Increasing Long-Term Major Vascular Events and Resource Consumption in Patients Receiving Off-Pump Coronary Artery Bypass

A Single-Center Prospective Observational Study

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***Background*—**Despite its widespread use and short-term efficacy, substantial uncertainty remains about the long-term outcomes and cost-effectiveness of off-pump coronary artery bypass (OPCAB).

***Methods and Results*—**A retrospective review of prospectively collected data was conducted of 6665 consecutive patients undergoing isolated coronary artery bypass graft (CABG) at our institution during 1999 to 2006. All patients were followed up until September 30, 2008. Short- and long-term outcomes were compared between OPCAB and conventional CABG. The 2 main long-term outcome measures were repeat revascularization and the composite outcome of major vascular events. Cost comparison at 2 years in a propensity-matched sample during follow-up was also a study interest. The overall mean baseline age was 60.3±8.6 years, and 17.0% were women. Compared with conventional CABG, patients who underwent OPCAB had lower rates of atrial fibrillation ($P=0.003$) and requirements for blood transfusion ($P=0.03$) and ventilation time >24 hours ($P<0.001$). After an average of 4.5 years of follow-up, the rates of repeat revascularization (adjusted hazard ratio, 1.40; 95% confidence interval, 1.03 to 1.89) and major vascular events (adjusted hazard ratio, 1.23; 95% confidence interval, 1.09 to 1.39) were significantly higher in the OPCAB than the conventional CABG group. At 2 years, OPCAB was associated with increased additional direct costs per patient compared with conventional CABG and had a similar survival rate.

***Conclusions*—**Compared with conventional CABG, OPCAB is associated with small short-term gain but increased long-term risks of repeat revascularization and major vascular events, especially among high-risk patients. Moreover, OPCAB consumes more resources and is less cost-effective in the long run. **(*Circulation*. 2010;121:1800-1808.)**

Key Words: coronary artery bypass grafting ■ coronary disease ■ coronary artery bypass, off-pump ■ surgery

Currently, increasing volume of off-pump coronary artery bypass (OPCAB) has been noted not only in Western countries but also in developing countries such as China and India. OPCAB was first introduced in China in 1996,[1] and >50 major cardiovascular centers across the country have routinely used the technique. On the basis of a large registration study involving ≈10 000 patients from 35 centers across China,[2] OPCAB accounts for >70% of all coronary artery bypass graft (CABG) surgeries done in these centers, a proportion that was ≈3 times as high as that reported in other populations such as the United States.[3] Unfortunately, when confronted with the growing volume, we seldom have adequate evidence from the literature. Several randomized controlled trials were reported but tended either to be small or to have short follow-up (seldom >5 years).[4–6] A recent randomized controlled trial involving 18 centers and 2203 patients was released, but the patients included were mostly male.[5] Studies with long-term follow-up exist but tend to emphasize primarily all-cause mortalities,[7] and data on long-term adverse events and costs have been unavailable.

Clinical Perspective on p 1808

There is suggestive evidence from observational studies that OPCAB may be associated with increased rates of repeat revascularization after hospital discharge,[3,8] but its long-term effects on other major morbidities such as myocardial infarction (MI), stoke, and rehospitalization are not well characterized. These outcomes are important from a health policy point of view because long-term adverse events place heavy burdens on healthcare systems and dictate medical resource allocation. However, although cost analysis is needed to maximize health gains within a limited budget, few data are

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available in the literature comparing off-pump and on-pump techniques.

To address some of these uncertainties, we report a large observational study of both the short-term and long-term effects of OPCAB compared with conventional CABG (cCABG), involving 6665 patients treated in our hospital during 1999 to 2006 and followed up for an average of 4.5 years.

Methods

Patients

Details of the study design, methods, and participants have been described previously.[9] The CABG database of Fuwai Hospital in Beijing, China, which was obtained prospectively, was studied retrospectively. In brief, 7822 consecutive patients who underwent CABG at Fuwai Hospital from January 1999 to December 2006 were considered for the study. Of them, 6665 patients who underwent isolated CABG were eligible for the study, whereas 1157 patients who, in addition to CABG, received other surgical procedures (such as valve replacement) were excluded (Figure I of the online-only Data Supplement). The choice of OPCAB or cCABG for a particular patient was made before surgery at the discretion of responsible surgeon. The study protocol was approved by the Institutional Review Board at Fuwai Hospital, and data collection began during 2002 with a standardized case report form with a range of variables and their corresponding definitions similar to those reported in the Society of Thoracic Surgeons database (http://www.sts.org/). All data were collected by trained clinical research staff and were subsequently double entered into computer databases. Baseline information on personal and clinical characteristics, as well as in-hospital events after CABG, was complete for all 6665 patients involved in the study. A total of 81 patients (1.2%) in the OPCAB group actually converted to cCABG, mainly because of surgical difficulty. Unlike many observational studies, intention-to-treat data were obtainable in the present study, so OPCAB cases that were converted to on-pump procedures remained in the OPCAB group on the basis of intention to treat.

