

Risk Factors for Myocardial Injury during Off-Pump Coronary Artery Bypass Grafting

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ABSTRACT

Background: Although off-pump coronary artery bypass grafting (CABG) is now used worldwide for coronary revascularization, the pre- and intraoperative risk factors for myocardial injury associated with the surgical procedure remain to be elucidated. We performed a multivariate analysis to investigate factors that contribute to myocardial injury during off-pump CABG.

Methods: The study population consisted of 22 patients who underwent off-pump CABG without apparent intraoperative complications. Blood samples were obtained before surgery and at 3 and 12 hours after the last anastomosis and serum Troponin T (cTnT) levels were measured to assess myocardial injury. Patient characteristics and factors related to preoperative cardiac function and the intraoperative process were analyzed to determine their correlation with serum cTnT levels, and the Spearman's correlation coefficient (r_s) was computed.

Results: Neither age, preoperative cardiac function, time required for anastomosis, the number of grafts, nor the total amount of bleeding were associated with serum cTnT levels. Serum cTnT at 3 and 12 hours after completed anastomosis correlated with the product of mean systolic blood pressure and mean heart rate (double product) during anastomosis. The r_s values at 3 and 12 hours were 0.62 ($P = .002$) and 0.58 ($P = .004$), respectively. With respect to the serum cTnT level at 12 hours, creatinine clearance (Ccr) had a slight effect on the serum cTnT values.

Conclusions: High blood pressure and an increased heart rate during anastomosis are unfavorable factors for off-pump CABG. However, strict control of the blood pressure and heart rate makes it possible to subject even patients at high-risk to off-pump CABG from the viewpoints of myocardial injury.

INTRODUCTION

Coronary artery bypass grafting on the beating heart without extracorporeal circulation (off-pump CABG) has

gained renewed acceptance for the treatment of patients requiring coronary artery revascularization. Compared to on-pump CABG, off-pump CABG is less invasive and therefore widely used in patients at high risk due to advanced age, poor left ventricular function, extensive arterial sclerosis, or renal insufficiency [van Dijk 2001, Puskas 2003, Mack 2004, Khan, 2004]. Reduced transfusion requirements, shorter hospitalization, and a lower incidence of neurologic complications have been reported in patients undergoing off- rather than on-pump grafting [Prifti 2000, Cleveland 2001, Roach 1996].

Troponin T (cTnT) is currently used to assess myocardial injury [Bennetts 2002, Bonnefoy 1998], and there is evidence that marginal serum cTnT elevation is related to the prognosis of patients with ischemic heart disease [Henrikson 2004]. To achieve better outcomes, especially in high-risk patients, the degree of myocardial injury due to off-pump CABG must be reduced. However, until the risk factors for myocardial injury associated with the surgical procedure are known, decisions regarding the safety of off-pump CABG remain difficult.

Compared to on-pump CABG, diffuse inflammatory responses and microcoagulopathy are reduced in patients undergoing off-pump CABG. However, myocardial injury persists [Puskas 2003, Khan 2004, Bennetts 2002] and factors that contribute to myocardial injury during the surgical procedure remain to be identified. Advance knowledge of the degree of possible myocardial injury may help to avoid cardiac complications that prolong the recovery time and may be useful for assessing operative indication. Therefore, we studied the factors that render patients scheduled for off-pump CABG vulnerable to myocardial injury, using cTnT as a marker of myocardial injury.

MATERIALS AND METHODS

Study Design

This was a prospective study with respect to measurements of the serum cTnT level. Risk factors for intraoperative myocardial injury were analyzed retrospectively. Only patients referred for isolated off-pump CABG were included in this study. The indication for off-pump CABG was based on ACC/AHA Practice Guidelines [Eagle 1999].

