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Cardiac Troponin T Levels in On- and Off-Pump Coronary Artery Bypass Surgery

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ABSTRACT

Background. Conventional coronary artery bypass graft surgery (CCAB) has been associated with greater myocardial injury than off-pump surgery (OPCAB). However, the extent of myocardial injury following CCAB and OPCAB has not been assessed by priority of surgery or the number of diseased vessels. We tested the hypothesis that the additional myocardial injury associated with CCAB compared with OPCAB is sustained when patients are stratified by priority and 2- or 3-vessel disease.

Methods and Results. In this prospective cohort, we measured 24-hour postoperative cardiac troponin T (cTnT) following CCAB and OPCAB surgery to determine if OPCAB results in less perioperative myocardial damage by priority (urgent or elective). We studied 1511 patients who underwent heart surgery in one hospital in northern New England between 2000 and 2004. Surgeons used either CCAB (778 patients) of OPCAB (733 patients). Unpaired *t* tests were used to test the mean difference in cTnT between CCAB and OPCAB subgroups. Mean cTnT levels were significantly higher in the CCAB group (0.94 ng/mL) than the OPCAB group (0.18 ng/mL) with $P < .001$; this difference was consistent across urgent and elective surgeries, and patients with both 2- and 3-vessel disease. CCAB patients consistently demonstrated higher cTnT levels. Similar results were evident when stratified by patient characteristics and surgeon.

Conclusions. In summary, higher postoperative cTnT levels are associated with CCAB than with OPCAB, regardless of priority, number of diseased vessels, patient characteristics, or surgeon. OPCAB results in less myocardial injury in patients, whether they present with 2- or 3-vessel disease and whether they undergo urgent or elective cardiac surgery.

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INTRODUCTION

The clinical usefulness of conventional coronary artery bypass surgery (CCAB) has enabled surgeons to operate on an arrested heart in patients with multi-vessel disease [Hernandez 2000, 2001]. However, some argue cardiopulmonary bypass (CPB) used in the conventional setting induces a harmful inflammatory cascade [Matata 2000; Biglioli 2003; Okubo 2003] and micro-embolic events, which may lead to a heightened risk of myocardial necrosis [Perrault 1997; Krejca 1999; Bennetts 2002; Kathiresan 2003; Sahlman 2003; Khan 2004], neurological deficits [Mazzone 2003], and renal failure [Tang 2002]. Off-pump coronary artery bypass surgery (OPCAB) was developed to minimize the morbidity and mortality from CPB-assisted CCAB surgery; this method leaves the heart beating (no CPB) and uses stabilization devices [Mitka 2004]. OPCAB has the potential to reduce the risk of perioperative-induced myocardial necrosis, making it a useful alternative in bypass surgery.

Cardiac troponin T (cTnT) has been utilized as a marker of myocardial damage and has been shown to be a more specific and sensitive marker than cardiac troponin I [Bennetts 2002]. Elevated postoperative cTnT has been associated with higher mortality rates at 1 year following CABG surgery [Kathiresan 2004]. Several studies have shown OPCAB procedures have less cTnT released into the blood during the perioperative period [Koh 1999; Krejca 1999; Gulielmos 2000; Masuda 2002; Ghosh 2003; Kathiresan 2003; Dybdahl 2004; Khan 2004]; this finding suggests that OPCAB does a better job protecting the myocardium [Krejca 1999; Bennetts 2002; Kathiresan 2003; Khan 2004]. However, all the studies to date have been small and not able to determine if this effect was consistent across subgroups, including priority (elective or urgent) and number of diseased vessels. In this study, we sought to measure the postoperative release of cTnT in CCAB and OPCAB procedures to determine if OPCAB results in lower cTnT release in relation to priority (elective and urgent) and among patients with 2- or 3-vessel disease to determine if this effect is indeed real and not specific only to elective surgeries or patients with less severely diseased cardiac anatomy.

