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Does Off-Pump Coronary Artery Bypass Grafting Offer Patients a Better Outcome than Conventional Bypass Surgery?: Retrospective Study Carried Out at Tokyo Women's Medical University Hospital

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[Background] For 3 decade's surgical coronary revascularization has been carried out with the use of cardiopulmonary bypass (CPB) as the gold standard. This is being challenged with the resurgence of an old technique involving operating on the beating heart, which is associated with lower morbidity. There is little long-term data on the success of off-pump coronary revascularization, hence this polarizing debate as to which surgery is superior continues.

[Aims] To evaluate whether off-pump coronary artery bypass grafting (OPCAB) reduces postoperative morbidity compared to conventional coronary artery bypass grafting (CABG) and to compare completeness of revascularization in both groups.

[Methods] Twenty patients who underwent OPCAB and 20 patients who underwent CABG with CPB were selected at random from May 2000–June 2005. Postoperative complications, completeness of revascularization and ICU stay were compared and analyzed.

[Results] The CK-MB in the on-pump group was (36.9 NG/ML) compared to (18.35 NG/ML) in the off-pump group ($p = 0.026$). Mean ICU stay was significantly different in both groups ($p = 0.043$). The index of completeness of revascularization was similar with no significant difference in graft number and patency.

[Conclusion] When compared to conventional CABG, OPCAB achieved significantly shorter ICU stay, less myocardial injury and similar completeness of revascularization indicating that it is an attractive alternative to conventional CABG.

Key words: off-pump coronary artery bypass grafting, cardiopulmonary bypass

Introduction

Fourteen percent of all coronary artery bypass grafting (CABG) worldwide is performed off-pump and in the USA this figure is 18%[1]. In Tokyo Women's Medical University (TWMU) Hospital, this figure is as high as 90% and even on-pump surgery is done without administering cardioplegic arrest, hence the heart is still beating during the surgery. This reflects the increased awareness of the morbidity associated with CPB and the need to perform beating heart surgery. Patients referred for CABG are older, have higher co-morbidities, worse ventricular function and more severe coronary disease than 20 years ago[2]. Therefore conventional coronary surgery in this high-risk group is associated with higher complication rates and potentially higher costs[3].

The main advantage of off-pump CABG (OP-

Table 1 Preoperative patient characteristics

Variables	On-pump (n=20)	Off-pump (n=20)
Male/Female	12/8	18/2
Mean age	61.9 ± 9.65	64.2 ± 11.08
Ejection fraction > 50%	12	14
Ejection fraction 30-50%	8	6
Previous MI	13	12
Chronic renal failure on haemodialysis	3	1
Diabetes	10	15
Patients with > 4 co-morbidities/	2	8

CAB) is the avoidance of the morbidity associated with cardioplegia and CPB. It is thought that coronary artery bypass grafting performed on the beating heart can achieve equivalent revascularization as compared to on-pump CABG and better short term outcomes especially in high risk groups[4]. Despite these apparent benefits, concern has been raised about this procedure and the debate continues. The main concern regarding this rediscovered operation is that incomplete revascularization may compromise patient outcome, it was recognized grafts to the lateral wall proved difficult off-pump and hence early studies omitted these patients from undergoing OPCAB[5)6)].

Other studies have also failed to evaluate completeness of revascularization by not directly assessing graft patency with coronary angiography. These reasons have further raised legitimate concerns as to whether there really are any tangible benefits of OPCAB as compared to the conventional surgery and this study carried out at TWMU Hospital seeks to investigate this.

Patients and Methods

1. Patients

This retrospective study was designed to compare clinical outcomes and completeness of revascularization in the two groups of patients who underwent coronary artery bypass surgery. To minimize variability all operations on the selected patients were performed by a single experienced cardiovascular surgeon (Kenji Yamazaki, MD, Ph D).

