

A propensity score analysis on the effect of on-pump versus off-pump coronary artery bypass grafting for patients with coronary artery disease

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Aim: The aim of this retrospective observational study was to investigate the effect of on-pump versus off-pump coronary artery bypass grafting (CABG) for patients with coronary artery diseases (CAD).

Methods: A retrospective observational study was performed using a propensity score analysis in 290 consecutive patients undergoing CABG between April 2009 and March 2014, of them, 54 patients undergoing off-pump CABG (OPCABG) were matched with 54 patients undergoing on-pump CABG (ONCABG) by propensity score. The perioperative complications and hospital mortality were documented.

Results: Preoperative characteristics were comparable in both groups following propensity matching. Postoperative myocardial infarction (MI) incidence was lower in OPCABG group than in ONCABG group (3.7% vs. 14.8%, $P=0.046$); both hospital mortality and the major complications rates were similar in the two groups after propensity adjustment for preoperative characteristics.

Conclusions: The perioperative complications are similar in both off-pump and on pump CABG groups, the short-term effect of OPCABG is similar to that of ONCABG.

Keywords: Coronary artery disease (CAD); coronary artery bypass grafting (CABG); cardiopulmonary bypass (CPB); propensity score analysis

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Introduction

Coronary artery diseases (CAD) are very common (1,2), and cause a significant morbidity and mortality in patients with severe stenosis of coronary artery (1-4). Medical therapy confers a poor survival advantage relative to surgical revascularization in some severe CAD patients. Coronary artery bypass grafting (CABG) is indicated for patients with severe stenosis of coronary artery (2), and can be finished by conventional on pump CABG (ONCABG) with cardiopulmonary bypass or off pump CABG (OPCABG) (1,5,6).

OPCABG is now an established procedure, recent studies show OPCABG reduced early operative mortality and the incidences of major complications in redo CABG (7), but it appears not to increase mid-term major adverse cardiovascular

and cerebrovascular events over ONCABG (1). There is no conclusion on which option is better than other. Moreover, the studies on OPCABG have reported on relative small cohorts of patients and have lacked statistical adjustment to reduce the differences in selection bias (8). In order to reduce the selection bias, we used a propensity score matching analysis to evaluate the early outcomes of OPCABG versus ONCABG in a consecutive cohort of CAD patients during four years periods.

Materials and methods

Patient selection

This was a retrospective, observational cohort study of data

from consecutive CAD patients who underwent CABG at the China-Japan Friendship Hospital between April 2010 and March 2014. The study followed the China-Japan Friendship Hospital ethical and legal requirements, and individual written consent was obtained for surgical management and related medical study.

Inclusion conditions were patients who underwent CABG with complete medical document, the exclusion conditions were those who underwent concomitant percutaneous coronary intervention or carotid thromboendarterectomy (2-4). Surgical procedure selection was at discretion of the operating surgeon. The resulting base sample contained detailed clinical information on 290 patients, including 192 (66.2%) undergoing OPCABG and 98 (33.8%) undergoing ONCABG. A propensity score matching analysis was used to minimize the impact of treatment selection bias and potential confounding, 54 patients who underwent OPCABG were matched with 54 patients who underwent ONCABG.

Definitions

Critical CAD disease was defined as a stenosis of greater than 50% of lumen based on a preoperative coronary angiogram. In-hospital mortality was all deaths after surgery occurring in hospital regardless of time after surgery. A postoperative myocardial infarction (MI) was diagnosed if new Q waves longer than 0.04 ms or a reduction in R waves greater than 25% in at least two continuous leads appear on electrocardiography. Stroke was defined as new onset of global or focal brain injury that persisted for over 72 hours. Acute postoperative renal failure was defined as new requirement of hemodialysis or an elevated creatinine level 50% or greater over baseline preoperative value or >200 mmol/L. Infection was defined septicemia, sternal or leg wound infections after harvesting of great saphenous veins or sternotomy with a positive culture and requiring antibiotics (9).

