Intraoperative cardiac troponin T release and lactate metabolism during coronary artery surgery: comparison of beating heart with conventional coronary artery surgery with cardiopulmonary bypass

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Abstract

Objective—To compare cardiac troponin T release and lactate metabolism in coronary sinus and arterial blood during uncomplicated coronary grafting on the beating heart with conventional coronary grafting using cardiopulmonary bypass.

Design—A prospective observational study with simultaneous sampling of coronary sinus and arterial blood: before and 1, 4, 10, and 20 minutes after reperfusion for analysis of cardiac troponin T and lactate. Cardiac troponin T was also analysed in venous samples taken 3, 6, 24, 48, and 72 hours after surgery.

Setting—Cardiac surgical unit in a tertiary referral centre.

Patients—18 patients undergoing coronary grafting on the beating heart (10 single vessel and eight two-vessel grafting) and eight undergoing two-vessel grafting with cardiopulmonary bypass.

Results—Cardiac troponin T was detected in coronary sinus blood in all patients by 20 minutes after beating heart coronary artery surgery before arterial concentrations were consistently increased. Peak arterial and coronary sinus cardiac troponin T values on the beating heart during single (0.03 (0 to 0.05) and 0.09 (0.07 to 0.16 µg/l, respectively) and two-vessel grafting (0.1 (0.07 to 0.11) and 0.19 (0.14 to 0.25) µg/l) were lower than the values obtained during cardiopulmonary bypass (0.64 (0.52 to 0.72) and 1.4 (0.9 to 2.0) µg/l) ($p < 0.05$). The area under the curve of venous cardiac troponin T over 72 hours for two-vessel grafting on the beating heart was less than with cardiopulmonary bypass (13 (10 to 16) v 68 (26 to 102) µg.h/l) ($p < 0.001$). Lactate extraction began within one minute of snare release during beating heart coronary surgery while lactate was still being produced 20 minutes after cross clamp release following cardiopulmonary bypass.

Conclusions—Lower intraoperative and serial venous cardiac troponin T concentrations suggest a lesser degree of myocyte injury during beating heart coronary artery surgery than during cardiopulmonary bypass. Oxidative metabolism also recovers more rapidly with beating

heart coronary artery surgery than with conventional coronary grafting. Coronary sinus cardiac troponin T concentrations increased earlier and were greater than arterial concentrations during beating heart surgery, suggesting that this may be a more sensitive method of intraoperative assessment of myocardial injury.

(Heart 1999;81:495–500)

Keywords: beating heart coronary artery surgery; troponin T; cardiopulmonary bypass; intraoperative assessment; myocardial injury

Beating heart coronary artery surgery, in avoiding the need for cardioplegic arrest and aortic clamping, may limit the ischaemic damage to the myocardium and interference with the cerebral circulation associated with conventional cardiopulmonary bypass. However, doubts have been expressed as to whether local coronary occlusion necessary to obtain a bloodless field may itself cause ischaemic damage in a warm metabolically active heart.¹ We have therefore correlated the early myocardial release and later venous concentrations of cardiac troponin T,^{2,3} a highly specific and sensitive marker of myocardial cell injury, with the recovery of oxidative metabolism in patients undergoing coronary artery bypass grafting on the beating heart. We have compared these results with those in patients undergoing conventional coronary artery surgery studied over the same period using identical techniques.

Methods

We studied 18 patients (median (range) age 62 (52 to 74) years; 14 men, four women) with chronic stable angina who underwent coronary artery surgery without cardiopulmonary bypass using the "Octopus" myocardial wall stabilisation device (Medtronic Inc, Grand Rapids, Michigan, USA). Ten patients underwent single vessel grafting (eight with left anterior descending and two with right coronary artery grafts) and eight had two-vessel grafting (all had left anterior descending and right coronary artery grafts).

Eight patients who underwent conventional coronary artery surgery with cardiopulmonary bypass were also studied. All eight patients had

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Accepted for publication
27 November 1998

two-vessel grafting, left anterior descending artery and right coronary artery grafts in five, and left anterior descending artery and circumflex grafts in three patients. Mean ejection fraction for patients undergoing grafting with and without cardiopulmonary bypass was similar, at 61 (6)%.