Twenty patients who underwent off-pump CABG (off-pump group) and 20 patients who underwent on-pump CABG (on-pump group) between May 2000 and June 2005 were selected at random. This randomization was done by randomly choosing 4 patients from each year in the five-year period therefore giving a more representative sample over five years. Patient identification numbers were placed in a box and cases selected randomly from each year to give 20 patients in each group (Table 1).

Exclusion criteria: Patients were not excluded on the basis of any preoperative co-morbid illnesses or extent of coronary artery disease. Those patients who underwent emergency CABG were excluded as well as those who had preoperative intraaortic balloon-pump counter pulsation as they are very high risk patients and may bias the results.

Patients were excluded if they were having concomitant major surgery for example CABG and a valve replacement. Redo CABG operations were also omitted from the study as the risks are very high and this would influence the postoperative outcome in a biased fashion.

2. Surgical technique

1) General

Surgical access to the heart was through a standard median sternotomy. All incision and closure techniques were the same in both groups limiting variability. Distal anastomosis in all cases were constructed with 8-0 polypropylene sutures. Most of the grafts performed were in situ arterial grafts, where proximal anastomosis was performed 6-0 Prolene sutures were used. A surgical blower humidifier was used to disperse blood from the anastomotic site in all cases. Routine CT scans were performed to assess the great arteries and epiaortic ul-

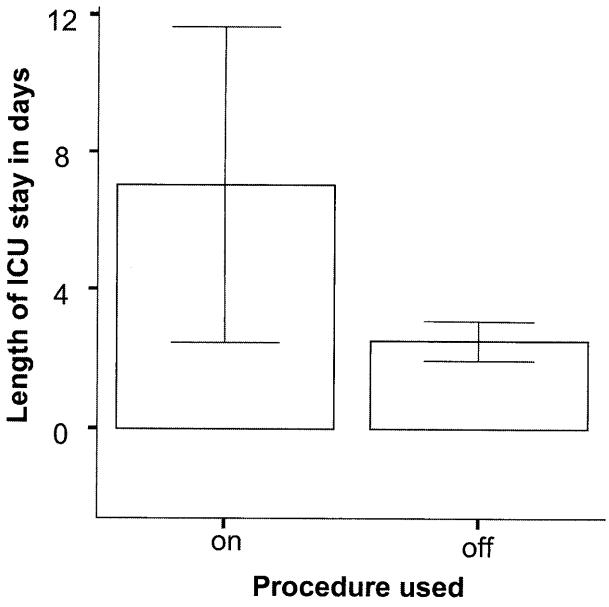

Fig. 1 Mean ICU stay
Bars show means. Error bars show 95.0% confidence interval of mean.

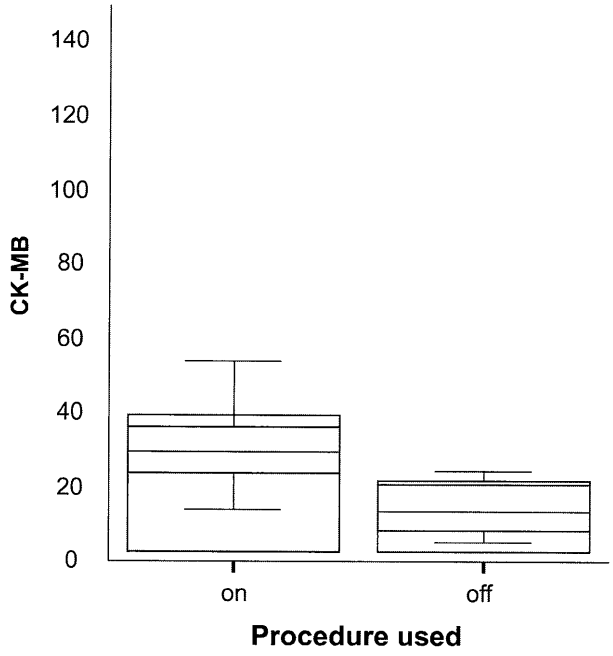

Fig. 2 Mean CK-MB
Bars show means. Box plot showing the mean CK-MB in the on- and off-pump group.

trasound performed on a case by case basis depending on whether there was calcification or atherosclerosis of the aorta.

