Long-Term Follow-up of Off-Pump and On-Pump Coronary Artery Bypass Grafting

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Objective: Despite increasing recognition of the benefits of off-pump coronary artery bypass grafting (CABG), concerns persist regarding its impact on long-term mortality and freedom from reintervention. In this study, we assessed the impact of off-pump CABG on long-term outcomes.

Methods: From January 2002 to December 2002, a total of 307 consecutive patients who underwent isolated multivessel off-pump CABG at our institution were compared with a control group of 397 patients who underwent multivessel on-pump CABG during the same period. Perioperative data were prospectively collected and compared. In addition, univariate and risk-adjusted comparisons between the two groups were performed at 10 years.

Results: After adjusting for clinical covariates, off-pump CABG did not emerge as a significant independent predictor of long-term mortality [hazard ratio (HR), 0.91; 95% confidence interval (CI), 0.70–1.12], readmission to hospital for cardiac cause (HR, 0.96; 95% CI, 0.78–1.10), or the need for reintervention (HR, 0.93; 95% CI, 0.87–1.05).

Conclusions: At long-term follow-up, off-pump CABG remains a safe and effective myocardial revascularization strategy with no adverse impact on survival or freedom from reintervention.

Key Words: Cardiopulmonary bypass, Coronary artery bypass grafting, Myocardial revascularization, Off-pump coronary artery bypass grafting, On-pump coronary artery bypass grafting.

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The expanding indications for angioplasty coupled with the successful short-term and midterm results of randomized controlled trials of drug-eluting stents have already had an unquestionable impact on the practice of coronary revascularization operations.[1–3] However, coronary artery bypass grafting (CABG) remains a major mode of therapy for coronary artery disease.[4] Coronary artery bypass grafting has been performed predominantly with the use of cardiopulmonary bypass (CPB) and cardioplegic arrest, which allows optimization of the surgical field and consistent placement of grafts. Despite these advantages, the use of CPB is also associated with numerous complications.[5] A surgical technique avoiding CPB should, in theory, reduce the incidence of such complications and lead to improved patient outcomes. This assumption has rekindled interest in performing off-pump coronary artery bypass (OPCAB) surgery.[5]

During the last decade, several randomized controlled trials[6–8] as well as meta-analyses and systematic reviews have rigorously scrutinized the safety and efficacy of OPCAB[9–11] and have demonstrated that OPCAB improves short-term and midterm clinical outcomes without measurable increased risk to the patient, with reduction in resource utilization and potential reduction in in-hospital costs compared with on-pump CABG.[6–11] Despite increasing recognition of the benefits of OPCAB grafting, concerns persist regarding its impact on long-term mortality and freedom from reintervention.[12–15]

In this study, we assessed the impact of OPCAB grafting on long-term outcomes.

METHODS

Study Sample

This study comprised a retrospective analysis of a prospectively collected cardiac surgery database (PATS; Dendrite Clinical Systems, Ltd, Oxford, UK) as well as a follow-up questionnaire approved by the institutional ethics committee. Because of its retrospective nature, informed consent was waived for this study. The PATS database captures detailed information on a wide range of preoperative, intraoperative, and hospital postoperative variables (including complications and mortality) for all patients undergoing cardiac surgery in our institution. Information from the database was collected and reported in accordance with the Society for Cardiothoracic Surgery in Great Britain & Ireland database criteria. In addition, the medical notes and charts of all the study patients were reviewed. For information on long-term outcomes, a questionnaire was mailed to all surviving patients or to the general practitioners of those patients who had died during the follow-up period.

From January 2002 to December 2002, a total of 307 consecutive patients who underwent isolated multivessel OPCAB grafting at our institution were compared with a control group

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of 397 patients who underwent multivessel on-pump CABG during the same period. Patient characteristics of both groups are shown in Table 1. This particular patient cohort was selected for two reasons: first, to have a follow-up that is truly long-term, and second, to exclude the influence of learning curve, which is a well-recognized influence on outcomes.[16] The surgeons performing OPCAB on the patients in this study had, on average, performed 100 or more OPCAB procedures individually since the inception of the OPCAB program at our institution in late 1996 and hence were assumed to have traversed their learning curve. Indications for surgical intervention were determined at a weekly review involving cardiologists, cardiac surgeons, and cardiac radiologists. The patients were placed on a specific waiting list according to the urgency of their procedure.