Surgical management

The heart was exposed via a median sternotomy, proximal aortic atheromatous disorder was palpated manually, and the anastomotic site was tailored to avoid atherosclerotic part. Cardiopulmonary bypass (CPB) was established in a standardized manner with mild hypothermia and a roller pump. For patients undergoing ONCABG, CPB was instituted with the use of ascending aortic cannulation and 2-stage venous cannulation of the right atrium. The proximal anastomosis to the ascending aorta was constructed during a single cross clamp

period. Myocardial protection was achieved with intermittent hyperkalemic antegrade warm blood cardioplegia. For OPCABG surgery, the up-to-date stabilizing retractor was used. Distal anastomosis was routinely constructed after proximal anastomosis. During surgery, heparin at 300 IU/kg for the ONCABG and 150 IU/Kg for the OPCABG were used. Activated clotting time was maintained over 480 s for ONCABG and over 300 s for OPCABG. The effect of heparin was reversed with protamine sulphate at 1:1 ratio. At the end of surgery, patients were transferred to the intensive care unit (ICU), a standardized protocol for immediate postoperative care was followed in ICU (10). Outcomes of care observed include reoperation for bleeding, hospital death, stroke, renal failure, and new MI.

Statistical analysis

A nonparsimonious multiple logistic regression analysis was used to determine the propensity for CABG. A propensity score was estimated from the logistic equation for each patient, and was used to match OPCABG patients with those undergoing ONCABG (1:1 match). Independent risk factors for in-hospital mortality were identified by a stepwise, multivariable logistic regression modeling. *Table 1* shows all baseline characteristics of covariates under consideration for models. All P values are reported as 2-sided. All statistical analyses were performed. A SPSS statistical software (version 13.0; IBM Corporation, Armonk, NY, USA) and R statistical software were used for study. The Kolmogorov-Smirnov test was used to check for normality of data in the two groups initially. Continuous data were expressed as mean \pm SD, and categorical data were expressed as percentages.

Differences between groups were compared with the chi-square statistic test for categorical variables and students' *t*-tests for continuous variables.

Results

Table 1 shows the baseline characteristics of patients with CAD, 192 patients (66.2%) with CAD underwent OPCABG; 98 patients (33.8%) underwent ONCABG. Compared with the OPCABG group, patients in ONCABG group had a higher prevalence of smoking and alcohol consumption, and lower ejection fraction less than 40% ($P<0.05$). In addition, patients undergoing ONCABG were more likely received urgent operation ($P=0.038$). There was no difference in the use of bilateral internal mammary artery between the two groups ($P>0.05$).

Table 1 Baseline characteristics of the entire cohort

Variable	OPCABG (n=192)	ONCABG (n=98)	P value
Age (years)	62.91±12.19	61.05±12.34	0.222
Female, n (%)	47 (24.5)	23 (23.5)	0.998
Creatinine (mol/L)	105.11±37.87	113.18±46.16	0.112
HPT, n (%)	126 (65.6)	68 (69.4)	0.52
DM, n (%)	26 (13.5)	16 (16.3)	0.524
Dyslipidemia, n (%)	43 (22.4)	23 (23.5)	0.837
Current smoker, n (%)	39 (20.3)	41 (41.8)	<0.001
Alcoholics, n (%)	25 (13.0)	22 (22.4)	0.039
COPD, n (%)	17 (8.9)	8 (8.2)	0.843
Stroke or TIA, n (%)	26 (13.5)	20 (20.4)	0.13
EF <40%, n (%)	33 (17.2)	31 (31.6)	0.005
No. of distal grafts	1.69±0.71	1.71±0.70	0.852
LIMA, n (%)	43 (22.4)	23 (23.5)	0.837
IABP, n (%)	117 (60.9)	64 (65.3)	0.468
Urgent surgery, n (%)	9 (4.7)	11 (11.2)	0.038

Data are presented as means ± SD; OPCABG, off-pump coronary artery bypass grafting; ONCABG, on-pump coronary artery bypass grafting; HPT, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; TIA, transient ischemia attack; EF, ejection fraction; LIMA, left internal mammary artery; IABP, intra-artery balloon pumping.