2) On-pump technique

On-pump CABG was done in a standardized fashion with ascending aortic cannulation and single venous cannulation of the right atrium. A standard circuit was used in all cases and the CPB priming solution contained Hartmann's solution, gelofusine, mannitol 0.5 g/ml, 7 ml 10% calcium gluconate and heparin 0.02 ml/kg. The body temperature was kept between 34 and 36℃. Myocardial protection was achieved by administering intermittent anterograde hyperkalaemic warm blood cardioplegia.

3) OPCAB technique

OPCAB was performed in most cases with the Medtronic Octopus 3 or 4 and Starfish stabilizing devices for coronary stabilization. In a few of the cases the CTS retractor and stabilization devices were used[7]. Deep pericardial traction sutures were used for cardiac displacement and presentation of the coronary vessels. With the use of these devices care is taken to maintain mean arterial blood pressure above 65 mmHg. An intracoronary shunt was used were there was electrocardiographic or haemodynamic instability.

3. Statistical analysis

Data are presented as means ± standard deviation except for the data regarding postoperative arrhythmias, which are presented as frequencies. Comparisons between the two groups were performed using a one way ANOVA and Pearson's chi-squared test were appropriate. Differences were considered significant if $p < 0.05$. The analysis was performed using SPSS 14.0 statistical package (©2005 SPSS Inc. Chicago, Illinois).

Results

There were no deaths in both groups of patients up to date. A significant difference existed in mean length of ICU stay (Fig. 1), with the on-pump group staying a mean 7.05 days compared with 2.5 ± 1.15 days in the off-pump group ($p = 0.046$).

However one patient in the on-pump group remained in ICU for 20 days due to respiratory failure and worsening of existing renal failure contributing to this difference in mean ICU stay between the two groups and hence the wide confidence interval in the on-pump group. A significant finding was the difference in mean CK-MB between the groups, 36.9 NG/Ml in the on-pump group and 18.35 in the off-pump group (Fig. 2) measured postoperatively on

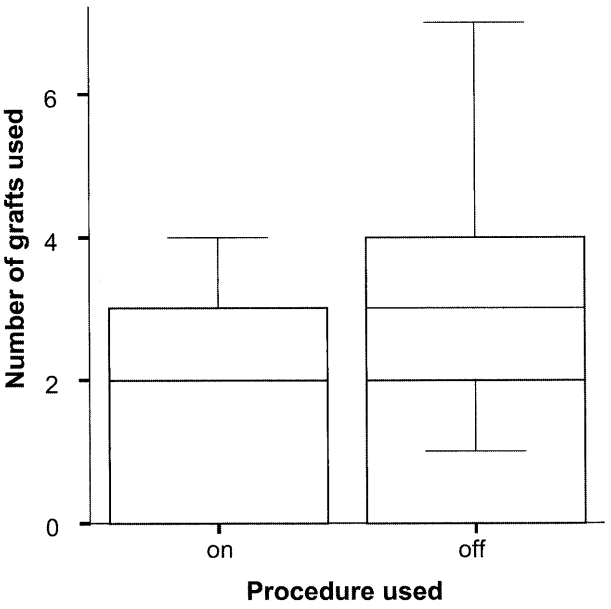

Fig. 3 Mean number of grafts
Bars show means. Box plot comparing mean number of grafts in both groups.

