)	<.001
Crossclamp time (min)	74 ± 34	74 ± 29	89 ± 34	1.13 (1.02-1.26)	.018
Cardioplegic solution					
Blood	91.9	92.0	87.0	1.00	
Crystalloid	8.1	8.0	13.0	1.72 (0.50-5.93)	.388
Temperature of cardioplegic solution					
Cold	69.0	69.3	56.5	1.00	
Warm	31.0	30.7	43.5	1.73 (0.75-4.00)	.197
Delivery of cardioplegic solution					
Antegrade	90.0	90.1	87.5	1.00	
Retrograde	1.1	1.1	0.0	—	
Both antegrade and retrograde	8.9	8.8	12.5	1.48 (0.44-5.09)	.527

Data presented as mean ± standard deviation or percentages. OR, Odds ratio; CI, confidence interval; NYHA, New York Heart Association. *OR per 10-unit increase in age, bypass time, and crossclamp time.

times. The different types of cardioplegic solutions used for myocardial protection had no influence on survival.

Figure 1 shows the percentile of cTnI peak values according to valve surgery type and in-hospital mortality after AVS and MVS. The percentile ranked cTnI peak values were greater in the MVS group than in the AVS group and in nonsurvivors than in survivors in both surgery groups. On multivariate regression analysis, the operative variables listed in Table 1 were not associated with the percentile ranked cTnI peak value, with the exception of the bypass duration and MVS, which showed a positive significant regression coefficient (both $P < .001$). The use of a cardioplegic solution, temperature of the cardioplegic solution, and delivery of the cardioplegic solution did not influence cTnI release ($P = .26$, $P = .17$, and $P = .32$, respectively). The accuracy of the postoperative cTnI level to discriminate between those patients who died and those

who survived, as quantified by the area under the receiver operating characteristics curve, was 0.717 (95% CI, 0.545-0.888) for AVS and 0.708 (95% CI, 0.534-0.881) for MVS. Figure E1 displays the receiver operating characteristic curve of the percentile ranked cTnI peak values for in-hospital mortality stratified by the surgery type. The 60th percentile of the cTnI level in the AVS group had 64% sensitivity and 72% specificity, with the greatest sum of sensitivity and specificity. The cTnI values of the 60th percentile ranged within each clinic from 4.48 to 8.6 ng/mL. After MVS, the 91st percentile of cTnI had 57% sensitivity and 86% specificity to distinguish nonsurvivors and survivors. The 91st percentile of cTnI ranged within each clinic from 12.27 to 38.90 ng/mL. The presence of a cTnI percentile greater than the 60th percentile in AVS and the 91st in the MVS group was significantly associated on univariate analysis for hospital mortality

FIGURE 1. Median with interquartile range of percentile ranked cardiac troponin I peak values stratified by (A) valve surgery and hospital mortality in (B) aortic and (C) mitral valve surgery.

(OR, 5.18; 95% CI, 2.29-11.70; $P < .001$, for the entire sample; OR, 4.58; 95% CI, 1.32-15.87; $P = .015$, for the AVS group; and OR, 7.85; 95% CI, 2.62-23.52; $P < .001$ for the MVS group).

The multivariate analysis results for hospital mortality are listed in [Table 2](#). Of the univariate predictors, only active

endocarditis, advanced New York Heart Association class, poor left ventricular ejection fraction, and bypass duration remained associated with in-hospital mortality. These variables were considered for the reference predictive model. When the cTnI peak percentile greater than the 60th in the AVS group and the 91st in the MVS group was added to the reference model, the biomarker remained significantly associated with mortality. Compared with the reference model, the addition of cTnI resulted in significant improvement in the goodness-of-fit (likelihood ratio, χ^2 , 69.9 vs 76.7, with $P = .009$ at the likelihood ratio test; Nagelkerke $R^2 = 0.327$ vs 0.358; Akaike information criterion, 172.2 vs 167.3), in discrimination (c-index, 0.832 vs 0.838), and reclassification (net reclassification improvement, 0.751; $P < .001$; and integrated discrimination improvement, 0.048; $P = .002$). The model incorporating cTnI had significant effects compared with reclassification. The net reclassification improvement indicated that 75.1% of patients were better classified when the cTnI level was included. Also, the significant value of integrated discrimination improvement showed that the addition of cTnI to the reference model led to significant improvement in the ability to stratify the risk of hospital mortality.