After propensity score matching, 54 pairs of patients were matched (*Table 2*). In the matched cohorts, no significant difference between the two groups for any covariate was observed. Patients undergoing OPCABG had a lower needs for postoperative intra-aortic balloon pump, but it did not reach a significant difference ($P>0.05$, *Table 2*).

Table 3 indicates that the incidence of postoperative MI in OPCABG group was lower than ONCABG group (3.7% vs. 14.8%, $P=0.046$), and other clinical outcomes of propensity matched patients were similar in both groups, including rates of blood transfusion, ICU stay and postoperative hospital stay, reoperation rate and hospital mortality. The incidence of wound infection in OPCABG group was higher than in ONCABG group (13% vs. 7.4%, $P=0.34$). One of the most common organisms cultured from the infected chest wounds was *Staphylococcus aureus*. Patients with wound infection had a poor healing of the sternal wound and wound dehiscence (*Figure 1*). The multivariate analysis revealed that a postoperative MI was an independent risk factor for surgical revascularization (odds ratio, 3.4; 95% CI: 0.45-1.09, $P=0.046$).

Discussion

Our propensity score analysis study demonstrates that OPCABG is safe for patients with coronary artery disease

and is associated with lower postoperative MI incidence and similar perioperative complications and hospital mortality with respect to ONCABG.

There are controversies about the possible benefits of OPCABG compared to ONCABG. Some institutes still use the ONCABG technique to treat severe CAD patients currently, the main reason is the hemodynamic instability that may occur in performing revascularization on a beating heart. Recent studies show that OPCABG resulted in significantly lower patency rate for arterial and saphenous vein graft conduits, and less effective revascularization than ONCABG. At one year after surgery, patients with less effective revascularization had higher adverse event rates (5). A meta analysis suggest that OPCABG may increase late all-cause mortality by a factor of 1.37 over ONCABG (11). Randomized controlled trials did not find, except for atrial fibrillation, the statistically significant reductions in short-term mortality and morbidity (12). Moreover, one systematic review did not demonstrate any significant benefit of OPCABG compared with ONCABG regarding mortality, stroke, or MI. In contrast, patients in ONCABG group had a better long-term survival (13). In another randomized study, a total of 2539 patients 75 years of age or older were randomly assigned for elective first-time CABG to undergo OPCABG or ONCABG, there was no significant difference between two groups with

Table 2 Baseline features of propensity-matched patients

Variable	OPCABG (n=54)	ONCABG (n=54)	P value
Age (years)	61.19±11.28	59.33±14.33	0.457
Female, n (%)	12 (22.2)	15 (27.8)	0.505
Creatinine (mol/L)	106.76±27.0	116.75±45.38	0.168
HPT, n (%)	36 (66.7)	35 (64.8)	0.839
DM, n (%)	20 (37.0)	12 (22.2)	0.092
Dyslipidemia, n (%)	14 (25.9)	10 (18.5)	0.355
Current smoker, n (%)	20 (37.0)	23 (42.6)	0.555
Alcoholics, n (%)	15 (27.8)	18 (33.3)	0.531
COPD, n (%)	11 (20.4)	5 (9.3)	0.104
Stroke or TIA, n (%)	16 (29.6)	14 (25.9)	0.667
EF <40%, n (%)	15 (27.8)	20 (37.0)	0.304
No. of distal grafts	1.69±0.72	1.72±0.71	0.789
LIMA, n (%)	12 (22.2)	15 (27.8)	0.505
IABP, n (%)	24 (44.4)	33 (61.1)	0.123
Urgent surgery, n (%)	3 (5.6)	9 (16.7)	0.066

Plus-minus values are means ± SD; OPCABG, off-pump coronary artery bypass grafting; ONCABG, on-pump coronary artery bypass grafting; HPT, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; TIA, transient ischemia attack; EF, ejection fraction; LIMA, left internal mammary artery; IABP, intra-artery balloon pumping.

