**Original
Article**

Comparison of Mid-Term Graft Patency between On-Pump and Off-Pump Coronary Artery Bypass Grafting

Tatsuya Seki, MD and Toshihito Yoshida, MD

Background: Multiple studies have compared on-pump coronary artery bypass (ONCAB) grafting with off-pump coronary artery bypass (OPCAB) grafting, but the optimal surgical strategy has yet to be established. Furthermore, there is limited evidence regarding mid-term graft patency rates.

Methods: Between April 2001 and March 2014, 365 consecutive patients underwent isolated coronary artery bypass grafting (CABG; male: 75%; mean age: 69 ± 10 years). After propensity-score-matched analysis, we assessed the results of 67 patients in each group (ONCAB: group A, OPCAB: group B). The mean follow-up period of graft patency and survival rate was 35 ± 37 months and 54 ± 47 months, respectively.

Results: There were no significant differences in baseline characteristics between the two groups. There was a trend for an increased number of distal anastomoses in group B as compared to group A (group A vs. group B: 3.8 ± 1.1 vs. 4.1 ± 1.6 , $P = 0.17$). The total graft patency rate was tend to be lower in group A, but not statistically significant (group A: 156 months, 45.2%; group B: 96 months, 72.6%; $P = 0.21$). There was no difference for survival and major-adverse-cardiac-and-cerebrovascular-events (MACCE) free rate ($P = 0.42$ and 0.76 , respectively).

Conclusion: Propensity-score-matched analysis revealed no difference in mid-term survival rate, MACCE free rate, graft patency rates, and number of distal anastomoses between ONCAB and OPCAB groups.

Keywords: CABG, graft patency, off-pump CABG, on-pump CABG

Introduction

Although many reports comparing on-pump coronary artery bypass (ONCAB) grafting with off-pump coronary artery bypass (OPCAB) have been published,^{1–5)} the optimal surgical strategy has not been well established.⁶⁾

Department of Cardiovascular Surgery, Japan Community Health Care Organization (JCHO) Hokkaido Hospital, Sapporo, Hokkaido, Japan

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Corresponding author: Tatsuya Seki, MD. Department of Cardiovascular Surgery, JCHO Hokkaido Hospital, 1 jo 8 chome 3-18 Nakanoshima, Toyohira-ku, Sapporo, Hokkaido 062-8618, Japan
Email: sekky48@yahoo.co.jp

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Despite the fact that many surgeons consider the off-pump approach to be more technically challenging, it remains the most commonly used approach in Japan, with more than 60% of coronary artery bypass grafting (CABG) performed by OPCAB.^{7,8)} OPCAB is superior to ONCAB because it avoids the use of cardiopulmonary bypass and aortic manipulation such as cannulation and aortic clamping; however, some studies have reported that the former is inferior in terms of patency rate and number of distal anastomoses.^{1,4)}

Puskas et al.⁹⁾ and Magee et al.¹⁰⁾ reported similar graft patency rates for OPCAB and ONCAB at 30 days and 1 year, but this result has been challenged by other studies that demonstrated a lower graft patency rate for OPCAB. The Randomized On/Off Bypass (ROOBY) trial, one of the largest randomized controlled studies

Fig. 1 (a) Trends in cardiopulmonary bypass strategies for CABG and patient details. Before 2007, the majority (67%) of CABG was performed in on-pump (ONCAB). After 2007, OPCAB was most commonly performed. (b and c) Number of distal anastomoses of CABG before (b) and after (c) propensity-score-matched analysis. The number of distal anastomoses was higher in the off-pump CABG (OPCAB) group than in the on-pump CABG (ONCAB) group ($P < 0.001$), but this difference was not significant after propensity-score-matched analysis ($P = 0.057$). CABG: coronary artery bypass grafting; OPCAB: off-pump coronary artery bypass; ONCAB: on-pump coronary artery bypass.

comparing the outcomes of ONCAB and OPCAB, demonstrated greater adverse composite outcomes and patency rates with OPCAB at 1 year follow-up.¹⁾ This finding was corroborated by the Danish On-pump Versus Off-pump Randomization Study (DOORS) randomized control trial which also showed a lower patency rate for OPCAB at 6 months follow-up.⁴⁾ These results were attributed to technical problems associated with OPCAB, but the studies were limited by the short duration of follow-up.