The protocol was approved by the ethics committee of the Royal Brompton Hospital and informed consent was obtained from all patients.

OPERATIVE PROCEDURE

Coronary artery surgery without cardiopulmonary bypass

General anaesthesia was induced by alfentanil and maintained with enflurane. The operation was performed through a median sternotomy. After harvesting the bypass conduits, heparin was given at a dose of 1.0 mg/kg. A DLP coronary sinus catheter was inserted to allow sampling of coronary venous blood. The Octopus myocardial stabilisation device (Medtronic Inc) consists of two paddles with suction cups on the underside.^{4,5} After pericardectomy, these were placed on the epicardial surface on either side of the coronary artery to be grafted. The device is fixed to the operating table by an articulating arm. A suction pump was connected to the paddles and adjusted to apply suction at 500–700 mm Hg to the epicardial surface, and thereby immobilising the region on either side of the coronary artery. Prolene sutures (2/0) were used as snares, positioned proximal and distal to the site of anastomosis. They were gently tightened to occlude coronary flow and therefore allow grafting of the coronary artery in a bloodless field. When the anastomosis was complete, the coronary snares were released to restore coronary blood flow. The proximal anastomosis was performed using a side biting clamp on the aorta when reversed saphenous vein was used as a conduit for grafting the right coronary artery. All left anterior descending coronary arteries were grafted with a pedicled left internal mammary artery.

Coronary artery surgery with cardiopulmonary bypass

Median sternotomy was performed. After harvesting the bypass graft conduits the patients were prepared for cardiopulmonary bypass. Heparin sulphate was given at a dose of 3 mg/kg. Cardiopulmonary bypass was established with ascending aortic and single right atrial cannulation with systemic hypothermia (32°C nasopharyngeal temperature), haemodilution (packed cell volume 20–25%), perfusion flow rate between 1.6 litres/min/m² at 32°C and 2.2 litres/min/m² at 37°C.

A DLP triple lumen catheter (Medtronic Inc) was positioned in the coronary sinus and its proximal pressure monitored and maintained at 30 to 40 mm Hg during retrograde perfusion. Cold blood cardioplegia was used for myocardial protection, the first two thirds of the cardioplegia given antegradely and subsequently maintained by potassium enriched

autologous blood given retrogradely into the coronary sinus catheter every 15 minutes.

After the distal anastomoses were complete the aortic cross clamp was removed and the proximal anastomoses fashioned with a side biting clamp on the aorta during myocardial perfusion. Immediately before release of the aortic cross clamp, a five minute period of warm reperfusion was given (600 ml of potassium enriched blood at 37°C through the coronary sinus catheter) while the patient's core temperature was 35–37°C.

ELECTROCARDIOGRAPHY

ECG leads in the aVf and V5 positions were positioned for monitoring during the operation. Serial 12-lead ECGs were obtained at the following time points: before operation, and 24, 48, and 72 hours after operation. The appearance of new Q waves of > 0.04 seconds duration or a loss of > 25% of R waves in two contiguous leads were taken as criteria for the diagnosis of myocardial infarction.

CARDIAC TROPONIN T AND LACTATE PROTOCOL

During beating heart coronary surgery, blood samples for estimation of cardiac troponin T and lactate were obtained simultaneously from the coronary sinus and radial artery at the following times: before coronary occlusion, and 1, 4, 10, and 20 minutes after release of the coronary snare.

In the case of coronary artery surgery with cardiopulmonary bypass, blood samples were obtained at the same times after cross clamp release to measure cardiac troponin T, lactate, and packed cell volume. The values of cardiac troponin T taken while on cardiopulmonary bypass were corrected for haemodilution by multiplying the measured concentration with a correction factor (CF) as described by Feindt *et al*⁶⁻⁸:

$$CF = \frac{PCV_0}{pPCV_0} \times \frac{pPCV_1}{PCV_1}$$

where PCV is packed cell volume (%), pPCV is plasma packed cell volume (100%–PCV%), 0 is the value before cardiopulmonary bypass, 1 is the value at the time of sampling.

