

Coronary artery bypass grafting on beating heart

Does it provide superior myocardial preservation than conventional technique?

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ABSTRACT

Objectives: To compare myocardial injury caused by 3 commonly used methods for coronary artery bypass grafting (CABG).

Methods: A prospective randomized study conducted at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia. The study started in February 2003 and concluded in April 2004 after including 45 patients (15 patients in each of 3 sub-groups) who fulfilled the inclusion and exclusion criteria. The subgroups included coronary artery bypass surgery performed by: a) conventional technique, b) off-pump technique, and c) on-pump beating-heart techniques. All patients had similar operative risk profiles. Their ages were 70 years or less with an ejection fraction of 30-50%. The creatine kinase, myocardial band (CKMB) levels were determined 2 hours after arrival from the operating room then, at 4 hours, 6 hours, and 12 hours. The comparison of creatine phosphokinase and CKMB levels was carried out using analysis of variance with repeated measures. The *p*-values were used to evaluate the significance of differences.

Results: The pre-operative characteristics including age, gender, ethnic origin, diabetes mellitus, hypertension, and left ventricular function, were similar in the 3 groups. All groups had a median number of 3 bypass grafts. The stay in the intensive care unit and the duration of inotropes were shortest in the off-pump group, but the difference was not significant. There was a peak of CKMB levels at 6 hours in all groups. The trend of CKMB level showed significantly higher values in the conventional CABG group as compared with the other 2 groups.

Conclusion: This study indicates that the off-pump technique provides better myocardial preservation than other methods.

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Coronary revascularization has undergone dramatic changes over the last few years. Recent improvements in invasive cardiology have left the surgeons with those patients for surgical revascularization who have multiple risk factors, diffuse coronary disease, significant left main stem stenosis, or poor left ventricular function.¹ Although the surgical technique of revascularization has become almost standardized, the myocardial protection is becoming more and more challenging due to these changes in the profile of patients referred for surgery. Off-pump coronary artery bypass (OPCAB) has become an established procedure. Meanwhile, on-pump beating heart coronary artery bypass (OBCAB) has also gained some recognition. It is, therefore, the time to compare the effectiveness and safety of these techniques in terms of myocardial preservation.

Methods. We conducted a prospective randomized study at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia from February 2003 to April 2004 after including 45 patients (15 patients in each group listed below) who fulfilled the inclusion and exclusion criteria. Group I: Conventional coronary artery bypass graft (CABG) by using standard cardiopulmonary bypass with aortic cross clamp and cold blood cardioplegia (ConCAB). Group II: OPCAB. Group III: OBCAB. The inclusion criteria were as following: Isolated coronary bypass grafting operation, age not over 70 years,

and moderate left ventricular dysfunction (ejection fraction 30-50%). The following patients were excluded from the study: (i) Re-do operations, (ii) those who required more than 5 grafts, (iii) patients with calcified coronaries, or diffuse coronary artery disease, (iv) patients with significant co-morbidities (significant carotid artery disease, peripheral vascular disease, pulmonary dysfunction, renal dysfunction, or previous stroke). (v) Those who required coronary endarterectomy during operation. (vi) Emergency or salvage operation resulting from unstable angina or catastrophic states. (vii) Localized perioperative myocardial infarction related to a grafted territory.

The study was conducted in strict compliance with the guidelines set by Helsinki declaration of 1975, as revised in 1983, and all patients received detailed counseling about the technical details of the operations for making an informed consent. The operating surgeons remained unaware of the information that which of their patients were included in the study. They had the full liberty to change over to the other group due to technical requirements. However, as mentioned earlier, patients who were converted to a different group during the course of operation were excluded from the study. The operations were carried out by 3 consultant surgeons. To obviate any effect of learning curve, the OPCAB and OBCAB techniques were used by 2 of the 3 consultant surgeons who have already performed over 500 operations and are routinely employing these techniques in more than 30% of their operations.