TABLE 1. Unmatched Preoperative Patient Characteristics

Variable	Off-pump (n = 307)	On-pump (n = 397)	*P*
Age, mean (SD), y	62.3 (11.8)	62.7 (9.9)	0.91
Male	219 (71.3)	216 (54.4)	0.02
BMI	29.1 (4.0)	28.7 (4.1)	0.87
Diabetes	108 (35.2)	106 (26.7)	0.03
Hypertension	163 (53.1)	212 (53.4)	0.97
Never smoked	99 (32.2)	137 (34.5)	0.76
Hypercholesterolemia	139 (45.3)	157 (39.5)	0.04
COPD	25 (8.1)	33 (8.3)	0.91
CCS ≥ 3	79 (25.7)	101 (25.4)	0.97
NYHA ≥ 2	166 (54.1)	219 (55.2)	0.87
PVD	27 (8.8)	21 (5.3)	0.03
MI in 30 d before CABG	79 (25.7)	101 (25.4)	0.99
Preoperative serum creatinine ≥ 200 μM/L	13 (4.2)	7 (1.8)	0.04
<30% ejection fraction	16 (5.2)	22 (5.5)	0.93
30%–49% ejection fraction	69 (22.5)	98 (24.7)	0.87
≥50% ejection fraction	222 (72.3)	277 (69.8)	0.76
Preoperative IV nitrates	20 (6.5)	31 (7.8)	0.65
Preoperative IV inotropes	1 (0.3)	2 (0.5)	0.79
Preoperative IABP	19 (6.2)	24 (6.0)	0.97
Previous PCI	13 (4.2)	17 (4.2)	1.0
CVA/TIA	5/4 (2.9)	3/9 (3.0)	0.91
LMS stenosis > 50%	119 (38.8)	159 (40.0)	0.6
Two vessels	112 (36.5)	110 (27.7)	0.04
Three vessels	195 (63.5)	287 (72.3)	0.06
Urgent	101 (32.9)	161 (40.6)	0.03
Logistic EuroSCORE, mean (SD)	3.3 (3.4)	3.4 (3.6)	0.76

Values are presented as number (percentage) unless otherwise indicated.

BMI indicates body mass index; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; IABP, intra-aortic balloon pump; IV, intravenous; LMS, left main stem; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack.

Operative Technique

Four surgeons performed both on-pump and OPCAB operations during the study period. All interventions were performed via a midline sternotomy. The choice of on- or off-pump strategy was based on the surgeon's preference. On-pump CABG was preferentially offered to the patients with poor ventricular function; those with diffusely diseased, calcified, poor-quality target vessels; and those requiring emergency surgical revascularization. On the other hand, OPCAB grafting was the procedure of choice for the patients with a higher risk for complications from CPB and aortic manipulation, particularly those with advanced ascending aortic disease. Overall, our institutional approach is that technical precision, anastomotic quality, and completeness of revascularization should not be compromised in an effort to avoid CPB unless the short-term risks outweigh any potential long-term benefit. The left and the right internal mammary artery (IMA) were harvested with minimal trauma as pedicled or skeletonized grafts, based on the surgeon's preference, and treated with papaverine solution before use. The great saphenous vein was harvested using open technique.

Conventional CABG on CPB was performed at 34°C. Cardiopulmonary bypass was instituted with single two-stage right atrial cannulation and an ascending aorta perfusion cannula. Standard bypass management included membrane oxygenators, arterial line filters, and nonpulsatile flow of 2.4 L/m^2 per minute, with a mean arterial pressure greater than 50 mm Hg. The myocardium was protected by using intermittent antegrade cold blood cardioplegia (4:1 blood-crystalloid ratio). Anticoagulation was achieved using 300 U/kg of heparin. If required, heparin was supplemented to maintain the activated clotting time of longer than 480 seconds and was reversed by protamine at the end of the procedure.

All patients underwent conventional multivessel CABG using varying combinations of left and/or right IMA and saphenous vein grafts. All distal and proximal anastomoses on CPB were performed during a period of single aortic cross-clamping.

For off-pump CABG, the heart was stabilized using the suction-irrigation tissue stabilization system. A deep pericardial retraction suture helped position the heart for grafting. Anticoagulation was achieved with 150 U/kg of heparin. If required, heparin was supplemented to maintain the activated clotting time of longer than 250 seconds and was reversed by protamine at the end of the procedure. Blood pressure was continually optimized during the procedure, and the mean arterial pressure was maintained higher than 50 mm Hg by repositioning the heart and by intravenous fluids or selective use of vasoconstrictors, or both. The proximal graft anastomoses to the aorta were performed with partial cross-clamping of the ascending aorta. Each distal anastomosis was followed by construction of the corresponding proximal anastomosis.

Postoperative Management

Postoperative intensive care unit management was standardized for all patients. All patients received intravenous nitroglycerin (0.17–8 μg/kg per minute) infusions for the first 24 hours unless hypotensive (systolic blood pressure of <90 mm Hg). Choice of inotropic agents was dictated by the hemodynamic data. Other routine medications included daily aspirin and resumption of cholesterol-lowering agents and β-blockers. Diuretics, angiotensin-converting enzyme inhibitors, and warfarin were gradually introduced when indicated clinically.

