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BRIEF COMMUNICATION

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Influence of impairment in renal function on the accuracy of high-sensitivity cardiac troponin T for the diagnosis of perioperative myocardial infarction after heart valve surgery

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Abstract

We aimed to assess the influence of impairment in renal function over the high-sensitivity cardiac troponin T (hs-cTnT) accuracy to diagnose perioperative myocardial infarction (MI) after heart valve surgery. Heart valve surgery was performed in 805 patients from June 2012 to January 2016. Patients with enzymatic curves of hs-cTnT suggestive of myocardial necrosis and electrocardiogram and/or transthoracic echocardiogram criteria were identified as patients with perioperative MI. Impairment in renal function was defined as a postoperative creatinine clearance <50 ml/min at 16 h after surgery and for at least 48 h. Patients included were divided into 2 groups at 16 h: (i) patients with normal renal function (creatinine clearance >50 ml/min) and (ii) patients with impairment in renal function (creatinine clearance <50 ml/min). From a total of 805 patients undergoing heart valve surgery, 88 patients developed perioperative MI. When comparing receiver operating characteristic curves in patients with perioperative MI according to renal function, the optimal threshold of hs-cTnT at 16 h differed in patients with impairment in renal function (1303 vs 1095 pg/ml, $P < 0.001$). The diagnostic accuracy of hs-cTnT at 16 h was 93.4% [95% confidence interval (CI) 89.98–96.86], with an area under receiver operating characteristic curve (0.993, 95% CI 0.988–0.999 vs 0.972, 95% CI 0.952–0.992; $P < 0.001$). Renal function might influence in hs-cTnT levels. However, a hs-cTnT threshold of 1303 pg/ml at 16 h may be applied according to renal function to diagnose perioperative MI after cardiac surgery.

Keywords: Cardiac surgery • High-sensitivity cardiac troponin T • Renal dysfunction • Perioperative myocardial infarction

INTRODUCTION

Cardiac surgery carries a well-established risk of perioperative myocardial infarction (MI) and renal dysfunction. Cardiac troponins have been recommended as the preferred biomarkers for diagnosing MI after cardiac surgery [1]. High-sensitivity cardiac troponin T (hs-cTnT) is a reliable biomarker with high sensitivity and high negative predictive value [1, 2]. It has been suggested that decreased renal clearance is a proposed explanation for troponin elevation in renal failure [3]. Therefore, we aimed to assess the influence of impairment in renal function over the hs-cTnT accuracy to diagnose perioperative MI.

METHODS

This was a prospective observational study where 805 consecutive patients, who underwent heart valve surgery with cardiopulmonary bypass (CPB), were included from June 2012 to January 2016; the follow-up continued until June 2016. Two patients died in the operating room. The target population consisted of patients who underwent heart valve surgery with CPB. Major exclusion criteria included patients <18 years, recent medical history of coronary artery disease, coronary artery bypass grafting, heart transplantation and patients with preoperative paced rhythms. The elevation of hs-cTnT is a frequent finding in the postoperative period of uncomplicated cardiac surgery. We did not include patients who underwent coronary artery bypass grafting because the mechanism of development of perioperative MI is usually the occlusion of a previous patency graft that should undergo percutaneous coronary intervention with the requirement of contrast administration which might influence the impairment in renal function. The surgical and anaesthetic techniques and the treatment the patient received in the intensive care unit (ICU) did not differ from ordinary procedures.

Diagnosis of perioperative myocardial infarction

According to The Third Universal Definition of MI and to our previous published article [4], criteria for diagnosing perioperative MI after heart valve surgery should be based on the elevation of biomarkers (requiring a stable baseline of hs-cTnT before

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Table 1: Demographic, clinical and pre-, intra- and postoperative characteristics of the group of patients with CCr >50 ml/min at 16 h and the group with CCr <50 ml/min at 16 h after cardiac surgery

	CCr >50 ml/min at 16 h (*n* = 574)	CCr <50 ml/min at 16 h (*n* = 228)	*P*-value
Preoperative characteristics			
Age (years)	66.9 ± 9.5	75.4 ± 6.4	**<0.001**
Male gender	314 (54.7)	102 (44.7)	**0.011**
Weight (kg)	75.5 ± 12.6	67.5 ± 11.3	**<0.001**
Ejection fraction (%)	60.3 ± 6.8	60.4 ± 6.9	0.974
Arterial hypertension	493 (85.9)	214 (93.9)	**0.002**
Dyslipidaemia	414 (72.1)	177 (77.6)	0.110
Diabetes mellitus type 2	110 (19.2)	52 (22.8)	0.246
Previous stroke	25 (4.4)	13 (5.7)	0.418
Peripheral arterial disease	13 (2.3)	9 (3.9)	0.188
Pulmonary chronic obstructive disease	46 (8.0)	18 (7.9)	0.955
Chronic renal failure	15 (2.6)	31 (13.6)	**<0.001**
Previous coronary artery disease	38 (6.6)	20 (8.8)	0.289
Previous heart valve surgery	67 (11.7)	29 (12.7)	0.680
Atrial fibrillation	198 (34.5)	94 (41.2)	0.074
EuroSCORE II (%)	1.6 ± 0.6	2.1 ± 0.9	**<0.001**
CCr (ml/min)	89.1 ± 24.1	67.5 ± 18.1	**<0.001**
Creatinine (mg/dl)	0.83 ± 0.2	0.88 ± 0.3	0.709
hs-cTnT (pg/ml)	0.02 ± 0.02	0.02 ± 0.01	0.339
Intraoperative characteristics			
CPB time (min)	101.5 ± 30.5	108.9 ± 40.8	0.102
Aortic cross-clamp time (min)	75.5 ± 25.4	79.4 ± 31.1	0.289
Postoperative characteristics			
Time of mechanical ventilation (h)	10.4 ± 21.7	34.6 ± 82.5	**<0.001**
Complications after surgery	50 (56.8)	171 (23.9)	**<0.001**
ICU stay (days)	3.8 ± 3.6	5.9 ± 6.2	**<0.001**
Hospital stay (days)	15.3 ± 10.0	19.1 ± 11.2	**<0.001**

