Patient Selection and Current Practice Strategy for Off-pump Coronary Artery Bypass Surgery

Mitchell J. Magee, MD; Laura P. Coombs, PhD; Eric D. Peterson, MD; Michael J. Mack, MD

Objective—Previous studies comparing off-pump coronary artery bypass surgery (OPCABG) to conventional techniques utilizing cardiopulmonary bypass (CABG-CPB) have failed to provide patient selection guidelines. We sought to determine guidelines, attempting to rectify the limitations of previous studies.

Methods and Results—A retrospective analysis of prospectively collected data from the Society of Thoracic Surgeons National Database, from January 1999 through December 2000, identified 204 602 multivessel coronary artery bypass (CABG) patients. Unadjusted and risk-adjusted odds ratios (OR) were calculated to compare OPCABG and CABG-CPB morbidity and mortality. A propensity model was developed to identify factors associated with selection for OPCABG. All off-pump patients were pair-matched with on-pump patients based on their propensity to receive an off-pump procedure. Off-pump patients, 8.8% of the total, had significantly different patient characteristics than the on-pump group. Characteristics associated with OPCABG selection included fewer diseased vessels, absence of left main disease, fewer bypass grafts, no previous CABG, older age, chronic lung disease, and renal failure. Unadjusted and risk-adjusted odds ratios indicate a significant off-pump survival benefit and decreased morbidity including stroke and renal failure in the overall group. Propensity matching also showed a significant OPCABG survival benefit [OR (95% CI) 0.83 (0.72, 0.96)]. Subgroup analysis of propensity-matched groups identified off-pump survival benefits in patients with previous CABG (OR=0.53), diabetics (OR=0.66), LVEF between 30% to 50% (OR=0.75), females (OR=0.79), and age 66 to 75 years (OR=0.80).

Conclusion—OPCABG imparts some survival benefit to most patient subgroups. Higher risk patients including those undergoing reoperative CABG, diabetics, and the elderly may gain the most benefit. **(*Circulation*. 2003;108[suppl II]: II-9-II-14.)**

Key Words: coronary disease ■ bypass ■ surgery ■ cardiopulmonary bypass ■ complications

Localized stabilization of the beating heart allowed for the limited successful introduction of off-pump coronary artery bypass surgery (OPCABG) prior to widespread adoption of cardiopulmonary bypass (CPB) in the late 1960s.[1] The still, bloodless field provided by cardioplegic arrest of the heart combined with the technological advances of cardiopulmonary bypass around the same time, overshadowed the off-pump approach to become the dominant modality in coronary surgery.[2,3] Resurgence in beating heart surgery began in the early 1990s in an attempt to decrease the morbidity associated with CABG without jeopardizing benefits, and was spurred by the observed benefits of avoiding CPB and its associated deleterious effects.[4–6] Early development of off-pump coronary artery bypass was hindered by crude instrumentation, as well as limited exposure through small incisions. Technological advancements have significantly facilitated the performance of beating heart surgery through a sternotomy in the past 8 years. Although numerous reports have demonstrated the safety and efficacy of off-pump coronary artery bypass and the associated benefits of avoiding CPB, large, randomized trials comparing the two techniques have been logistically difficult due to the reluctance of patients, their referring physicians, and surgeons to participate because of the perceived benefits of off-pump surgery.[7–10]

Through a large retrospective study utilizing prospectively collected data from the Society of Thoracic Surgery database, we sought first to analyze the contemporary use of off-pump surgery in patients undergoing multivessel coronary artery bypass. Second, we sought to determine the benefits in terms of mortality and morbidity associated with beating heart techniques and avoidance of CPB. Finally, we examined subsets of patients most likely to benefit from off-pump surgery.

Methods

The STS National Cardiac Database

The STS National Cardiac Database (NCD) was established as a voluntary database in 1989 for the purpose of outcomes assessment following adult cardiac surgery.[11] STS NCD data are harvested semiannually from a majority of U.S. hospitals performing open

From the Cardiopulmonary Research Science and Technology Institute (CRSTI), Dallas, Texas (M.J.M., M.J.M.); and Duke Clinical Research Institute, Duke University School of Medicine, Durham, North Carolina (L.P.C., E.D.P.).