Variables and Data Collection

Preoperative variables of interest included age, sex, body mass index, smoking history, chronic obstructive pulmonary

TABLE 2. Unmatched Intraoperative Data

Variable	Off-pump (n = 307)	On-pump (n = 397)	*P*
LIMA use	307 (100)	397 (100)	1.00
RIMA use	122 (39.7)	61 (15.4)	<0.01
SVG use	185 (60.3)	336 (84.6)	<0.01
Grafts per patient, mean (SD)	2.91 (1.06)	3.4 (0.4)	<0.01
CPB time, mean (SD), min	—	79.7 (35.2)	—
Aortic cross-clamp time, mean (SD), min	—	49.4 (29.5)	
Conversion to CPB	3 (0.9)	—	—
ICOR, mean (SD)	1.09 (0.17)	1.11 (0.19)	0.87

Values are presented as number (percentage) unless otherwise indicated.
CPB indicates cardiopulmonary bypass; ICOR, index of completeness of revascularization; LIMA, left internal mammary artery; RIMA, right internal mammary artery; SVG, saphenous vein graft.

disease, diabetes, hypercholesterolemia, renal insufficiency (preoperative serum creatinine of ≥200 μM/L), hypertension, peripheral vascular disease, cerebrovascular disease, left ventricular ejection fraction, urgency (operation performed <24 hours vs >24 hours from time of referral), previous myocardial infarction (MI), prior percutaneous coronary interventions, preoperative intravenous nitrates, preoperative intravenous inotropes, number of diseased vessels, preoperative intra-aortic balloon pump, and logistic EuroSCORE. Intraoperative variables of interest included types of grafts used, grafts per patient, CPB time, aortic cross-clamp time, conversion to CPB, and index of completeness of revascularization (ICOR). The ICOR was defined as the total number of distal grafts constructed divided by the number of the affected coronary vessels reported on the preoperative coronary angiogram.[17] Complete revascularization was assumed when the ICOR was 1 or greater.

Postoperative variables of interest included in-hospital mortality, postoperative intra-aortic balloon pump, stroke or transient ischemic attack, prolonged ventilation of longer than 24 hours, atrial fibrillation, deep sternal infection, superficial sternal infection, mediastinitis, vein harvest site infection, use of blood products, hemofiltration, inotropes upon leaving the operating room (OR), chest infection, return to OR for bleeding, gastrointestinal complications, and length of intensive care unit and hospital stay.

The long-term outcomes of interest were all-cause mortality after discharge from a hospital, coronary reintervention (percutaneous or CABG), or readmission for any cardiac cause defined by the following codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification*[18]: 410 (acute MI), 411 (unstable angina), 412 (old MI), 413 (angina pectoris), 414 (other forms of chronic ischemic heart disease), 426 (conduction disorders), 427 (cardiac dysrhythmias), 428 (heart failure), and 429 (ill-defined descriptions and complications of heart disease).

Statistical Analysis

The patients who underwent OPCAB grafting were compared with those who did not, using *t* tests and the Kruskal-Wallis test for continuous variables and the χ^2 test for categorical variables. A propensity analysis was performed modeling the probability of receiving OPCAB grafting. Briefly, a nonparsimonious multivariate logistic regression model using clinically relevant variables was generated to compute a propensity score for each patient. All clinically relevant variables were included in the model. The propensity score (or probability of receiving OPCAB grafting) was then used to obtain a one-to-one match of all OPCAB grafting patients with CPB controls by a "greedy 5 → 1 matching" technique.[19] In-hospital outcomes were compared between these matched groups.

Logistic regression was used to examine the association of OPCAB grafting with in-hospital adverse events after adjusting for differences between the patients on the basis of each of the abovementioned preoperative variables. The association between OPCAB grafting and the long-term outcomes of interest was analyzed using adjusted survival curves and Cox proportional hazards modeling techniques. All baseline characteristics were included in the fully adjusted multivariate Cox models.

Statistical significance was indicated by a two-tailed *P* value of less than 0.05. All analyses were performed with the Statistical Analysis Systems software package (Release 9.1.3; SAS Institute, Cary, NC USA). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the article as written.

RESULTS

A total of 704 patients formed the final study population. Compared with the patients who had on-pump grafting, those receiving OPCAB grafting were more likely to be men and more likely to have diabetes, hypercholesterolemia, renal insufficiency, peripheral vascular disease, two-vessel disease, and elective surgery (Table 1). Off-pump grafting unmatched (39.7% vs 15.4%; $P < 0.01$) and propensity-matched (39.7% vs 10.4%; $P < 0.01$) patients also received more bilateral IMAs than the control group, as listed in Tables 2 and 3. Overall, there were fewer distal anastomoses performed in the OPCAB group compared with the control group [2.91 (1.06) grafts vs 3.4 (0.4) grafts; $P < 0.01$). Unadjusted hospital mortality was 1.3% for the OPCAB group and 1.5% for the control group ($P = 0.76$). The overall in-hospital mortality for the entire cohort was 1.4%.

