Influence of On-Pump Versus Off-Pump Techniques and Completeness of Revascularization on Long-Term Survival After Coronary Artery Bypass

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Background. **Off-pump coronary artery bypass graft surgery (OPCABG) may be associated with reduced morbidity and in-hospital mortality. In this study, we report the influence of surgery type, number of grafts, and the Index of Completeness of Revascularization (ICOR), namely, the number of grafts/number diseased vessel systems, on long-term survival.**

Methods. **From 1997 to 2006, 12,812 consecutive patients underwent isolated CABG at a single academic center. Ten-year survival data were obtained by cross-referencing patients with the national Social Security Death Index. A propensity score analysis of 46 preoperative characteristics balanced risk factors between surgical groups. A proportional hazards regression analysis modeled the hazard of death as a function of surgery type (on versus off), distal group (1 to 3 versus 4 to 7 vessels), ICOR, and propensity score.**

Results. **Proportional hazards regression analysis showed no significant influence of surgery type or number of grafts on long-term survival within the four groups: OPCABG 1 to 3 grafts (n = 3,946; ICOR 1.11), OPCABG 4 to 7 grafts (n = 1,721; ICOR 1.56), on-pump CABG 1 to 3 grafts (n = 3,380; ICOR 1.21), and on-pump CABG 4 to 7 grafts (n = 3,765; ICOR 1.64). Irrespective of technique of revascularization, there was a survival advantage for patients with higher ICOR.**

Conclusions. **Long-term survival was similar for patients receiving 1 to 3 or 4 to 7 grafts by either on-pump or off-pump techniques. However, higher ICOR was associated with improved long- term survival within all groups.**

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The last decade's increasing interest in lessening the dependence on cardiopulmonary bypass by an increasing number of surgeons adopting use of off-pump coronary artery bypass graft surgery (OPCABG) was met by concerns that such a shift could be fraught with hazards [1]. Such concerns have been amply refuted by numerous recent reports on the short-term safety, improved benefits, and the decreased morbidity and mortality associated with beating-heart surgical revascularization techniques [2–8]. Off-pump technique benefits have been affirmed for men, women, patients with compromised ejection fractions, and elderly patients as well as for patients with other comorbid factors such as diabetes mellitus, renal insufficiency, chronic obstructive pulmonary disease, and history of cerebrovascular diseases [9–11]. The growing confidence in the short-term benefits of OPCABG revascularization due to increasingly established safety and short-term efficacy has led to the supportable conclusion that OPCABG surgery should remain a therapeutic option in modern cardiac surgery; however, it was advised that long-term clinical results are still warranted. Thus, a natural follow-up question was raised on the impact of such OPCABG techniques on intermediate- and long-term patient benefits and on event-free survival [12, 13] and whether such short-term benefits are maintained on long-term follow-up.

The concern that OPCABG techniques may be safe for single- or double-vessel revascularization but not for extended multiple-vessel revascularization was addressed in a large series of patients presented at the

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Table 1. Demographics and Clinical Characteristics