Correspondence to: Mitchell J. Magee, MD, 7777 Forest Lane, Suite A323, Dallas, Texas 75230. Phone: (972)566-4866, Fax: (972)490-5457, E-mail: mmagee@csant.com

© 2003 American Heart Association, Inc.

Circulation is available at http://www.circulationaha.org

DOI: 10.1161/01.cir.0000089187.51855.77

TABLE 1. On-Pump Versus Off-Pump Patient Characteristics

Variable	Level	On-Pump (N=186,633)	Off-Pump (N=17,969)	*P*-value
Number of bypass grafts	Two	13.9	34.6	<0.0001
	Three	34.3	39.2	
	Four or more	51.8	26.2	
Age	Median	66	68	<0.0001
	25th/75th	57/73	59/75	
Congestive heart failure	Yes	13.6	13.2	<0.0001
Cardiogenic shock	Yes	2.9	1.7	<0.0001
Cerebrovascular accident	Yes	6.8	7.5	<0.0001
Cerebrovascular disease	Yes	11.2	14.0	<0.0001
Chronic lung disease	Yes	14.4	17.1	<0.0001
NYHA classification	I	13.5	12.8	<0.0001
	II	15.6	17.3	
	III	35.6	37.3	
	IV	22.7	25.4	
Current smoker	Yes	20.9	19.7	<0.0001
Diabetes	Yes	33.4	30.9	<0.0001
Diabetes control	Oral	17.3	15.7	<0.0001
	Insulin	10.6	10.0	
Dialysis	Yes	1.1	1.6	<0.0001
Ejection fraction	Median	50	53	<0.0001
	25th/75th	40/60	45/60	
Gender	Female	27.7	31.6	<0.0001
Intra-aortic balloon pump	Yes	9.8	6.4	<0.0001
Immunosuppressive treatment	Yes	1.7	2.8	<0.0001
Left main disease	Yes	22.7	20.3	<0.0001
Recent myocardial infarction	<1 day	2.8	1.6	<0.0001
Number diseased vessels	One	1.7	5.5	<0.0001
	Two	20.2	30.9	
	Three	70.8	61.6	
Peripheral vascular disease	Yes	15.4	16.5	<0.0001
Prior PTCA	Yes	17.1	20.1	<0.0001
Race	Caucasian	85.2	89.2	<0.0001
	Black	4.3	3.8	
	Hispanic	2.5	1.9	
Renal failure	Yes	4.5	5.7	<0.0001
Operative status	Emergent	5.1	3.0	<0.0001
	Salvage	0.3	0.1	

heart surgery. Clinical patient data are entered at the sites using uniform definitions and certified software systems. Data includes 30-day, but no longer term, postoperative follow-up. Data quality standards must be met before a local dataset can be entered into the aggregate national dataset. Data are warehoused at the Duke Clinical Research Institute in Durham, NC, which produces semi-annual site-specific reports to STS participants for outcomes analysis and quality improvement efforts.

Patients

A retrospective review of prospectively collected data voluntarily submitted to the Society of Thoracic Surgeons (STS) National Cardiac Database identified 234 145 patients that underwent isolated coronary artery bypass (CABG) surgery from January 1999 through December 2000. All single vessel CABG procedures as well as any CABG combined with another cardiac surgical procedure, such as valve replacement, were excluded. The total number of multivessel isolated CABG procedures with complete data suitable for analysis was 204 602 of which 91.22% (186 663/204 602) were performed in a conventional fashion with cardiopulmonary bypass (CABG-CPB), whereas 8.78% (17969/204602) were performed without cardiopulmonary bypass (OPCABG). For purposes of this study, an OPCABG procedure was defined based on a reported cardiopulmonary bypass time of zero, and use of cardioplegia as “no”. Selection criteria utilized in determining which CABG procedure individual patients would receive, with or without CPB, was neither specified nor