TABLE 3. Propensity-Matched Intraoperative Data

Variable	Off-pump (n = 307)	On-pump (n = 307)	*P*
LIMA use	307 (100)	307 (100)	1.00
RIMA use	122 (39.7)	32 (10.4)	<0.001
SVG use	185 (60.3)	275 (89.6)	<0.01
Grafts per patient, mean (SD)	2.91 (1.06)	3.4 (0.2)	<0.01
CPB time, mean (SD), min	—	78.3 (31.3)	—
Aortic cross-clamp time, mean (SD), min	—	47.9 (28.7)	
Conversion to CPB	3 (0.9)	—	—
ICOR, mean (SD)	1.09 (0.17)	1.10 (0.17)	0.83
Operative time, mean (SD), min	145.3 (22.1)	174 (11.7)	0.01

Values are presented as number (percentage) unless otherwise indicated.
CPB indicates cardiopulmonary bypass; ICOR, index of completeness of revascularization; LIMA, left internal mammary artery; RIMA, right internal mammary artery; SVG, saphenous vein graft.

The propensity score model included 26 patient variables listed in Table 1. The *c* statistic for this model was 0.81 (Hosmer-Lemeshow goodness-of-fit P = 0.3057). All 307 OPCAB grafting patients could be matched to 307 control patients. The two groups were well matched for all the patient variables (Table 4).

The in-hospital mortality for the propensity-matched OPCAB group was similar to that of the control group (1.3% vs 1.6%; P = 0.71). The length of hospitalization was a median of 7 days in both groups with an interquartile range of 4 to 13 days (P = 0.98). Major morbidity was not statistically different between the OPCAB and matched groups (Table 5). However, significantly more patients in the control group required inotropes (17.6% vs 8.5%; P < 0.001), required hemofiltration (6.2% vs 1.3%; P = 0.01), received blood products (29.6% vs 6.2%; P < 0.001), and were re-explored for bleeding (5.5% vs 2.6%; P = 0.01) compared with the matched OPCAB patients. After adjusting for clinical covariates, OPCAB grafting was not an independent predictor of in-hospital adverse events [odds ratio, 0.78; 95% confidence interval (CI), 0.66–0.85; P = 0.31].

TABLE 4. Preoperative Characteristics of Propensity-Matched Patients

Variable	Off-pump (n = 307)	On-pump (n = 307)	*P*
Age, mean (SD), y	62.3 (11.8)	62.6 (7.9)	0.93
Male	219 (71.3)	211 (68.7)	0.87
BMI	29.1 (4.0)	28.6 (3.5)	0.91
Diabetes	108 (35.2)	99 (32.2)	0.76
Hypertension	163 (53.1)	172 (56.0)	0.87
Never smoked	99 (32.2)	114 (37.1)	0.78
Hypercholesterolemia	139 (45.3)	143 (46.6)	0.83
COPD	25 (8.1)	27 (8.8)	0.91
CCS ≥ 3	79 (25.7)	82 (26.7)	0.87
NYHA ≥ 2	166 (54.1)	179 (58.3)	0.74
PVD	27 (8.8)	20 (6.5)	0.42
MI in 30 d before CABG	79 (25.7)	81 (26.4)	0.89
Preoperative serum creatinine ≥ 200 μM/L	13 (4.2)	7 (2.3)	0.34
<30% ejection fraction	16 (5.2)	19 (6.2)	0.83
30%–49% ejection fraction	69 (22.5)	76 (24.8)	0.87
≥50% ejection fraction	222 (72.3)	212 (69.0)	0.81
Preoperative IV nitrates	20 (6.5)	23 (7.5)	0.87
Preoperative IV inotropes	1 (0.3)	1 (0.3)	1.0
Preoperative IABP	19 (6.2)	20 (6.5)	0.91
Previous PCI	13 (4.2)	13 (4.2)	1.0
CVA/TIA	5/4 (2.9)	3/6 (2.9)	1.0
LMS stenosis > 50%	119 (38.8)	159 (40.4)	0.54
Two vessels	112 (36.5)	101 (32.9)	0.29
Three vessels	195 (63.5)	209 (68.1)	0.45
Urgent	101 (32.9)	113 (37.1)	0.53
Logistic EuroSCORE, mean (SD)	3.3 (3.4)	3.3 (2.9)	0.71

Values are presented as number (percentage) unless otherwise indicated.

BMI indicates body mass index; CABG, coronary artery bypass grafting; CCS, Canadian Cardiovascular Society; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; IABP, intra-aortic balloon pump; IV, intravenous; LMS, left main stem; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease; TIA, transient ischemic attack.