Table 1. Patient Characteristics*

	CCAB	OPCAB	P†
Number of procedures by group	778	733	
Patient age, %			
<60 y	31.0	28.8	.469
60-69 y	32.0	32.2	
70-79 y	31.1	31.2	
≥80 y	5.9	7.8	
Female, %	25.1	28.1	.181
Body mass index			
<31	67.2	69.2	.755
31-36 (obese)	24.3	22.9	
≥37 (severely obese)	8.0	7.6	

*CCAB indicates conventional coronary artery bypass; OPCAB, off-pump coronary artery bypass.

†*P* for χ^2 value.

MATERIALS AND METHODS

Data Collection

The Northern New England Cardiovascular Disease Study Group (NNECDSG) was founded in 1987 as a regional voluntary consortium capturing 100% of the coronary revascularizations and/or valve procedures in northern New England including those from 8 medical centers in Vermont, New Hampshire, and Maine. The group consists of clinicians, hospital administrators, and health care research personnel who seek to continually improve the quality, safety, effectiveness, and cost of medical interventions in cardiovascular disease. The Institutional Review Board approved the NNECDSG for data collection and analysis of these data.

We prospectively enrolled 1511 consecutive CCAB and OPCAB procedures at a single medical center between January 2000 and June 2004. There were 778 CCAB and 733 OPCAB procedures. Postoperative cTnT (ng/mL) levels were analyzed 24 hours after the surgery.

Data were recorded prospectively for all patients; methods for data collection have been described previously [Hernandez 2000, 2001]. Cardiac catheterizations were performed using standard methods during the course of regular clinical care. The number of diseased coronary vessels were assessed using criteria established by the National Heart, Lung, and Blood Institute Coronary Artery Surgery Study [1981]. Priority of the surgical procedure was assessed by the cardiothoracic surgeons as previously described [O'Connor 1991; Surgenor 2001].

For these analyses, we excluded patients undergoing CABG operation incidental to heart valve repair, resection of ventricular aneurysm, or another surgical procedure (n = 686). We excluded patients operated on by surgeons who had performed fewer than 100 OPCAB procedures during the study period (n = 407), restricting the analysis to high-volume surgeons using both CCAB and OPCAB. We excluded patients not undergoing urgent or elective priority with 2- or 3- vessel disease (n = 90).

Surgical Procedures

Surgical methods have been described previously [Hernandez 2000, 2001]. The decision to perform the operation with or without a heart-lung machine was made by the operating surgeon. All procedures were done using a median sternotomy incision. The choices of conduit used and vessels grafted were made by the surgeon. Heparin doses varied by surgeon. Various techniques were used to afford exposure of all coronary artery segments, and several retractor-stabilizer systems were used according to the individual surgeon's preference. Management of CCAB cases with regard to CPB measurements, use of hypothermia, and myocardial protection technique used was determined by individual surgeons' preferences. Hypothermic cardioplegia and blood was used for CPB patients with no variation by surgeon.

The Medtronic Octopus (Minneapolis, MN, USA) and Genzyme Cohn Cardiac (Cambridge, MA, USA) stabilizer systems were used for the OPCAB procedures. Shunts were rarely used. Only small sections of the myocardium (the area just distal to the artery being bypassed at the point of the anastomosis) were made ischemic for a very brief period of time (the time required to perform that particular distal anastomosis). Once that anastomosis was completed, that area of myocardium was completely revascularized and reperfused while the remainder of the operation was performed. There were no periods of global ischemia as one would see with a cross-clamp applied.

cTnT

Postoperative cTnT was collected the morning after incision at 24 hours in the intensive care unit. The clinical laboratory measured the cTnT levels directly following sample collection (Roche Diagnostics, Indianapolis, IN, USA). We reported the geometric mean for cTnT (ng/mL). The lower limit of this assay was 0.01 (ng/mL), and the threshold for myocardial necrosis was diagnosed at 0.20 (ng/mL) [Coudrey 1998; Bennetts 2002].