TABLE 2. OPCAB Selection Propensity Model

Risk Factor	Odds Ratio	*t*-statistic	*P*-value
Number of grafts	0.51	−62.98	<0.0001
Reoperation (one)	0.40	−21.48	<0.0001
Number of diseased vessels	0.70	−20.25	<0.0001
Age	1.02	20.04	<0.0001
Left main disease	0.78	−11.48	<0.0001
Chronic lung disease	1.29	9.96	<0.0001
Renal failure/dialysis	1.32	9.44	<0.0001
Intra-aortic balloon pump	0.75	−5.92	<0.0001
Hypercholesterolemia	1.10	4.89	<0.0001
Reoperation (two or greater)	0.64	−3.77	0.0002
Immunosuppressive Rx	1.23	3.75	0.0002
Diabetes–Insulin Rx	0.90	−3.65	0.0003
Ejection fraction	1.00	3.37	0.0008
Peripheral or cerebral vascular disease	1.06	3.36	0.0008
Diabetes–Oral Rx	0.92	−3.25	0.0012
Male	1.06	2.24	0.0248
Race–Black	1.11	2.11	0.0353
Recent myocardial infarction	0.98	−2.07	0.0383
CVA	1.08	2.04	0.0413

obtainable from the database. Treatment assignment of individual patients was at the discretion of each operating surgeon and varied accordingly by patient, surgeon, and institution; however medical comorbidities that increase the risks of CPB are often used to select patients for OPCABG. The CABG-CPB and OPCABG patients were contemporaneous and not sequential cohorts.

Patient data were collected and analyzed according to The Society of Thoracic Surgeons (STS) National Cardiac Database guidelines and definitions (http://www.ctsnet.org/doc/2167). Outcomes definitions in the STS NCD include operative mortality (determined as death within 30 days of surgery, regardless of location (in-hospital or out of hospital) or death in-hospital regardless of length of stay), stroke (new-onset CVA persisting >72 hours); renal failure (acute postoperative renal insufficiency with one or more of: (1) increase in serum creatinine >2.0; (2) 50% or greater increase in creatinine over baseline preoperative value; (3) new requirement for dialysis); re-operation (reexploration for any reason including bleeding, graft occlusion, other cardiac problem, other noncardiac problem), and prolonged ventilation (pulmonary insufficiency requiring ventilatory support for 48 hours or more). Preoperative data included diabetes, chronic pulmonary disease (COPD), prior cerebrovascular event (CVA), peripheral vascular disease (PVD), obesity, hypertension, hypercholesterolemia, family history of CAD, renal failure, renal failure on dialysis, current smoking, prior myocardial infarction, preoperative IABP use, preoperative cardiogenic shock, left main coronary disease, age, gender, left ventricular function, and prior CABG

Statistical Analysis

Patients were grouped and compared according to surgical treatment, OPCABG versus CABG-CPB. First, preoperative patient characteristics and individual risk factors, intraoperative course, and operative outcomes including mortality were compared. Data are reported as a percentage for categorical variables or as the median and first and third quartile for continuous variables. Categorical variables were compared using a chi-square test and comparisons of continuous data were done using the Wilcoxon rank sum test. All tests are two-sided. probability values less than or equal to 0.05 were considered significant.

Unadjusted odds ratios (OR) and confidence intervals (CI) to compare off-pump OPCABG and on-pump CABG-CPB procedures were calculated for several outcome measures including operative mortality and four morbidities. Patients were also divided into three clinically meaningful risk groups based on the current STS mortality model, and odds ratios and confidence intervals were calculated for mortality within these risk groups.

To control for selection bias as a result of nonrandom treatment assignment, two methods were used: risk-adjustment and propensity analysis. For risk-adjustment, a hierarchical mixed-effects logistic regression model was used to determine the effect of off-pump surgery after simultaneously adjusting for site as well as up to 27 preoperative patient risk factors contained in the STS CABG mortality and morbidity models.

For the propensity analysis, a hierarchical mixed-effects logistic regression model, which included both site and patient factors, was used to create OPCABG-selection propensity scores (ie, probability of receiving an off-pump procedure). Patients whose status were classified as emergent or salvage were excluded from the propensity-matched analysis. After these exclusions, the 16,937 off-pump patients were all pair-matched (in a 1:1 ratio) to the on-pump patient with the most similar propensity to receive an off-pump procedure. Propensity scores were required to be within 0.01 of each other to be considered a match. This propensity score analysis allows for the comparison of outcomes between groups that have a similar likelihood of receiving off-pump surgery. Once patients were matched, conditional logistic regression was then used to determine the overall effect of off-pump surgery for the resulting 16 937 matched pairs. Subgroups were selected for further analyses based on results from previous studies of selected high risk patient populations. Odds ratios and confidence intervals for subgroups were calculated by adding interaction terms to the logistic regression model.