Boldface values: Values with statistical significance ($P < 0.05$).

Data are expressed as median ± standard deviation, absolute rate and percentage. Statistical significance was defined as *P*-value <0.05.

CCr: creatinine clearance; CPB: cardiopulmonary bypass; EuroSCORE: European System for Cardiac Operative Risk Evaluation; hs-cTnT: high-sensitivity cardiac troponin T; ICU: intensive care unit; SD: standard deviation.

surgery) with enzymatic curves suggestive of ischaemia and peak values reached at similar times for spontaneous criteria (the onset of new pathological Q-waves or new bundle branch block or imaging evidence of new wall motion abnormality). Thus, patients with enzymatic curves of hs-cTnT suggestive of myocardial necrosis and electrocardiogram and/or transthoracic echocardiogram criteria were identified as patients with perioperative MI, and details are described in our previous published article [4]. An experienced cardiologist, blinded to outcomes, analysed electrocardiogram and transthoracic echocardiogram before and after heart valve surgery. Blood samples, for the measurements of hs-cTnT, were taken by qualified personnel at ICU admission and 8, 16, 24, 48 and 72 h after surgery.

Assessment of renal function

Creatinine was measured at ICU admission and at 8, 16, 24, 48 and at 72 h after surgery. Creatinine clearance (CCr), which is defined as the volume of plasma that is completely cleared of creatinine in a unit of time and is a widely used test to estimate the glomerular filtration rate, was estimated using the Cockcroft formula [5]. Impairment in renal function was defined as a postoperative CCr <50 ml/min at 16 h after surgery and during at least 48 h. Patients included were divided into 2 groups at 16 h after surgery: (i) patients with normal renal function (CCr > 50 ml/min) and (ii) patients with impairment in renal function (CCr < 50 ml/min).

Statistical analysis

Data are expressed as mean ± standard deviation or median. Comparisons between the 2 groups were performed using the Student's *t*-test, the Mann–Whitney test and the Fisher's exact method, when appropriate. Receiver operating characteristic (ROC) analysis was used to assess postoperative hs-cTnT levels after heart valve surgery. The cut-off for hs-cTnT was estimated with the highest Youden index [(sensitivity + specificity) - 1]. The area under the ROC curve and the corresponding 95% confidence intervals (CI) and *P*-values were calculated using the Wald test for pairwise comparison with chance. The accuracy of the test depends on how well the test separates the group being tested and is reflected by the area under the ROC curve. Comparison of areas under the ROC curve was performed using a non-parametric technique.

RESULTS

From a total of 805 patients undergoing heart valve surgery, 88 (10.9%) patients developed perioperative MI showing a hs-cTnT

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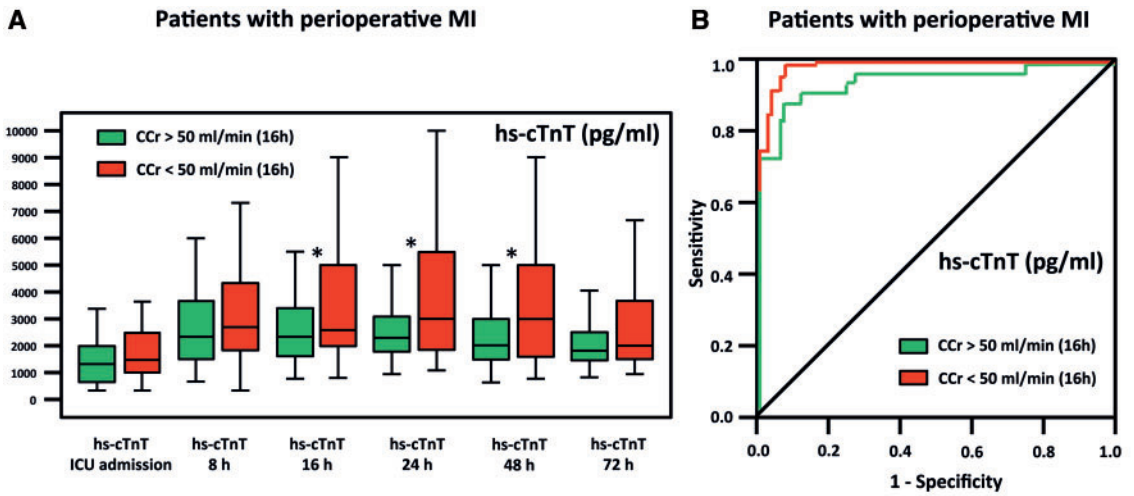