Patients

Between March 2003 and April 2004, we performed 25 elective off-pump CABG operations. Excluded from this

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Table 1. Baseline Characteristics of the 22 Patients*

Variable	
Age, yr	71.1 ± 8.3
Sex, n (%)	
Male	16 (73)
Female	6 (27)
Co-morbidity, n (%)	
Diabetes	11 (50)
Hypertension	12 (55)
Hyperlipidemia	7 (32)
Renal insufficiency (Ccr ≤ 30)	3 (14)
COPD	3 (14)
Obesity†	1 (5)
History of CVA	8 (36)
Diseased vessels, n (%)	
Single	3 (14)
Double	7 (32)
Triple	9 (41)
LMT	6 (27)
Prior PTCA, n (%)	8 (36)
Re-CABG, n (%)	1 (5)

*Ccr (mL/min) indicates creatinine clearance; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accidents; LMT, left main trunk; PTCA, percutaneous coronary angioplasty.

†Body Mass Index >30.

study were 1 patient with preoperative cTnT elevation and 2 patients with intraoperative cardiac complications. The baseline characteristics of the 22 remaining patients, 16 males and 6 females, are listed in Table 1. Their ages ranged from 52 to 83 years (mean 71.1 ± 8.3); 8 patients (36.4%) had a history of cerebrovascular accidents (CVA) that included status lacunar without accompanying symptoms.

Operative Technique

All operations were performed by the authors, who had 27 years of combined experience in the field. The patients were under general endotracheal anesthesia and cardiac output was continuously monitored using a continuous-output Swan-Ganz catheter (Vigilance; Edwards Lifesciences, Irvine, CA, USA). Left ventricular wall motion was monitored by transesophageal echocardiography. An arterial pressure-monitoring line was also placed. The chests of all patients were opened via median full sternotomy. After the conduits were harvested, the pericardium was opened widely. Full systemic heparinization during anastomosis and complete protamine sulfate reversal were carried out. A heart stabilizer (Octopus; Medtronic, Minneapolis, MN, USA) and intracoronary shunting were used during anastomosis.

The flow in the conduits after anastomosis was measured with an electromagnetic flow meter.

Follow-up

ECG were monitored in the perioperative periods. Symptoms were checked daily and at any time on demand. Stress ECG and echocardiograms were obtained approximately 60

Table 2. Preoperative Cardiac Function and Operative Data*

Variable	
Preoperative cardiac functions	
Previous myocardial infarction, n (%)	7 (32)
Preoperative CI	2.50 ± .44
Dd/BSA, mm/m ²	30.5 ± 4.0
BNP† (mean), pg/mL	110.1
Ccr, mL/min	73.1 ± 33.7
Degree of mitral regurgitation, n (%)	
None	17 (77)
1/4-2/4	4 (18)
3/4-4/4	1 (5)
Operative data	
Territory grafted, n (%)	
Left anterior descending artery	22 (52)
Circumflex artery	9 (21)
Right coronary or posterior descending artery	11 (26)
Mean blood loss, mL	974
Blood transfusion required, n (%)	11 (50)
Mean HR/min during anastomosis	65.1 ± 8.3
Mean systemic blood pressure during anastomosis, mm Hg	112.0 ± 15.1

*CI indicates cardiac index; Dd/BSA, left ventricular diastolic diameter/body surface area; BNP, brain natriuretic peptide; Ccr, creatinine clearance.

†BNP was not normally distributed and ranged from 2.7 to 546.

days after surgery. Patients with suspected cardiac ischemia underwent coronary angiography.

Measurements of cTnT

Venous blood samples were obtained before surgery and at 3 and 12 hours after completion of the last anastomosis. Serum cTnT levels were measured using the conventional enzyme-linked immunoassay.

Statistical Analysis

Age, creatinine clearance (Ccr), preoperative cardiac function, and intraoperative factors were assessed as possible risk factors for myocardial injury. Preoperative cardiac functions included previous myocardial infarction, the serum level of brain natriuretic peptide (BNP), cardiac index (CI), left ventricular diastolic diameter/body surface area (Dd/BSA) measured by echocardiography, and the degree of mitral regurgitation. Intraoperative factors considered were the heart rate and blood pressure during anastomosis, the product of the heart rate and blood pressure (double product) during anastomosis, the time required for anastomosis, the number of grafts, and the total amount of bleeding. As the serum cTnT values at 3 and 12 hours were not normally distributed, the Spearman's correlation coefficient (r_s) was computed [Glantz 2002]. The association between the serum cTnT level and other discrete variables was examined by the Mann-Whitney test. After the correlation matrix was computed, repeated-measures analyses were performed. A confidence level of 95% was required to consider correlations and statistical values to be significant. For statistical calculations we used JMP software (version 5.01, SAS Institute Inc.).