Surgical Procedures

A total of 10 faculty surgeons were involved in the present study. As part of standard institutional requirements, all of them had to have specialized in congenital or valve heart surgery for >3 years before undertaking any CABG procedures. With respect to OPCAB, which was first performed in our institution in 1996,[1] the surgeon had to perform at least 100 cCABG procedures before being considered qualified to carry out the off-pump procedure. Once qualified, the choice of OPCAB as opposed to cCABG for a particular patient was generally at the discretion of the individual surgeons. For the OPCAB procedure, several standard cardiac positioning techniques and coronary artery stabilizers were adopted[10]; for cCABG, standard cardiopulmonary bypass techniques were used that incorporated cold antegrade and retrograde blood cardioplegia and moderate systemic hypothermia (28°C to 32°C). Apart from differences in surgical procedures, all other aspects of in-hospital management for patients were done similarly according to standard protocols.

Long-Term Follow-Up

As part of institutional standard procedures, all surgical patients discharged alive from hospital are required to return for an outpatient follow-up visit at 6 months after surgery and then once every year. Hospital databases were checked annually to identify and review any routine follow-up information for study participants. In addition, all surviving study participants were contacted by telephone again by the research staff during 2007 to 2008 using standard procedures and forms. Overall, by September 30, 2008, follow-up information was available for 97.6% of study participants, with the rate of loss to follow-up being somewhat higher in the cCABG (4.2%) than in the OPCAB (0.5%) group (Figure I of the online-only Data Supplement). The medical records in outpatient clinics of those who reported any adverse events after discharge were reviewed further for confirmation. When any major clinical events were reported by other hospitals, patients were asked to mail a copy of all relevant medical records. Overall, a total of 1737 copies (99.5%) of medical records were provided for further review.

Cost, Cost-Effectiveness, and Sensitivity Analyses

The analyses were carried out on propensity score–matched data and direct costs. In-hospital costs were obtained directly from medical records of Fuwai Hospital. Follow-up cost analyses were limited to cardiovascular hospitalization and other procedure-related costs. Costs per patient were calculated by multiplying the number of resource uses by the unit costs. We used the diagnostic related group price in the Medicare claims data from the Beijing Medical Insurance Center as unit cost estimates. The costs of repeat CABG were estimated by using the cost of on-pump CABG. The time horizon for cost analysis was set at 2 years during follow-up. The costs were adjusted to 2006 Ren Min Bi (RMB) with the Beijing consumer price index released by the Chinese National Bureau of Statistics (http://www.stats.gov.cn). We estimated cost-effectiveness as the difference in costs and the difference in survival rate. Mortality rate was expressed as events per 1000 person-years.

In our primary analysis, follow-up cost estimates were based on Medicare claims from the Beijing Medical Insurance Center. As a sensitivity analysis, we also calculated follow-up costs using data from the Guangzhou and Lanzhou Medical Insurance Centers. Guangzhou is a typical coastal city; Lanzhou is located in northwest China. The costs were adjusted to 2006 RMB with the Guangzhou and Lanzhou consumer price indexes as appropriate.

Statistical Analysis

The 2 prespecified coprimary end points that related to long-term outcome were repeat revascularization alone and major vascular events (MVEs), which consisted of cardiac death, repeat revascularization, MI, or stroke. Secondary end points were cardiac deaths, nonfatal MI, nonfatal stroke, angina pectoris, heart failure, and hospitalization for any vascular conditions. If a patient experienced the same type of clinical event more than once, only the first one was used in the analysis.

To minimize potential selection bias in the comparisons of surgery, a propensity score analysis was undertaken[11,12] for which age and various other baseline variables (see Table 1) were used in a logistic regression model to calculate the probability of each patient having the different surgical options. The discrimination and calibration of the model were evaluated by area under the receiver-operating characteristic curve and Hosmer-Lemeshow test for goodness of fit. The estimated propensity score showed good discriminatory power (C statistic, 0.76; 95% confidence interval [CI], 0.74 to 0.77) and calibration characteristics (P=0.36).

Odds ratios (ORs) were estimated by a logistic regression model for in-hospital outcomes with surgical type (OPCAB or cCABG) as the exposure variable and propensity score as the covariate; hazard ratios (HRs) were estimated by a Cox proportional-hazards model with surgical type (OPCAB or cCABG) as the exposure variable, propensity score as the covariate, and various primary and secondary end points as the outcomes. All analyses were stratified by individual surgeons and year of surgery. In addition, the Kaplan-Meier method and log-rank test were used to compare the difference in the long-term outcomes between the 2 groups. The patients lost to follow-up were treated as censored data in survival analyses.

To help minimize any residual selection bias, an additional propensity score that included year of surgery and surgeon was calculated, and a greedy matching algorithm was used to match patients based on the logit of the propensity score. For a subset of 4176 patients from both groups (2088 OPCAB and 2088 cCABG) who were matched on baseline characteristics, Cox models stratified on matched pairs were used to examine the difference in long-term prognosis.