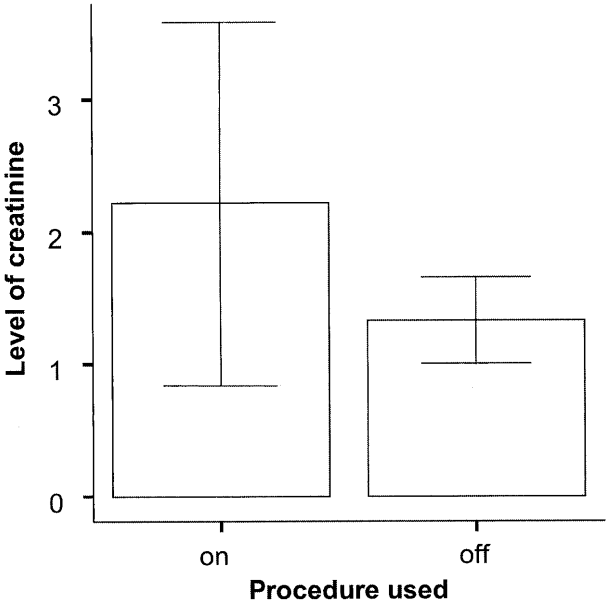

Fig. 4 Mean level of creatinine
Bars show means. Error bars show 95.0% confidence interval of mean. Box plot showing mean creatinine in both groups.

the first day in ICU ($p = 0.026$). The rise in this enzyme is thought to be a marker of myocardial injury and necrosis. There were no strokes in either group as well. Completeness of revascularization was similar in both groups with postoperative graft patency 98% and 96.3% in the off- and on-pump group. Graft patency at three months assessed by angiography was also the same as above. The mean number of grafts in the on-pump groups was 2.95 ± 0.94 and 3.3 ± 1.59 in the off-pump group ($p = 0.403$). The greatest number of distal anastomosis was performed in the off-pump group were one patient received 7 bypass grafts, all patent to date.

The box plot (Fig. 3) illustrates the similar number of grafts achieved in both groups, and also the wide confidence interval for the off-pump group, where a range of one to seven grafts were performed in this group.

The incidence of postoperative atrial fibrillation was not significantly different in both groups with 8 patients having atrial fibrillation in the on-pump group and 4 in the off-pump group ($p = 0.168$). Similarly there was no significant difference with regard to ventricular arrhythmias in the on- and off-pump group ($p = 0.151$).

No patients developed acute renal failure (defined as a creatinine > 2.0 mg/dl). However 2 patients in the on-pump group with a preoperative diagnosis of chronic renal failure on haemodialysis had worsening of preexisting renal failure. The first patient's creatinine increased from 5.95 mg/dl preoperatively to 7.4 g/dl on day 2 of ICU stay. The second patient's creatinine increased to 9.65 from 9.0 on day 1 of ICU stay. There was no significant difference in the mean postoperative creatinine (day 1 ICU stay) between the on- and off-pump group, 2.2 and 1.3 mg/dl respectively ($p = 0.199$) (Fig. 4).

Discussion

The results of this nonrandomized retrospective analysis indicate that there is a significant difference in the length of ICU stay ($p = 0.046$) and in the mean CK-MB ($p = 0.026$) between the two groups. The length of ICU stay was longer by 4.5 days in the on-pump group. This is in keeping with other large retrospective studies. Racz et al[8] in a retrospective study where $> 9{,}000$ patients had off-pump revascularization found the length of ICU stay was longer by one day in the on-pump group. Similarly in a meta-analysis of the BHACAS 1 and 2 (beating heart against cardioplegic arrest) randomized prospective studies, ICU stay and mean hospital stay

Table 2 Completeness of revascularization

Variables	Off-pump group (n=20)	On-pump group (n=20)	p-value
Grafts per patient	3.3 ± 1.59	2.95 ± 0.94	0.403
ICOR	1.01	1.03	NS
Graft patency	98%	97%	NS

were significantly shorter in the off-pump group.

To appreciate the results obtained, one needs to consider the large confidence interval for the mean hospital stay in the on-pump group. One patient remained in the ICU for 20 days due to numerous complications not all of which were related to the cardiac surgery. This would have an effect on the results, as there were only 20 patients in each group. Shorter ICU and hospital stay needless to say would have a significant impact on reducing the costs of managing these patients postoperatively.