Table 3A. Relationship between Serum cTnT Levels and the Indicated Factors*

	cTnT at 3 hr		cTnT at 12 hr	
	P	r_s	P	r_s
Age	.75	0.07	.08	0.39
Previous MI	.94	/	.18	/
CI	.65	-.10	.77	0.06
BNP	.85	0.04	.20	0.29
Dd/BSA	.19	0.29	.02†	0.51
Degree of mitral regurgitation	.38	/	.14	/
Ccr	.48	-0.16	.03†	-0.46
Blood pressure during anastomosis	.15	0.32	.08	0.38
Heart rate during anastomosis	.002†	0.63	.04†	0.44
Double Product†	.002†	0.62	.004†	0.58
Blood loss	.34	0.21	.09	0.37
Time required for anastomosis	.10	0.36	.13	0.33
Number of grafts	.10	/	.07	/

* r_s indicates Spearman's correlation coefficient; MI, myocardial infarction; CI, cardiac index; BNP, brain natriuretic peptide; Dd/BSA, left ventricular diastolic diameter/body surface area; Ccr, creatinine clearance.

† $P < .05$.

‡ Product of blood pressure and heart rate during anastomosis.

RESULTS

Operative Data

In this series of 22 patients we encountered no postoperative acute cardiac ischemia and no operative deaths. One patient suffered minor brain infarction in the perioperative period. Although 3 patients manifested preoperative renal insufficiency, none required postoperative hemodialysis. Preoperative cardiac function and operative data are listed in Table 2.

Troponin T

The absence of serum cTnT was confirmed preoperatively. As shown in Table 3A, patient's age, previous myocardial infarction, serum BNP, CI, Dd/BSA, degree of mitral regurgitation, time required for anastomosis, the number of grafts, and total amount of bleeding were not associated with serum cTnT levels. The serum cTnT level at 3 hours was correlated with the product of mean systolic blood pressure and mean heart rate (double product) during anastomosis (Figure A). The r_s value was 0.65 ($P = .002$). The heart rate during anastomosis was also correlated with serum cTnT levels (Table 3A), however, the double product and heart rate correlated with each other. In addition, the serum cTnT level at 12 hr correlated with the double product (Figure B). The r_s value was 0.58 ($P = .004$). Based on the correlation matrix we obtained, the double product, Dd/BSA, and Ccr were candidate risk factors for intraoperative myocardial injury (Table 3A, Figure). Multivariate analysis that included these 3 factors and the serum cTnT level at 12 hr revealed the double product and Ccr as risk factors for intraoperative myocardial injury (Table 3B). The serum cTnT level at 3 and 12 hr did not correlate when the double product was multiplied by the time required for anastomosis.

Table 3B. Repeated-Measures Analysis of Variance with Serum cTnT Level at 12 hr*

	t value	P value
Dd/BSA	0.27	.79
Ccr	-2.43	.03†
Double Product‡	3.09	.006†

*Regression equation was significant (Adjusted $R^2 = .50$, F value = 7.86, $P = .002$). Dd/BSA indicates left ventricular diastolic diameter/body surface area; Ccr, creatinine clearance.

† $P < .05$.

