Postoperative Functional Outcome After Off-Pump Versus On-Pump Coronary Artery Bypass Grafting Using Gated Myocardial SPECT: A Comparison by Propensity Score Analysis

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Received: 2 December 2009 / Revised: 29 January 2010 / Accepted: 1 February 2010 / Published online: 22 April 2010
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Abstract

Purpose We evaluated the short-term and mid-term differences in perfusion and function after off-pump and on-pump coronary artery bypass grafting (CABG) using gated myocardial single photon emission computed tomography.

Materials and Methods A total of 70 patients with coronary artery disease who underwent CABG were included based on the propensity score matching results from 165 patients. Thirty-five patients underwent off-pump and 35 patients on-pump CABG. Rest ^{201}Tl /dipyridamole stress $^{99\text{m}}\text{Tc}$ -methoxyisobutylisonitrile gated single photon emission computed tomographies were performed preoperatively and postoperatively at short-term (103 ± 23 days after surgery) and mid-term follow-up (502 ± 111 days after surgery). Changes in left ventricular ejection fraction, end systolic volume, stress and rest segmental perfusion, and

segmental wall thickening were compared between the two groups. The segments with preoperative rest ^{201}Tl uptake under 60% of maximum uptake were included in the segmental analysis.

Results Left ventricular ejection fraction ($P=0.001$) and end systolic volume ($P=0.008$) showed significant improvement in both groups. There were no significant short-term and mid-term differences between the two groups in terms of left ventricular ejection fraction ($P=0.309$) and end systolic volume ($P=0.938$). Likewise, segmental rest ($P=0.178$) and stress perfusion ($P=0.071$), and systolic wall thickening ($P=0.241$) showed significant improvement in both groups with similar time courses.

Conclusion Off-pump CABG resulted in significant improvements in left ventricular ejection fraction, end systolic volume, and regional myocardial perfusion and function that are comparable to on-pump CABG at short-term and mid-term. Gated myocardial SPECT successfully revealed that off-pump CABG is as good as on-pump CABG from the viewpoint of myocardial perfusion and function.

Keywords Gated myocardial single photon emission computed tomography · Off-pump coronary artery bypass grafting · Cardiopulmonary bypass · Coronary artery disease

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Introduction

Coronary artery bypass grafting (CABG) without cardiopulmonary bypass (off-pump CABG or OPCAB) has been widely used as an alternative surgical technique even in high-risk patients [1–3] as well as in low-risk patients [4, 5].

Mid-term angiographic and clinical outcomes after OPCAB were reported in recent studies showing that OPCAB outcomes were at least as good as those of on-pump CABG (ONCAB) [5–11]. However, little is known about the short-term and mid-term differences in myocardial perfusion and contractility between OPCAB and ONCAB.

Gated myocardial single photon emission computed tomography (SPECT) is used for the determination of myocardial viability and prediction of prognosis in CABG patients [12, 13]. Serial changes in myocardial perfusion and function after bypass surgery can be evaluated objectively using gated myocardial SPECT.

The aim of this study was to evaluate whether there are short-term and mid-term differences in the improvements of myocardial perfusion and left ventricular function between ONCAB and OPCAB using the short-term and mid-term postoperative gated myocardial SPECT.

Materials and Methods

Subjects

Of the 698 patients (224 ONCABs and 474 OPCABs) who underwent isolated CABG between July 1996 and November 2003, 165 patients (49 ONCABs and 116 OPCABs) who had available SPECT preoperatively and postoperatively in the short- and mid-term were initially enrolled in this study. The subjects were selected in a nonrandomized, prospective manner. All patients were confirmed to have coronary disease by coronary angiography when the luminal narrowing greater than 80% was considered to be significant. For the group comparison, propensity score was calculated for each patient. After matching the propensity scores, each group comprised 35 patients. There was no difference between the two groups in terms of sex, age, preoperative left ventricular ejection fraction (LVEF), preoperative end diastolic volume (EDV), previous myocardial infarction history, diabetes, hypertension, hypercholesterolemia, smoking, and number of affected vessels (Tables 1, 2). To evaluate temporal changes in the segments that benefit from revascularization, only hypoperfused segments in the preoperative myocardial SPECT were enrolled in the analysis. Hypoperfused segments were defined as those with rest ^{201}Tl uptake less than 60% of maximum uptake. Segmental analysis based on the vascular territory was not done because of the individual heterogeneity and large portion of three-vessel disease in the study population.