Risk Factor	CABG on CPB 1 to 3 Grafts (n = 3,380)	CABG on CPB 4 to 7 Grafts (n = 3,765)	OPCABG 1 to 3 Grafts (n = 3,946)	OPCABG 4 to 7 Grafts (n = 1,721)	OPCABG Versus CPB *p* Value	1 to 3 Versus 4 to 7 *p* Value	OPCABG 1 to 3 Versus OPCABG 4 to 7 *p* Value	CABG on CPB 1 to 3 Versus CABG on CPB 4 to 7 *p* Value	OPCABG 1 to 3 Versus CPB 1 to 3 *p* Value	OPCABG 4 to 7 Versus CPB 4 to 7 *p* Value
Patient age (SD)[a]	62.4 (11.0)	62.5 (10.4)	63.3 (11.6)	62.4 (10.4)	0.003	0.039	0.005	0.62	< 0.001	0.78
Last creatinine level (SD)[b]	1.23 (1.08)	1.19 (0.82)	1.28 (1.34)	1.18 (0.94)	0.043	< 0.001	0.003	0.12	0.12	0.92
Ejection fraction (SD)[b]	50.0 (12.9)	49.0 (13.0)	50.9 (12.6)	50.7 (12.1)	< 0.001	< 0.001	0.69	0.004	0.004	< 0.001
Number of diseased vessels (SD)[b]	2.45 (0.70)	2.80 (0.46)	2.31 (0.75)	2.82 (0.42)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	0.23
STS mortality risk (SD)[b]	0.022 (0.033)	0.020 (0.027)	0.024 (0.032)	0.021 (0.032)	0.001	< 0.001	< 0.001	0.011	0.022	0.56
Female	1,118 (33.1)	806 (21.4)	1,393 (35.3)	393 (22.8)	< 0.001	< 0.001	< 0.001	< 0.001	0.046	0.24
Year: before 2001	2,177 (64.4)	2,448 (65.0)	887 (22.4)	238 (13.8)	< 0.001	< 0.001	< 0.001	0.59	< 0.001	< 0.001
Caucasian (%)[b]	2,723 (84.9)	3,068 (86.5)	3,107 (81.4)	1,371 (83.2)	< 0.001	< 0.001	0.11	0.051	< 0.001	0.002
Cerebrovascular disease (%)	400 (11.8)	415 (11.0)	622 (15.8)	240 (14.0)	< 0.001	< 0.001	0.08	0.28	< 0.001	0.002
Cerebrovascular accident (%)	247 (7.3)	263 (7.0)	369 (9.4)	142 (8.3)	< 0.001	0.034	0.18	0.60	0.002	0.10
Diabetes mellitus (%)	1,149 (34.0)	1,386 (36.8)	1,360 (34.5)	659 (38.3)	0.86	< 0.001	0.006	0.013	0.67	0.29
Diabetes control					< 0.001	0.008	0.034	0.12	0.004	0.011
No control (%)	166 (4.9)	181 (4.8)	130 (3.3)	53 (3.1)						
Diet (%)	96 (2.8)	120 (3.2)	113 (2.9)	54 (3.1)						
Oral (%)	552 (16.3)	681 (18.1)	679 (17.2)	352 (20.5)						
Insulin (%)	334 (9.9)	404 (10.7)	438 (11.1)	200 (11.6)						
Family history CAD (%)	1,558 (46.1)	1,792 (47.6)	1,436 (36.4)	627 (36.4)	< 0.001	< 0.001	0.98	0.20	< 0.001	< 0.001
Hypertension (%)	2,456 (72.7)	2,724 (72.4)	3,071 (77.8)	1,405 (81.6)	< 0.001	0.82	0.001	0.77	< 0.001	< 0.001
Peripheral vascular disease (%)	240 (7.1)	202 (5.4)	475 (12.0)	158 (9.2)	< 0.001	< 0.001	0.002	0.002	< 0.001	< 0.001
Renal failure (%)	228 (6.8)	247 (6.6)	314 (8.0)	94 (5.5)	< 0.001	0.009	< 0.001	0.75	0.048	0.12
Dialysis (%)	54 (1.6)	33 (0.9)	106 (2.7)	26 (1.5)	0.22	< 0.001	0.007	0.006	0.002	0.035
Current smoker (%)	843 (24.9)	935 (24.8)	1,057 (26.8)	504 (29.3)	< 0.001	0.71	0.052	0.92	0.07	< 0.001
Angina (%)	2,886 (85.4)	3,190 (84.7)	3,332 (84.4)	1,441 (83.7)	0.20	0.47	0.50	0.44	0.26	0.34
CCS classification 5 (%)[b]	1,068 (36.5)	1,156 (35.1)	1,026 (29.9)	395 (26.1)	< 0.001	0.74	0.004	0.58	< 0.001	< 0.001
Congestive heart failure (%)	515 (15.2)	556 (14.8)	745 (18.9)	291 (16.9)	< 0.001	0.008	0.08	0.58	< 0.001	0.042
Myocardial infarction (%)	1,646 (48.7)	1,948 (51.5)	1,879 (47.6)	839 (48.8)	0.009	0.003	0.43	0.01	0.36	0.04
Myocardial infarct < 24 hours (%)	177 (5.2)	254 (6.8)	125 (3.2)	68 (4.0)	< 0.001	< 0.001	< 0.001	0.001	< 0.001	< 0.001
ACE inhibitors (%)	527 (15.6)	606 (16.1)	885 (22.4)	460 (26.7)	< 0.001	0.82	< 0.001	0.56	< 0.001	< 0.001
Anticoagulants (%)	1,184 (35.0)	1,390 (36.9)	1,515 (38.4)	686 (39.9)	< 0.001	0.25	0.30	0.10	0.003	0.037
Antiplatelets (%)	115 (3.4)	105 (2.8)	160 (4.1)	59 (3.4)	0.015	0.019	0.26	0.13	0.14	0.20
Aspirin (%)	2,030 (60.1)	2,299 (61.1)	2,701 (68.5)	1,252 (72.8)	< 0.001	0.86	0.001	0.39	< 0.001	< 0.001
Beta-blockers (%)	1,663 (49.2)	1,854 (49.2)	2,440 (61.8)	1,128 (65.5)	< 0.001	0.06	0.008	0.97	< 0.001	< 0.001
Diuretics (%)	565 (16.7)	587 (15.6)	706 (17.9)	276 (16.0)	0.069	0.015	0.09	0.20	0.19	0.67
Inotropes (%)	17 (0.5)	11 (0.3)	24 (0.6)	11 (0.6)	0.07	0.20	0.89	0.15	0.55	0.059
Intravenous nitrates (%)	465 (13.8)	650 (17.3)	664 (16.8)	305 (17.7)	0.023	0.002	0.41	< 0.001	< 0.001	0.68