The net release of cardiac troponin T was quantified as the arteriovenous difference (coronary sinus concentration minus arterial concentration).⁷ Lactate extraction was calculated as:

$$\frac{(\text{arterial lactate} - \text{coronary sinus lactate})}{\text{arterial lactate}}$$

expressed as a percentage.⁹ A negative value for lactate extraction therefore represents net myocardial production of lactate. Peripheral venous blood samples were obtained 3, 6, 24, 48, and 72 hours after the operation for cardiac troponin T estimation, and the area under the curve of cardiac troponin T concentration derived. All samples were centrifuged within 20 minutes and the plasma was stored at –20°C until analysis.

Table 1 Characteristics of the patients

	No cardiopulmonary bypass (CPB)		CPB
	One-vessel grafting (n = 10)	Two-vessel grafting (n = 8)	Two-vessel grafting (n = 8)
Age (years) (median (range))	63 (52 to 74)	58 (43 to 69)	62 (56 to 70)
Sex (male/female)	7/3	7/1	5/3
Ischaemic time (min) (mean (SD))	17 (4)	32 (8) [†]	44 (7)*
Vessels grafted (n)			
LAD	8	8	8
RCA	2	8	5
Cx	0	0	3
LVEF (%) (mean (SD))	60 (7)	62 (5)	62 (8)
Previous MI (n)			
Anterior	1	1	1
Inferior	1	0	1
Drug treatment (n)			
β Blockers	8	5	4
Calcium antagonists	7	4	7
Nitrates	4	5	4

* $p < 0.01$ v non-CPB one- and two-vessel grafting; [†] $p < 0.001$ v non-CPB one-vessel grafting. Cx, circumflex coronary artery; LAD, left anterior descending coronary artery; LVEF, left ventricular ejection fraction; MI, myocardial infarction; RCA, right coronary artery.

BIOCHEMICAL ANALYSIS

Cardiac troponin T was measured using a commercially available enzyme linked immunosorbent assay kit (ELISA troponin T, Boehringer Mannheim, Mannheim, Germany) and batch ELISA analyser (Enzygum test system ES 300, Boehringer Mannheim). The cardiac troponin T ELISA used was a second generation assay with improved specificity and reproducibility compared with previously available assays.¹⁰ The lower detection limit of the assay was 0.05 µg/l, and concentrations above the discriminator value of 0.1 µg/l were considered raised.^{10–12} Coefficient of variation for cardiac troponin T measurements was 7% for concentrations between 0.1 and 2 µg/l. Lactate was measured by the lactate oxidase method using a Analox LM3 analyser (Analox Instruments, London, UK). The coefficient of variation of lactate at a concentration of 2.3 mmol/l was 5.7%.

STATISTICAL ANALYSIS

Cardiac troponin T values are presented as median and interquartile range (25–75%) and non-parametric statistical tests used, as normal distribution could not be assumed.^{7 13 14} The area under the curve was calculated using the

Figure 1 Cardiac troponin T concentration in coronary sinus and arterial blood during two-vessel grafting on the beating heart. Cardiac troponin T concentrations were increased in both coronary sinus and arterial blood within one minute of cross clamp release and increased progressively. Coronary sinus concentrations were consistently higher than arterial concentrations. * $p < 0.01$ between coronary sinus and arterial concentrations. Data are expressed as median and interquartile (25th and 75th centile) range.

Figure 2 Cardiac troponin T concentrations in coronary sinus and arterial blood during two-vessel grafting using cardiopulmonary bypass. Note that cardiac troponin T concentrations are greater than for beating heart coronary artery surgery for the entire period (fig 1). * $p < 0.01$ between coronary sinus and arterial concentrations. Data are expressed as median and interquartile (25th and 75th centile) range.

method of Matthews and Altman.¹⁵ A Wilcoxon signed rank test was used to evaluate differences between time points, while differences between groups were compared using the Kruskal–Wallis test. Differences within and between groups were assessed by repeated measures analysis of variance (ANOVA) as appropriate or χ^2 test for categorical variables. The level of significance was taken as $p < 0.05$.