Few studies have provided long-term follow-up data of OPCAB and ONCAB grafts. Furthermore, the limited data available is from Europe and the United States, where OPCAB was used in only 20% of CABG procedures,¹¹⁾ and therefore it is unclear whether these results are applicable in Japan, where a much greater proportion of CABG is performed using OPCAB. In this study, we used coronary computed tomography angiography

(CCTA) to compare graft patency at regular 2-yearly intervals for up to 10 years after surgery, and conducted a propensity-matched analysis adjusted for multiple risk factors.

Materials and Methods

This study was approved by the institutional review board of Japan Community Health Care Organization Hokkaido Hospital. Retrospective data were collected for 365 consecutive patients (ONCAB, $n = 116$ and OPCAB, $n = 249$) who underwent isolated CABG at our institution between April 2001 and March 2014. Following the exclusion of patients who did not undergo median sternotomy, we conducted propensity-score-matched analysis for 67 patients in each group (ONCAB: group A, OPCAB: group B). We identified 179 patients who underwent isolated CABG between April 2001 and March

2007 (ONCAB: $n = 112$, 67% and OPCAB: $n = 67$, 33%), and 186 patients who underwent isolated CABG between April 2007 and March 2014 (ONCAB: $n = 9$, 4% and OPCAB: $n = 177$, 96%). Since CABG was performed mainly by off-pump in the latter half of the study, after propensity-score-matched analysis, we selected 93% (62/67) of patients from before 2007 in group A and 70% (47/67) of patients from after 2007 in group B (**Fig. 1a**). We aimed to perform traditional complete revascularization, which revascularize every stenosed branch even if there was an adjacent area of perfusion. The grafting strategy and preoperative and postoperative strategy has not been changed thorough all period.

Graft patency was assessed mainly by CCTA performed every 2 years after CABG until 10 years after surgery, even in the absence of ischemic symptoms. Cardiovascular surgeon and radiologist evaluated graft patency by CCTA. After 10 years, graft patency was assessed only in symptomatic patients. The mean follow-up period of patency for all patients was 35 ± 37 , group A was 30 ± 42 months and for group B was 40 ± 31 months ($P = 0.93$). The maximum follow-up period of patency was 156 months for group A and 96 months for group B. Major adverse cardiac and cerebrovascular events (MACCE) was defined as all-cause death, myocardial infarction, cerebrovascular events, and repeat revascularization. The mean follow-up period of survival and MACCE free rate for all patients was 54 ± 47 months, for group A was 56 ± 55 months and for group B was 52 ± 38 months ($P = 0.28$). The maximum follow-up period of survival and MACCE rate was 168 months for group A and 132 months for group B.

Surgical techniques

All procedures were performed through a median sternotomy. In on-pump CABG, cardiopulmonary bypass was commenced through the ascending aorta and the right atrium. In on-pump arrest CABG, the ascending aorta was cross-clamped and cardiac arrest was achieved and maintained with intermittent administration of tepid blood cardioplegic solution through the aortic root and the coronary sinus. Then, distal anastomoses were constructed during cardiac arrest using a continuous 7-0 or 8-0 polypropylene suture. In off-pump CABG, the anastomoses were constructed without cardiac arrest using intraluminal shunts and a dedicated positioner and stabilizer. The internal thoracic arteries (ITA) and radial arteries (RA) were harvested in a skeletonized fashion using electronic scalpels and/or a Harmonic scalpel (Ethicon,