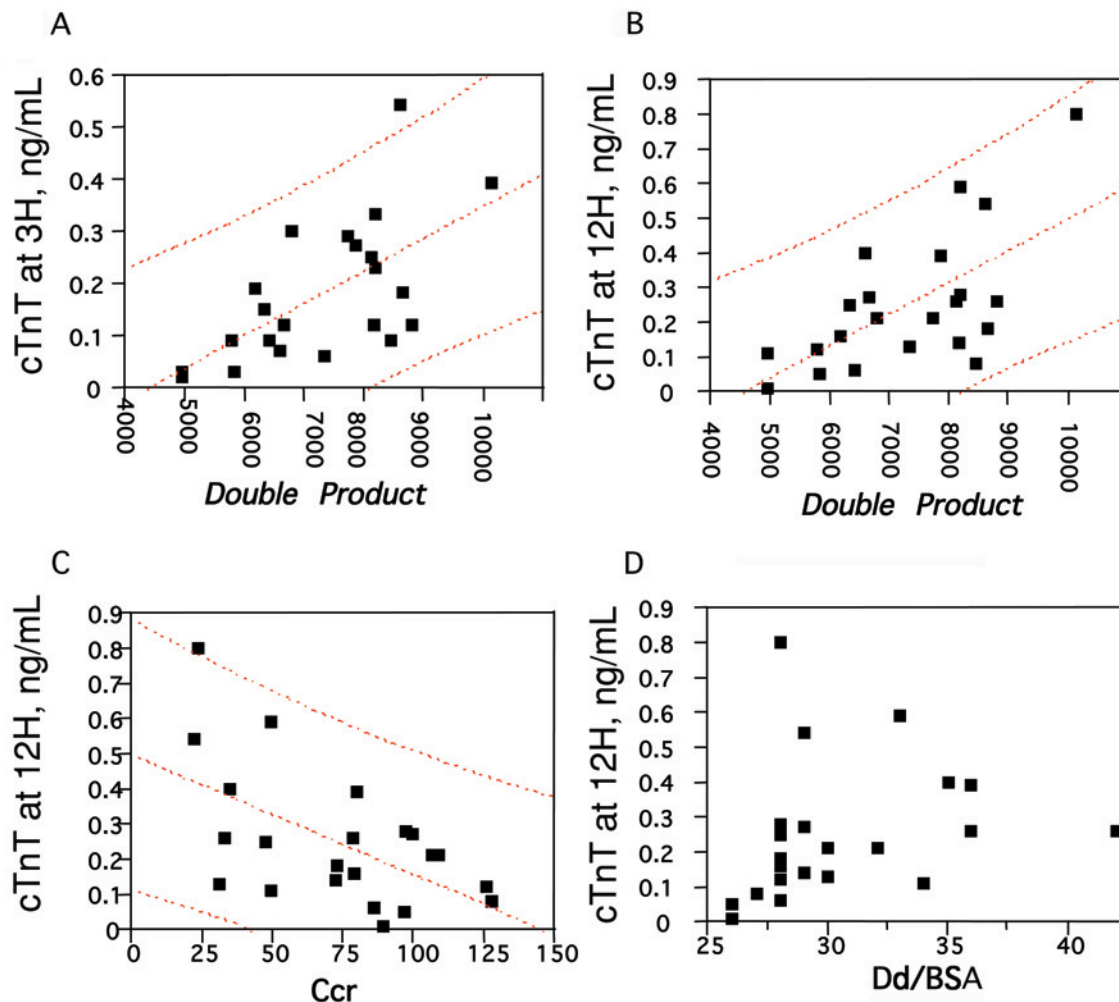
‡ Product of blood pressure and heart rate during anastomosis.

DISCUSSION

Because of improvements in technology and techniques, off-pump CABG is now used worldwide in patients requiring coronary revascularization. However, clear indications for off-pump CABG must be identified and, in some patients, on-pump CABG remains the appropriate procedure for myocardial revascularization. Patients of advanced age and other high-risk patients are now considered eligible for off-pump CABG [Beauford 2003, Bittner, 2004] and some have reported that myocardial injury due to surgical procedures was lower in patients treated by off- rather than on-pump CABG [Puskas 2003, Bennetts 2002, Kathiresan 2003]. To minimize surgical invasion in high-risk patients, the degree of myocardial injury has to be low, irrespective of whether on- or off-pump CABG is considered. In the current retrospective study we attempted to identify risk factors for myocardial injury in patients treated by off-pump CABG.

