

Off-Pump Coronary Bypass Grafting Is Associated with Less Myocardial Injury Than Coronary Bypass Surgery with Cardiopulmonary Bypass

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ABSTRACT

Background: Excessive myocardial necrosis following coronary artery bypass grafting is associated with adverse outcome. The present study was designed to assess the extent of myocardial injury after conventional coronary artery bypass grafting with cardiopulmonary bypass (ONCAB) compared with off-pump coronary artery bypass (OPCAB).

Methods: Measurements of serum cardiac troponin T (TnT) were obtained in 137 consecutive, unselected patients who underwent coronary artery bypass grafting. Serial blood sampling was performed at 3 time intervals after surgery: immediately postoperatively, 6 to 12 hours postoperatively, and 18 to 24 hours postoperatively.

Results: ONCAB patients totaled 122, and OPCAB patients numbered 15. Ten patients in the ONCAB group suffered perioperative complications, compared with no patients in the OPCAB group. At each time point examined, OPCAB patients exhibited significantly less release of TnT than ONCAB patients (immediately postoperative TnT, 1.99 ± 4.75 ng/mL versus 0.20 ± 0.32 ng/mL, $P = .004$; 6- to 12-hour TnT, 2.28 ± 3.66 ng/mL versus 0.37 ± 0.32 ng/mL, $P = .001$; and 18- to 24-hour TnT 1.59 ± 3.49 ng/mL versus 0.30 ± 0.32 ng/mL, $P = .01$). When ONCAB patients with perioperative ischemic complications were excluded, the differences between the 2 groups remained. The OPCAB patients still demonstrated less TnT release, typically 5- to 6-fold less than for ONCAB patients.

Conclusions: The nearly 6-fold reduction of postoperative TnT associated with OPCAB suggests that off-pump surgery may offer superior cardioprotection than coronary artery bypass grafting with conventional cardiopulmonary bypass.

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INTRODUCTION

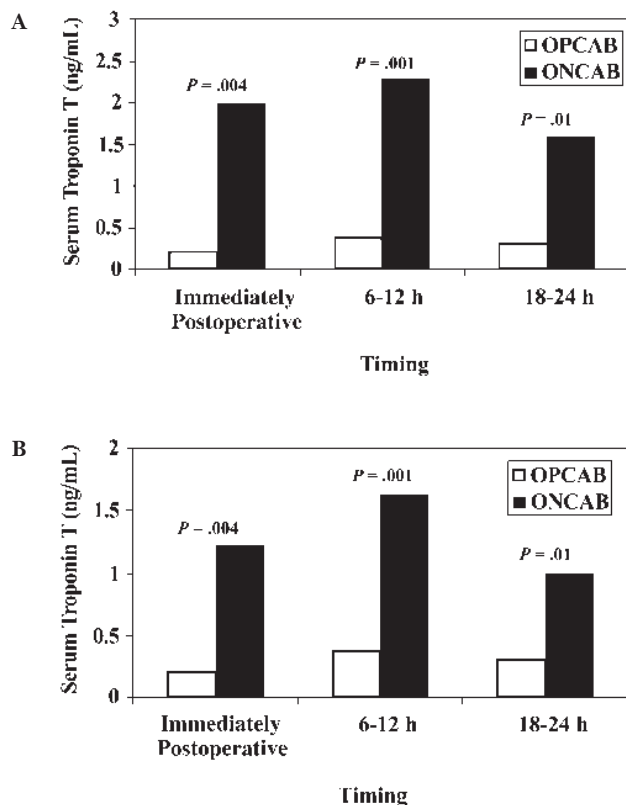
Coronary artery bypass grafting (CABG) performed with cardiopulmonary bypass (ONCAB) has been the gold standard for myocardial revascularization over the last 3 decades [Favaloro 1998]. Recently, off-pump coronary artery bypass (OPCAB), a technique performed on a beating heart without aortic cross-clamping or cardiopulmonary bypass (CPB), has garnered great attention due to theoretical benefits including decreased inflammation, coagulopathy, and atheroembolic complications [Ascione 1999b, Wan 1999, Diegeler 2000, Yokoyama 2000]. OPCAB may avoid the morbidity related to cardioplegic arrest, aortic cross-clamping, and CPB. The procedure, however, poses risk of ischemic myocardial injury related both to the necessity for temporary occlusion of a coronary artery supplying normothermic, metabolically active myocardium and to epicardial placement of stabilizer devices, which might be expected to lead to injury to underlying myocardium or a coronary vessel [Bredee 1998, Svennevig 2000]. In addition, because of the manipulation of the coronary artery required in the OPCAB technique, early postoperative complications due to coronary artery trauma might be expected to be more common [Boncheck 1998, Jegaden 2001].