Cincinnati, OH, USA). The left anterior descending coronary artery was revascularized primarily using the *in situ* left ITA. The diagonal branch and left circumflex coronary artery were revascularized using grafts from the right ITA, RA, or saphenous vein graft (SVG). Gastroepiploic artery (GEA) grafts were used to revascularize the right coronary artery in young patients, whereas SVGs were used for this purpose in elderly patients. The RA was not used in patients with chronic kidney disease in case of future need for hemodialysis access. Proximal anastomoses of free grafts were made on the ascending aorta using a continuous 6-0 polypropylene suture during aortic cross-clamping for those with on-pump arrest CABG and on the beating heart with a dedicated suture assistant device (Enclose II, Vitalitec, Plymouth, MA, USA) for those without cardiac arrest. We use heparin 100 U/kg for OPCAB and 300 U/kg for ONCAB. The target of activated whole blood clotting time was 300 sec for OPCAB and 500 sec for ONCAB. The postoperative anticoagulant protocol for all patients consisted of heparin infusion from immediately after hemostasis until postoperative day 5, followed by dual-antiplatelet drug therapy thereafter. CABG was mainly performed by two and one surgeons before and after 2007, respectively.

Statistical analysis

Continuous variables are presented as mean $\pm$ standard deviation and categorical data as numbers and percentages. The Mann–Whitney U test was used for the comparison of continuous values. The chi-square test or Fisher's exact test was used for the comparison of categorical data as appropriate. The survival curve, the MACCE free curve, and the graft patency curves were estimated using the Kaplan–Meier method, and between-group differences were compared using the log-rank test.

Propensity scores were developed based on 15 baseline characteristics. Age, sex, body surface area, smoking history, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, hemodialysis, peripheral vascular disease, cerebral vascular disease, old myocardial infarction, chronic obstructive pulmonary disease, number of diseased vessels, and impaired left ventricular ejection fraction (LVEF) were variables used to developed propensity score. Logistic regression analysis was conducted to calculate propensity score. The C-statistics was 88.9%. In all, 67 matched ONCAB and OPCAB pairs were selected from propensity matching. There was no significant difference in the preoperative characteristics of matched patients (**Table 1**). Statistical analysis was

Table 1 Patients' baseline characteristics before and after propensity-score-matched analysis

	Before PS match			After PS match		
	ONCAB	OPCAB	P value	ONCAB	OPCAB	P value
	(Group A)	(Group B)		(Group A)	(Group B)	
	N = 116	N = 249		N = 67	N = 67	
Age, year	67 ± 10	69 ± 10	0.989	69 ± 10	69 ± 9	0.558
Male, n (%)	92 (79)	200 (80)	0.915	50 (75)	50 (75)	1
Body surface area, m ²	1.7 ± 0.3	1.6 ± 0.2	0.08	1.6 ± 0.1	1.6 ± 0.2	0.507
Smoking, n (%)	47 (41)	61 (24)	0.0018	20 (30)	19 (14)	0.849
Hypertension, n (%)	62 (53)	110 (44)	0.098	36 (54)	40 (60)	0.486
Diabetes mellitus, n (%)	56 (48)	145 (58)	0.075	35 (52)	33 (49)	0.729
Dyslipidemia, n (%)	49 (42)	112 (45)	0.624	29 (43)	25 (37)	0.481
COPD, n (%)	12 (10)	35 (14)	0.324	6 (9)	5 (7)	0.753
Old myocardial infarction, n (%)	33 (28)	44 (18)	0.018	21 (31)	18 (27)	0.568
Cerebral vascular disease, n (%)	36 (31)	59 (24)	0.137	18 (27)	18 (27)	1
Peripheral vascular disease, n (%)	32 (28)	77 (31)	0.517	16 (24)	20 (30)	0.436
Chronic kidney disease, n (%)	16 (14)	63 (25)	0.0129	13 (19)	12 (18)	0.825
Hemodialysis, n (%)	10 (9)	30 (12)	0.329	7 (5)	5 (7)	0.545
Impaired LVEF, n (%)	13 (11)	37 (15)	0.345	8 (6)	8 (6)	1
Number of diseased vessels						
1 vessel disease	4 (3)	9 (4)	0.906	0 (0)	2 (3)	0.38
2 vessel disease	29 (25)	57 (23)		19 (28)	14 (21)	
3 vessel disease	83 (72)	183 (74)		44 (66)	48 (72)	

Values are mean ± SD. COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; ONCAB: on-pump coronary artery bypass; OPCAB: off-pump coronary artery bypass; PS: propensity score

performed using JMP 12.0.1 (SAS Inc., Cary, NC, USA). The significance threshold was set at 0.05.