hs-cTnT (16h)	CCr > 50 ml/min (16h) (n = 574)	CCr < 50 ml/min (16h) (n = 228)	P value
Threshold of hs-cTnT	1095 pg/ml	1303 pg/ml	< 0.001
AUC	0.972 (0.952-0.992)	0.993 (0.988-0.999)	< 0.001
Sensitivity %	93.02	97.78	< 0.001
Specificity %	93.51	96.60	< 0.001
Accuracy %	93.42	96.69	< 0.001

Figure 1: (**A**) Box plot of hs-cTnT levels in patients with perioperative MI at ICU admission and at 8, 16, 24, 48 and 72 h after heart valve surgery in the groups of patients with or without impairment in renal function. Data are expressed as median (25th–75th interquartile range). *$P < 0.05$: Statistically significant differences. (**B**) Comparison of receiver operating characteristic curves showing the relationship between sensitivity and 1-specificity in determining the predictive value of hs-cTnT for the diagnosis of perioperative MI in patients with or without postoperative impairment in renal function. AUC: area under receiver operating characteristic curve; CCr: creatinine clearance; hs-cTnT: high-sensitivity cardiac troponin T; ICU: intensive care unit; MI: myocardial infarction.

level of 1057 pg/ml at 16 h after surgery ($P < 0.001$), with the highest sensitivity and specificity, and electrocardiogram and/or transthoracic echocardiogram criteria. In the perioperative period, 46 (5.7%) patients had an estimated CCr <50 ml/min at 16 h. Before surgery, the group of patients with CCr <50 ml/min at 16 h had a mean estimated CCr of 67.5 ± 18.1 ml/min vs 89.1 ± 24.1 ml/min in the group with CCr >50 ml/min at 16 h ($P < 0.001$). Levels of serum creatinine were numerically higher in the group of patients with CCr <50 ml/min at 16 h than in the group of patients with CCr >50 ml/min at 16 h (0.88 ± 0.3 vs 0.83 ± 0.2 mg/dl; Table 1).

Postoperative impairment in renal function was observed in 228 (28.3%) patients. Renal function might influence hs-cTnT levels in patients with or without perioperative MI. In patients with perioperative MI, the peak value of hs-cTnT reached at 16 h was significantly higher in patients with impaired renal function (median = 2885 pg/ml vs 2247 pg/ml, $P = 0.002$) (Fig. 1A).

When comparing ROC curves in patients with perioperative MI according to renal function, the optimal threshold of hs-cTnT at 16 h differed in patients with impairment in renal function (1303 vs 1095 pg/ml, $P < 0.001$). The diagnostic accuracy of hs-cTnT at 16 h was 93.4% (95% CI 89.98–96.86) with an area under the ROC curve (0.993, 95% CI 0.988–0.999 vs 0.972, 95% CI 0.952–0.992; $P < 0.001$) (Fig. 1B).

DISCUSSION

The main findings of this study are as follows: (i) hs-cTnT levels were increased in patients with postoperative impairment in renal function, either with or without perioperative MI and (ii) the diagnostic accuracy of hs-cTnT was significantly increased when the threshold at 16 h was adapted to renal function showing an increase of 208 pg/ml in patients with perioperative MI and CCr <50 ml/min.

In patients undergoing cardiac surgery, a decreased renal function was associated with higher cardiac morbidity and mortality [5, 6]. We observed that renal function might influence hs-cTnT levels. High levels of hs-cTnT have been reported in patients undergoing non-complicated cardiac surgery with end-stage renal failure [2, 4, 5]. The interference of renal function with hs-cTnT levels might be explained because troponins are large macromolecules that are small enough to be cleared by healthy kidneys, but renal impairment leads to clearance decrease [3, 5, 6].

Although hs-cTnT levels were also increased in patients without perioperative MI with impaired renal function, the magnitude of the increases related to impairment in renal function were higher in patients with perioperative MI. The current study improves the definition of perioperative MI after cardiac surgery with impairment in renal function providing a new threshold of hs-cTnT with the highest sensitivity and specificity.

However, the elevation of hs-cTnT after heart valve surgery might be due to several factors that may provide some insights into its mechanism: (i) direct trauma of the myocardium, which can be produced by sutures or direct manipulation of the heart, (ii) myocardial ischaemia related to an inadequate intraoperative cardioprotection, (iii) microvascular embolisms related to reperfusion and (iv) myocardial damage induced by the release of oxygen free radicals. Therefore, the results should be interpreted with caution.

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CONCLUSION

Renal function might influence the hs-cTnT levels. However, a hs-cTnT threshold of 1303 pg/ml at 16 h should be applied according to renal function impairment to diagnose perioperative MI after cardiac surgery.

Conflict of interest: none declared.

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