Postoperative Complications

The patients with a greater cTnI peak value in the entire sample and, specifically, after MVS had significantly greater rates of creatinine clearance reduction, postoperative dialysis, reopening for complications and bleeding, reintubation, insertion of a permanent pacemaker, sepsis, intra-aortic balloon pump use, and hospital mortality ([Table 3](#)). In AVS, a high cTnI peak value was associated with creatinine clearance reduction, postoperative dialysis, reopening for complications, sepsis, and hospital mortality.

Follow-up

For the 593 residents in Puglia, the link between patients in the registry and the regional Health Information System with the vital status updated after hospital discharge, was obtained. Five patients died after discharge within 3 months postoperatively. Troponin I values greater than the cutoff value showed a significant effect compared with mid-term mortality on univariate (hazard ratio, 4.58; 95% CI, 2.19-9.59; $P < .001$) and multivariate (hazard ratio, 3.38; 95% CI, 1.44-7.93; $P = .005$) analysis, correcting for variables in the reference model. [Figure 2](#) shows the cumulative mortality in the AVS and MVS subgroups according to the postoperative cTnI peak values.

DISCUSSION

In the present study, we assessed whether adding the postoperative cTnI level to the clinical variables resulted in improved risk reclassification of the patients who had

TABLE 2. Multivariate logistic regression analysis for in-hospital mortality

Variable	OR (95% CI)	P value	Reference model		Reference model plus cTnI	
			OR (95% CI)	P value	OR (95% CI)	P value
Renal impairment requiring dialysis	2.37 (0.32-17.72)	.401				
Previous cardiac surgery	1.64 (0.50-5.41)	.416				
Active endocarditis	8.24 (2.29-29.6)	.001	16.22 (5.68-46.31)	<.001	15.12 (5.08-45.01)	<.001
Critical preoperative state	1.44 (0.23-9.19)	.700				
Diabetes requiring insulin	2.29 (0.60-8.72)	.225				
NYHA class III-IV	3.83 (1.03-14.25)	.045	4.56 (1.29-16.13)	.019	5.42 (1.49-19.72)	.010
Left ventricular ejection fraction ≤ 30%	17.98 (4.52-71.43)	<.001	24.51 (6.89-87.18)	<.001	26.59 (7.14-99.04)	<.001
Systolic pulmonary artery pressure > 55 mm Hg	1.74 (0.53-5.75)	.363				
Nonelective operation	2.20 (0.47-10.25)	.314				
Bypass time (min)*	1.18 (1.09-1.28)	<.001	1.20 (1.11-1.29)	<.001	1.14 (1.06-1.24)	.001
High cTnI peak	—	—	—	—	3.88 (1.41-10.69)	.009

High cTnI peak refers to values greater than the 60th in the AVS and 91st in the MVS group. OR, Odds ratio; NYHA, New York Heart Association; cTnI, cardiac troponin I. *OR per 10-unit increase in bypass time.

undergone AVS or MVS. The major finding of the present study was that the postoperative cTnI level was significantly associated with the in-hospital and mid-term mortality, with significant improvement in the risk reclassification measures in both AVS and MVS.

To date, far few smaller studies have evaluated this aspect. Adabag and colleagues,⁵ in a retrospective, single-center study, evaluated 696 CABG patients and 490 valve patients and demonstrated that greater cTnI elevation after surgery was associated with increased mortality and a greater incidence of myocardial infarction.⁵ The analysis of the 490 valve patients was performed combining AVS and MVS, and no information regarding survival after hospital discharge was available. Monaco and colleagues⁶ reported on about 185 patients undergoing MVS; however, owing to the limited population, they could only evaluate the predictors of cTnI release after surgery, without establishing a significant effect on the patients' prognosis.