To study the effects of incomplete revascularization on long-term MVEs, we introduced the index of completeness of revasculariza-

Table 1. Main Baseline Characteristics of Patients by Type of Surgery

Risk Factors	OPCAB (n=3266)	cCABG (n=3399)	P*
Mean age, y	60.9	59.8	<0.001
Women, %	16.7	17.3	0.27
Mean BMI, kg/m^2	26.0	26.4	0.12
Family history of CAD, %	6.9	7.9	0.23
Current smoker, %	20.5	20.6	0.68
Diabetes mellitus, %	26.6	26.2	0.96
History of stroke, %	6.7	7.1	0.17
Mean creatinine, μmol/L	91.4	91.8	0.05
eGFR $\leq$60 mL $\cdot$ min^{-1} $\cdot$ 1.73 m^{-2}, %	20.3	23.0	0.03
Diseased territories, %†			<0.001
1	4.7	2.9	
2	14.4	13.5	
3	80.9	83.6	
Left main stenosis ($\geq$50%), %	29.5	31.0	0.18
Previous MI, %	44.8	50.2	<0.001
Congestive heart failure, %	3.8	5.2	0.004
Atrial fibrillation, %	2.1	4.1	<0.001
COPD, %	13.7	11.6	0.14
PVD, %	2.6	2.1	0.22
Mean ejection fraction, %	59.8	59.0	0.01
Mean cholesterol, mmol/L‡	4.7	4.7	0.54
Mean LDL, mmol/L‡	2.6	2.7	0.15
Previous open heart surgery, %	0.3	0.4	0.15
Preoperative intraaortic balloon pump, %†	1.1	2.3	<0.001
Emergent/urgent surgery, %	2.8	4.0	0.006
Additive EuroSCORE >6, %	11.6	13.7	0.01
Surgeon's experience with OPCAB, %			
Fair (100–150 OPCABs)	20.3	33.2	
Good (151–300 OPCABs)	29.8	35.9	
Excellent (>300 OPCABs)	49.8	30.9	

BMI indicates body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; COPD, chronic obstructive pulmonary disease; PVD, peripheral vascular disease; and LDL, low-density lipoprotein.

*All comparisons between the 2 groups were adjusted for age through the use of a general linear model for various continuous variables (eg, BMI, LDL) and logistic regression for noncontinuous variables (eg, gender, smoking).

†Territory refers to the 3 coronary vessel trees (left anterior descending, left circumflex, and right coronary arteries). Diseased territory refers to those territories with stenosis >70%.

‡Data are available only for those recruited since 2004.

tion, defined as the ratio of the total number of distal vessels bypassed to the number of diseased territories. A revascularization with an index of completeness of revascularization <1 was considered incomplete revascularization. The Kaplan-Meier method and log-rank test were used after patients were stratified according to incompleteness and a combination of incompleteness and surgery types. Moreover, an additional Cox model was built with surgical type and incompleteness as the exposure variables, propensity score as the covariate, and long-term MVEs as outcomes. Again, the analyses were stratified by individual surgeons and year of surgery. The interaction between surgery type and incompleteness was evaluated through the use of a likelihood ratio test.

As for cost analysis, because the distribution of cost data tends to be skewed, in-hospital costs and total costs, including in-hospital charges and charges during follow-up, are expressed as median, whereas total costs during follow-up and costs for repeat CABG; percutaneous coronary intervention; angiography; and rehospitalization for MI, stroke, angina, and heart failure are expressed as means. Comparisons were performed by the Wilcoxon signed-rank test. All patients who finished a 2-year follow-up were included. The costs of those who died within 2 years after discharge were also counted. In cost-effectiveness analysis, survival was compared by the Kaplan-Meier method and log-rank test. All statistical analyses were performed with SAS version 9.13 (SAS Institute Inc, Cary, NC). The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Patient Characteristics

Of the 6665 patients included in the study, 3266 patients underwent OPCAB and 3399 underwent cCABG. During the study period, the number of patients undergoing OPCAB increased significantly from <100 in 1999 to ≈700 in 2006; for cCABG, it remained relatively constant at ≈400 patients per year. Consequently, the proportion of patients who underwent off-pump procedures rose sharply from 15% in 1999 to 66% in 2006. Compared with patients in the cCABG group, those in the OPCAB group were older (60.9 versus 59.8 years) and more often were female, smoked, had a history of diabetes and stroke, and had mean levels of cholesterol, low-density lipoprotein, and body mass index (Table 1). On the other hand, patients in the cCABG group were more likely to have triple-vessel disease and a history of MI, congestive heart failure, atrial fibrillation, preoperative insertion of intraaortic balloon pump, and emergent/urgent surgeries. Moreover, the proportion with EuroSCORE >6 was greater in the cCABG group than the OPCAB group.

As shown in Table I of the online-only Data Supplement, patients in the OPCAB group had significantly lower rates of circumflex territory bypass compared with those in the cCABG group (69.9% in OPCAB versus 73.8% in cCABG; $P<0.001$). There was also a significant difference between the 2 groups in the proportion receiving internal mammary artery grafts (90.8% in OPCAB versus 92.7% in cCABG; $P=0.005$) and the proportion receiving venous grafts (91.3% versus 97.9%; $P<0.001$). More patients had incomplete revascularization in the OPCAB group than the cCABG group (12.8% in OPCAB versus 4.0% in cCABG; $P<0.001$).