Despite the concerns, early outcome of OPCAB surgery appears to be quite good, particularly compared with outcome of conventional ONCAB techniques. One mechanism that might explain the good outcome among patients treated with the OPCAB technique may be superior operative myocardial protection compared with conventional CABG with CPB. Because there exist limited data on the relationship between OPCAB and perioperative myocardial injury, we prospectively studied the differences between ONCAB and OPCAB with respect to perioperative myocardial protection, as assessed by serial measurement of troponin T (TnT).

MATERIALS AND METHODS

Patients and Clinical Data Collection

Over a 6-week period, 137 consecutive patients admitted to the cardiac surgical intensive care unit at the Massachusetts General Hospital were enrolled after CABG. Patients were identified on admission to the intensive care unit, and clinical variables were collected in a prospective



A, Comparison of postoperative serum troponin T (TnT) levels between patients treated with off-pump coronary artery bypass (OPCAB) ($n = 15$) and patients treated with coronary artery bypass grafting with cardiopulmonary bypass (ONCAB) ($n = 122$). At all time points, relative to those treated on pump, patients in the OPCAB group demonstrated lower serum TnT levels. B, Comparison of postoperative serum TnT levels between patients free of complications treated with OPCAB ($n = 15$) versus those treated with ONCAB ($n = 112$). Patients treated off pump demonstrated similar significantly lower amounts of perioperative myocardial necrosis.

manner by a study coordinator blinded to the results of cardiac biomarker values. Clinical factors collected included demographics, past medical history, prior medication use, cardiac catheterization results, and presenting cardiac syndrome. Additional data regarding surgical procedures, including type of surgery, number of bypass grafts, bypass/ischemic times, and intraoperative complications, also were collected. Postoperative variables gathered included length of intensive care unit stay and the results of postoperative electrocardiography (ECG). The patients' cases were followed through the end of hospitalization for clinical outcome.

Complications were prospectively defined as (1) new ECG Q-wave myocardial infarction or new left bundle branch block; (2) cardiogenic shock, defined as sustained impairment in cardiac index (≤ 1.5 L/min) necessitating either prolonged (≥ 24 hours) or significant need for (≥ 2 drugs) vasopressor therapy; and (3) death. End points were adjudicated at the end of hospitalization.

Biomarkers of Myocardial Necrosis

Serial samples of blood, approximately 5 mL each, were drawn on arrival to the surgical intensive care unit (immediately postoperative) and 6 to 8 hours and 18 to 24 hours after surgery. Serum TnT levels were measured with the third-generation Enzygnost TnT assay (Roche Diagnostics, Indianapolis, IN, USA) on an Elecsys 1010 platform (Roche Diagnostics). The lower limit of detection of this TnT assay is 0.01 ng/mL, and the conventional threshold for diagnosis of myocardial necrosis at our institution is 0.10 ng/mL.

Surgical Technique

For OPCAB surgery, exposure was obtained via full median sternotomy and deep pericardial traction sutures. Target coronary artery stabilization was achieved with an immobilizer system (Genzyme Biosurgery, Cambridge, MA, USA). ONCAB was performed with full CPB and tepid cooling. Myocardial protection strategy with ONCAB was left to the discretion of the surgeon and included cold or warm potassium cardioplegia provided via antegrade, retrograde, or both routes.

Statistical Analysis

All statistical analyses were performed with SPSS software (Chicago, IL, USA). Differences between the treatment groups were tested with the chi-square test for categorical variables and the rank sum test for continuous variables. Mean cardiac marker levels were assessed for the group as a whole as well as for patients with or without complications. Comparisons of mean cardiac marker levels between patients with or without complications were made with the Wilcoxon rank sum test. All P values were 2-sided, values $< .05$ considered significant.

RESULTS

Baseline Demographics

The baseline clinical characteristics of the study patients are detailed in the Table, which demonstrates our institutional bias with respect to the use of the OPCAB technique. Compared with ONCAB patients, OPCAB patients tended to be older (mean age, 72 versus 67 years, $P = .10$) and more likely to have diabetes (67% versus 30%, $P = .06$) or hypertension (87% versus 72%, $P = .06$). In addition, more OPCAB patients presented with congestive heart failure (CHF) (40% versus 10%, $P = .10$), whereas a significantly higher percentage of ONCAB patients presented with stable angina pectoris (20% versus 0%, $P = .03$). Preoperative medication use was comparable in the two groups. Although the severity of coronary artery disease as measured by number of coronary vessels diseased was similar between the ONCAB and the OPCAB groups (2.7 ± 0.7 versus 2.6 ± 0.7 , $P = .33$), compared with patients undergoing ONCAB, patients undergoing OPCAB tended to receive significantly fewer bypass grafts (3.6 ± 1.2 versus 2.4 ± 1.1 , $P = .002$), a finding consistent with those of prior studies of the OPCAB technique.