Results

CLINICAL AND ECG DATA

The patient characteristics are shown in table 1. All patients who underwent coronary surgery on the beating heart were successfully grafted without the need to employ back-up cardiopulmonary bypass. No pharmacological agents were given to slow the heart rate during surgery. Three patients undergoing single vessel grafting developed ST segment elevation during coronary occlusion—two during left anterior descending artery (lead V5) and one during right coronary artery grafting (lead aVf). Three patients developed ST elevation (lead V5) during left anterior descending artery occlusion in the course of two-vessel grafting. All ECG changes resolved rapidly after release of the coronary snare.

No patient required inotropic support or pacing in the perioperative period for coronary grafting with or without cardiopulmonary bypass. None sustained perioperative myocardial infarction on the basis of serial electrocardiography. There were no complications during the study.

Cross clamp time for two-vessel grafting with cardiopulmonary bypass was significantly longer than the duration of coronary occlusion required for two-vessel grafting on the beating heart (44 (7) v 32 (8) minutes, $p < 0.01$). Total coronary occlusion time for two-vessel grafting was greater than for single vessel grafting on the beating heart, at 32 (8) v 17 (4) minutes ($p < 0.001$).

INTRAOPERATIVE TROPONIN T RELEASE

Beating heart coronary artery surgery

Troponin T concentrations were not raised in coronary sinus or arterial blood before coronary occlusion in any patient grafted without

Figure 3 Serial changes in cardiac troponin T concentrations in peripheral venous blood for grafting with (CPB) and without cardiopulmonary bypass (non-CPB) over a 72 hour period. Data are expressed as median and interquartile (25th and 75th centile) range.

cardiopulmonary bypass. By one minute of snare release, cardiac troponin T concentration was raised in one patient in arterial blood compared with three patients in coronary sinus blood during single vessel grafting. By 20 minutes of snare release, cardiac troponin T was raised in two patients in arterial blood but was detectable in all 10 patients in coronary sinus blood. In five patients coronary sinus cardiac troponin T concentrations were greater than 0.1 µg/l, and in the remaining five patients cardiac troponin T concentrations ranged between 0.05 and 0.09 µg/l.

During two-vessel grafting without cardiopulmonary bypass, arterial cardiac troponin T concentrations were raised in three patients, while all eight patients had raised coronary sinus cardiac troponin T concentrations by one minute of snare release. By 20 minutes of snare release cardiac troponin T concentrations were increased in five patients in arterial blood and remained raised in all eight patients in coronary sinus blood. Coronary sinus and arterial cardiac troponin T concentrations increased progressively between one and 20 minutes after snare release. These data are shown in fig 1. Coronary sinus cardiac troponin T concentrations were higher than arterial concentrations at all time points ($p < 0.01$ for 1, 4, 10, and 20 minutes).

Net cardiac troponin T release increased progressively after snare release to a peak after 20 minutes during single (0.08 (0.05 to 0.12) µg/l) and two-vessel grafting (0.1 (0.07 to 0.16) µg/l) without cardiopulmonary bypass.

Cardiopulmonary bypass

Cardiac troponin T concentrations were not raised in coronary sinus or arterial blood before coronary grafting in patients who underwent surgery with cardiopulmonary bypass. Within one minute of cross clamp release, cardiac troponin T concentrations were increased in both arterial and coronary sinus blood in all patients. Arterial and coronary sinus cardiac troponin T concentrations increased progressively over the 20 minutes of reperfusion studied (fig 2). Cardiac troponin T concentrations in coronary sinus were consistently higher than those in arterial blood, suggesting continuing net myocardial release of cardiac troponin T throughout the period of sampling ($p < 0.01$ for 1, 4, 10, and 20 minutes).

Figure 4 Area under the curve of cardiac troponin T concentration in peripheral venous blood during two-vessel grafting using cardiopulmonary bypass (CPB) is significantly greater than for coronary artery grafting on the beating heart (non-CPB). Data are expressed as median and interquartile (25th and 75th centile) range.

Peak arterial and coronary sinus cardiac troponin T concentrations during coronary surgery with cardiopulmonary bypass (0.64 (0.52 to 0.72) and 1.4 (0.9 to 2.0) µg/l, respectively) were significantly higher than during coronary grafting without cardiopulmonary bypass for single (0.03 (0 to 0.05) and 0.09 (0.07 to 0.16) µg/l, $p < 0.001$) and two-vessel grafting (0.1 (0.07 to 0.11) and 0.19 (0.14 to 0.25) µg/l, $p < 0.05$). Peak cardiac troponin T concentrations in arterial and coronary sinus blood for two-vessel grafting did not differ significantly from values with single vessel grafting.