Table 1. Continued

Risk Factor	CABG on CPB 1 to 3 Grafts (n = 3,380)	CABG on CPB 4 to 7 Grafts (n = 3,765)	OPCABG 1 to 3 Grafts (n = 3,946)	OPCABG 4 to 7 Grafts (n = 1,721)	OPCABG Versus CPB *p* Value	1 to 3 Versus 4 to 7 *p* Value	OPCABG 1 to 3 Versus OPCABG 4 to 7 *p* Value	CABG on CPB 1 to 3 Versus CABG on CPB 4 to 7 *p* Value	OPCABG 1 to 3 Versus CPB 1 to 3 *p* Value	OPCABG 4 to 7 Versus CPB 4 to 7 *p* Value
Steroids (%)	76 (2.3)	77 (2.1)	108 (2.7)	28 (2.2)	0.11	0.12	0.25	0.55	0.18	0.70
Left main stenosis $> 50\%$	797 (23.6)	808 (21.4)	850 (21.5)	369 (21.4)	0.20	0.17	0.93	0.032	0.037	0.99
Intra-aortic balloon pump (%)	198 (5.9)	246 (6.5)	113 (2.9)	54 (3.1)	< 0.001	0.001	0.57	0.24	< 0.001	< 0.001
ICOR	1.21 (0.50)	1.64 (0.55)	1.11 (0.45)	1.56 (0.43)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

[a] Because a direct adjustment is made for patient age, it is not included in the propensity score. [b] Contains some missing data.

ACE = angiotensin-converting enzyme; CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; ICOR = Index of Completeness of Revascularization; STS = The Society for Thoracic Surgeons.

forty-third annual meeting at The Society of Thoracic Surgeons (STS). In this study, OPCABG conferred a greater safety margin for patients requiring extensive revascularization than did on-pump coronary artery bypass graft surgery (ONCABG) [14]. Furthermore, analysis of the STS National Database conducted and reported by Dr Fred Edwards at the aforementioned meeting has confirmed the 30-day morbidity and mortality reduction in OPCABG cohorts as compared with the patient groups treated on cardiopulmonary bypass. Thus, the growing body of evidence affirms the safety and efficacy of OPCABG in coronary artery revascularization. The increasing reports in support of OPCABG application, the continued technical advancements and new positioning and stabilization devices being introduced, and the improved monitoring and hemodynamic support that have significantly facilitated the performance of, and broadened the application of, beating-heart surgery, OPCABG as a safe, reliable, and cost-effective method for surgical coronary revascularization has been broadly adopted [2–8].

Despite the early observed morbidity and mortality benefits of OPCABG, concerns remain about long-term graft patency [15], thus raising the question of long-term benefits of OPCABG, and hence suggesting that specific consents should be obtained when performing OPCABG [16]. Heretofore, it was not known whether the number of grafts or the method of revascularization impacted the long-term, risk-adjusted outcomes for OPCABG versus ONCABG patients. The present study was designed to assess the long-term outcomes, to determine whether multiple-vessel OPCABG is safe, and to compare the results to a similar cohort of patients who underwent ONCABG. Additionally, we wanted to examine the impact of the index of completeness of revascularization on long-term survival for patients in each subgroup.

Material and Methods

In compliance with the Health Insurance Portability and Accountability Act regulations and the Declaration of Helsinki, and after Institutional Review Board approval granted by Emory University, the STS adult cardiac database was examined for all patients who underwent primary isolated CABG at Emory University or Emory Crawford Long Hospitals between January 1, 1997, and December 30, 2006. The study cohort consisted of 12,812 consecutive patients, including patients with emergent and urgent status. The time frame was chosen to include the entire period during which OPCABG procedures were performed at the institution. Medical records from this retrospective, single-institution cohort study included demographics, preexisting diseases, surgeon identity, operative strategy, and clinical outcomes.

Demographic and Preoperative Data

Before analysis, preoperative risk factors for the outcomes of interest were identified and harvested from the STS database (Table 1). Standard STS definitions of each risk factor and outcome were used. The timing of each patient's most recent cerebrovascular accident and myocardial infarction (if any) were recoded as separate nominal variables as were surgeon identity and diabetes mellitus control method (diet, oral, insulin, none). Race was dichotomized as Caucasian or non-Caucasian. The family history of cardiac diseases, smoking history, systemic arterial hypertension, congestive heart failure, number of diseased vessels, ejection fractions, STS mortality risks, renal function status, preoperative use of cardiac, antiplatelet, anticoagulant, and anti-inflammatory drugs (steroids) were each coded also as separate nominal values. The index of completeness of revascularization (ICOR) was computed by dividing the total number of distal vessels bypassed by the number of diseased vessels.