Results

Table 1 summarizes the baseline characteristics of the study population before and after the propensity-score-matched analysis. Before propensity-score matching, patients in the ONCAB group had a higher rate of smoking and old myocardial infarction, whereas patients in the OPCAB group had a higher rate of chronic kidney disease. However, there were no significant differences in baseline characteristics after propensity-score matching. The incidence of hemodialysis and impaired LVEF decreased in both groups after propensity-matched analysis. The rate of triple vessel disease was approximately 70% in both groups. **Table 2** shows the operative and postoperative data. There was a trend for an increased number of distal anastomoses in group B as compared to group A, but this difference was not statistically significant (group A vs. group B: 3.8 ± 1.1 vs. 4.1 ± 1.6 , respectively, $P = 0.17$). Cardiopulmonary bypass time and cross-clamp time were calculated only in patients receiving extracorporeal circulation. The clinical course of three (5%) patients in group A was complicated by

postoperative stroke, but there were no cases of postoperative stroke in group B ($P = 0.08$). Postoperative delirium occurred in five patients (8%) and one patient (2%) in groups A and B, respectively ($P = 0.095$). There was no significant difference in the rate of reoperation due to bleeding ($P = 1$), operative death ($P = 0.315$), and hospital death ($P = 0.315$). There was one case of operative death on postoperative day 7 due to non-occlusive mesenteric ischemia and multi-organ failure, and one case of hospital death at 3 months after surgery due to respiratory failure. Graft selection differed between the two groups (Group A; ITA: 35%, SVG: 38%, RA: 20%, GEA: 8%. Group B; ITA: 39%, SVG: 48%, RA: 11%, GEA: 3%, $P < 0.01$). In group A, SVGs were less commonly used and RAs were more frequently used than in group B.

Figures 1b and **1c** show the number of distal anastomoses before (**b**) and after (**c**) propensity-score-matched analysis. Before propensity-score-matched analysis, the mean distal anastomoses numbers were 3.7 ± 1.2 for group A and 4.5 ± 1.7 for group B ($P < 0.001$). After propensity-score-matched analysis, the mean distal anastomoses numbers were 3.8 ± 1.1 for group A and 4.1 ± 1.6 for group B ($P = 0.057$). **Figure 2a** shows the survival curve. Survival rate was not different between two

Table 2 Operative and early postoperative data

	Group A (N = 67)	Group B (N = 67)	P value
Number of distal anastomoses	3.8 ± 1.1	4.1 ± 1.6	0.17
Total graft number	251	271	-
ITA, n (%)	87 (35)	105 (39)	<0.01
SVG, n (%)	94 (38)	130 (48)	
RA, n (%)	51 (20)	29 (11)	
GEA, n (%)	19 (8)	8 (3)	
CPB time, minutes	189 ± 52	NA	NA
Cross-clamp time, minutes	129 ± 37	NA	NA
Intubation >48 hour, n (%)	9 (13)	4 (6)	0.144
Stroke, n (%)	3 (5)	0 (0)	0.08
Delirium, n (%)	5 (8)	1 (2)	0.095
Deep sternum infection, n (%)	1 (2)	1 (2)	1
Reoperation for bleeding, n (%)	1 (2)	1 (2)	1
Operative death, n (%)	0	1 (2)	0.315
Hospital death, n (%)	1 (2)	0	0.315

CPB: cardiopulmonary bypass; GEA: gastroepiploic artery; ITA: internal thoracic artery; NA: not applicable; RA: radial artery; SVG: saphenous vein graft