The variables ultimately included in the propensity score model were age (OR, 1.01; 95% CI, 1.00 to 1.02), current smoker (OR, 0.76; 95% CI, 0.64 to 0.88), chronic obstructive pulmonary disease (OR, 1.32; 95% CI, 1.14 to 1.54), MI (OR, 0.81; 95% CI, 0.72 to 0.90), left main disease (OR, 0.86; 95% CI, 0.77 to 0.97), intraaortic balloon pump insertion (OR, 1.01; 95% CI, 1.00 to 1.02), and single-vessel disease (OR, 2.54; 95% CI, 1.78 to 3.61).

In-Hospital Complications

Table 2 shows the adjusted ORs for OPCAB versus cCABG for various short-term outcome measures recorded during hospitalization. Overall, the mortality was low in both groups, and the use of OPCAB was associated with a nonsignificant

Table 2. Short-Term (In-Hospital) Outcomes and Adjusted ORs and HRs for OPCAB Versus cCABG

	OPCAB (n=3266)		cCABG (n=3399)		Adjusted OR (95% CI)‡	*P*
	Events, n*	%†	Events, n	%		
Deaths	32	1.0	52	1.5	0.74 (0.46–1.18)	0.21
Stroke (fatal and nonfatal)	9	0.3	25	0.7	0.46 (0.21–1.02)	0.06
MI (fatal and nonfatal)	6	0.2	10	0.3	0.71 (0.26–1.96)	0.51
Atrial fibrillation	267	8.2	331	9.7	0.80 (0.66–0.97)	0.02
Blood transfusion	2139	65.6	2438	71.8	0.85 (0.73–0.97)	0.03
Reoperation for bleeding	37	1.2	49	1.5	0.88 (0.55–1.41)	0.60
Prolonged ventilation (>24 h)	120	4.7	256	8.7	0.62 (0.49–0.78)	<0.001

*Refers to total number of events observed.
†The occurrence of in-hospital outcomes is given in percentages.
‡Adjusted by propensity score, surgeon identity, and year of surgery.

26% (adjusted OR, 0.74; 95% CI, 0.46 to 1.18) lower in-hospital mortality. Lower risks of any stroke ($P=0.06$) and any MI ($P=0.51$) were noted in the OPCAB group but did not reach statistical significance. There was a significant reduction in atrial fibrillation ($P=0.02$) and the need for blood transfusion ($P=0.03$) and prolonged ventilation ($P<0.001$) with OPCAB.

Long-Term Outcomes

After an average of 4.5 years of follow-up, a total of 268 patients died of various causes, among whom 176 died of cardiac causes. No differences of all-cause deaths were noted between the OPCAB (n=112) and cCABG (n=156) groups (adjusted HR, 0.94; 95% CI, 0.72 to 1.22; $P=0.64$). A total of 1112 patients (16.9%) developed MVEs. There were no significant differences in the use of various secondary preventive treatments between the OPCAB and cCABG groups (aspirin, 85.9% versus 84%; angiotensin-converting enzyme inhibitor, 30.7% versus 30.5%; β-blocker, 53.6% versus 53.0%; lipid-lowering agent, 45.3% versus 43.4%). However, there was a significant 23% (95% CI, 8% to 41%; $P=0.002$) higher rate of MVEs among patients who underwent OPCAB than those in cCABG group (Table 3 and Figure 1). Moreover, the rate of repeat revascularization was significantly higher in the OPCAB group than in the cCABG group (adjusted HR, 1.40; 95% CI, 1.03 to 1.89; $P=0.03$). Except for cardiac mortality, the rates of various secondary outcome measures were generally higher in the OPCAB than in the cCABG group, and the differences for angina (adjusted HR, 1.41; 95% CI, 1.21 to 1.63) and rehospitalization for any cardiovascular conditions (adjusted HR, 1.37; 95% CI, 1.21 to 1.55) were all statistically significant. In the non–intention-to-treat analysis that excluded 81 patients in the OPCAB group who were converted to cCABG, the estimated risk ratio was not materially changed for MVEs (adjusted HR, 1.17; 95% CI, 1.03 to 1.33) or repeat revascularization (adjusted HR, 1.41; 95% CI, 1.04 to 1.91).

In the propensity score–matched analyses involving 2088 OPCAB patients and 2088 cCABG patients, no differences in all-cause deaths were noted between the 2 groups (adjusted HR, 0.85; 95% CI, 0.64 to 1.13; $P=0.27$). There remained statistically significant 19% (95% CI, 3 to 37; $P=0.02$) higher rates of MVEs and 38% (95% CI, 3 to 86; $P=0.03$) higher rates of repeat revascularization in the OPCAB group (Table II of the online-only Data Supplement). Similarly, the results for various secondary outcome measures were largely unchanged in these matched analyses, with the excess risks associated with OPCAB being statistically significant for