Results

Patient Population

Overall, the on-pump and off-pump groups were widely disparate. Patients receiving off-pump surgery had significantly more single and double vessel rather than triple vessel

TABLE 3. Unadjusted and Risk-Group Survival Outcomes

	On-pump		Off-pump		
	Total	% Mortality	Total	% Mortality	OR (95% CI)
Overall Risk Group	186 633	2.91	17 969	2.40	0.82 (0.74, 0.91)
<1	48 630	0.49	4754	0.34	0.69 (0.41, 1.14)
1–2.5	72 686	1.38	6682	1.35	0.98 (0.79, 1.22)
2.5–5	39 432	3.71	3916	3.06	0.82 (0.68, 0.99)
>5	25 885	10.56	2617	7.87	0.72 (0.62, 0.84)

TABLE 4. Unadjusted and Risk-Adjusted Postoperative Morbidity

Complication	On-pump Incidence (%)	Off-pump Incidence (%)	Unadjusted Outcome OR (95% CI)	Risk-Adjusted Outcome OR (95% CI)
Stroke	1.75	1.23	0.70 (0.61, 0.80)	0.65 (0.56, 0.75)
Renal failure	3.97	3.85	0.97 (0.90, 1.05)	0.82 (0.75, 0.89)
Reoperation for any reason	2.74	2.01	0.73 (0.66, 0.81)	0.74 (0.69, 0.80)
Prolonged ventilation	6.77	4.71	0.68 (0.64, 0.73)	0.62 (0.57, 0.67)

coronary disease, less left main disease, less recent myocardial infarction, less pre-operative shock and intra-aortic balloon pump use, less emergent status, and less diabetes. The off-pump patient group also were older and more often female, had more class III and IV heart failure, more chronic lung disease, more history of stroke and cerebral vascular disease, renal failure, peripheral vascular disease, and previous percutaneous interventions (PTCA) (Table 1).

Characteristics associated with off-pump selection in the hierarchical logistic regression model included fewer diseased vessels, fewer bypass grafts, no prior cardiac surgery, older age, absence of left main coronary disease, chronic lung disease (COPD), and renal failure (Table 2).

Outcomes

Unadjusted odds ratios indicate an off-pump survival benefit in the overall group [OR=0.82, 95%CI=0.74, 0.91] that persisted and was more pronounced after risk adjustment [OR=0.76, 95%CI=0.68, 0.84]. Risk stratification of the entire group into 4 mortality risk groups indicates an increasing survival benefit of off-pump surgery as predicted risk increases (Table 3). Off-pump patients also had less morbidity that was more pronounced with risk-adjustment including a 40% reduction in risk of stroke, a 20% reduced risk of post-operative renal failure, a 40% relative risk reduction in the incidence of prolonged ventilation, and a 30% relative risk reduction in reoperation (Table 4).

There was a 100% match on propensity score between the off-pump and on-pump patients. Patient characteristics for the propensity-matched pairs were similar (Table 5). The survival benefit of off-pump surgery based on the conditional logistic regression model using the propensity-matched pairs was significant with a computed odds ratio of 0.833 (95% CI (0.724, 0.957)). Subgroup analysis of propensity-matched groups identified off-pump survival benefits in many patient groups including those with previous CABG [OR 0.53 (CI 0.32 to 0.87)], diabetics [0.66 (0.52 to 0.85)], LVEF between 30% to 50% [0.75 (0.59 to 0.95)], females [0.79 (0.64 to 0.99), and age 66 to 75 years [0.80 (0.70 to 0.93)] (Figure 1).