By including a large number of patients from 5 different centers and removing the differences that might exist among the different assays using percentile ranking, the present study investigated the effects of cTnI on mortality after isolated AVS and MVS in patients without coronary artery disease. We have shown that in valve surgery, myocardial damage is a strong determinant of the postoperative outcome, emphasizing the importance of myocardial protection in this type of surgery. In MVS, the cTnI values will be greater than those in AVS, probably reflecting the need for left atrial muscle incision, vigorous retraction to expose the valve, and the implantation of a prosthesis directly into the muscular part of the mitral annulus when the valve is replaced. It is, therefore, important to determine the different cutoff for each type of surgery. A cTnI value of 15 ng/mL at 12 hours could be a relatively normal finding after mitral valve replacement surgery but could be a worrisome finding after aortic valve replacement. Future studies are needed to clarify the influence of the initial

aortic and mitral valve pathologic features (stenosis vs insufficiency) on postoperative myocardial damage.

The incidence of postoperative complications was enhanced in patients with cTnI levels greater than the cutoff. After both AVS and MVS, acute kidney injury and the need for permanent pacemaker insertion was significantly influenced by myocardial damage.

Considering that perioperative myocardial infarction can lead to increased mortality and morbidity after hospital discharge, we extended the follow-up period to the first 3 months after surgery and found a significant negative effect for greater cTnI release in the mid-term.

In our study, cTnI determinations were obtained using different assays with different upper reference limits for the 5 participating centers. The cTnI measurements could not be directly compared among the different assays owing to differences in the lower detection limits, upper reference limits, diagnostic cutpoints, assay imprecision with difficult standardization, and harmonization.⁹ Normalization is required when the data have different measurement units or in the case of absolute determinations not comparable among manufacturers. The measures must be transformed to a common scale before being combined. Some methods of rescaling include (1) dividing each measure by its standard deviation, (2) dividing each measure by its range, (3) assigning a score according to a certain comparable threshold, and (4) assigning a score according to the group's percentile ranking. The first 2 methods can be influenced by extreme values or outliers and the third requires that the commonly used 99th percentile concentrations should be comparable among manufacturers. Ranking is the simplest normalization technique and will not be affected by outliers. To overcome this issue and to facilitate comparisons, the cTnI peak values were transformed into percentile ranks for each patient within each center; then, the ranked data of the centers were combined for the global analysis. It is important to note that we also performed the analysis with

TABLE 3. Postoperative complication stratified by troponin I peak value

Variable	cTnI peak			p value
	Overall	Low	High	
Entire sample (n)	965	739	226	
Creatinine clearance reduction > 50%	5.9	3.3	14.7	<.001
Dialysis	2.7	1.5	6.8	<.001
Atrial fibrillation	30.9	30.9	31.0	.973
Reopening for complications	0.7	0.1	2.7	<.001
Reopening for bleeding	6.0	5.0	9.3	.018
Reintubation	3.6	2.7	6.6	.006
Permanent pacemaker insertion	3.0	2.3	5.3	.020
Wound infection	0.3	0.4	0.0	.337
Sepsis	1.2	0.5	3.5	<.001
Stroke	0.6	0.5	0.9	.565
TIA	0.3	0.1	0.9	.076
Confusion or delirium	1.2	1.1	1.8	.414
Overall stay > 30 d	2.1	1.8	3.1	.217
Intra-aortic balloon pump use	1.1	0.7	2.7	.024
Hospital mortality	2.6	1.4	6.6	<.001
AVS (n)	579	415	164	
Creatinine clearance reduction > 50%	7.0	4.6	13.2	<.001
Dialysis	2.6	1.7	5.0	.026
Atrial fibrillation	33.9	34.2	32.9	.768
Reopening for complications	0.7	0.0	2.4	.001
Reopening for bleeding	6.2	5.3	8.5	.146
Reintubation	2.9	2.4	4.3	.233
Permanent pacemaker insertion	2.6	1.9	4.3	.110
Wound infection	0.3	0.5	0.0	.373
Sepsis	1.0	0.5	2.4	.036
Stroke	0.5	0.2	1.2	.139
TIA	0.2	0.0	0.6	.111
Confusion or delirium	1.0	1.0	1.2	.784
Overall stay > 30 d	2.4	1.9	3.7	.222
Intra-aortic balloon pump use	1.0	0.7	1.8	.359
Hospital mortality	1.9	1.0	4.3	.009
MVS (n)	386	324	62	
Creatinine clearance reduction > 50%	4.2	1.6	18.6	<.001
Dialysis	2.9	1.2	11.9	<.001
Atrial fibrillation	26.4	26.5	25.8	.904
Reopening for complications	0.8	0.3	3.2	.017
Reopening for bleeding	5.7	4.6	11.3	.038
Reintubation	4.7	3.1	12.9	.001
Permanent pacemaker insertion	3.6	2.8	8.1	.041
Wound infection	0.3	0.3	0.0	.661
Sepsis	1.6	0.6	6.5	.001
Stroke	0.8	0.9	0.0	.447
TIA	0.5	0.3	1.6	.190
Confusion or delirium	1.6	1.2	3.2	.246
Overall stay > 30 d	1.6	1.5	1.6	.968
Intra-aortic balloon pump use	1.3	0.6	4.8	.031
Hospital mortality	3.6	1.9	12.9	<.001