We found that only the double product during anastomosis correlated well with serum cTnT levels at 3 and 12 hours after completion of the last anastomosis. The heart rate during anastomosis alone also correlated with serum cTnT levels. However, as the heart rate and the double product were associated with each other, we regarded the double product as a risk factor for intraoperative myocardial injury and suggest that it is of clinical relevance. As the double product correlates well with O_2 consumption/min, we postulate that O_2 consumption/min during anastomosis may be a predictor of intraoperative myocardial injury. Control of the heart rate and blood pressure is important not only for minimization of myocardial injury but also for easing operative techniques; a short-acting beta-blocker is useful for this purpose.

With respect to the serum cTnT level at 12 hr, multivariate analysis revealed that Ccr played a role. We considered two possibilities to explain the relationship between Ccr and the serum cTnT level. In patients with decreased renal function, the excretion of serum cTnT may be delayed. Alternatively, decreased renal function may lead to circulatory congestion and result in increased O_2 consumption by the heart. According to cardiac physiology, O_2 consumption is determined by the sum of potential energy (internal work) and the external work done by the ventricular muscle. Cardiac congestion may increase tension in the myocardium and decrease the compliance of the left ventricle, resulting in an increase in the internal work.



Distribution of serum cTnT and regression lines. Double Product indicates the product of blood pressure and heart rate during anastomosis; Ccr, mL/min, creatinine clearance; Dd/BSA, mm²/m², left ventricular diastolic diameter/body surface area.

The patency of off-pump CABG is reportedly lower than that of conventional CABG [Khan 2004], possibly because successful anastomosis with the heart beating requires a high skill level. Contrary to our expectations, the time required for anastomosis was not correlated with the degree of intraoperative myocardial injury, indicating that anastomotic precision, rather than speed, is the most important factor. The increased blood loss due to some prolongation of the time required for precise anastomosis did not have a significant effect on the outcome.

As preoperative cardiac function did not appear to affect markedly the level of intraoperative myocardial injury, we suggest that even patients at high-risk due to advanced age or poor left ventricular function can be treated by off-pump CABG.

Because the serum cTnT level, considered an indicator of myocardial injury, began to increase at 3 hr and leveled off at 12 hr, we chose those time points for blood sampling [Bonney 1998].

The relationship between myocardial injury and postoperative morbidity and mortality in patients undergoing coronary artery surgery is not well understood, although some risk factors have been reported [Eagle 1999, Kurki 2001,

Al-Ruzzeh 2003, Bernstein 2000]. However, those risk indices were developed primarily for patients undergoing on-pump CABG and considered the entire course of treatment and the outcomes in patients with ischemic heart disease, and included postoperative mortality due to severe complications such as cerebrovascular accidents, respiratory failure, and infections. The left ventricular ejection fraction was reported as a prognostic marker of mortality in patients with ischemic heart disease and chronic heart failure, and the plasma BNP concentration correlated well with the left ventricular ejection fraction. BNP is now considered a possible marker for the prognosis of these patients [de Denu 2004].

At present, there are no clear guidelines to aid in the selection between on- or off-pump CABG in low-risk and younger patients. Surgical patency is an important consideration as is the diameter of the target arteries, heart size, and coexisting valvular disease. We suggest that coronary artery surgery without cardiopulmonary bypass represents a promising new alternative in patients where the adverse effects of extracorporeal circulation may exacerbate their clinical status and in patients at risk for cardioplegic arrest due to preexisting complications and disorders.

Study Limitations

There were several study limitations. Ours was a retrospective analysis of risk factors for intraoperative myocardial injury in a relatively small number of patients undergoing coronary revascularization. Data on larger study populations must be collected and mid- and long-term outcomes must be analyzed. In addition, it remains unclear whether the improved myocardial performance associated with off-pump CABG surgery translates into clinically significant benefits reflected in improvement of the quality of life of these patients.

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