Table 3. Long-Term Outcomes and Adjusted ORs and HRs for OPCAB Versus cCABG

	OPCAB (n=3234)		cCABG (n=3347)		Adjusted HR (95% CI)†	*P*
	Events, n	Rate*	Events, n	Rate		
Primary						
MVE	493	43.8	619	41.2	1.23 (1.08–1.41)	0.002
Repeat revascularization	112	9.4	125	7.6	1.40 (1.03–1.89)	0.03
Secondary						
Cardiac mortality	71	5.9	105	6.5	1.07 (0.77–1.49)	0.70
Nonfatal MI	39	3.2	44	2.7	1.46 (0.93–2.30)	0.10
Nonfatal Stroke	306	26.3	397	25.1	1.17 (0.98–1.38)	0.05
Angina	449	39.0	426	26.9	1.41 (1.21–1.63)	<0.001
Heart failure	197	16.7	234	14.5	1.21 (0.99–1.49)	0.06
CVD-related hospitalization	629	56.5	634	41.6	1.37 (1.21–1.55)	<0.001

CVD indicates cardiovascular disease.
*The occurrence of long-term outcomes is given as number of events per 1000 person-years.
†Adjusted by propensity score, surgeon identity, and year of surgery.

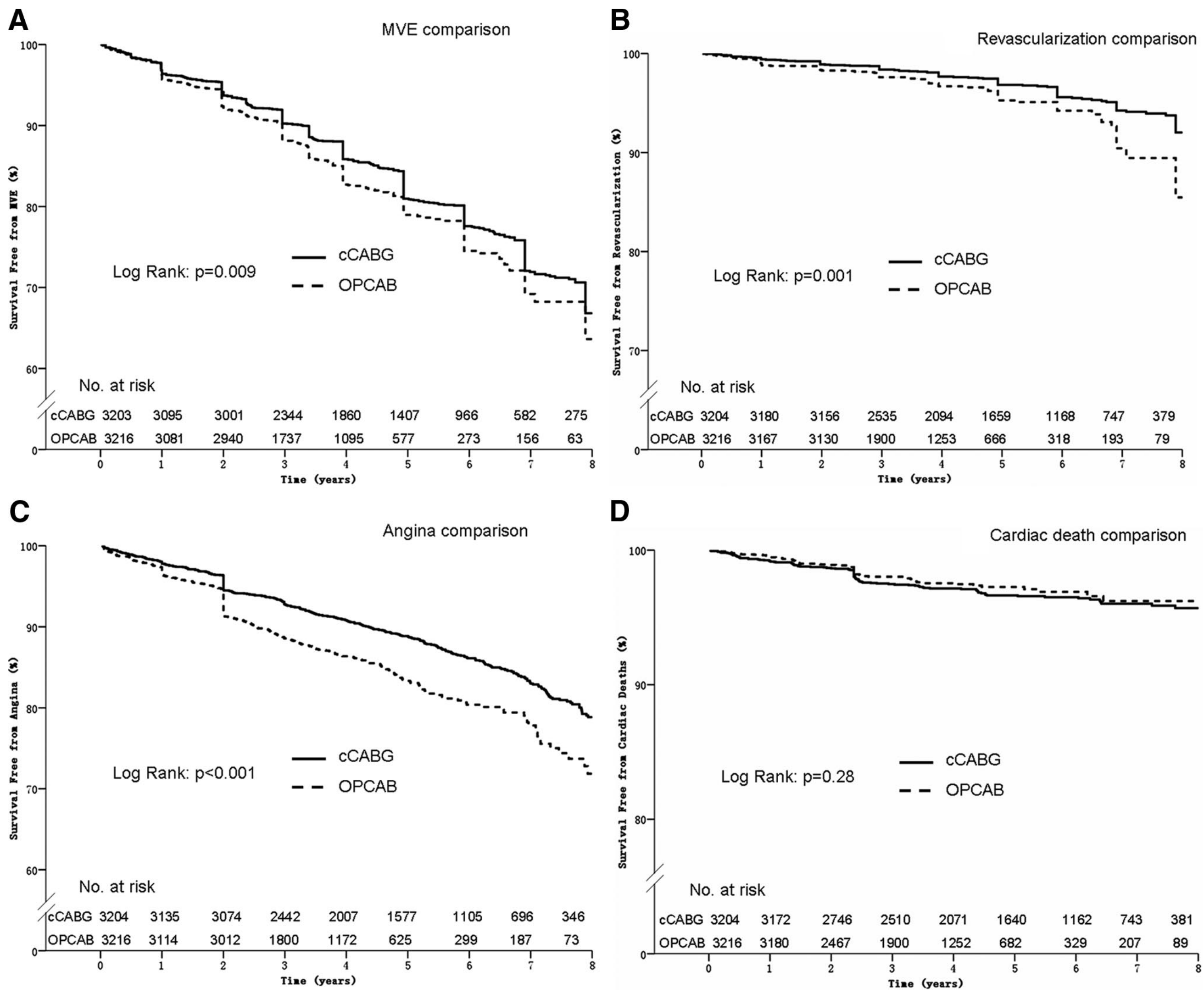

Figure 1. Crude time-to-event curve by surgery type at different end point for patients discharged alive. A, MVEs (P=0.009, log-rank test). B, Repeat revascularization (P=0.001, log-rank test). C, Angina (P<0.001, log-rank test). D, Cardiac deaths (P=0.28, log-rank test).