Patients were premedicated with lorazepam 2mg orally the night before surgery, and morphine 0.1mg/kg intramuscular 1 hour before operation. Anaesthesia was induced with sufentanil 1-1.5 µg/kg, midazolam 0.05-0.1 mg/kg, and rocuronium 0.9 mg/kg, and was maintained with infusion of sufentanil 0.2 µg/kg/hr, midazolam 1.5ug/kg/hr, and rocuronium 0.5mg/kg/hr. It was further supplemented with sevoflurane as required. Supplementation of further doses for induction or maintenance was guided by signs of lack of analgesia correlated with hemodynamics changes. In the ConCAB group, the standard cardiopulmonary bypass (CPB) was established with aortic and 2 stage right atrial cannulae. The CPB circuit was primed with a crystalloid solution with addition of albumin. The heparin was administered in a dose of 300 U/Kg. The systemic temperature was lowered to 28-30°C. The local cooling was carried out with topical ice-cold saline. Cold blood cardioplegia was given through a cannula in the ascending aorta. The cardioplegia solution was prepared by mixing the commercially available solution Plegisol (Abbot) into the oxygenated blood in a 4 to 1 ratio. Potassium was added to achieve a concentration

of 16 mmol/L for the first dose and was 6-8 mmol/L for the subsequent doses of cardioplegia. For the first dose, 1000 ml of cardioplegia solution was infused. This was followed by 600 ml repeated every 20 minutes. In the OPCAB group, the coronary artery immobilization was achieved with mechanical stabilizers, Octopus and Urchin devices (Medtronic). Vessel occlusion was achieved by external encircling with silicone rubber bands. Intra-coronary shunts were used in those vessels where stenoses were significant but not critical. In the OBCAB group, the CPB was established just like the ConCAB group. However, the aorta was not clamped and hence cardioplegia was not administered. The body temperature was kept normo-thermic, and the coronary bypass grafting was carried out by using the mechanical stabilizers in a similar manner to the OPCAB technique. After completion of surgery, the patients were transferred to the cardiac intensive care unit (ICU). All patients underwent elective mechanical ventilation until they were ready for extubation. During their stay in ICU, all patients had invasive hemodynamic monitoring. Patients were transferred to the ward on the morning of the first post-operative day, except those who still needed mechanical ventilation or significant inotropic support. Those who did not require ventilation but were not ready for mobilization or still required significant oxygen therapy were transferred to a high dependency unit. Blood samples were taken at the following 4 times in each patient: first sample - 2 hours after arrival from the operating room (OR). Second sample - 6 hours after arrival from the OR. Third sample - 12 hours after arrival from the OR. Fourth sample - 24 hours after arrival from the OR. Those samples which showed creatine kinase, myocardial band (CKMB) levels below one u/liter were converted to one for conducting analysis of variance (ANOVA).

The data were stored in a Microsoft Excel (MS Excel version 2003, Microsoft Co. USA) data sheet and the statistical analysis was carried out using SPSS (SPSS version 10 for Windows, SPSS Inc, Chicago, IL) and StatsDirect (StatsDirect Statistical Software version 2.4.5 Cheshire, UK). The continuous variables were compared by ANOVA, and the categorical variables were compared by chi-square test. The analysis of variance with repeated measures were used to compare the trends in rise and fall of CKMB and CK levels. The significance of the differences between the groups was expressed as *p*-value and a value of <0.05 was considered significant.

Results. Tables 1 and 2 show that patients in the 3 groups had similar pre-operative characteristics including age, gender, ethnic origin, diabetes

mellitus, hypertension, and left ventricular function. The age in the OBCAB was higher than OPCAB and conventional groups, but this difference was not significant. The mean number of bypass grafts was 3.2 in the OBCAB, 2.47 in the OPCAB, and 2.8 in the ConCAB groups. This difference was statistically significant by ANOVA ($p=0.04$). However, as we know that the mean is not a valid estimate for ordinal variables such as the number of grafts, hence, ANOVA is not an appropriate method for comparison. We therefore compared the number of grafts by median test as well. The median number was 3 in all the

groups and did not show any statistically significant difference ($p=0.34$). The duration of stay in the ICU and the duration of inotropes were shortest in the off-pump group but the difference was not significant. The **Table 3** and **Figure 1** show that there was a peak of CKMB levels at 6 hours in all groups. The trend of CKMB level showed significantly higher values in the conventional CABG group as compared with the other 2 groups. These values were very similar in the off-pump and on-pump beating groups. **Table 4** shows that the rise in CK levels had a similar pattern to CKMB levels. However, the difference

Table 1 - Patients characteristics in continuous variables.