A preoperative SPECT was performed 20 ± 29 days before surgery, and short-term follow-up SPECT was performed 103 ± 23 days after surgery. Mid-term follow-up SPECT was performed 502 ± 111 days after surgery. There

Table 1 Patient demographics and clinical data

	OPCAB (<i>n</i> =116)	ONCAB (<i>n</i> =49)	<i>P</i> -value
Sex (M:F)	85:31	38:11	0.565
Age (years) ^a	60.7 $\pm$ 9.6	58.7 $\pm$ 8.6	0.216
LVEF ^a	51.9 $\pm$ 12.6	50.7 $\pm$ 14.7	0.604
EDV ^a	109.4 $\pm$ 45.4	112.8 $\pm$ 47.4	0.664
Stable:unstable	41:75	13:36	0.270
Previous MI	13 (11.2%)	6 (12.2%)	0.849
Risk factors			
Diabetes	49 (42.2%)	14 (28.6%)	0.099
Hypertension	81 (69.8%)	24 (49.0%)	0.011
Hypercholesterolemia	21 (18.1%)	7 (14.3%)	0.551
Smoking	64 (55.2%)	30 (61.2%)	0.473
Number of diseased arteries			
One-vessel disease	6 (5.2%)	1 (2.0%)	0.648
Two-vessel disease	17 (14.7%)	8 (16.3%)	
Three-vessel disease	93 (80.2%)	40 (81.6%)	

OPCAB Off-pump coronary artery bypass grafting, ONCAB on-pump coronary artery bypass grafting, LVEF left ventricular ejection fraction, EDV end diastolic volume, MI myocardial infarction

^a Values are expressed as mean $\pm$ standard deviation

were no cases of acute complications during or after the bypass surgery.

Myocardial SPECT Protocol

Dual isotope-separate acquisition myocardial perfusion SPECT was performed in all patients. Patients refrained from caffeine-containing beverages for 24 h and fasted for 4 h, prior to the study. A rest ^{201}Tl /dipyridamole stress $^{99\text{m}}\text{Tc}$ -methoxyisobutylisonitrile (MIBI) gated SPECT was performed. Ten minutes after an injection of 111 MBq of ^{201}Tl , the rest SPECT images were acquired. For the stress study, 0.56 mg/kg of dipyridamole was continuously injected over 4 min. At 3 min after the completion of the stress procedure, 925 MBq of $^{99\text{m}}\text{Tc}$ -MIBI was injected. After taking a fatty meal of two raw eggs and 180 ml of milk, the post-stress $^{99\text{m}}\text{Tc}$ -MIBI gated SPECT was performed 90 min after stress with the same camera.

The SPECT was performed using a dual-head camera and low-energy high-resolution collimator (Vertex EPIC, ADAC Labs, CA, USA). Thirty-two step-and-shoot images were acquired at intervals of 3° at 25 s/step. For gating, 16 steps per cardiac cycle with pre-set RR intervals and 40% windows were used. The ^{201}Tl SPECT was reconstructed using a Butterworth filter with a cut-off frequency of 0.35 and order of 10, and the $^{99\text{m}}\text{Tc}$ -MIBI SPECT was reconstructed using a Butterworth filter with a cut-off frequency of 0.45 and an order of 10.