Postoperative Serum TnT Levels

Mean TnT levels among the study patients are detailed in part A of the Figure. Mean postoperative TnT level

Table 1. Baseline Clinical Characteristics*

Variable	ONCAB (n = 122)	OPCAB (n = 15)	P
Age, mean \pm SD (range), y	66.9 \pm 11.7 (16-84)	71.6 \pm 10.5 (47-85)	.10
Male sex	78.7%	60.0%	.10
Past medical history			
Diabetes	29.5%	66.7%	.06
Arterial hypertension	72.1%	86.7%	.06
Hypercholesterolemia	85.2%	93.3%	.32
Tobacco use	41.0%	46.7%	1.00
History of coronary artery disease	67.2%	66.7%	.71
Prior myocardial infarction	33.6%	46.7%	1.00
History of valve disease	4.1%	13.3%	.56
Prior congestive heart failure	13.1%	26.7%	.16
Prior coronary artery bypass grafting	8.2%	6.7%	1.00
Prior percutaneous coronary intervention	16.4%	26.7%	.18
Presenting syndrome†			
Chest pain	18.0%	26.7%	1.00
Congestive heart failure	9.8%	40%	.10
Cardiac arrest	2.5%	0%	.32
Stable angina pectoris	19.7%	0%	.03
Unstable angina pectoris	41.0%	26.7%	.71
Non-Q-wave myocardial infarction	18.0%	26.7%	.32
ST elevation myocardial infarction	9.8%	6.7%	1.00
Prior medication use			
β -Blocker	81.1%	93.3%	.18
Aspirin	93.4%	93.3%	.32
Nitrates	66.4%	86.7%	.06
Calcium channel blockers	27.9%	6.7%	.10
Heparin	37.7%	53.3%	.16
Statins	74.6%	86.7%	.06
No. of diseased vessels, mean \pm SD	2.7 \pm 0.69	2.6 \pm 0.74	.33
Ejection fraction, mean \pm SD (range), %	50.7 \pm 14.7 (15-78)	41.3 \pm 18.3 (12-73)	.64

*OPCAB indicates off-pump coronary artery bypass; ONCAB, coronary artery bypass grafting with cardiopulmonary bypass.

†Some patients presented with more than one syndrome.

between the entire ONCAB group (n = 122) and the OPCAB patients (n = 15) was 1.99 ± 4.75 ng/mL versus 0.20 ± 0.32 ng/mL ($P = .004$) immediately postoperatively. Mean 6- to 12-hour level was 2.28 ± 3.66 versus 0.37 ± 0.32 ($P = .001$), and mean 18- to 24-hour level of TnT was 1.59 ± 3.49 ng/mL versus 0.30 ± 0.32 ng/mL ($P = .01$). To more clearly delineate the extent of myocardial injury with or without CPB, we excluded all patients with in-hospital ischemic complications, including shock, death, or new ECG Q-wave myocardial infarction (Figure, B). Although none of the OPCAB patients developed in-hospital complications, 10 ONCAB patients suffered complications (8 developed shock, 4 developed ECG evidence of new myocardial, and 1 died). Even after exclusion of ONCAB patients with complications (who therefore might be expected to have incrementally higher TnT levels), patients who underwent OPCAB surgery still had 5- to 6-fold less myocardial injury at each time point examined (Figure, B) (postoperative, 1.22 ± 0.32 versus 0.20 ± 0.32 ng/mL, $P = .004$; 6-12 hours, 1.62 ± 1.04 versus 0.37 ± 0.32 ng/mL, $P = .001$; 18-24 hours, 1.0 ± 0.74 versus 0.26 ± 0.32 , $P = .01$).

DISCUSSION

With avoidance of global cardiac arrest and aortic manipulation, it has been suggested that in appropriately selected patients, surgery with the OPCAB technique may reduce early postoperative morbidity and mortality. Conversely, epicardial placement of a stabilizer platform as well as temporary occlusion of a coronary artery feeding metabolically active myocardium during OPCAB may induce intraoperative myocardial ischemia and injury. We sought to compare the extent of myocardial injury after conventional CABG with CPB versus that associated with the OPCAB technique. In this consecutive, unselected series of 137 patients undergoing CABG surgery at our institution, the serial TnT levels suggested, despite theoretical risks of OPCAB and the relatively high-risk patient population who underwent OPCAB at our institution, that beating-heart myocardial revascularization was associated with less myocardial injury than conventional ONCAB surgery.