Statistical Analysis

The goal of this analysis was to compare OPCAB with CCAB with respect to patient and disease characteristics and perioperative outcomes. The analysis was conducted using Stata release 8.0 software (Stata, College Station, TX, USA).

Table 2. Patient Comorbidities*

	CCAB	OPCAB	P†
Vascular disease, %	23.4	26.1	.230
Diabetes, %	34.8	34.0	.724
Preoperative renal failure or creatinine ≥2, %	3.1	2.7	.681
COPD, %	6.4	8.3	.158
Urgent, %	67.1	64.1	.224

*CCAB indicates conventional coronary artery bypass; OPCAB, off-pump coronary artery bypass; COPD, chronic obstructive pulmonary disease.

†*P* for χ^2 value.

Table 3. Cardiac History, Function, and Anatomy*

	CCAB	OPCAB	P†
Ejection fraction, %			
<40	9.4	7.9	.527
40-49	10.9	12.8	
50-59	22.6	21.5	
≥60	57.1	57.9	
Prior CABG, %	2.1	1.4	.301
Number of diseased vessels, %			
2	28.8	30.8	.386
3	59.1	52.8	.013
Coronary artery stenosis, %			
Left main ≥50%	27.1	25.8	.556
LAD ≥70%	85.4	86.1	.682
RCA ≥70%	82.4	78.0	.033
CX ≥70%	73.5	67.4	.009
PDA ≥70%	5.1	1.4	<.001

*CCAB indicates conventional coronary artery bypass; OPCAB, off-pump coronary artery bypass; CABG, coronary artery bypass grafting; LAD, left anterior descending artery; RCA, right coronary artery; CX, left circumflex artery; PDA, posterior descending coronary artery.

†*P* for χ^2 value.

Chi-square tests and unpaired *t* tests were used to examine the differences between CCAB and OPCAB in patient and disease characteristics. Mean postoperative cTnT (ng/mL) values with 95% confidence intervals between CCAB and OPCAB in the 1511 CABG procedures were compared using unpaired *t* tests.

RESULTS

There were 778 CCAB and 733 OPCAB procedures with measures of postoperative cTnT levels performed during the data collection period. Patient and disease characteristics were similar in the two groups. No significant differences were found between CCAB and OPCAB procedures with regard to patient characteristics (Table 1) and comorbidities (Table 2). This suggests the patient populations in CCAB and OPCAB were virtually identical patient populations during the study time.

Patients were similar with regard to cardiac history, function, and anatomy (Table 3). We stratified patients according to preoperative ejection fraction categories (<40%, 40%-49%, 50%-59%, and ≥60%) and found no difference in any category ($P = .527$). However, OPCAB patients tended to have slightly less coronary disease than CCAB patients in the right coronary, left circumflex, and posterior descending arteries. In regard to procedural data, OPCAB patients on average received fewer distal anastomoses, but there was not a difference in the ratio of the number of distal anastomoses to the number of diseased vessels (Table 4). There was no difference in the adjusted mean predicted mortality risk, as calculated from the NNECDSG preoperative mortality risk model [O'Connor 1992]. This evidence suggests that although the patient populations were similar with respect to patient and disease characteristics and adjusted preoperative mortality risk, they did differ with respect to coronary disease and revascularization classifications.