TABLE 5. Postoperative Data of Propensity-Matched Patients

Variable	Off-pump (n = 307)	On-pump (n = 307)	*P*
Inotropes leaving OR	26 (8.5)	54 (17.6)	<0.001
Stroke/TIA	1/1 (0.7)	2/1 (1.0)	0.87
Atrial fibrillation	37 (12.1)	47 (15.3)	0.73
Chest infection	14 (4.6)	19 (6.2)	0.76
Hemofiltration	4 (1.3)	19 (6.2)	0.01
Postoperative IABP	5 (1.6)	7 (2.3)	0.79
Ventilation >24 h	7 (2.3)	11 (3.6)	0.67
Superficial sternal infection	3 (0.9)	4 (1.3)	0.84
Deep sternal infection	2 (0.7)	3 (0.9)	0.91
Mediastinitis	0 (0)	1 (0.3)	0.76
Vein harvest site infection	7 (2.3)	10 (3.3)	0.83
Blood product use	19 (6.2)	91 (29.6)	<0.001
Return to OR for bleeding	8 (2.6)	17 (5.5)	0.01
Tracheostomy	1 (0.3)	3 (0.9)	0.67
GI complications	2 (0.6)	3 (0.9)	0.79
Length of ICU stay, median (IQR)	1 (1–3)	1 (1–3)	0.98
Length of hospital stay, median (IQR)	7 (4–13)	7 (4–13)	0.98
In-hospital mortality	4 (1.3)	4 (1.3)	1.00
Late mortality	11 (3.6)	12 (3.9)	0.91
Readmission	10 (3.3)	11 (3.6)	0.93
Reintervention	2 (0.7)	2 (0.7)	1.00

Values are presented as number (percentage).

GI indicates gastrointestinal; IABP, intra-aortic balloon pump; ICU, intensive care unit; IQR, interquartile range; OR, operating room; TIA, transient ischemic attack.

The follow-up was 100% complete at 10 years. During the entire follow-up period, 11 patients (3.6%) died in the OPCAB group and 19 patients (4.8%) died in the control group (P = 0.67). After adjusting for clinical covariates, OPCAB grafting did not emerge as a significant independent predictor of long-term mortality: the hazard ratio (HR) was 0.91 (95% CI, 0.70–1.12; P = 0.87). Risk-adjusted survival was 85% after OPCAB grafting and 84% after on-pump grafting (P = 0.89) during the long-term follow-up (Fig. 1). After discharge, 3.3% of the OPCAB grafting patients and 3.8% of the on-pump grafting patients were readmitted to a hospital for cardiac reasons (P = 0.81). These included two (0.7%) OPCAB grafting and three (0.9%) on-pump grafting patients who were readmitted for repeat revascularization (percutaneous or surgical; P = 0.93); repeat CABG was performed in one (0.3%) OPCAB and one (0.3%) on-pump grafting patient (P = 1.00). After adjusting for clinical covariates, OPCAB grafting did not emerge as a significant independent predictor of readmission to a hospital for cardiac cause (HR, 0.96; 95% CI, 0.78–1.10) or the need for reintervention (HR, 0.93; 95% CI, 0.87–1.05). Risk-adjusted freedom from readmission for any cardiac reason and repeat reintervention are illustrated in Figures 2 and 3, respectively.

Subgroup analysis of the patients with diabetes revealed similar outcomes in terms of survival and freedom from reintervention, with reduced postoperative complications for the OPCAB cohort. There was a statistically significant reduction in the need for inotropes (8.3% vs 17.9%; P < 0.001) and hemofiltration (1.8% vs 9.4%; P < 0.001). Further clinical but not statistically significant advantage was noted in terms of reduced

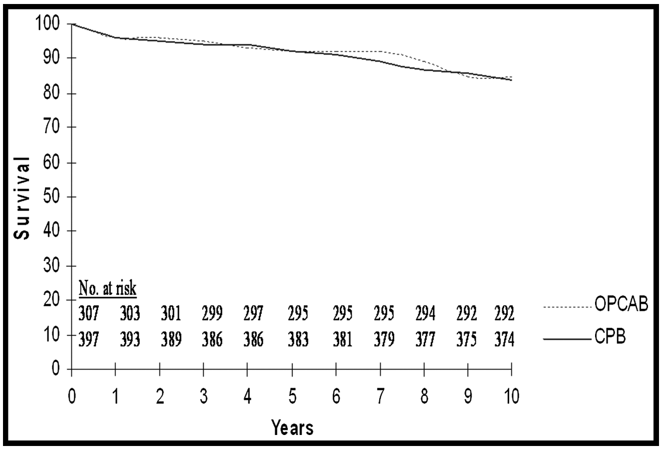

FIGURE 1. Comparison of risk-adjusted freedom from mortality between the off-pump coronary artery bypass (OPCAB) grafting and on-pump cardiopulmonary bypass (CPB) grafting groups.