The baseline characteristics of the OPCAB patients were at least similar to those of the ONCAB group, if not actually

predictive of higher operative risk. This finding is reflective of our institutional bias, wherein patients considered at high risk during CPB are generally selected for OPCAB. The fact that the OPCAB group was older, had a greater percentage of patients with diabetes mellitus and CHF, and had a lower mean ejection fraction reflects this selection bias. Despite higher-risk baseline characteristics, the OPCAB patients consistently suffered less myocardial necrosis, with nearly 6-fold less TnT release at all time points, compared with ONCAB patients.

In other small studies of the OPCAB technique, levels of cardiac biomarkers after OPCAB procedures have been shown to be lower compared with levels after ONCAB. In a study with 80 patients, Ascione et al found that cardiac troponin I (TnI) release was constantly lower in their OPCAB group at multiple postoperative time points [Ascione 1999a]. Kilger et al also documented lower TnI levels after minimally invasive coronary surgical procedures (either minimally invasive direct CABG or use of the Octopus method by median sternotomy) versus conventional coronary bypass [Kilger 2000]. In the only other study to assess cardiac TnT levels among OPCAB patients, Krejca et al found 12-fold higher TnT levels 24 hours postoperatively in their ONCAB group compared with 13 patients revascularized via OPCAB [Krejca 1999]. These data are in accordance with ours. A recent larger randomized study of OPCAB versus ONCAB also found significantly less myocardial injury with off-pump surgery, as demonstrated by serial assessment of the creatine kinase muscle-brain isoenzyme (CK-MB) [van Dijk 2001]. In that study, CK-MB release was 41% lower in the OPCAB group, and this was the only major short-term outcome found to be reduced with OPCAB [van Dijk 2001, Yacoub 2001]. We have previously shown TnT to be superior to CK-MB for quantifying myocardial necrosis and predicting impending complications following cardiac surgery [Januzzi 2002]. Because TnT results are far superior to those of CK-MB, the results for the latter marker are not included in this paper but were nonetheless similarly lower in OPCAB patients (data not shown).

We have previously demonstrated elevated TnT levels after cardiac surgery to be an important predictor of early complications and a reliable method for estimating perioperative myonecrosis. In a separate analysis of 224 patients undergoing cardiac surgery, we found that a TnT level ≥ 1.58 ng/mL immediately postoperatively or at the 18- to 24-hour time point was the strongest predictor of impending postoperative complications, such as cardiogenic shock and death [Januzzi 2002]. In the ONCAB group as a whole, the mean postoperative TnT levels at each time point were elevated beyond this threshold, in part reflecting the 10 patients with complications. Even after exclusion of the patients with complications in the ONCAB group, the mean levels of TnT were still significantly higher among patients undergoing surgery with CPB, suggesting that OPCAB may be associated with superior myocardial protection.

The long-term impact of excessive perioperative myonecrosis (estimated biochemically) is becoming clearer.

Results of a recent analysis suggested that excessively elevated CK-MB levels following cardiac surgery may be associated with poorer long-term prognosis [Klatte 2001] irrespective of early outcome. Despite the relationship between TnT and early postoperative complications, the long-term significance of less TnT release following coronary bypass surgery has not been defined. Preliminary results from long-term follow-up of a patient cohort suggest that the superiority of TnT over CK-MB for predicting outcome remains strikingly superior at 1 year (J.L.J., unpublished data). Whether strategies to attenuate myocardial necrosis following cardiac surgery will have an impact on longer-term outcome remains speculative.

Our study was limited by the following 3 factors. First, because the study was nonrandomized, patient selection may have systematically altered baseline clinical characteristics, potentially leading to lower TnT levels in the OPCAB group. However, the baseline demographics revealed that the OPCAB patients tended to have higher operative risk features, and thus their outcomes (and TnT levels) would have been predicted to be higher, not lower. Second, the myocardial protection and surgical strategies in the ONCAB group were not standardized. The variation in cardioplegic and surgical access route strategies reflects general cardiac surgical practice, however. Finally, the number of OPCAB patients in our study was small; however, our results were significant, consistent with the results of previous studies of OPCAB, and extended to include serum TnT assessment.

In conclusion, we demonstrated that, compared with conventional CABG with CPB, surgical coronary revascularization by the OPCAB technique is associated with a nearly 6-fold reduction in perioperative myocardial necrosis, as assessed with postoperative serum TnT levels. These reductions were significant despite the technical aspects of the OPCAB procedure, which includes the need for occlusion of coronary vessels subtending beating, metabolically active myocardium. Whether the significant reductions in perioperative myocardial necrosis following OPCAB can be expected to result in superior long-term outcome (compared with ONCAB) remains to be determined. Long-term randomized studies directly comparing these two surgical strategies are needed. Finally, our data are of value in that they help to define the expected magnitude of TnT following uncomplicated OPCAB, which will be important as the use of TnT testing after cardiac surgery increases.

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