angina (adjusted HR, 1.33; 95% CI, 1.11 to 1.58), heart failure (adjusted HR, 1.19; 95% CI, 0.95 to 1.49), and hospitalization for any cardiovascular conditions (adjusted HR, 1.39; 95% CI, 1.27 to 1.51). To further explore the long-term difference, a subgroup analysis was carried out in the propensity score–matched sample for MVEs. Overall, the proportional excess risk of MVEs associated with OPCAB did not differ significantly in the different subcategories of patients studied (Figure 2). There was, however, a trend toward a higher relative risk of MVE among higher-risk patients (such as those who were elderly, had a history of MI, presented with triple-vessel disease, or had abnormal renal function), with the event rate being 66.1 per 1000 person-years in OPCAB group versus 50.5 per 1000 person-years in cCABG group, which is an absolute excess of 15.6 per 1000 person-years.

As shown in Figure II of the online-only Data Supplement, patients with incomplete revascularization did significantly worse. Figure III of the online-only Data Supplement shows that OPCAB patients with incomplete revascularization had poorer MVE outcomes than the other strata. After adjustment, both surgery type (adjusted HR, 1.14; 95% CI, 1.00 to 1.30; P=0.03) and incomplete revascularization (adjusted HR, 1.34; 95% CI, 1.07 to 1.67; P=0.01) remained as correlates of long-term MVEs. The interaction between surgery type and incomplete revascularization did not reach statistical significance (P=0.68).

Cost, Cost-Effectiveness, and Sensitivity Analyses

The median in-hospital costs were 59 905.3 RMB in the OPCAB group and 61 012.1 RMB in cCABG group (P=0.77). However, as shown in Table 4, the costs of stroke and angina and as the total amount during follow-up were higher in the OPCAB group than the cCABG group. Moreover, the total amounts, including both in-hospital charges and charges during follow-up, were much higher in OPCAB patients than in cCABG patients (62 718.6 versus 62 442.5 RMB; P=0.02).

After 2 years of follow-up, survival free from cardiac deaths was not different between the 2 groups (5.3 versus 6.5