Characteristics	ConCAB (n=15)	OPCAB (n=15)	OBCAB (n=15)	P value
Age	54.87 ± 12.46	54.6 ± 11.06	63.13 ± 10.16	0.07*
Height	163.8 ± 6.59	164.93 ± 6.34	161.87 ± 6.72	0.44*
Weight	76.4 ± 11.70	72.55 ± 5.18	77.13 ± 13.41	0.45*
Body surface area	1.84 ± 0.14	1.76 ± 0.13	1.85 ± 0.19	0.23*
Echocardiography				
Ejection fraction	46 ± 7.60	45 ± 8.01	40 ± 8.63	0.17*
Left ventricular dimension in diastole	50.33 ± 5.79	52.66 ± 5.86	54.46 ± 5.87	0.16*
Left ventricular dimension in systole	30.60 ± 6.44	32.73 ± 5.86	37.26 ± 7.54	0.03*
Bypass time	102.54 ± 29.93	NA	96.2 ± 39.99	0.68†
Cross clamp time	57.92 ± 20.23	NA	NA	NA
Number of grafts				
Mean	2.8 ± 0.86	2.47 ± 0.64	3.2 ± 0.77	0.04*
Median	3	3	3	0.34‡
Intensive care unit stay	55.06 ± 26.34	40.00 ± 18.35	52.20 ± 39.14	0.33*
Duration of inotropes	26.80 ± 19.63	10.8 ± 9.78	21.40 ± 24.19	0.72*

Values are expressed as number and (%).

*Analysis of variance, †student's t-test, ‡median test, ConCAB - cold blood cardiopelgia. OPCAB - off-pump coronary artery bypass, OBCAB - on-pump beating coronary artery bypass.

Table 2 - patient characteristics in categoric variables.

Characteristics	Number (%)			P values
	ConCAB n=15	OPCAB n=15	OBCAB n=15	
Male gender	15 (100)	14 (93.3)	8 (53.3)	0.15
Diabetes mellitus	6 (40)	6 (40)	7 (46.7)	0.9
Hypertension	6 (40)	2 (13.3)	8 (53.3)	0.07
Arab ethnic origin	12 (80)	14 (93.3)	15 (100)	0.14
Use of LIMA	10 (66.6)	13 (86.7)	8 (53.3)	0.139

Values are expressed as number and (%). P values estimated by chi-square test.

LIMA - left internal mammary artery. ConCAB - cold blood cardiopelgia. OPCAB - off-pump coronary artery bypass. OBCAB - on-pump beating coronary artery bypass.

Table 3 - Creatine kinase myocardial bound levels following coronary artery bypass.

Levels	CKMB 1 (U/lit)	CKMB 2 (U/lit)	CKMB 3 (U/lit)	CKMB 4 (U/lit)
ConCAB (n=15)	11.07±10.6	13.13 ± 23.23	12.0 ± 19.72	4.4 ± 3.1
OPCAB (n=15)	1.33 ± 0.49	3.13 ± 2.61	3.6 ± 2.47	1.8 ± 2.24
OBCAB (n=15)	2.8 ± 2.04	2.8 ± 2.04	2.87 ± 2.61	2.07 ± 1.62
<i>P</i> value	0.0001	0.10	0.07	0.009

Values are expressed as mean ± SD. *P* values estimated by ANOVA. CKMB - creatine kinase myocardial bound, ConCAB - cold blood cardioplegia, OPCAB - off-pump coronary artery bypass, OBCAB - on-pump beating coronary artery bypass

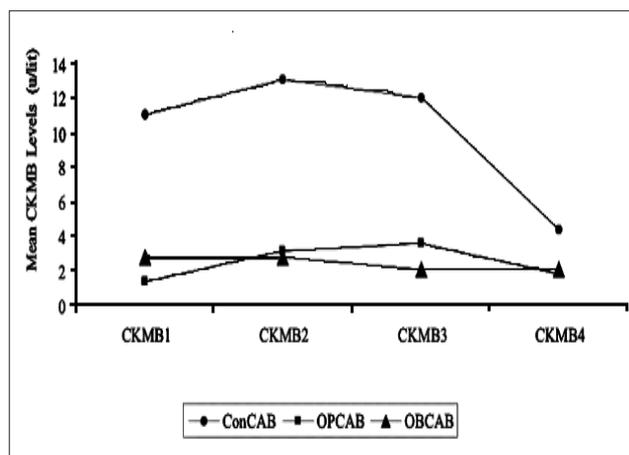


Figure 1 - Trend of postoperative creatine kinase, myocardial bound (CKMB) levels. Comparison of cold blood cardioplegia (ConCAB), off-pump coronary artery bypass (OPCAB) and on-pump beating coronary artery bypass (OBCAB).