The institutional database was populated by trained and dedicated personnel; consequently, missing data were scarce. Data were 100% complete for the critical risk factors of interest (surgery type and sex) as well as for each major postoperative hospital outcome. Data were missing for the following variables: Caucasian race (n = 596, 4.7%), last creatinine level (n = 2,640, 20.6%), Canadian Cardiovascular Society (CCS) classification (n = 1,654, 12.9%), ejection fraction (n = 1,687, 13.2%), number of diseased vessels (n = 975, 7.6%), and STS predicted risk of mortality (n = 4, < 0.1%). To address this, several imputation strategies described by Rubin and associates [17, 18] and Molenberghs and associates [19] were employed to impute values that reflect the uncertainty surrounding the missing data. Data were assumed to be missing at random.

Interventions, Surgeons, and Surgical Technique

Each patient underwent one surgical session consisting of OPCABG or ONCABG, performed at the discretion of any of 17 faculty surgeons, who varied in their adoption of off-pump surgery. Institutional adoption of OPCABG over time is displayed in Figure 1. Off-pump CABG was performed with one of several commercially available cardiac positioning and coronary artery stabilizing devices, using techniques that have been previously described [6]. On-pump CABG was performed with standard techniques, utilizing roller head pumps, membrane oxygenators, cardiotomy suction, arterial filters, cold antegrade and retrograde blood cardioplegia, and moderate systemic hypothermia (30° to 34°C). Patients who had to be converted intraoperatively from OPCABG to ONCABG were entered into the database and analyzed according to the operation they ultimately received. Intraoperative conversion began to be measured and routinely recorded as part of the institutional database in 2004.

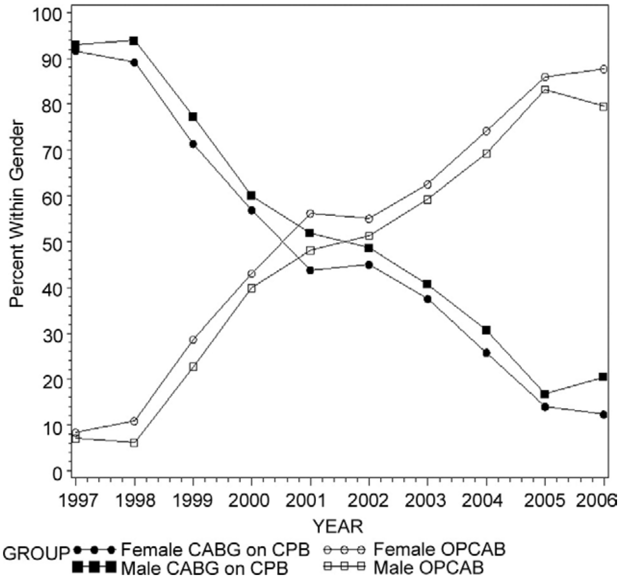

Fig 1. Trends in surgical procedure type over time by vessel group. (Solid circles = female coronary artery bypass graft surgery [CABG] on cardiopulmonary bypass [CPB]; open circles = female off-pump CABG; solid boxes = male CABG on CPB; open boxes = male off-pump CABG.)

The extent of coronary revascularization in each individual patient was typically planned by the operating surgeon in consultation with the referring cardiologist. The final number of vessels revascularized, specific location of surgical anastomoses, and type of conduit utilized were usually and ultimately determined intraoperatively by the operating surgeon in accordance with locations of coronary lesions, extent of lesions, size of target vessel, and extent of target vessel calcifications. Additionally, quality of conduits available, adequacy and suitability of radial arteries, and presence and extent of diabetes mellitus were deciding factors for utilization of only arterial conduits or a combination of arterial and venous conduits. Diabetes mellitus and severe patient obesity weighed against the use of two internal mammary arteries. The great majority of patients had at least one internal mammary artery, except in conditions of extreme hemodynamic instability; patients going into the operating room in cardiogenic shock with active closed chest massage received all venous conduits without an arterial graft. In our institution, the usual approach is to pursue the most complete revascularization procedure possible and to utilize at least a single internal mammary artery. The use of bilateral internal mammary arteries and radial arteries is increasing.

Long-Term Follow-Up

The Social Security Death Index (SSDI) is a database of death records extracted from the United States Social Security Administration's death master file extract. Persons who have died since 1963 and who had a social security number and whose death has been reported to the Social Security Administration will be listed in the SSDI.

To assess the mortality status of individual study patients, the institutional data manager first referenced the social security number of all patients in the study cohort. The SSDI may be accessed free through the Internet by entering one social security number at a time; however, arrangements were made with the SSDI whereby individual death records for all patients in the study cohort were purchased in bulk. Thus, for each patient who died before the cutoff date of March 31, 2007, a mortality date was provided. The number of days between the date of surgery and the mortality date is the primary variable of interest in the long-term portion of the study. For patients still alive at the study cutoff date, no mortality date was given, and these patients were considered to be censored for the purposes of the survival analysis. Importantly, the cause of death was not considered, nor available, in this study; thus, the study seeks to compare all-cause mortality between the surgery types.