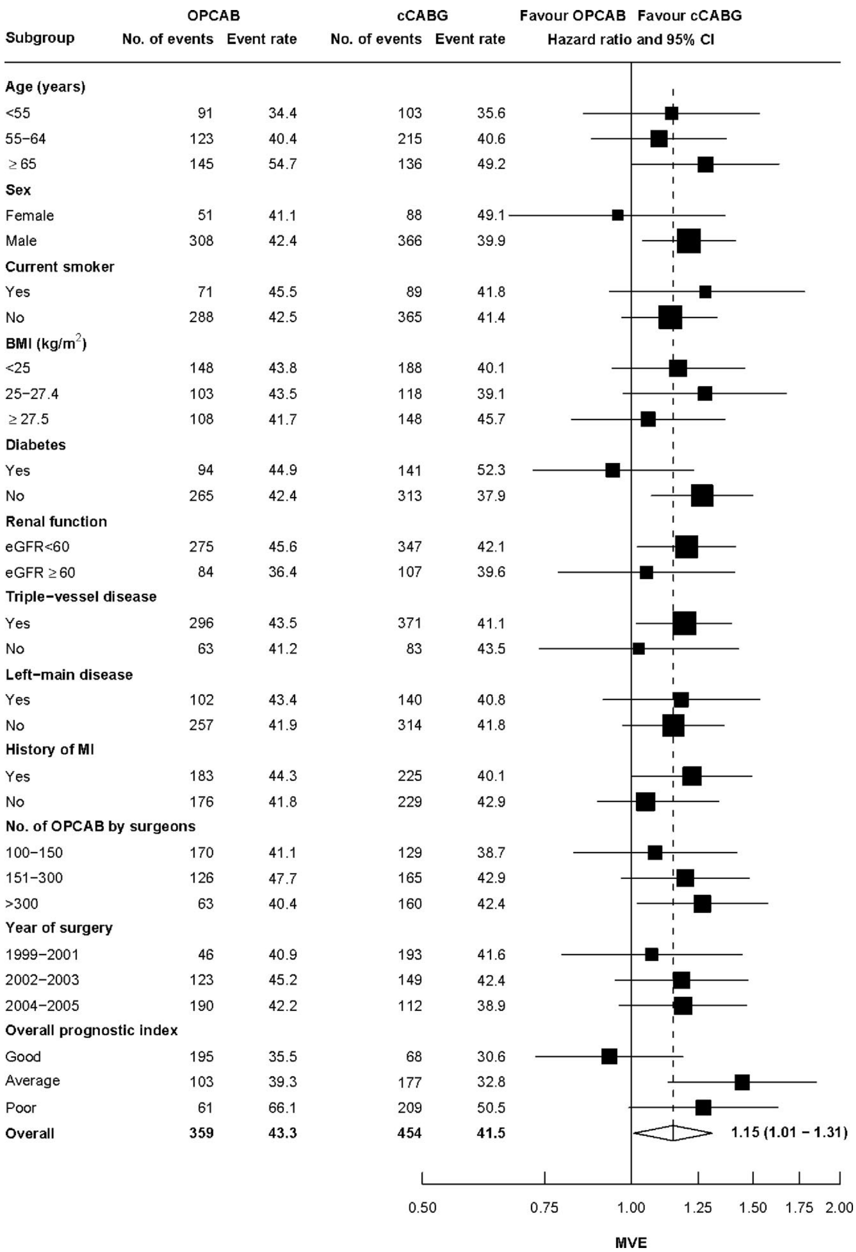

Figure 2. Subgroup analysis for long-term outcomes. HR (and 95% CI) for risk of MVEs during follow-up by major categories in propensity-matched patients. The area of the square is proportional to the number of events. Dashed vertical line indicates overall result; diamond, 95% CI. Three similar-sized prognostic index groups were based on absolute risk of primary composite outcome (MVEs) for each patient calculated from baseline prognostic variables (ignoring the surgical type) with a Cox regression model. Event rate is given in number of events per 1000 person-years.

per 1000 person-years; $P=0.47$). Over the same period, OPCAB patients incurred significantly more healthcare costs ($P=0.02$; Table 4). On-pump surgery was the dominant treatment because it was as effective as OPCAB and resulted in significantly lower costs.

After recalculation of the follow-up cost estimates by applying unit cost data from the Medical Insurance Centers in Guangzhou and Lanzhou, the sensitivity analysis did not alter the primary results. By Guangzhou estimates, the total costs, including both in-hospital charges and charges during follow-up, were significantly higher in the OPCAB group than the cCABG group (63 322.8 versus 62 645.8 RMB; $P=0.009$). By Lanzhou estimates, the total costs were still significantly higher in OPCAB patients than in cCABG patients (62 092.4 versus 61 990.7 RMB; $P=0.02$). This suggested the robustness of the primary cost analysis.

Discussion

This is by far the largest study of the effects of OPCAB procedures in China. It involved a large number of patients who were operated on by a small number of surgeons with OPCAB experience in a single cardiac center with standardized surgical and postsurgical management. It has been shown that, compared with cCABG, OPCAB is associated with limited in-hospital benefits and moderate long-term hazards, especially among patients who were older or had multivessel conditions or other major comorbidities at baseline. Moreover, OPCAB consumes more resources than cCABG in the long run.

In the present study population of largely unselected CABG patients, the in-hospital mortality of 1.3% (84 of 6665) compares favorably with the rate reported in studies conducted in the United States or Western European popula-

Table 4. Cost Analysis at 2 Years of Follow-Up

	Average Resource Use, % (n)*		Cost Data, RMB†		
	Off Pump	On Pump	Off Pump	On Pump	*P*‡
Coronary bypass surgery	0.1 (3)	0.1 (2)	113.8	76.1	0.69
Percutaneous coronary intervention	1.4 (29)	1.3 (27)	835.6	780.2	0.83
Coronary angiography only	3.7 (77)	3.5 (72)	795.0	745.5	0.73
Hospitalization for myocardial infarction	0.6 (13)	0.4 (9)	311.4	216.2	0.41
Hospitalization for stroke	4.7 (98)	2.7 (57)	629.5	367.2	0.002
Hospitalization for angina pectoris	4.8 (100)	3.9 (82)	1905.9	1567.3	0.19
Hospitalization for heart failure	3.6 (75)	1.7 (36)	903.7	435.0	<0.001
Subtotal costs at 2 y§	...	...	5494.8	4187.5	<0.001
Total costs at 2 y‖	...	...	62 718.6	62 442.5	0.02

Two-year follow-up for 2088 off-pump and 2088 on-pump patients' cost data.

*Calculated by dividing number of events by total number of patients in corresponding groups.

†Total costs including in-hospital charges and charges during follow-up are expressed as medians. Total costs during follow-up and costs for repeat CABG, percutaneous coronary intervention, angiography, and rehospitalization for MI, stroke, angina, and heart failure are expressed as means.

‡Mann-Whitney test.

§Costs during follow-up.

‖Total costs of in-hospital charges and charges during follow-up.

tions.[13,14] This may reflect in part the prolonged training required for cardiovascular surgeons in our hospital and in part the relatively younger age of our patient population (mean, 60 years compared with 67 years in most other studies). There was no difference between the 2 groups in terms of in-hospital mortality, but there was a reduced risk of atrial fibrillation, blood transfusion, and ventilation for >24 hours in patients having OPCAB. These in-hospital findings are similar to those reported in a number of large observational studies.[3,8]

To help compare the effects of OPCAB versus cCABG unbiasedly, a few dozen randomized trials have been conducted, but all were small (typical sample size, ≈200 patients) and tended to have relatively short follow-up. In a recent meta-analysis of 37 randomized trials involving ≈3500 CABG patients,[15] there were only 29 in-hospital deaths and a nonsignificant reduction in in-hospital mortality among OPCAB patients (OR, 0.91; 95% CI, 0.45 to 1.83). There was a significant 41% risk reduction in atrial fibrillation associated with OPCAB and a tendency toward lower rates of stroke and MI that were not significant because of the extremely small number of events involved. Much larger randomized evidence is needed to compare the effects of off-pump procedures and conventional procedures reliably.