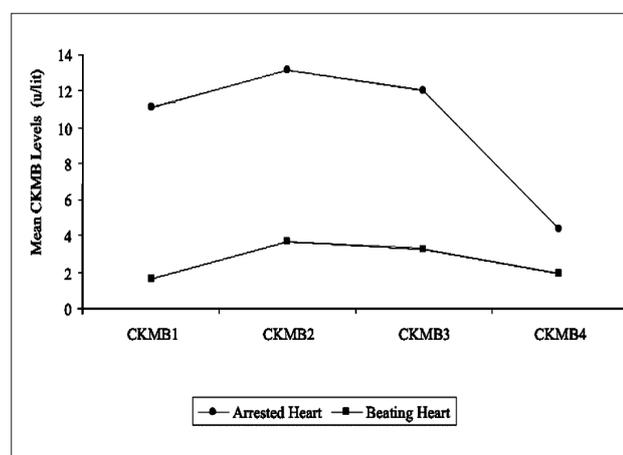


Figure 2 - Trend of postoperative CKMB levels. Comparison of pooled beating versus arrested heart coronary artery bypass grafting (CABG).

was significant only at 2-hours following the arrival from the OR. Since the enzyme levels in the OPCAB and OBCAB had similar values, we also compared the pooled data of both of these groups with the ConCAB group (arrested heart group). This resulted in uniformly higher and significant values of CKMB levels in the conventional group as compared with the beating heart group (**Figure 2 & Table 5**). However, although the CK levels also showed uniformly higher values in the conventional group, the difference was significant only at 2 hours following arrival from the OR (**Table 6**).

Discussion. Myocardial protection is a serious issue in those cases of CABG who are relatively high risk due to left ventricular dysfunction or diffuse nature of coronary artery disease. Recent advances in coronary interventions have shown a potential to take away a large proportion of patients previously referred for coronary bypass surgery.² In our practice, we have noticed a sharp decrease in referral for coronary

Table 4 - Creatine kinase levels following coronary artery bypass grafting.

Levels	CK 1 (U/lit)	CK 2 (U/lit)	CK 3 (U/lit)	CK 4 (U/lit)
ConCAB (n=15)	623 ± 315	762 ± 379	767 ± 390	534 ± 283
OPCAB (n=15)	322 ± 103	578 ± 273	555 ± 198	516 ± 728
OBCAB (n=15)	445 ± 336	706 ± 612	739 ± 655	770 ± 1160
<i>P</i> values	0.016	0.5	0.39	0.63

Values are expressed as mean ± SD.
P values estimated by analysis of variance.
 CK - creatine kinase. OPCAB - off-pump coronary artery bypass.
 OBCAB - on-pump beating coronary artery bypass.

Table 5 - Creatine kinase myocardial bound levels following coronary artery bypass grafting.

CKMB levels	CKMB 1 (U/lit)	CKMB 2 (U/lit)	CKMB 3 (U/lit)	CKMB 4 (U/lit)
Arrested heart group (n=15)	11.07 ± 10.6	13.13 ± 23.23	12.0 ± 19.72	4.4 ± 3.1
Beating heart group (n=15)	2.07 ± 1.6	3.7 ± 3.45	3.23 ± 2.53	1.93 ± 1.93
<i>P</i> values	0.0001	0.033	0.02	0.002

Values are expressed as mean±SD. *P* values estimated by analysis of variance. CKMB - creatine kinase myocardial bound.

Table 6 - Creatine kinase (CK) levels following coronary artery bypass grafting.

CKMB levels	CK 1 (U/lit)	CK 2 (U/lit)	CK 3 (U/lit)	CK 4 (U/lit)
Arrested heart group (n=15)	623 ± 315	762 ± 379	767 ± 390	534 ± 283
Beating heart group (n=15)	384 ± 252	642 ± 460	647 ± 484	643 ± 960
<i>P</i> values	0.009	0.389	0.409	0.670

Values are expressed as mean±SD. *P* values estimated by analysis of variance.