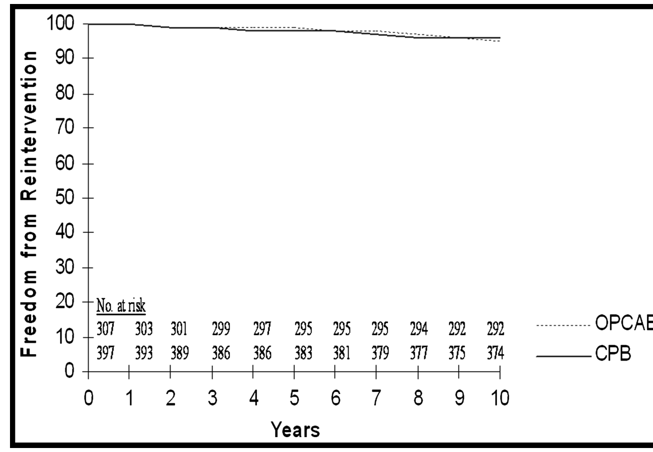

FIGURE 3. Comparison of risk-adjusted freedom from reintervention between the off-pump coronary artery bypass (OPCAB) grafting and on-pump cardiopulmonary bypass (CPB) grafting groups.

blood product use, shorter duration of ventilation, and return to OR for bleeding.

DISCUSSION

The results of our study demonstrated that OPCAB grafting is associated with similar in-hospital and long-term outcomes compared with on-pump grafting. Comparable results have been reported by Puskas and associates[20] as well as Angelini and colleagues[21] for the long-term follow-up of their randomized on- and off-pump cohorts. A large volume of data has been accumulated during the past decade highlighting the advantages of OPCAB grafting for myocardial revascularization. These advantages include improved in-hospital and midterm outcomes.[4–11] However, concerns persist regarding its impact on long-term mortality and freedom from reintervention.[12–15]

Takagi and associates[14] have recently published a meta-analysis of randomized controlled trials suggesting that OPCAB grafting may increase late (≥1 year) all-cause mortality by a factor of 1.37 over on-pump grafting. However, the findings of this meta-analysis must be interpreted with caution because the results are strongly influenced by the ROOBY (Randomized On/Off Bypass) trial,[22] which has attracted a lot of criticism and has several important limitations. It is a well-established fact that incomplete revascularization and lower graft patency have a negative impact on long-term survival. Bell and colleagues[23] performed a retrospective analysis of 3372 nonrandomized surgical patients from the Coronary Artery Surgery Study Registry (three-vessel coronary disease). In patients having class I or II angina (Canadian Cardiovascular Society criteria), adjusted cumulative 4-year survivals according to the number of vessels bypassed were 85% (one vessel), 94% (two vessels), 96% (three vessels), and 96% (more than three vessels) ($P = 0.022$). Placing grafts to three or more vessels was independently associated with improved survival (RR [relative risk], 0.745; 95% CI, 0.591–0.940; $P = 0.0132$) in patients having class III or IV angina. One of the major criticisms of OPCAB grafting has been low revascularization rates and suboptimal anastomotic quality resulting in poor graft patency and long-term outcomes.[12–15] These concerns are no longer valid particularly in large-volume centers and for surgeons who have traversed their learning curve. Our results strongly back this claim because we have clearly shown that all patients in our study had complete revascularization (ICOR, ≥1) translating into improved long-term outcomes. Similar findings have been reported by Puskas and associates[7,20] for their SMART (Surgical Management of Arterial Revascularization Therapies) trial.

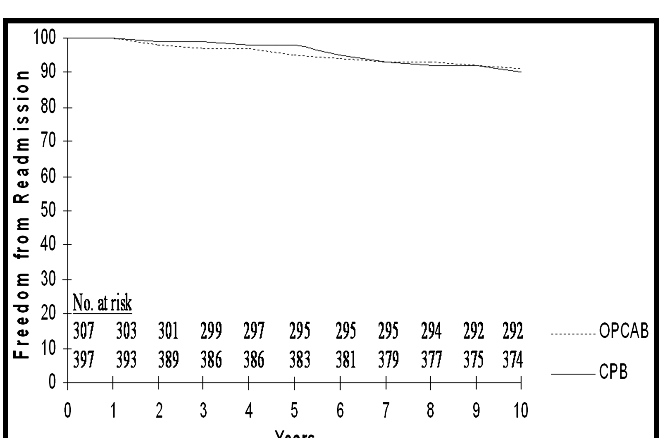

FIGURE 2. Comparison of risk-adjusted freedom from readmission to a hospital for cardiac cause between the off-pump coronary artery bypass (OPCAB) grafting and on-pump cardiopulmonary bypass (CPB) grafting groups.