A few large observational studies have previously reported on the long-term effects of OPCAB, but most typically involved only 1 to 2 years of follow-up, tended to focus primarily on total mortality, and have produced inconsistent findings. In a meta-analysis involving ≈300 000 patients from 22 observational studies, follow-up information at an average of 1 to 2 years was available for only <2000 patients in 2 studies, and there was no difference in overall survival between OPCAB and cCABG patients, although there was a tendency toward increased risk of repeat revascularization with OPCAB.[15] In the recently published New York State CABG registry involving 35 941 cCABG and 13 889 OPCAB patients recruited during 2001 to 2004,[3] there was no significant difference in 3-year overall survival between OPCAB and cCABG patients (89.4% versus 90.1%), but there was a significant excess risk of repeated revascularization among OPCAB patients (10.1% versus 6.3%). Similar results were also reported in another single-center study in the United States involving 5026 cCABG and 641 OPCAB patients who were followed up for ≈3 years.[16]

To help understand the potential mechanism underlying the long-term effects of the off-pump procedure and to improve statistical power, we prespecified MVEs and repeat revascularization as the 2 primary long-term outcome measures. Patients who underwent OPCAB were found to have significantly increased rates not only of repeated revascularization but also of MVEs compared with cCABG patients. Overall, the excess risk of MVEs associated with OPCAB was modest, corresponding to about an extra 2 events per 1000 person-years in the propensity score–matched analysis. However, in high-risk individuals (such as those presenting with advanced age, triple-vessel disease, impaired renal function, or history of diabetes), the absolute excess risk was ≈8 times higher. In addition, there were significantly higher rates of angina and CVD-related hospitalization with OPCAB, all of which contributed significantly to adverse postoperative quality of life and are common reasons for readmission after CABG.[17,18]

The present study revealed a strong association between OPCAB surgery and incomplete revascularization. This finding provides further supporting evidence for concerns about incomplete revascularization associated with off-pump technique.[19] Good evidence is available that incomplete revascularization at CABG can lead to poor long-term prognosis.[13,20] Consistent with the above reports, the present study suggested that incomplete revascularization contributes significantly to long-term MVE (Figures II and III of the online-only Data Supplement).

Although cost comparison is important, few articles discuss this issue when OPCAB and cCABG are compared. It was previously suggested in randomized trials that cCABG is associated with increasing short-term (1-year follow-up) costs,[4,6] which could potentially affect strategy decisions. However, midterm to long-term cost comparisons are still lacking. We looked into the medical expenditure data up to 5 years after discharge. To the best of our knowledge, no other series has followed cost data for such a long period. In the present study, OPCAB incurs low in-hospital costs, but this benefit is offset by high rehospitalization rates or costs of late procedures. Somewhat different from the findings of others,[4,6] we found that the cost at 1 year is significantly higher in the OPCAB group than the cCABG group. It is likely that the cost-effectiveness of cCABG was blurred by the low-risk nature of selected populations in previous studies.

The present study has a number of strengths, including a prospective study design, large sample size, nonselective nature of the patient population from a single center, experienced surgeons, long-term follow-up for a number of major outcomes, and highly compatible use of long-term secondary prevention in the 2 groups. Despite these strengths and the use of various statistical measures (such as propensity analysis and matching) to help minimize selection biases between the surgery groups, the findings should be interpreted cautiously given the nonrandomized design of the study. In addition, no angiographic follow-up data were available to allow direct assessment of any differences in postoperative atherosclerotic progression of the grafts (although the major end points used in the study are more directly relevant clinical measures). In addition, although previous studies have consistently found that graft flow after anastomosis, which is another major concern related to off-pump techniques, is significantly lower after OPCAB than cCABG,[21,22] no information is available on the quality of anastomosis in the present study. To what extent the reduced quality of anastomosis associated with off-pump procedures affects long-term prognosis remains to be established.

Conclusions

Use of the off-pump procedure appeared to be associated with a reduced risk of hospital complications, but this saving was not translated into long-term benefits. The increased risk of MVEs was particularly noticeable among high-risk patients. In addition, OPCAB may be less cost-effective in the long run. The choice between such procedures should be considered extremely carefully; in particular, any potential short-term gain should be balanced against the potential for long-term hazard.

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Disclosures

None.

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CLINICAL PERSPECTIVE

Worldwide, ≈1 million patients undergo coronary artery bypass grafting procedures each year. Off-pump procedures, which involve performing anastomoses on a beating heart, have gained in popularity over the last decade. A rising trend in off-pump surgery volume is seen in developing countries such as China and India. In sharp contrast to the experience in the United States, where off-pump surgery accounts for ≈20% of all coronary artery bypass grafting procedures, two thirds are performed with this technique in China. Unfortunately, substantial uncertainties remain about the long-term outcomes. A number of studies have addressed this issue, but several inadequacies exist in the currently available literature. First, besides mortality, long-term adverse events that are important from a healthcare point of view are less frequently documented. Second, studies with long-term follow up are needed. Finally, analyses of resource use are still lacking. Therefore, more evidence is needed to guide surgeons in making decisions for patients undergoing coronary artery bypass graft.