Table 3 Postoperative outcomes of propensity score matched patients

Variable	OPCABG (n=54)	ONCABG (n=54)	P value
Transfusion rate			
Plasma, n (%)	30 (55.6)	33 (61.1)	0.558
Platelet, n (%)	3 (5.6)	9 (16.7)	0.066
Intensive care unit stay	1.69±0.72	1.72±0.71	0.789
Postoperative length of stay	16 [12, 22.5]	15 [12, 19]	0.568
Tracheostomy, n (%)	9 (16.7)	5 (9.3)	0.252
Wound infection, n (%)	7 (13.0)	4 (7.4)	0.340
Reoperation, n (%)	6 (11.1)	5 (9.3)	0.750
Postoperative MI, n (%)	2 (3.7)	8 (14.8)	0.046
Stroke/TIA, n (%)	1 (1.9)	4 (7.4)	0.169
Mortality, n (%)	2 (3.7)	1 (1.9)	0.558

Data are expressed as means ± SD or median (25th percentile-75th percentile); OPCABG, off-pump coronary artery bypass grafting; ONCABG, on-pump coronary artery bypass grafting; MI, myocardial infarction; TIA, transient ischemic attack.

regard to the composite outcome of death, stroke, MI, repeat revascularization, or new renal-replacement therapy within 30 days and within 12 months after surgery (14).

In order to reduce the patient selection bias, we used propensity score analysis in this study. Our study results were consistent with the data reported (6,9,15-17). The randomized

trial and observational study show OPCABG now becomes an established procedure with results comparable to ONCABG, both procedures were associated with similar early and late graft patency, incidence of recurrent or residual myocardial ischemia, need for reintervention, long-term survival, and the similar late mortality (6,9,15-17). Moreover, in comparison to ONCABG,