Data Management and Statistical Analysis

All data for consecutive patients were entered into a computerized cardiac surgical database, utilizing the data fields and definitions of the STS national adult cardiac database. Checks for data quality are employed both at the institutional level and before final entry into the STS national adult cardiac database. Patients were primarily classified according to number of grafts (1 to 3 or 4 to 7) and the surgery type (OPCABG or CABG on cardiopulmonary bypass) they received. To control for potential selection bias, propensity scores, described by Blackstone [20] and D'Agostino [21] were calculated for each patient based on 40 risk factors (including surgeon identity, year of surgery, and six indicators of missingness) available preoperatively. For the propensity score calculation, a multiple logistic regression model was used nonparsimoniously to model OPCABG (yes or no) as a function of all 40 risk factors (Table 1). The resulting conditional probability of a patient receiving OPCABG is the propensity score. Importantly, because patient age is the single most reliable risk factor for long-term survival, it was left out of the propensity score calculation so that its effect was directly adjusted for in the final survival regression modeling. To account for 17 different surgeons who performed coronary artery bypass surgery during the study period, surgeon identity was included in the propensity score.

Long-term survival estimates were made at 1-, 3-, 5-, and 10-year intervals using Kaplan-Meier product-limit methods. Life-table curves were plotted for each graft/surgery type combination. After verifying the proportional hazards assumptions through Schoenfeld residual analysis, long-term survival comparisons were made using Cox proportional hazards regression models. The proportional hazards regression modeled the instantaneous hazard of death as a function of grafts (1 to 3 or 4 to 7), surgery type (OPCABG or CABG on cardiopulmonary bypass) and their interaction, adjusted for the propensity score, ICOR, and patient age. Hazard ratios were generated for grafts (1 to 3 or 4 to 7) and surgery type, along with 95% confidence intervals. The data were managed and analyzed using SAS version 9.1 (SAS Institute, Cary, North Carolina) and STATA 9.0 (Stata Corp, College Station, Texas). All statistical tests were two-sided, using an $\alpha = 0.05$ level of significance.

Results

Preoperative Patient Characteristics

Table 1 shows preoperative demographics, clinical characteristics, and risk factors for a combination of number of vessels grafted and surgery type within the cohort of 12,812 consecutive patients. The patients requiring OPCABG 1 to 3 grafts (63.3 years; n = 3,946) were older than the patients requiring CABG 1 to 3 grafts (62.4 years; n = 3,380; $p <$ 0.001), whereas the age of patients requiring OPCABG 4 to 7 grafts (62.4 years; n = 1,721) was similar to those requiring CABG 4 to 7 grafts (62.5 years; n = 3,765; $p =$ 0.78). In comparison with the group requiring OPCABG 1 to 3 grafts, the group requiring CABG 1 to 3 grafts had more females (35.3% versus 33.1%, $p = 0.046$) and a higher STS predicted risk of mortality (0.024 versus 0.022, $p = 0.022$). The group requiring OPCABG 4 to 7 grafts when compared with the group requiring CABG 4 to 7 grafts had similar numbers of females (22.8% versus 21.4%, $p = 0.24$), fewer incidences of myocardial infarction (48.8% versus 51.5%, $p = 0.04$), and a slightly higher STS predicted risk of mortality, although not statistically significant (0.021 versus 0.020, $p = 0.56$). Further, patients requiring OPCABG 1 to 3 grafts had more renal failure (8.0% versus 6.8%, $p = 0.048$), preoperative dialysis treatment (2.7% versus 1.6%, $p = 0.002$), congestive heart failure (18.9% versus 15.2%, $p < 0.001$), and cerebrovascular disease (15.8% versus 11.8%, $p = 0.002$), but less postoperative myocardial infarction (3.2% versus 5.2%, $p < 0.001$) than patients requiring CABG 1 to 3 grafts. Similarly, the group requiring OPCABG 4 to 7 grafts had more congestive heart failure (16.9% versus 14.8%, $p =$ 0.042) and cerebrovascular disease (14% versus 11%, $p =$ 0.002), and less postoperative myocardial infarction (4.0% versus 6.8%, $p < 0.001$); however, renal failure was not different among the groups (5.5% versus 6.6%, $p = 0.12$).

Table 2 shows vessel groups (1 to 3 grafts versus 4 to 7 grafts) with respect to on-pump versus off-pump and long-term survival estimates at 1, 3, 5, and 10 years of follow-up. The survival estimates at those yearly intervals reveal no discernable differences between the respective groups. An apparent sharp drop in survival at

Table 2. One-, 3-, 5-, and 10-Year Product-Limit Survival Estimates

Survival Group	1-Year Survival (95% CI)	3-Year Survival (95% CI)	5-Year Survival (95% CI)	10-Year Survival (95% CI)
CPB 1 to 3 (n = 3,380)	0.942 (0.934, 0.950)	0.900 (0.889, 0.910)	0.850 (0.837, 0.862)	0.651 (0.622, 0.679)
CPB 4 to 7 (n = 3,765)	0.951 (0.944, 0.958)	0.915 (0.905, 0.923)	0.864 (0.852, 0.875)	0.696 (0.669, 0.721)
OPCABG 1 to 3 (n = 3,946)	0.946 (0.938, 0.952)	0.894 (0.883, 0.904)	0.828 (0.812, 0.842)	0.685 (0.628, 0.735)
OPCABG 4 to 7 (n = 1,721)	0.966 (0.956, 0.973)	0.916 (0.900, 0.930)	0.856 (0.832, 0.877)	0.381 (0.017, 0.796)

CI = confidence interval; CPB = cardiopulmonary bypass; OPCABG = off-pump coronary artery bypass graft surgery.