There is general agreement from randomized[9)10)] and non-randomized prospective[11)] studies that on-pump bypass grafting with cardioplegic arrest is associated with significantly greater myocardial injury than OPCAB. The results in this study showed the mean CK-MB enzyme release in the on-pump group was 36.9 NG/ML, twice that of the off-pump group ($p = 0.026$). Some of the CK-MB release can be explained by cannulation of the right atrium whilst setting up the cardiopulmonary bypass in the on-pump group. However the differences in the myocardial injury are largely the result of aortic cross clamping, which results in myocardial ischemia and reperfusion injury despite even optimal myocardial protection and hence most of the enzyme arises from the ventricular myocardium. However patients would need to be followed up to correlate any long-term outcomes with the elevation in the CK-MB. It has been reported that elevated serum troponin post cardiac surgery is an independent predictor of in hospital mortality and postoperative complications in high-risk patients[12)].

The results illustrate that off-pump group achieved similar and slightly superior graft patency rates (98%) than on-pump group (96.3%). The index of completeness of revascularization (ICOR) and the mean number of grafts 2.95 ± 0.94 and 3.3 ± 1.59 were similar. Therefore it is possible to achieve equivalent completeness of revascularization and similar graft numbers using the off-pump technique. These results reflect the high level of success in terms of surgical outcomes attained by our team in both modems of surgery (Table 2).

Due to the fact the cardiovascular surgery center in Tokyo is one of the main referral centers, it is up to date with all the new stabilization devices required to perform difficult grafts off-pump, particularly the marginal branches of the circumflex. Some studies have reported significantly fewer grafts in the OPCAB group. Sabik et al[13)] found in their registry of patients that the mean number of grafts in the OPCAB group was 2.8 compared with 3.5 in the on-pump group ($p < 0.001$). This resulted in higher cardiac related events and mortality due to incomplete revascularization. Improvements in stabilization techniques have allowed grafting to difficult areas and smaller vessels thus allowing complete revascularization off-pump. Some patients in the OPCAB study group carried out at Tokyo received 7 successful bypass grafts. This may be due to the fact the surgeon can spend more time on grafting difficult vessels without worrying about myocardial ischemia, which occurs predominately in on-pump bypass surgery. Also the cardiac surgery team now carry out the majority of CABG off-pump hence are now proficient in grafting nearly all vessels and achieving complete revascularization (Distal marginal grafts on the beating heart were once considered off limits).

No patients developed acute renal failure. Two patients in the on-pump group who were on haemodialysis had worsening of there pre-existing renal failure. No patients in the OPCAB group with chronic renal failure had a worsening of their renal function. Cardiopulmonary bypass in the elderly

and those with co-morbid illness is associated with an increased risk of dialysis dependant renal failure and this may indicate the use of OPCAB in this patient subgroup[14].

The small numbers in the study may have meant it would be difficult to detect any significant difference in the renal function between the two groups. It is also important to realize there are many other factors most of which are patient related that increase the risk of developing acute renal failure. Previous retrospective studies have also failed to show any significant renoprotective effect from using OPCAB techniques[15].

The similar rate of postoperative arrhythmias was also similar in both groups. However large studies for example a large multivariate analysis from Bristol (990 patients) have found decreased intraoperative and postoperative arrhythmias in the off-pump group[16].

At present there are no specific indications or guidelines for which patients should undergo on- or off-pump surgery. This is largely the choice of the operating surgeon, but it appears that the benefits of off-pump surgery are most marked in the elderly and those where CPB may be detrimental (diabetics, renal failure, cerebral co-morbidity) and in patients with severe aortic calcification[17]. There is now a significant body of evidence suggesting that OPCAB can achieve better short term and similar midterm outcomes than conventional CABG. This small study is in keeping with other studies in which multivessel revascularization success rates are as successful compared with the on-pump CABG, these studies have also demonstrated a 25% reduction in cost and better outcomes particularly in high risk groups[3]. OPCAB has also been found to be associated with reduced use of inotrops, blood loss and transfusion requirements compared to and conventional CABG[4]. Despite all these benefits, the lack of long term data and other factors have halted the widespread use OPCAB, and it may be a while before OPCAB becomes the new gold standard in surgical coronary revascularization.