bypass surgery in recent years.³ Since the pioneer experimental work by Melrose,⁴ the concept of elective cardioplegic arrest of the heart for cardiac surgery has made tremendous progress. Experimental work by Buckberg et al⁵ provided important information about the oxygen requirements of various heart conditions.⁵ Since then, composition of cardioplegia solutions has undergone tremendous clinical evaluations,⁶⁻¹⁰ and at present blood cardioplegia has almost replaced the older crystalloid solutions. However, the preference between hypothermia and normothermia still varies among the cardiac surgeons.¹¹⁻¹⁴ Despite all improvements in myocardial preservation, the patients with recent myocardial infarction have remained a well-recognized subset that fares poorly after conventional CABG.^{15,16} In the recent years, OPCAB has gained popularity as it does not require cardioplegia and has opened new vistas in the understanding of myocardial preservation. A pooled analysis randomized control trial has proved OPCAB has good short as well as midterm results.¹⁷ This has established the role of OPCB as a safe and effective method of coronary bypass surgery. The long term follow-up results have also suggested that OPCAB is more beneficial, particularly in high risk patients.¹⁸ Since the heart is not deprived of its blood supply, there is theoretically no period of global ischemia and hence no ischemic reperfusion injury. Ischemic reperfusion injury is a very well-recognized phenomenon, which is considered to be a major cause of postoperative mortality in sick hearts.¹⁹ However, there is still a large proportion of patients where the OPCAB technique cannot be applied due to various technical reasons.

In such patients, we prefer to do revascularization by the on-pump beating technique. The support of heart-lung machine enables us to carry out complete revascularization in patients who require complex or extensive techniques such as reconstruction of coronary arteries or endarterectomies even in the presence of impaired left ventricular function. We observed, in our practice, that patients operated electively by off-pump as well as on-pump beating techniques required inotropes in much lesser doses and for much shorter durations, which resulted in a bias to perform on-pump beating heart surgery upon relatively high risk patients. A very similar experience was reported by Edgerton et al.²⁰ These observations prompted us to conduct this prospective study. The selection of CKMB levels as a marker of injury due to global ischemia can be criticized as troponin-T and troponin-I are considered to be more specific and sensitive markers. We acknowledge the fact that troponins are superior markers for the clinical diagnosis of myocardial infarction. However, in this study the aim is not to detect the myocardial infarction. Our aim was to compare the myocardial injury during surgery, and since the same marker is used in all 3 groups, we believe that its sensitivity is not an issue. Moreover, there is also sufficient evidence that although, the troponin-I is better than troponin-T, and CKMB for diagnosing fresh infarcts, yet this superior diagnostic capacity is not statistically significant.²¹ Another matter of contention could be the timing of collecting the blood samples for CKMB levels. Our selection of times are based on the knowledge that the CKMB level starts rising soon after the myocardial injury and reaches a peak between 18-24 hours after

which it starts receding back to base line. We initially included samples taken immediately after grafting, but these are not worth comparing due to wide variations in the hemodilutions in these patients. Similarly, samples taken immediately after arriving from the OR had very low levels and were not suitable for comparisons. We therefore used 2 hours after arrival from the OR as a reasonable starting point. However, even at this time, many samples showed CKMB levels far below one u/liter. We therefore, converted all such values to one for statistically analysis in ANOVA.

Tables 3 and 4 show that the patients operated by OPCAB and OBCAB techniques had a lower rise in the levels of CK and CKMB levels as compared to the levels in the ConCAB group. Due to smaller size of samples and internal variations within the groups the differences did not reach statistical significance at all 4 times of sample collection. However, since we believe that the off-pump and on-pump beating are similar groups in terms of avoiding ischemic-reperfusion injury, we repeated the analysis by pooling up these 2 groups and then comparing their values with the conventional CABG group. This analysis produced interesting results proving that the rise in CKMB levels in the pooled beating heart group is significantly lower at all timings of sample collection. Moreover, we believe that ischemic reperfusion injury caused by an aortic cross clamp might have a major role in initiating systemic inflammatory response,²² which can result in far reaching multiple organ injury. The on-pump beating heart surgery therefore has a theoretical advantage, as it does not involve any aortic clamping. Recently published articles have confirmed similar observations regarding the use of on-pump beating heart revascularization. Izumi et al²³ reported better postoperative outcome in the on-pump beating group in patients undergoing CABG following recent infarction. Similarly, Glucan et al²⁴ reported more favorable outcome by the on-pump beating-heart CABG technique in patients with severe left ventricular dysfunction. However, when OPCAB is compared to the on-pump beating technique, the results are almost consistently in favor of OPCAB.¹⁸

In conclusion, CABG on the beating heart appears to result in less myocardial injury as compared to the conventional CABG on the arrested heart. This difference may remain unnoticed in patients with normal myocardial function, but can become critically significant in patients with poor ventricles.

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Related topics

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