Table 2 Patient demographics and clinical data after propensity score matching

	OPCAB (n=35)	ONCAB (n=35)	P-value
Sex (M:F)	29:6	27:8	0.502
Age (years) ^a	58.5±12.6	59.1±8.5	0.842
LVEF ^a	48.5±13.3	51.2±16.3	0.448
EDV ^a	118.7±44.8	113.5±54.3	0.667
Stable:unstable	11:24	9:26	0.792
Previous MI	6 (17.1%)	4 (11.4%)	0.734
Risk factors			
Diabetes	11 (31.4%)	9 (25.7%)	0.792
Hypertension	16 (45.7%)	17 (48.6%)	1.000
Hypercholesterolemia	6 (17.7%)	7 (20.0%)	1.000
Smoking	20 (57.1%)	22 (62.9%)	0.808
Number of diseased arteries			
One-vessel disease	0 (0.0%)	1 (2.9%)	0.602
Two-vessel disease	4 (11.4%)	4 (11.4%)	
Three-vessel disease	31 (88.6%)	30 (85.7%)	

^a Values are expressed as mean ± standard deviation

Quantification of Regional Perfusion and Wall Function

The reconstructed images were analyzed using an automatic quantifying software package (AutoQUANT, ADAC Labs) without manual intervention. For the regional analysis, a 20-segment model was adopted. The segmental perfusion was quantified by measuring the radioactivity and was expressed as the percentage of the maximum uptake. The segmental wall thickening was also quantified and expressed as the percentage of the end-diastolic thickness on the gated images. The LVEF and end systolic volume (ESV) were calculated using quantitative gated SPECT software on the stress ^{99m}Tc-MIBI SPECT.

Statistical Analysis

Probability of being assigned to OPCAB and ONCAB is obtained using logistic regression. Independent variables were sex, age, preoperative LVEF, preoperative EDV, unstable angina, previous myocardial infarction history, diabetes, hypertension, hypercholesterolemia, smoking, number of affected vessels, and average of segmental preoperative rest

²⁰¹Tl uptake. Patients were matched according to the propensity score and the difference was under 0.04 for every match. The significance of the difference between the demographic parameters of OPCAB and ONCAB groups was tested using Pearson chi-squared test or independent samples *t*-test. The significance of difference between the preoperative segmental parameters of OPCAB and ONCAB groups was tested using independent samples *t*-test. The significance of the time-course difference between the two groups in terms of the segmental parameters, EF and ESV was tested using repeated measures analysis of variance. All values are expressed as percentage or mean ± SD. A *P*-value of less than 0.05 was considered significant. SPSS (version 12.0, Chicago, IL, USA) was used for the statistical analysis.

Results

Global Function Change

LVEF was improved and ESV decreased significantly in both OPCAB and ONCAB groups. There were no

Table 3 Time courses of global parameters

	OPCAB (n=35)	ONCAB (n=35)	Within group P-values	Between group P-values	Interaction P-values
Values are expressed as mean ± standard deviation. P-values come from the repeated measures analysis of variance					
OPCAB Off-pump coronary artery bypass grafting, ONCAB on-pump coronary artery bypass grafting, EF ejection fraction, EDV end diastolic volume					
EF (%)					
Preoperative	48.5±13.3	51.2±16.3	0.001	0.309	0.900
Short-term follow-up	51.7±13.3	55.2±14.5			
Mid-term follow-up	52.0±13.3	55.7±16.4			
ESV (ml)					
Preoperative	65.4±37.8	62.2±48.9	0.008	0.846	0.937
Short-term follow-up	53.8±30.7	52.0±43.0			
Mid-term follow-up	58.8±33.3	58.1±61.1			