We have attempted to make meaningful comparisons between the OPCAB grafting group and a contemporaneous group of on-pump grafting control patients. To do this, we have used two statistical approaches based on propensity modeling, a technique that has been strongly advocated in several recent publications, in an effort to better evaluate treatment comparisons from nonrandomized clinical experiences.[24] The propensity score is the probability of a patient receiving a given intervention (in this case, OPCAB grafting) on the basis of a nonparsimonious model derived from preoperative patient variables. The propensity model thus reduces many variables to a single balancing score, facilitating meaningful intergroup comparisons. We used two approaches, namely, the creation of matched pairs on the basis of propensity score and logistic regression analysis of outcomes in which propensity score participated as a variable.

Using the propensity matching technique, the OPCAB and control groups were remarkably well matched in terms of known risk predictors of outcomes after CABG. The overall mortality and major morbidity between the groups were not statistically different. However, the incidence of re-exploration for bleeding and transfusion of blood products in the on-pump group was significantly higher than in the OPCAB group. The incidence of re-exploration for bleeding in this study (2.2% vs 5.5%) compares quite well with incidences of 2% to 6% mentioned in the literature.[25] Continuation of aspirin until the day of surgery and increased number of distal anastomoses with more potential bleeding sites in the on-pump patients could be some of the plausible explanations for this phenomenon. In addition, it is well established that patients undergoing OPCAB do not show any impairing effect of CPB on hemostasis.[26] Because of the absence of the artificial surfaces of the heart-lung machine, the various platelet activation mechanisms and depletion caused by contact activation with extracorporeal surfaces, bubble oxygenator, cardiotomy suction, and filters are avoided, leading to reduced postoperative bleeding.[26] In addition, excessive bleeding may be related to a coagulopathy resulting from greater heparin doses during CPB, as guided by dosing protocols based on body weight and activated coagulation time values or with maintenance of a defined heparin concentration.[26] In contrast, a low level of intraoperative heparinization in OPCAB patients preserves hemostasis.[26] Finally, markedly reduced systemic inflammatory response after OPCAB surgery may also contribute to reduction in postoperative blood loss.[27]

An additional advantage of OPCAB grafting was a significantly less need for hemofiltration despite significantly more patients having preoperative serum creatinine of 200 μM/L or greater. Patients undergoing CABG have several risk factors that predispose them to develop acute kidney injury (AKI). These include but are not limited to advanced age; presence of multiple comorbid illnesses such as diabetes, hypertension, congestive heart failure, and peripheral vascular disease; and, most importantly, preexisting renal insufficiency.[28] However, the risk for developing AKI is related to the surgical procedure itself. One of the major causes is the application of CPB circuit that requires placement of aortic cross clamp and the inevitable reduction in blood supply, albeit for a short time, and loss of pulsatile blood flow to the kidney.[28] In addition, exposure of blood to circuit membranes stimulates the release of inflammatory mediators such as catecholamines and free hemoglobin that may be involved in the development of AKI.[28] The length of the use of the bypass circuit further dictates likelihood of development of AKI. At a pathological level, although no biopsy-based studies have been done, based on the pathophysiology of developing AKI, acute tubular necrosis is suspected to be the most likely cause.[28] There is evidence both from randomized controlled trials and observational studies that avoiding CPB may reduce the AKI risk because OPCAB grafting is not associated with constellation of changes described above.[28]

Another important finding of this study was the increased use of bilateral IMAs in the patients receiving OPCAB grafting. There is evidence to support the concept that the greater the number of arterial conduits used, the better are the long-term results.[29] Two meta-analyses have proven the advantages of bilateral IMA grafting compared with single IMA grafting.[30,31] Because more patients in the OPCAB cohort had two-vessel coronary artery disease, they were possibly preferentially offered two IMAs to achieve complete revascularization. This revascularization strategy not only offered a survival benefit but also reduced the need for reintervention.

Subgroup analysis of the patients with diabetes revealed a beneficial impact of OPCAB in reducing postoperative morbidity without compromising long-term survival or freedom from repeat reintervention. These findings are in general agreement with previously published reports highlighting beneficial impact of OPCAB on outcomes in patients with diabetes.[32,33] Diabetes is a systemic illness with a huge inflammatory component that has been shown to have a significant exacerbation after surgery on CPB.[27] Avoidance of CPB by performing OPCAB in this patient group possibly blunts this systemic inflammatory response syndrome and translates into improved outcomes.[27]