Table 3. Cox Proportional Hazards Regression Hazard Ratio Estimates (Adjusted for Propensity Score)

Factor	Hazard Ratio for Death (95% Confidence Interval)	*p* Value
Off-pump versus on-pump	1.00 (0.88, 1.14)	0.98
4 to 7 versus 1 to 3 grafts	0.97 (0.88, 1.06)	0.49
Index of completeness of revascularization	0.85 (0.77, 0.93)	< 0.001
Patient age	1.059 (1.054, 1.063)	< 0.001

year 10 (38.1%, 95% confidence interval: 0.017 to 0.796) in the OPCABG 4 to 7 group is based on small sample sizes (n = 3) and is not statistically different from the other groups at 10 years.

Risk-Adjusted Comparisons of Outcomes

The c-index for the propensity model was 0.91, indicating that the model exhibits very good discrimination in separating dichotomies. Table 3 shows the hazard ratio for death to be equivalent between all of the OPCABG groups as compared with the CABG group ($p = 0.98$), as well as for all the 4 to 7 group as compared with the 1 to 3 group ($p = 0.49$). No interaction existed between surgery type and vessels grafted. Because no significant interactions exist, the investigators concluded that OPCABG in the 1 to 3 vessels group as well as in the 4 to 7 vessels group provided similar benefits to patients in terms of intermediate- and long-term survival benefit. In contrast, the hazard for death was highest among patients who had a lower index for completeness of revascularization ICOR (hazard ratio = 0.85, 95% confidence interval: 0.77 to 0.93, $p < 0.001$). As expected on long-term follow-up, older patients had a higher hazard ratio for death ($p < 0.001$).

Possible Confounder of the Impact of Number of Vessels and Surgical Technique on Outcomes: Completeness of Revascularization

Concerns about multivessel revascularization with OPCABG techniques have included incompleteness of revascularization. To evaluate this, the number of diseased vessels was included in the multivariable logistic regressions that generated the propensity score reported above. Moreover, an index of completeness of revascularization (ICOR) was calculated for each patient and compared between groups. The ICOR was defined as the number of distal grafts constructed divided by the number of diseased vessels reported on the preoperative coronary arteriogram. Table 1 shows that the ICOR was significantly lower among patients with 1 to 3 grafts than among patients with 4 to 7 grafts ($p < 0.001$) and was also significantly lower for patients treated with OPCABG than for those treated with ONCABG ($p < 0.001$). The longer-term clinical implications of these differences are examined in depth in this paper.

Comment

Although numerous retrospective as well as randomized prospective studies have demonstrated that OPCABG is associated with decreased risk-adjusted morbidity and mortality compared with on-pump coronary artery bypass [6, 7, 22], the overall rate of OPCABG technique utilization remains relatively low. In 2006, US surgeons performed approximately 20% of all coronary bypass operations off pump [23]. Despite improved short-term results, early adopters of OPCABG techniques continue to be challenged to exercise judgment in patient selection for application of OPCABG techniques and to ensure that such techniques should never be chosen for inappropriate reasons such as cost alone, marketing, or machismo [1].

Our increasing experience with coronary stabilization devices and our improved understanding of hemodynamic management during off-pump coronary revascularization have led to a level of skill maturation that has enabled us to expand OPCABG techniques to patients needing complex multivessel revascularization. The increased confidence of the surgeon and anesthesiologist in the management and control of hemodynamic parameters has led to a substantial shift in our overall approach in coronary revascularization in favor of OPCABG. Encouraged by our institutional retrospective observations as well as by prospective randomized clinical trials [10], we have continued to expand the utilization of off-pump techniques to the point that in 2006, 75% of patients receiving 4 to 7 vessel grafts and 87% of patients receiving 1 to 3 vessel grafts were revascularized without the use of cardiopulmonary support (Fig 1). In this study, we conducted a retrospective review of all consecutive patients who underwent isolated primary coronary artery revascularization. The objective of this study was to investigate the long-term outcome of the OPCABG patients requiring limited (1 to 3 vessels) or extensive (4 to 7 vessel) bypass operations as compared with outcomes of patients undergoing similar grafting requirements utilizing cardiopulmonary bypass.