Table 4 Time courses of global parameters for patients with EF<60%

	OPCAB (n=26)	ONCAB (n=21)	Within group P-values	Between group P-values	Interaction P-values
Values are expressed as mean $\pm$ standard deviation. P-values come from the repeated measures analysis of variance					
OPCAB Off-pump coronary artery bypass grafting, ONCAB on-pump coronary artery bypass grafting, EF ejection fraction, EDV end diastolic volume					
EF (%)					
Preoperative	42.6 $\pm$ 9.7	40.9 $\pm$ 12.5	0.000	0.820	0.283
Short-term follow-up	46.8 $\pm$ 11.1	48.7 $\pm$ 13.0			
Mid-term follow-up	47.4 $\pm$ 11.0	49.4 $\pm$ 14.4			
ESV (ml)					
Preoperative	77.2 $\pm$ 36.2	86.5 $\pm$ 49.7	0.003	0.555	0.925
Short-term follow-up	62.3 $\pm$ 30.7	67.8 $\pm$ 48.2			
Mid-term follow-up	68.1 $\pm$ 32.2	75.0 $\pm$ 71.3			

significant short-term and mid-term differences between the two groups in terms of LVEF and ESV (Table 3). For the patients whose preoperative LVEF values were less than 60%, LVEF improved and ESV decreased significantly in both groups, and there were also no significant short-term and mid-term differences between the two groups (Table 4).

Segmental Perfusion and Functional Change of Hypoperfused Segments

A total of 220 segments in the OPCAB group and 189 segments in the ONCAB group had preoperative rest ^{201}Tl uptake that was less than 60% of maximum uptake. Percentages of hypoperfused segments were not different between OPCAB and ONCAB groups ($P=0.07$). Preoperative rest ^{201}Tl uptake ($P=0.314$), preoperative stress $^{99}\text{Tc-MIBI}$ uptake ($P=0.070$), and wall thickening ($P=0.560$) were not different between the two groups.

Rest ^{201}Tl uptake, stress $^{99}\text{Tc-MIBI}$ uptake, and wall thickening improved in OPCAB and ONCAB groups. There were no significant short-term and mid-term differences between the two groups in terms of rest ^{201}Tl uptake, stress $^{99}\text{Tc-MIBI}$ uptake, and wall thickening (Table 5).

Discussion

The major finding of this study is that there was no difference between OPCAB and ONCAB groups in the improvement of global left ventricular function at both short-term and mid-term follow-up after surgery. We used LVEF and ESV calculated from gated post-stress $^{99}\text{Tc-MIBI}$ SPECT as markers of global left ventricular function because LVEF and ESV are good predictive markers for clinical outcome after bypass surgery [14–16]. These results indicate that left ventricular global functional improvement by OPCAB is comparable to ONCAB.

Another finding is that there were no significant short-term and mid-term differences between the two groups in terms of regional perfusion and contractility such as rest ^{201}Tl uptake, stress $^{99}\text{Tc-MIBI}$ uptake, and wall thickening. Our results support previous studies that reported OPCAB yielded comparable angiographic or clinical outcomes to those of ONCAB both in short-term and mid-term results [5–11].

Operator-independence and robustness of measuring myocardial perfusion and function on gated myocardial SPECT made it possible to investigate the short-term and mid-term differences with more confidence [17–20]. Myocardial motion was beyond our scope because of

Table 5 Time courses of segmental parameters

	OPCAB (n=220)	ONCAB (n=189)	Within group P-values	Between group P-values	Interaction P-values
Rest ^{201}Tl uptake (%)					
Preoperative	51.0 $\pm$ 6.1	50.3 $\pm$ 7.4	<0.000	0.178	0.775
Short-term follow-up	55.5 $\pm$ 10.8	56.6 $\pm$ 11.3			
Mid-term follow-up	56.8 $\pm$ 10.1	57.0 $\pm$ 10.7			
Stress $^{99}\text{Tc-MIBI}$ uptake (%)					
Preoperative	49.0 $\pm$ 12.0	46.9 $\pm$ 10.9	<0.000	0.071	0.645
Short-term follow-up	54.1 $\pm$ 11.6	54.4 $\pm$ 10.8			
Mid-term follow-up	54.1 $\pm$ 12.1	54.7 $\pm$ 12.8			
Segmental wall thickening (%)					
Preoperative	17.1 $\pm$ 10.5	17.7 $\pm$ 11.5	<0.000	0.241	0.669
Short-term follow-up	22.7 $\pm$ 13.2	21.3 $\pm$ 12.1			
Mid-term follow-up	21.4 $\pm$ 13.1	20.9 $\pm$ 14.3			