Finally, it is extremely important to highlight that central to all the concerns associated with OPCAB grafting is the issue of learning curve. Surgeons of low or even moderate OPCAB experience have been found to be predictive of emergency conversion[34] as well as responsible for poor graft patency and incomplete revascularization.[35] The technical difficulty of OPCAB grafting means that it involves a steep learning curve that applies to both trainees and consultant surgeons new to OPCAB grafting. The key skill in OPCAB surgery is to be able to perform coronary anastomoses on a beating target myocardium rather than a stationary one. Exposure to OPCAB techniques during training is infrequent; and the acquisition of proficiency, even less so. In a study of residents undergoing cardiothoracic training in the United States, only 22% of residents had performed 20 or more OPCAB procedures during their training.[36] Of these, only 4% had performed OPCAB circumflex coronary artery revascularization. Similarly in the United Kingdom, only 51% of trainees surveyed (76% of all trainees) had experienced OPCAB in their training program, although 96% believed that OPCAB training was essential.[16] Among established surgeons, the adoption of OPCAB has also been highly variable, with rates varying between 0% and 100% of revascularization cases per surgeon, even within a single institution. The reasons for the variation in the adoption of OPCAB techniques are multifactorial. These include the lack of established training programs; the perception that success with the technique is limited to more proficient surgeons; and a fear of deleterious patient outcomes, especially during the learning curve.[16]

The learning curve in OPCAB surgery can be safely negotiated with appropriate patient selection, individualized grafting strategy, peer-to-peer training of the entire team, and graded clinical experience (preoperative planning; adequate exposure; proximal anastomoses to the aorta; and distal anastomoses initially to the anterior wall vessels, followed by the inferior wall vessels, and then the lateral wall vessels).[37] In our experience, the surgeon's learning curve is approximately 75 to 100 cases, and good proficiency with the technique is usually associated with a low 1% to 2% conversion rate and good short- as well as long-term outcomes, as shown by the findings of this study.

The primary limitation of this study is its retrospective nature. Propensity score adjustment is no substitute for a properly designed randomized controlled trial. The retrospective nature of the study cannot account for the unknown variables affecting the outcome that are not correlated strongly with measured variables. However, retrospective comparisons with propensity score adjustment are more versatile and offer a useful way of interpreting large amounts of audit data and of seeking answers to questions that may present insuperable difficulties in the design of randomized controlled trials. Despite the retrospective and observational nature of this study, we provided data on a large cohort of patients undergoing OPCAB grafting for comparison with an on-pump grafting control group, with the longest follow-up that has not been reported before, and demonstrated the safety of OPCAB grafting and its potential for providing complete revascularization that translates into long-term outcomes comparable with a contemporaneous cohort of on-pump grafting patients who also underwent complete revascularization. Lastly, our analysis would have been enhanced substantially if long-term graft patency comparisons were available. However, because of costs, routine follow-up coronary angiography was not performed. The need for coronary angiography was dictated by the occurrence of angina, instability, or electrocardiogram changes in the perioperative or late follow-up period.

On the basis of our findings, we can confidently conclude that at long-term follow-up, OPCAB grafting remains a safe and effective myocardial revascularization strategy with no adverse impact on survival or freedom from reintervention.

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CLINICAL PERSPECTIVE

This is a report from Dr. Raja and his colleagues at Harefield Hospital, which followed 307 consecutive patients that underwent isolated multi-vessel, off-pump coronary artery bypass grafting at their institution from January 2002 to December 2002. They were compared to a control group of 397 patients. They used a propensity analysis to match the groups. They followed these patients for 10 years and compared clinical outcomes. Off-pump coronary artery bypass grafting did not emerge as a significant independent predictor of mortality, readmission to the hospital for cardiac cause, or need for reintervention. The authors concluded that off-pump coronary artery bypass grafting remains a safe and effective myocardial revascularization strategy with no adverse impact on survival or freedom from reintervention at 10 years.

This study is unique in that it examined 10-year followup. The authors are to be congratulated for this longitudinal analysis of their results. However, there are significant shortcomings to this report. It is an observational, retrospective study and thus subject to significant selection bias. Also, while they looked at clinically relative outcome variables, the analysis would have been enhanced if long-term graft patency comparisons were available. Finally, this is a relatively small study considering the low incidence of adverse outcomes following routine coronary artery bypass grafting. In order to determine the efficacy of off-pump coronary artery bypass grafting compared to traditional on-pump procedures, a prospective randomized trial is required. Unfortunately, randomized trials have suggested worse outcomes (Shroyer AL, Grover FL, Hattler B, Collins JF, McDonald GO, Kozora E, Lucke JC, Baltz JH, Novitzky D; Veterans Affairs Randomized On/Off Bypass (ROOBY) Study Group. On pump versus off-pump coronary-artery bypass surgery. N Engl J Med 2009;361:1827-37. Møller CH, Penninga L, Wetterslev J, Steinbrüchel DA, Gluud C. Off-pump versus on-pump coronary artery bypass grafting for ischaemic heart disease. Cochrane Database Syst Rev. 2012;3:CD007224).