Net cardiac troponin T release during coronary grafting with cardiopulmonary bypass increased from 0.4 (0.24 to 0.8) µg/l at one minute to a peak of 1.1 (0.48 to 1.36) µg/l 10 minutes after cross clamp release. Peak net cardiac troponin T release was significantly higher for the cardiopulmonary bypass patients than for non-cardiopulmonary bypass patients for single (0.08 (0.05 to 0.12) µg/l, $p < 0.001$) and two-vessel grafting (0.1 (0.07 to 0.16) µg/l, $p < 0.05$).

VENOUS CARDIAC TROPONIN T CONCENTRATIONS

Beating heart coronary artery surgery

Cardiac troponin T was increased in peripheral venous blood in every patient who underwent coronary grafting without cardiopulmonary bypass within 24 hours of surgery. Peak cardiac troponin T concentration for one-vessel grafting was 0.28 (0.19 to 0.49) µg/l at six hours after operation. The data are shown in fig 3. Peak cardiac troponin T concentration for two-vessel grafting was 0.40 (0.34 to 0.43) µg/l at three hours after surgery. Cardiac troponin T concentration in venous blood remained raised 72 hours after surgery in seven of 10 patients having single vessel grafting and in six of eight patients with two-vessel grafting without cardiopulmonary bypass.

The area under the curve of cardiac troponin T concentration in venous blood for two-vessel grafting did not differ significantly from single vessel grafting, at 13 (10 to 16) v 7 (5 to 11) µg.h/l).

Cardiopulmonary bypass

Cardiac troponin T concentrations in peripheral venous blood peaked (1.1 (0.7 to 1.8) µg/l) three hours after coronary grafting with

Figure 5 Lactate extraction data showing maximum lactate production one minute after reperfusion for grafting with cardiopulmonary bypass (-31 (10)% *v* 4 (8)% and 14 (10)%, $p < 0.05$) compared with lactate extraction in single and two-vessel grafting on the beating heart. Lactate was still being produced after 20 minutes reperfusion for grafting with cardiopulmonary bypass (-5 (3)% *v* 25 (8)%, $p < 0.05$) compared with lactate extraction for two-vessel grafting on the beating heart. Data are means, error bars = SEM.

cardiopulmonary bypass (fig 3). All patients who underwent coronary surgery with cardiopulmonary bypass had raised cardiac troponin T concentrations in venous blood at all time points throughout the 72 hour period.

The area under the curve of cardiac troponin T concentration in venous blood (68 (26 to 102 $\mu\text{g.h/l}$) for patients undergoing grafting with cardiopulmonary bypass was significantly greater than for single (7 (5 to 11) $\mu\text{g.h/l}$, $p < 0.001$) and two-vessel grafting (13 (10 to 16) $\mu\text{g.h/l}$, $p < 0.05$) without cardiopulmonary bypass (fig 4).

LACTATE METABOLISM

Lactate extraction was found before coronary grafting in patients operated with cardiopulmonary bypass (12 (9)%) and without (25 (12)% for single and 11 (18)% for two-vessel grafting) (fig 5). Within one minute of reperfusion, patients grafted without cardiopulmonary bypass showed lactate extraction during single (4 (8)%) and two-vessel grafting (14 (10)%) compared with patients who were grafted with cardiopulmonary bypass, who showed marked lactate production (-31 (10)%, $p < 0.05$ *v* both single and two-vessel). Lactate production continued at 20 minutes after reperfusion in patients grafted with cardiopulmonary bypass (-5 (3)%), while lactate extraction increased in patients having single (18 (10)%) and two-vessel grafting without cardiopulmonary bypass (25 (8)%, $p < 0.05$ *v* cardiopulmonary bypass values).