We assessed the 24-hour postoperative cTnT levels between CCAB and OPCAB and stratified the analysis by priority (elective and urgent) and by the number of diseased vessels (2- or 3- vessel disease). The CCAB surgical group had significantly higher cTnT levels than the OPCAB group across acuity and number of diseased vessels, thereby confirming the heightened degree of elevations in cTnT levels from CCAB procedures regardless of priority or number of diseased vessels. This effect is visually obvious when graphed side-by-side with 95% confidence intervals (Figure). A subset of 200 patients in this cohort was enrolled in a randomized controlled trial for CCAB and OPCAB. The analysis of the randomized controlled trial subgroup was consistent with the cohort: mean 24-hour postoperative cTnT was 0.89 (95% confidence interval, 0.66-1.11) for CCAB and 0.24 (95% confidence interval, 0.17-0.31) for OPCAB. Due to the large sample size of this cohort, we were able to assess the effect on cTnT release across additional subgroups. We determined the observed effect (greater cTnT release following CCAB versus OPCAB) was consistent across patient sex, surgeon, preoperative medication use (aspirin, beta-blockers, and ace-inhibitors), and among patients without a preoperative myocardial infarction within 7 days of the procedures. All of these subgroups showed CCAB had significantly more release of cTnT than OPCAB ($P < .001$). We also addressed the association of cTnT release and ischemic time and demonstrated that cTnT levels were correlated with cross-clamp time ($r = 0.13$; $P < .001$) and pump time ($r = 0.16$; $P < .001$).

We assessed the relationship between CCAB and OPCAB procedures with respect to clinical outcomes. The crude and adjusted outcome rates for CCAB and OPCAB did not differ with regard to mortality or low-output syndrome (use of intraoperative or postoperative intra-arterial balloon pump, or use of 2 or more postoperative inotropes at 48 hours). However, low-output syndrome was 30% lower in the OPCAB group (adjusted odds ratio, 0.70; 95% confidence interval, 0.37-1.35). This finding suggests the 4-fold excess in cTnT release evidenced in the CCAB group was a precursor to postoperative heart failure. However, in-hospital mortality did not differ between CCAB and OPCAB (adjusted odds ratio, 1.20; 95% confidence interval, 0.61-2.37). Odds ratios were adjusted for risk factors used in the prediction model (see Table 4).

DISCUSSION

In this paper we examined the effect of CCAB and OPCAB on the myocardium through the measurement of postoperative cTnT to determine if OPCAB results in less perioperative myocardial damage in a large cohort of patients. After examining 1511 consecutive isolated procedures, we found CCAB resulted in higher postoperative cTnT levels across priority, number of diseased vessels, and additional subgroups.

Table 4. Procedural Data and Predicted Mortality*

	CCAB	OPCAB	*P*†
Number of distal anastomoses	3.3	3.0	<.001
Number of distals/number of diseased vessels	1.4	1.4	.181
IMA used, %	94.6	92.6	.117
Mean predicted mortality risk‡	2.4	2.4	.977

*CCAB indicates conventional coronary artery bypass; OPCAB, off-pump coronary artery bypass; IMA, internal mammary artery.

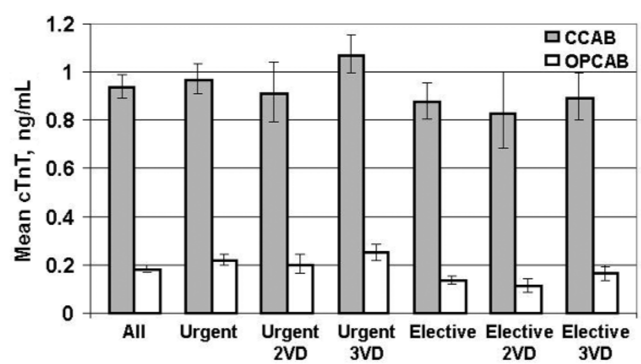
†*P* for χ^2 value, Student *t* test.

‡Predicted risk model includes age, sex, body mass index, peripheral vascular disease, diabetes, pre-existing renal failure or creatinine ≥2, chronic obstructive pulmonary disease, prior coronary artery bypass grafting surgery, preoperative ejection fraction <0.40, left main stenosis ≥50%, and number of diseased vessels.