Discussion

This analysis represents the largest contemporary multicenter comparison of outcomes in multivessel coronary artery bypass patients performed with and without cardiopulmonary bypass. As shown in previous studies, early operative mortality without adjusting for risk was less in the off-pump group compared with the on-pump group, 2.4% versus 2.9%. Morbidity was also decreased in the off-pump group including decreased incidence of stroke, renal failure, prolonged ventilation, and reoperation. The significance of these findings is limited by the markedly different patient characteristics in the off-pump and on-pump treatment groups as expected in any large nonrandomized comparison, however, risk adjustment helps to offset some of these differences. The mortality and morbidity benefits of off-pump surgery per-

TABLE 5. Patient Characteristics of OPCAB Propensity-Matched Groups

Variable	Level	On-Pump (N=16 937)	Off-Pump (N=16 937)	*P*-value
Number of grafts	Two	30.8	34.0	<0.0001
	Three	42.8	39.3	
	Four or more	26.4	26.7	
Age	Median	68	68	0.3892
	$25^{th}/75^{th}$	59/75	59/75	
Gender	Female	31.3	31.4	0.7786
Chronic lung disease	Yes	16.3	16.9	<0.0001
Left main disease	Yes	19.9	19.7	<0.0001
Number of diseased vessels	One	4.4	5.3	<0.0001
	Two	31.8	30.6	
	Three	60.2	62.0	
Renal failure	Yes	5.4	5.6	0.3252

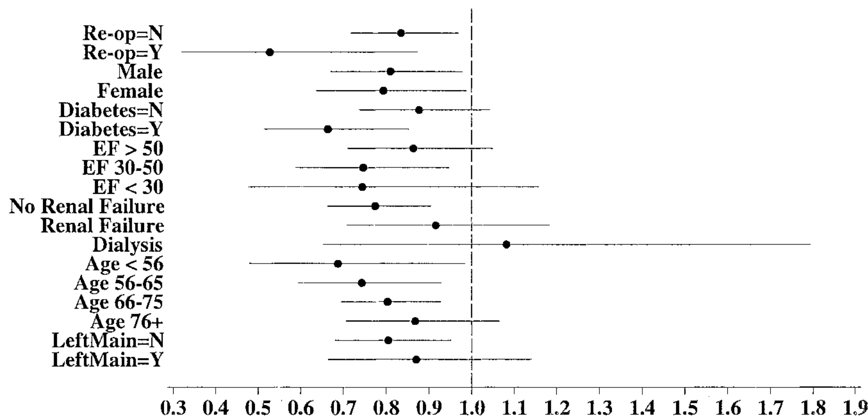

Figure 1. Subgroup analysis of propensity-matched patients. OPCAB propensity-matched patient groups (excludes emergent/salvage). Odds ratios and 95% confidence intervals. Off-pump=16 937; on-pump=16 937

sisted with risk-adjustment and in addition were more significant.

We also identified those specific patient characteristics that influenced selection of patients for off-pump surgery. The factors associated with OPCAB selection included among others: no prior cardiac surgery, fewer numbers of diseased vessels and corresponding need for fewer bypass grafts, absence of left main coronary disease, absence of preoperative intra-aortic balloon pump (IABP), older age, presence of chronic lung disease (COPD), and renal failure. These characteristics were used to develop propensity scores to computer match off-pump patients with patients in the on-pump group who had equivalent likelihood to receive off-pump surgery, thereby minimizing differences between the two treatment groups inherent in nonrandom selection. The resulting propensity-matched pairs represent comparable patient populations with similar characteristics for comparison of treatment. The survival benefit of off-pump surgery in the propensity-matched analysis was similar to that found in other studies (OR=0.83).

A prime objective of this study was to identify subgroups of patients who, based on projected improved outcomes, should be preferentially selected for off-pump or on-pump coronary artery bypass surgery. Previous studies have shown that high-risk coronary artery bypass patients may particularly benefit from avoiding cardiopulmonary bypass.[12–15] Risk stratification into four risk groups based on predicted operative mortality revealed a significant survival benefit of off-pump surgery as predicted risk of mortality increased. Lower-risk patients as a group also appear to benefit from off-pump surgery but this comparison lacked statistical significance because of wide confidence intervals. This may be a result of greater diversity within the low-risk groups representing some patient characteristics that predispose benefit and others that do not. Note that no risk group had significantly better survival or trended toward better outcomes with on-pump surgery.

Subgroup analysis of the propensity-matched pairs, in further attempts to identify specific patients who might derive greater benefit from off-pump or on-pump surgery, revealed no group that failed to benefit from off-pump surgery, with the exception perhaps of dialysis patients. Because of the relatively small number of dialysis patients in this study, the benefit of off-pump surgery in this high-risk subgroup is inconclusive.