Fig. 2 (a) The survival curve and (b) the major adverse cardiac and cerebrovascular event free curve.

groups (group A: 168 months survival rate, 80.3%; group B: 132 months survival rate, 76.3%; log-rank: $P = 0.42$; **Fig. 2a**). **Figure 2b** shows the MACCE free curve. MACCE free rate was not different between two groups (group A: 168 months MACCE free rate, 30.5%; group B: 132 months MACCE free rate, 28.2%; log-rank: $P = 0.76$; **Fig. 2b**). **Figures 3a–3e** show the graft patency rate. The mean follow-up period was 30 ± 42 months in group A and 40 ± 31 months in group B, and the maximum follow-up period was 156 months in group A and 96 months in group B. The all-graft patency rate tended to be lower in group B compared to group A, but this difference was not statistically significant (group A: 156 months patency, 45.2%; group B: 96 months patency,

72.6%; log-rank: $P = 0.21$; **Fig. 3a**). There was no significant difference in the patency rate of ITA and RA grafts between groups (ITA graft: group A: 156 month patency, 76.3%; group B: 96 months patency, 90.6%; log-rank: $P = 0.88$; **Fig. 3b**. RA graft: group A: 156 month patency, 98.0%; group B: 60 months patency, 100%; log-rank: $P = 0.45$; **Fig. 3c**). The patency rate of SVG in group A was 0% at 156 months and in group B was 83% at 84 months (log-rank: $P = 0.54$) (**Fig. 3d**). GEA grafts were used infrequently in the study cohort (group A: 19 grafts, group B: 8 grafts), and the patency rate of GEA grafts was significantly lower in group B compared to group A (group A: 132 month patency, 100%; group B: 96 months patency, 0%; log-rank: $P < 0.01$; **Fig. 3e**).

Fig. 3 Plot of time-related graft patency (or freedom from graft occlusion) for (a) all graft, (b) internal thoracic artery graft, (c) radial artery graft, (d) saphenous vein graft, (e) gastroepiploic artery graft in groups A and B. The number of grafts at each time point is listed in the figure.

Discussion

In the current study, we made two important clinical observations. First, the mid-term graft patency rate did not differ between ONCAB and OPCAB groups in a propensity-score-matched analysis. Second, there was no difference in the number of distal anastomoses between groups. However, there was a trend for an increased number of anastomoses in the OPCAB group, and this contributed to the higher use of the SVG grafts in the OPCAB group compared to that in the ONCAB group.

The ROOBY trial, one of the largest randomized controlled studies comparing the outcome of ONCAB and OPCAB, showed greater adverse composite outcomes and lower patency rates with OPCAB at 1-year follow-up.¹⁾ However, the ROOBY trial was criticized for the fact that it had a high conversion rate (12.4%) to cardiopulmonary bypass, which suggests that the surgeons who participated in the trial did not have sufficient expertise in OPCAB. The DOORS trial is another randomized controlled study which showed a lower patency rate with OPCAB at 6-month follow-up.⁴⁾ The latter study was limited by a low rate of angiography at 6 months (56%), as well as by a short follow-up period and surgical inexperience with OPCAB. The Japanese Off-Pump Coronary

Revascularization Investigation (JOCRI) trial is a randomized controlled study from Japan which revealed that OPCAB was the most common modality performed in 60% of CABG procedures, and this study found no differences in the early patency rate.⁵⁾ Puskas et al.¹²⁾ also reported that the 8-year patency rate did not differ between ONCAB and OPCAB. In our institute, surgeons had sufficient experience in performing OPCAB, as evidenced by the fact that OPCAB was performed in 96% of CABG cases after 2007. In previous studies evaluating graft patency rates, the follow-up period was limited to less than 12 months,^{9,13–16)} with limited follow-up data available beyond 1 year.^{12,17)} In this study, we used CCTA to routinely follow-up graft patency at 2-year intervals even in asymptomatic patients, and thus provided data on mid-term graft patency, which was missing in previous studies.