Discussion

Beating heart surgery allows coronary artery bypass grafting to be performed without the attendant disadvantages, both cerebral and myocardial, of cardiopulmonary bypass.¹⁶ It was our aim in the present study to compare the extent of myocardial damage associated with these two techniques using cardiac troponin T,^{13 17 18} a specific marker with negligible cross reactivity with skeletal muscle.¹⁰ In addition, we aimed to increase the sensitivity of

this method still further by estimating cardiac troponin T in both coronary sinus and peripheral artery, so that myocardial release could be detected.⁷

Using this approach, we found that all patients undergoing beating heart coronary artery surgery had detectable cardiac troponin T in coronary sinus blood within 20 minutes of release of the coronary snare. In contrast, even by 20 minutes peripheral arterial concentrations were consistently less raised, and remained less than coronary sinus concentrations throughout the intraoperative period, showing net myocardial release of the protein. Peripheral venous samples, taken up to 72 hours, showed raised cardiac troponin T concentrations in the majority of patients, regardless of whether they had undergone single or two-vessel grafting. Since cardiac troponin T has a half life of two hours,³ a prolonged increase in blood levels suggests continuing release from myofilaments,^{2 14 19} and thus some degree of irreversible myocardial damage.

The pattern of cardiac troponin T release following conventional cardiopulmonary bypass was significantly different. Within one minute of release of the aortic cross clamp, cardiac troponin T was already detectable in arterial as well as coronary sinus blood, and concentrations were nearly an order of magnitude higher. When patients undergoing two-vessel grafting were compared, the area under the curve of cardiac troponin T release was also significantly greater with conventional cardiopulmonary bypass. This finding was similar to that of Birdi *et al.*,²⁰ who noted that cardiac troponin I concentrations in peripheral venous blood collected over a 48 hour period were significantly higher with coronary surgery using the conventional approach compared with single vessel grafting without cardiopulmonary bypass using the LAST (lateral anterior small thoracotomy) approach. Our findings are also compatible with a study by Swaanenburg and colleagues, who reported that cardiac troponin T concentrations in peripheral venous blood six hours after minimally invasive coronary artery bypass grafting were significantly lower than after conventional surgery with cardiopulmonary bypass.²¹ In addition, we found that lactate production was undetectable after beating heart coronary artery surgery, but persisted for the whole intraoperative course after conventional cardiopulmonary bypass, in spite of a period of warm reperfusion before cross clamp release.²² In percutaneous transluminal coronary angioplasty, where the duration of occlusion is much shorter (one to three minutes), the reported increase in cardiac troponin T is only 0–24%.^{23–25} We conclude that taken together, these results provide strong evidence that the lesser degree of myocardial injury with beating heart coronary surgery reflects a shorter occlusion time and a localised region of myocardium.

LIMITATIONS

The number of patients undergoing conventional surgery was small, but the results were

similar to those we have reported previously.⁷ The opportunity to study any significant number of patients undergoing single vessel grafting with cardiopulmonary bypass is rare in the current era of percutaneous angioplasty and interventional devices. We were therefore limited to studying patients undergoing conventional surgery for two-vessel grafting, but the findings clearly differed from those in patients having the same extent of revascularisation performed on the beating heart. The release kinetics of cardiac troponin T during beating heart coronary surgery for single vessel grafting by itself are revealing in that cardiac troponin T is still released, especially in coronary sinus blood, even when coronary occlusion time is expected to be very short; however, any comparison with conventional coronary surgery in our study must necessarily also reflect the difference in extent of revascularisation. We think it unlikely that myocardial trauma owing to stabilisation by the Octopus device contributed significantly to cardiac troponin T release, since histological studies suggest that this is minimal.⁴ We studied a series of low risk patients, so we are unable to correlate our results with clinical outcome.

CONCLUSIONS

Cardiac troponin T release occurs after beating heart coronary surgery, indicating some degree of myocardial injury. However, levels approximately an order of magnitude lower than those seen after conventional cardiopulmonary bypass would imply that the degree of injury is correspondingly less. We believe that the sensitivity of this approach in detecting intraoperative injury can be increased by using coronary sinus as well as arterial samples, and suggest that this approach may be useful in assessing future myocardial protection strategies.²⁶

TWK is supported by a British Heart Foundation Junior Research Fellowship.

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