Limitations of the study

The study was intended to analyse 80 patients (40 in each group). However over the last 5-8 years most of the surgery for coronary revascularization in TWMU Hospital has been performed off-pump or on-pump beating (on-pump without cardioplegic arrest). We could only gather 20 patients over the last five years who underwent conventional CABG hence had to reduce the number of patients in the study to 40 limiting the power of the study. It is also recognized that randomized prospective studies comparing clinical outcomes in on and off-pump groups of patient are the gold standard and reduce recall bias which occurs in retrospective analysis.

No follow up data in this study are presented and this would be most useful especially with regard to graft patency in assessing completeness of revascularization. Long-term data and longitudinal studies from off-pump CABG are needed in order to truly appreciate any longer term benefit it offers.

Conclusion

In comparison to conventional CABG, off-pump CABG yielded similar completeness of revascularization; less myocardial injury and shorter ICU stay. This indicates that this rediscovered operation is a viable alternative to conventional CABG with superior short-term outcomes and comparable graft patency, which is ultimately the gold standard in coronary bypass surgery. Excellent surgical outcome can be attained by both types of operation as evidenced by the results of our team.

Acknowledgement

Thanks to the whole department of cardiovascular surgery at TWMU. A particular mention goes for supervising the audit and for providing case series for bypass operations he carried out.

Appendix Statistical data and analysis

One-way ANOVA statistical test used to compare the means in each group.

ANOVA

	Sum of squares	df	Mean square	F	Sig.
Level of creatinine					
Between groups	7.709	1	7.709	1.705	0.199
Within groups	171.782	38	4.251		
Total	179.491	39			
CK-MB					
Between groups	3,444.736	1	3,444.736	5.394	0.026
Within groups	24,265.588	38	638.568		
Total	27,710.324	39			
Length of ICU stay in days					
Between groups	207.025	1	207.025	4.271	0.046
Within groups	1,841.950	38	48.472		
Total	2,048.975	39			
Number of grafts used					
Between groups	1.225	1	1.225	0.715	0.403
Within groups	65.150	38	1.714		
Total	66.375	39			

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心拍動下冠動脈バイパス術は従来の冠動脈バイパス術と比較して優位性があるか
—東京女子医科大学における検討—

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過去30年間に渡って冠動脈再建術は人工心肺の使用が必要不可欠とされてきたが，またその使用が死亡率，合併症率を高める一因とも考えられてきた．現在では人工心肺非使用心拍動下冠動脈バイパス術は広く一般に行われつつあるが，依然としていずれの方法が優位性を持つかは議論が続けられている．

［目的］人工心肺使用冠動脈バイパス術（on-pump CABG：on-pump 群）と心拍動下冠動脈バイパス術（off-pump CABG：off-pump 群）における優位性を比較検討した．

［方法］2000年5月～2005年6月までに行われたすべての冠動脈再建術患者のうち，on-pump 群患者20名と off-pump 群患者20名を無作為に抽出し，死亡率，合併症発生率，完全血行再建率，グラフト開存率，集中治療室滞在日数等を比較検討した．

［結果］術後クレアチニンキナーゼの MB 分画（CK-MB）は on-pump 群で 36.9NG/Ml，off-pump 群で 18.35NG/Ml と off-pump 群で有意に低値であった（$p=0.026$）．平均集中治療室滞在日数は on-pump 群で 4.5 日長期であった（$p=0.043$）．完全血行再建率は両群で有意差を認めなかった．