Data presented as n or %. High cTnI peak refers to values greater than the 60th in AVS and 91st in MVS. cTnI, Cardiac troponin I; TIA, transient ischemic attack; AVS, aortic valve surgery; MVS, mitral valve surgery.

row cTnI values (data not shown), with results similar to those obtained with percentile rank values. Therefore, for

each cardiac procedure, according to the cTnI assays adopted, a cutoff value for MVS and AVS able to predict the risk of adverse outcome after surgery, should be determined.

What is the clinical utility of measuring myocardial damage biomarkers after surgery? In many postoperative intensive care units, they are not routinely evaluated because they are considered less essential than other clinical parameters. In contrast, we believe it is of paramount importance to perform a routine assessment of the postoperative myocardial damage biomarkers. A simple and inexpensive test can have critical prognostic power that can be used to change routine therapy, enhancing cardiovascular management with the possibility of reducing the rate of adverse events. It has recently been shown that even modest postoperative cTnI release will be associated with new areas of myocardial infarction as assessed using cardiac magnetic resonance imaging with late gadolinium enhancement¹⁵; therefore, the importance of assessing the efficacy of myocardial protection techniques and solutions used for each operation cannot be denied. The determinants of myocardial injury have been assessed for CABG¹⁶ but not comprehensively for valve operations. In our study, we did not examine the determinants of cTnI release after surgery because of limited space; however, several triggers not easily recordable in any registry should be considered, including muscle incision and retraction, iatrogenic coronary lesion, inadequate delivery of cardioplegia in the case of aortic insufficiency or because of retraction of the heart during administration, type of cardioplegia used, and route of cardioplegia delivery.¹⁷⁻¹⁹ Increased postoperative cTnI values could help the identification of specific treatment in the intensive care unit (ie, early angiography, intra-aortic balloon pump support) or might indicate a need for revision of myocardial protection strategies.

The present study had some limitations. Different assays for cTnI evaluation were adopted in the different hospitals, although a single, high-sensitivity assay would have been preferable. However, we overcame this limitation by percentile ranking. The accuracy of the cTnI peak evaluation could have been influenced by the timing of postoperative blood samples collected at intensive care unit acceptance and serially thereafter every day of the intensive care unit stay. Also, the mid-term follow-up data were not complete, being limited to residents of the Puglia region. The treating physicians were not unaware of the cTnI results; therefore, we could not exclude the bias that might have resulted from this knowledge.

The principle strength of our report was that the cTnI values and clinical data were prospectively collected in a institutional registry, with a link to an administrative database to gather the midterm vital status. For the first time, a specific assessment of the prognostic implications

FIGURE 2. Cumulative mortality in (A) aortic and (B) mitral valve surgery according to postoperative troponin I peak value. A high troponin I peak refers to values greater than the 60th in aortic and 91st percentile after mitral valve surgery.

of myocardial injury after AVS and MVS has been reported in a large sample size showing that cTnI is a powerful predictor of mortality and morbidity and could be added to validated preoperative and intraoperative risk factors.

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FIGURE E1. Receiver operating characteristic curve of percentile ranked cardiac troponin I peak values for in-hospital mortality stratified by surgery type (aortic valve and mitral valve surgery).