OPCAB Off-pump coronary artery bypass grafting, ONCAB on-pump coronary artery bypass grafting

post-CABG inaccuracy in examinations of septal or lateral wall motion. Instead, we used segmental systolic wall thickening as myocardial functional index. Segmental systolic wall thickening is the best parameter to represent segmental myocardial contractility [20, 21].

This study was prospective but not randomized. We should consider that the patients enrolled in this investigation might reflect the effect of learning curve since the introduction of OPCAB. After 1998, ONCAB tapered off and OPCAB increased. As in other institutions [2, 4, 5, 22], in the earlier years more low-risk patients were enrolled to the OPCAB group as we were on the up-slope of the learning curve. Now, in our institution, almost all the patients are operated on without cardiopulmonary bypass. Only the minority of difficult patients are operated with cardiopulmonary bypass. Over the period of patient enrollment, surgeons learned OPCAB, and the learning curve flattened out [22].

In our previous pilot study of retrospective serial sampling of these cohort groups, segmental wall thickening was significantly better in the OPCAB group at short-term follow-up, however the better wall thickening disappeared at mid-term. The demographic characteristics of the two groups in that study showed differences in the number of affected vessels. Because three-vessel disease was more prevalent in the ONCAB group, which suggested that more myocardium was at risk, we introduced the propensity score in the data sampling to overcome the bias of data distribution between the two groups.

In the observational study, especially to investigate the treatment effect, randomization is important to eliminate the systemic differences between groups. However, when random assignment is difficult or impossible, propensity score matching can be a solution [23–25]. Propensity score is the probability of being assigned to each group. As the statistical concept is similar to survival analysis, propensity score can be calculated using the logistic regression model. In this study, we matched patients to each group according to the propensity scores. After propensity score matching, there were no significant demographic differences between the groups, including the numbers of affected vessels.

Ischemic injury during cardiopulmonary bypass procedure and microembolism might cause damages to the myocardium as is the case for other organs [1, 26]. Several studies reported that troponin or cardiac enzyme level was higher in the on-pump group [10, 27, 28]. It is probable that perioperative myocardial damage causes the myocardial perfusion or thickening impairment assessed by gated myocardial SPECT. In this study, however, rest ^{201}Tl uptake, stress $^{99\text{m}}\text{Tc}$ -MIBI uptake, and wall thickening of the OPCAB group were not significantly different from the ONCAB group at 3 months after operation.

It is interesting that a previous similar study using cardiac MRI showed that the OPCAB group achieved earlier left

ventricular function improvement at 6 postoperative days but no significant difference at 6 months follow-up compared to the ONCAB group [29]. Our results add to this finding the fact that the results of OPCAB and ONCAB were the same at 3 months after operation. The acute effects of cardiopulmonary bypass, if any, would have gone away as early as 3 months after operation, and so we could not find additional benefit in terms of myocardial perfusion and contractility in the OPCAB group as compared to the ONCAB group. Considering that global indices such as LVEF and ESV were similar in both groups, we suggest that the risks of possible additional perioperative myocardial damage due to ONCAB are not significant when the patients have similar clinical characteristics before CABG operation.

Conclusion

OPCAB showed significant improvements in LVEF, ESV, and myocardial perfusion and function that were comparable to ONCAB at short-term and mid-term. Gated myocardial SPECT successfully revealed that OPCAB is as good as ONCAB in terms of myocardial perfusion and function.

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