We know from previous reports that elevated levels of cTnT are associated with higher rates of 1-year mortality [Kathiresan 2004]. Recent studies have supported our findings that cTnT levels are higher for CCAB surgery, yet small sample sizes limited the ability to analyze important patient subgroups. Krejca [1999] randomized 38 patients into 3 groups: (1) 13 patients who underwent surgery with intermittent cross clamp; (2) 12 patients who underwent surgery with a beating heart, but on pump without the cross clamp; and (3) 13 patients who underwent OPCAB surgery. They demonstrated—through serial measurement of perioperative cTnT levels—that patients in group 1 had the largest rise in cTnT from baseline through 72 hours postoperative, and these levels were statistically different from the OPCAB group at 48 and 72 hours. They also demonstrated that group 2 showed similar low levels of cTnT, suggesting damage to the heart was due to the cross-clamp and ischemic time rather than the pump itself. Bennetts [2002] investigated 27 OPCAB and 27 CCAB patients with equal preoperative cTnT levels; CCAB patients had higher cTnT levels over the course of the perioperative period, with significant differences at 12 and 24 hours. Katherisan [2003] examined 137 patients; only 15 had OPCAB procedures and 122 CCAB. That report showed CCAB patients had significantly higher cTnT levels immediately postoperatively and 6 to 12 and 18 to 24 hours following the procedure. Khan [2004] conducted a randomized trial that included 49 OPCAB and 47 CCAB patients. They showed CCAB patients had significantly higher cTnT levels at 6 and 12 hours postoperatively, but not at 24, 48, or 72 hours. Dybdahl [2004] reported a nonsignificant difference in cTnT between 10 CCAB and 10 OPCAB procedures at 24 hours with CCAB again having higher cTnT levels. Gulielmos [2000] reported similar findings, where 10 CCAB patients had elevated cTnT levels compared to 10 OPCAB patients. Koh [1999] assessed the postoperative cTnT levels of 10 patients with single-vessel disease and 8 with 2-vessel disease undergoing OPCAB compared to 8 patients undergoing CCAB and found that patients with 2-vessel disease undergoing CCAB had higher postoperative cTnT levels indicative of myocardial injury. Masuda [2002] studied 217 patients, of whom only 28 had an OPCAB procedure, and reported CCAB results in significantly ($P < .01$) higher release of cTnT than OPCAB. These studies uniformly report CCAB is associated with higher cTnT release, suggestive of more myocardial injury. However, all of these studies are limited in their ability to (1) confirm this effect on a large cohort and (2) adequately assess this effect in subgroups of patients who regularly present for surgery. Our study is in agreement with the above studies and represents the largest cohort to date in examining the effects of OPCAB and CCAB with 1511 patients evenly split between the procedures (778 CCAB and 733 OPCAB). Our study not only confirms the excessive release of cTnT following CCAB in a large cohort of patients, but more importantly adds confirmatory information about key subgroups of patients.

We conducted a prospective observational study and not a randomized study, making the study susceptible to unmeasured confounding from baseline patient and disease characteristics and selection bias. Although we did not randomize, we controlled for baseline patient characteristics and severity of cardiovascular disease. Both groups of patients had equal preoperative mortality risk scores, suggesting that surgeons were not biased in their selection of patients for one procedure over the other. A subset of the cohort was part of a CCAB and OPCAB randomized trial; the analysis of the trial was consistent with the findings for the large cohort.

In summary, we conclude that CCAB is associated with higher postoperative cTnT levels across priority (elective and urgent) and number of diseased vessels. The results were confirmatory of small studies and gave important insight into the susceptibility of the myocardium to damage with respect to the type of procedure, but irrespective of patient subgroups. There is a distinct myocardial benefit to OPCAB surgery, which is consistent across all subgroups of patients, regardless of their priority or coronary disease.



Mean postoperative cardiac troponin T (cTnT, ng/mL) values plotted for conventional coronary artery bypass graft surgery (CCAB) and off-pump coronary artery bypass graft surgery (OPCAB). The abscissa stratifies mean cTnT levels by priority classification at the time of surgery. 2VD indicates 2-vessel disease; 3VD, 3-vessel disease. Vertical lines represent 95% confidence intervals. All *P* values demonstrate statistical difference <.001.

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