Patients that receive the most survival benefit from off-pump surgery include those with previous CABG (OR=0.53), diabetics (OR=0.66), mild to moderate left ventricular dysfunction (OR=0.75), females (OR=0.79), and age 66 to 75 years (OR=0.80).

The small number of patients in the off-pump group (8.8% of the total), relative to the on-pump group may be an additional limitation of this study, although any impact this may have on the conclusions is not apparent. A larger cohort of off-pump patients may be associated with different selection criteria that may in turn alter the propensity analysis. Factors not taken into account in this retrospective analysis due to limitations of the database and that may impact conclusions include (1) variations in coronary anatomy such as calcified, intramyocardial, or small coronary arteries, (2) variations in individual surgeon skill and experience, (3) long-term patency and event-free survival. These questions can only be answered in a large, multicenter, prospective, randomized trial with long-term follow-up. The limited adoption of off-pump surgery, despite apparent benefits as demonstrated clearly in this large, contemporary, retrospective, multicenter comparison with sophisticated methods to control for nonrandom treatment selection bias, suggests the need and timeliness for such a study.

References

1. Kolessov VI. Mammary artery-coronary artery anastomosis as a method of treatment for angina pectoris. *J Thorac Cardiovasc Surg* 1967;54: 535–544.
2. Johnson WD, Flemma RJ, Harding HW, Cooper GN, Lepley D Jr. Surgical principles in the direct reconstruction of the left coronary flow. *Ann Thorac Surg.* 1970;10:141–152.
3. Favaloro RG, Effler DB, Groves LK, Shelton WC, Sones FM Jr. Direct myocardial revascularization by saphenous vein graft. Present operative techniques and indications. *Ann Thorac Surg.* 1970;10:97–111.
4. Buffolo E, Andrade JC, Branco JN, Aguiar LF, Ribeiro EE, Jantene AD. Myocardial revascularization without extracorporeal circulation. Seven year experience in 593 cases. *Eur J Cardiothorac Surg.* 1990; 4:504–508.
5. Benetti F, Naselli G, Wood M, et al. Direct myocardial revascularization without extracorporeal circulation: experience in 700 patients. *Chest.* 1991;100:312–316.

6. Edmunds LH. Inflammatory response to cardiopulmonary bypass. *Ann Thorac Surg.* 1998;66:S12–16.
7. Puskas JD, Wright CE, Ronson RS, et al. Off-pump multivessel coronary bypass via sternotomy is safe and effective. *Ann Thorac Surg.* 1998;66: 1068–1072.
8. Magee MJ, Jablonski KA, Stamou SC, et al. Elimination of cardiopulmonary bypass improves early survival for multivessel coronary artery bypass patients *Ann Thorac Surg.* 2002;73:1196–1203.
9. Plomondon ME, Cleveland JC, Ludwig ST, et al. Off pump coronary artery bypass is associated with improved risk-adjusted outcomes. *Ann Thorac Surg.* 2001;72:114–119.
10. Calafiore AM, Di Mauro M, Contini M, et al. Myocardial revascularization with and without cardiopulmonary bypass in multivessel disease: impact of the strategy on early outcome. *Ann Thorac Surg.* 2001;72:456–463.
11. Ferguson TBJr, Dziuban SW, Edwards FH, et al. The STS National Database: current changes and challenges for the new millennium. *Ann Thorac Surg.* 2000;69:680–691.
12. Stamou SC, Corso PJ. Coronary revascularization without cardiopulmonary bypass in high-risk patients: a route to the future. *Ann Thorac Surg.* 2001;71:1056–1061.
13. Yokoyama T, Baumgartner FJ, Gheissari A, et al. Off-pump versus on-pump coronary bypass in high-risk subgroups. *Ann Thorac Surg.* 2001;72:1630–1635.
14. Koutlas TC, Elbeery JR, Williams JM, et al. Myocardial revascularization in the elderly using beating heart coronary artery bypass surgery. *Ann Thorac Surg.* 2000;69:1042–1047.
15. Trehan N, Mishra YK, Malhotra R, et al. Off-pump redo coronary artery bypass grafting. *Ann Thorac Surg.* 2000;70:1026–1029.