We found no difference in the number of distal anastomoses between the OPCAB and ONCAB groups. A meta-analysis of randomized trials showed a lower number of grafts per patient in the OPCAB group compared with ONCAB (2.6 for OPCAB and 2.8 for ONCAB).¹⁸⁾ However, these results were not supported by the JOCRI trial, which showed that the number of grafts per patient were similar between OPCAB and ONCAB (3.5 ± 1.0 for OPCAB and 3.6 ± 0.9 for ONCAB).⁵⁾

We believe that OPCAB is a suitable technique for coronary artery revascularization, especially multiple vessel revascularization. In ONCAB, anastomosis is performed during cardiac arrest, and therefore cardiac ischemia is inevitable. Therefore, if a surgeon is qualified to perform OPCAB, we believe that this technique is superior to ONCAB because it eliminates the need for cardiac arrest during anastomosis. In OPCAB, we performed traditional complete revascularization, and aimed to revascularize every stenosed branch even if there was an adjacent area of perfusion, without worrying about cardiac ischemic time. We believe that this approach led to the increased number of anastomoses in OPCAB compared to ONCAB before propensity-score matching. In OPCAB, we could avoid cardiopulmonary bypass use, which was the risk factor of stroke. In this study, there was no perioperative stroke in OPCAB group. OPCAB has been indicated for high-risk patients. In one randomized control trial, Lemma et al.¹⁹⁾ reported that the composite primary endpoint (operative mortality, myocardial infarction, stroke, renal failure and reoperation for bleeding, and acute respiratory distress syndrome) was significantly lower for high-risk patients treated by OPCAB compared to ONCAB. This finding was supported by the results of Puskas²⁰⁾ who reported that OPCAB was associated with a lower risk for operative mortality in high-risk patients, and that the mortality benefit increased with increasing predicted risk of mortality. Furthermore, OPCAB has been shown to be beneficial in high-risk patients with advanced age,^{21,22)} severe atheromatous aortic disease,^{23,24)} chronic kidney disease,²⁵⁾ and left ventricular dysfunction.²⁶⁾ We believe that all CABG should be performed by off-pump technique. Although good target of OPCAB was high-risk patients as mentioned above, to perform multiple revascularization for high-risk patients safely, we should perform revascularization in all patients including lower risk patients to keep surgical technique.

Conducting propensity-score-matched analysis method was the limitation in this study. Ours is not the first study to conduct a propensity-score-matched analysis comparing OPCAB and ONCAB.^{27,28)} We found that the rate of hemodialysis and impaired LVEF decreased after propensity-score matching. This is important since previous studies have identified that high-risk patients on hemodialysis²⁵⁾ and with impaired LVEF²⁶⁾ were good candidates for OPCAB, and therefore these patients may have been partly excluded in this study. The number of distal anastomoses in the OPCAB group also decreased after

propensity-score-matched analysis. The examples above highlight a limitation of using propensity-score-matched analysis.

This study has other limitations in addition to those listed above. First, the number of patients was limited. Second, this is a retrospective study which used observational data obtained from a single institution. Third, we did not control for differences in surgical expertise throughout the study period. This is important since the decision to perform off-pump versus on-pump CABG was determined by surgeons' preferences. Fourth, the follow-up periods of patency rates differed between groups due to the different time course of performing ONCAB and OPCAB procedures. Fifth, patency rate data extending beyond 10 years was limited. We routinely assessed graft patency until 10 years after surgery, following which graft patency was only evaluated in patients with ischemic symptoms. We assumed that asymptomatic patients had a patent graft, but this was not evaluated objectively.

Conclusion

In a propensity-score-matched analysis of consecutive patients who underwent CABG at our institution, there was no difference in mid-term survival, MACCE free and graft patency rates or number of distal anastomoses between OPCAB and ONCAB groups.

Disclosure Statement

The authors have declared that no conflict of interest exists.

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