Few and multiple-vessel OPCABG patients were similar in age and had STS predicted risk of mortality equivalent to that of the ONCABG cohorts. The number of diseased vessels in the OPCABG 1 to 3 group was less than that of the ONCABG 1 to 3 group (2.31 versus 2.45, $p < 0.001$); whereas it was slightly higher for the OPCABG 4 to 7 groups as compared with the ONCABG 4 to 7 group (2.82 versus 2.80, $p = 0.23$; see Table 1). Although there was a lower degree of ICOR in the OPCABG 1 to 3 vessel group (n = 3,946; ICOR 1.11) than in the ONCABG 1 to 3 group (n = 3,380; ICOR 1.21, $p < 0.001$), and the same applied when comparing the ICOR between the OPCABG 4 to 7 grafts group (n = 1,721; ICOR 1.56) and the ONCABG 4 to 7 grafts cohort (n = 3,765; ICOR 1.64, $p < 0.001$), the predicted risk of mortality was slightly higher in the 1 to 3 vessel OPCABG group compared with 1 to 3 vessel ONCABG group (0.024 versus 0.022, $p = 0.022$), and was also higher in the 4 to 7 vessel OPCABG as compared with the ONCABG cohort (0.021 versus 0.020, $p = 0.56$). Of great interest for the purpose of this paper is the

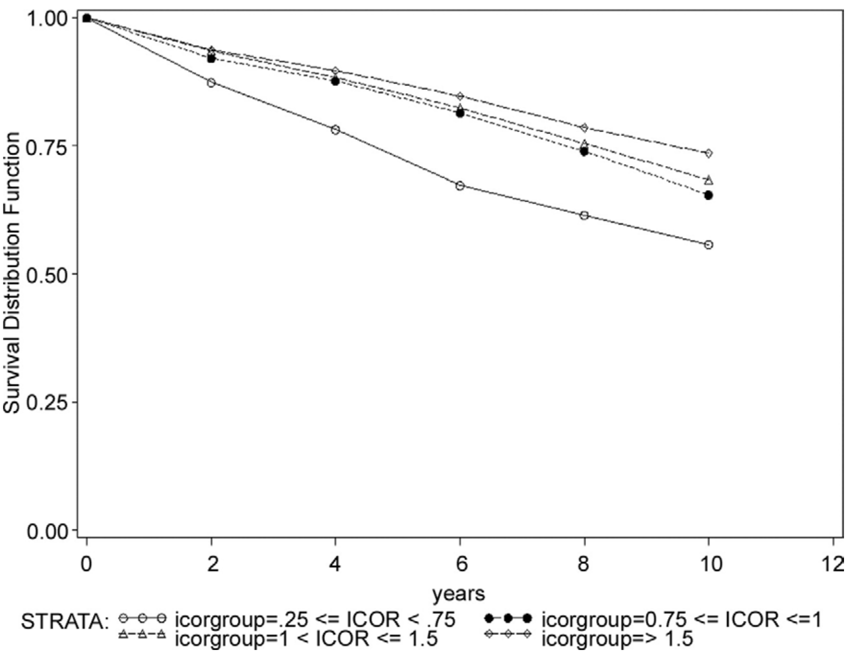

Fig 2. Life-table survival curves by number of grafts (1 to 3 or 4 to 7) and surgery type. (Open circles = index of completeness of revascularization [ICOR] group = 0.25 ≤ ICOR < 0.75; solid circles = ICOR group = 0.75 ≤ ICOR ≤ 1; triangles = ICOR group = 1 < ICOR ≤ 1.5; diamonds = ICOR group = > 1.5.)

finding that the observed long-term product-limit survival estimate was equivalent among all surgery type and vessel groups (Table 2, Fig 2). Table 3 shows that the hazard ratio for death analysis reveals that age and ICOR significantly disadvantaged long-term survival while the method or extent of revascularization did not. Additionally, life-table survival curves by ICOR ranges revealed gradual worsening of long-term survival by lower rates of ICOR (see Fig 3).

Further analysis of the data at four different intervals of postoperative survival tracking at years 1, 3, 5, and 10 reveals equivalence of survival between all the four subgroups irrespective of number of vessels grafted or methods of revascularization (Table 2). It is important to note that historically the use of on-pump revascularization has long preceded the off-pump technique particularly in the multivessel group; hence, more patients in the 1 to 3 vessel group have reached the 10-year postoperative follow-up evaluation.