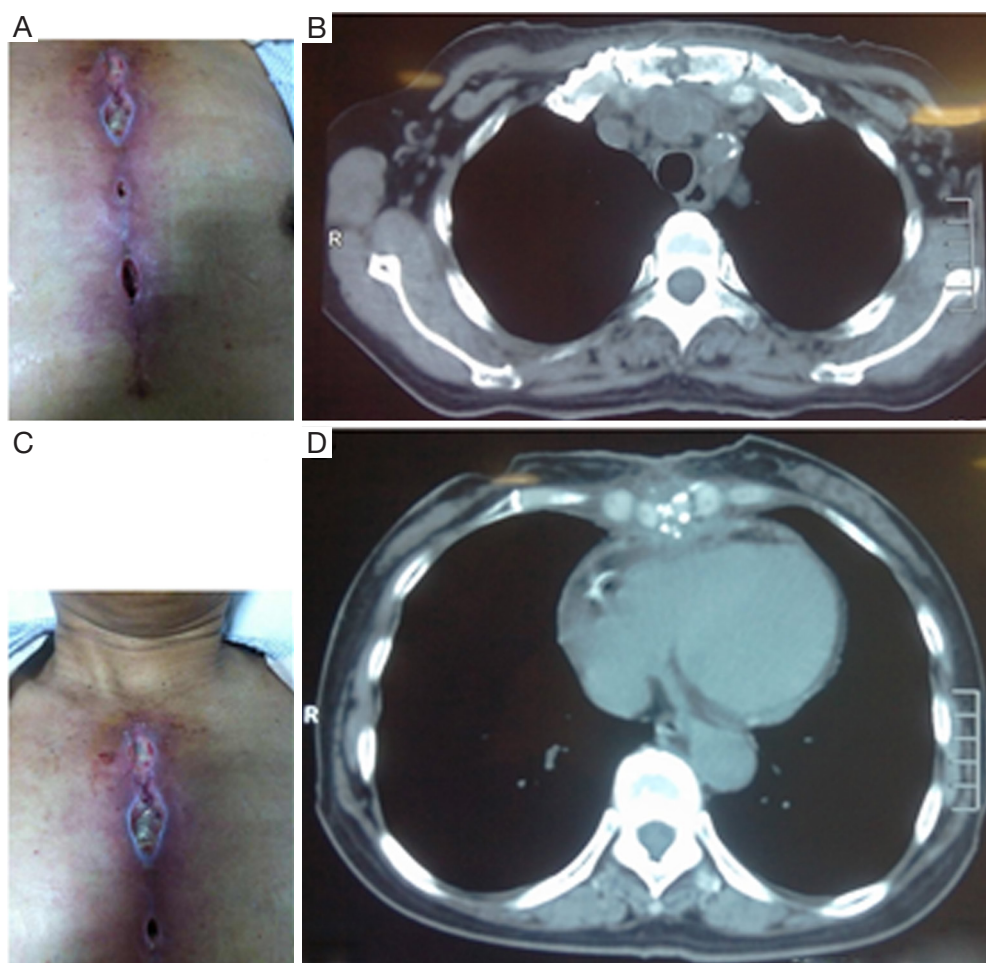


Figure 1 A female patient underwent OPCABG procedure 2.5 months earlier had chest wound dehiscence and infection (A,C), no healing of sterna wound (B) and pericardial effusion (D) demonstrated on CT scan. OPCABG, off-pump coronary artery bypass grafting.

Meta analysis demonstrates that OPCABG reduces the incidence of post-operative stroke and has no substantial effect on mortality or MI (18). Furthermore, other studies showed that OPCABG significantly reduces perioperative mortality with long-term good outcome (19-21). Use of CPB is an independent predictor of in-hospital mortality (14).

Complete revascularization remains the gold standard of CABG. The main goal of surgical revascularization is to reestablish the blood supply to the ischemic cardiac region and to prevent MI (22). One of the great concerns is the early graft patency with OPCABG did not match the excellent outcomes of conventional ONCABG (5,11). The postoperative MI in OPCABG group was higher than in OCCPB group, which might be induced by the blocked graft, as coronary angiography could not be performed in all patients with postoperative MI to verify the presence of blocked graft, it

is difficult to assure the graft patency rate in CABG patients. Another concern regarding OPCABG is possible reduced quality of anastomosis on beating heart. As a patient with complete revascularization is more likely free from severe angina than one with incomplete revascularization (22).

The surgical options for ischemic heart disease should be tailored individually to optimize the benefits and minimize the risk of adverse effects, the surgeon should consider bypass options and bypass graft conduit to maximize the long-term benefits of coronary revascularization while minimizing the risks (6,23).

The cause of wound infection in our study is most likely due to the jeopardized immunity of patients leading to the growth of bacteria such as staphylococcus in surgical area, and poor healing of sternal wound and surgical wounds (24) (*Figure 1*). The preventive approach is to observe the sterilization rule carefully to sterilize the surgical wound area and use antibiotics

prophylactically (24).

Study limitations

This is an observational retrospective study rather than a randomized controlled trial; even though a propensity score matched analysis was used in this study, it still has some limitations. Only perioperative outcomes but not long-term follow up results are reported, and data on surgical revascularization rates and graft patency following surgery are not available. There is no report on the degree of stenosis of carotid artery, which is associated with stroke before or after CABG. Long-term follow-up of patients from current study will offer additional evidence.

Overall, our propensity score matching showed that patients in OPCABG group had lower postoperative MI incidence and similar other clinical outcomes in comparison with those in ONCABG group. The short-term effect of OPCABG was similar to that of ONCABG. Based on the current evidence, ONCABG should continue to be the standard surgical option. Yet, OPCABG may be an alternative when there are contraindications for cannulation of the aorta and CPB. Further long-term follow up and randomised clinical trials are warranted to address the optimal treatment.

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