This dataset confirmed equivalence in intermediate- and long-term safety and efficacy of OPCABG as a whole (1 to 7 grafts) compared with ONCABG. Most importantly, long-term survival outcomes for patients receiving multiple-vessel grafts were equivalent between the two

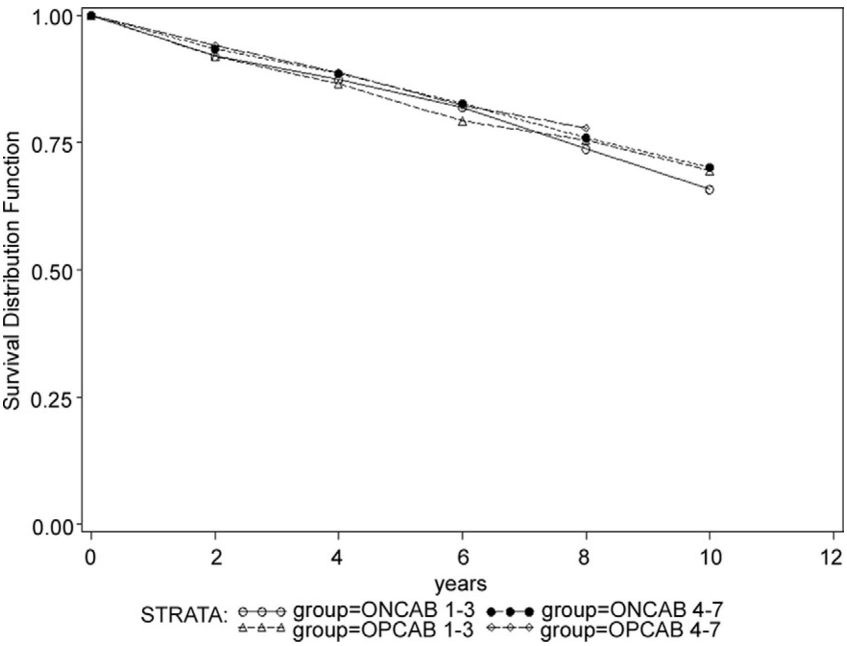

Fig 3. Life-table survival curves by index of completeness of revascularization (ICOR) ranges. (Open circles = on-pump coronary artery bypass graft surgery [ONCABG] 1 to 3; solid circles = ONCABG 4 to 7; triangles = off-pump CABG [OPCABG] 1 to 3; diamonds = OPCABG 4 to 7.)

groups. Previously reported short-term morbidity and mortality benefits of OPCABG techniques are maintained at the intermediate- and long-term levels for all patients undergoing off-pump CABG. From a historical perspective, it is of interest to note that the findings of Jones and associates [24, 25] reported nearly 3 decades ago revealed that completeness of revascularization was a key determinant in long-term patient survival. That stands true today despite all of the advancements in diagnostic and therapeutic interventions available in the operating rooms and the postoperative care units.

Limitations

This study has several limitations. Its retrospective nature does not permit complete accounting for all sources of bias, despite advanced statistical methodology designed to correct for both treatment selection bias and potential confounders of outcomes in preplanned analyses. Another limitation of this study is the utilization of all-cause mortality data, reliably obtained from the Social Security Death Index, rather than the more specific cardiac-related mortalities, which were not readily available for the purpose of this study. The study also did not address the relative incidence of nonfatal cardiac-related events and the requirements for repeat revascularization between the respective groups during the follow-up period. In addition, the database utilized in this study reported surgical cases according to the ultimate surgery type performed. This meant that patients whose coronary revascularization was initially attempted without cardiopulmonary bypass and who required conversion to cardiopulmonary bypass (typically owing to hemodynamic instability) were included in the ONCABG group. That may disadvantage ONCABG in the comparison of outcomes with OPCABG. Reciprocally, patients converted from ONCABG to OPCABG (usually because of intraoperative discovery of severe aortic atherosclerosis) were included from the OPCABG group. Additionally, our data analysis did not address the extent of coronary calcification and the utilization of coronary endarterectomy in each group or the incidence of conversion from OPCABG to ONCABG in the occasional cases of severe calcified coronary arteries. Such patients' potential increased incidence of complications may disadvantage one method for revascularization in comparison with the other. The database does not allow reconciliation of these data to an intention-to-treat analysis. Fortunately, intraoperative conversion is an infrequent event, affecting approximately 2% of cases [9]. Finally, although the 17 surgeons who performed coronary revascularization in this study varied greatly in their interest in OPCABG (several rarely performed OPCABG, whereas several used OPCABG in the majority of their cases), our center has maintained a strong institutional interest in OPCABG since 1997. Thus, faculty surgeons in the present study may have average experience with OPCABG that exceeds the national norm, limiting the ability to generalize these results.

In conclusion, OPCABG techniques have been shown here to provide intermediate- and long-term survival trends equivalent to those for patients treated on pump. This equivalence in survival applies for patients undergoing single-, or double-, or multiple-vessel OPCABG revascularization. The unfounded concern that the short-term benefits of OPCABG techniques may jeopardize the long-term survival of the coronary artery bypass patient can no longer be supported. Indeed, our results ascertain the intermediate- and long-term survival equivalence of off pump to on pump. For patients who need limited or extensive revascularization, cardiopulmonary bypass techniques do not contribute an intermediate- or long-term survival advantage; therefore, the perceived notion of special benefits offered by cardiopulmonary bypass cannot be supported by our data. Further studies are still required to address important unanswered questions on the relative incidence of nonfatal cardiac-related events and the requirements for repeat revascularization between the respective groups during the follow-up periods.

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