Off-Pump Coronary Bypass Provides Reduced Mortality and Morbidity and Equivalent 10-Year Survival

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Background. **This study compared in-hospital major adverse cardiac events (MACE) and long-term survival after off-pump (OPCAB) vs on-pump (CPB) coronary artery bypass grafting (CABG).**

Methods. **Reviewed were 12,812 consecutive isolated CABG patients from 1997 to 2006. A propensity score (PS), including 40 preoperative risk factors, balanced characteristics between OPCAB and CPB groups. Multiple logistic regression models tested whether gender or surgery type, or their interaction, were associated with in-hospital mortality and MACE. A proportional hazards regression model and Kaplan-Meier curves related long-term survival with gender, surgery type, and their interaction, adjusted for PS and age.**

Results. **OPCAB was associated with a significant reduction in operative mortality (adjusted odds ratio [AOR], 0.68; $p = 0.045$), stroke (AOR, 0.48; $p < 0.001$), and MACE (AOR, 0.66; $p = 0.018$). Female gender was associated with higher rates of death (AOR, 1.93), stroke (AOR, 1.82), myocardial infarction (AOR, 2.19), and MACE (AOR, 1.97; each $p < 0.001$). Women disproportionately benefited from OPCAB in operative mortality ($p = 0.04$). Odds of death for women on CPB were higher than for women treated with OPCAB (AOR, 2.07, $p = 0.005$). Odds of death for men on CPB were not significantly higher than for men treated with OPCAB (AOR, 1.16, $p = 0.51$). Male gender was associated with longer-term survival ($p = .011$), but surgery type (OPCAB vs CPB) was not ($p = 0.23$).**

Conclusions. **OPCAB provides significant early mortality and morbidity advantages, especially for women. During the 10-year follow-up, OPCAB and CPB result in similar survival, regardless of gender.**

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Comparisons of early outcomes for male and female patients undergoing coronary artery bypass grafting (CABG) have, with few exceptions [1, 2], shown a higher morbidity and mortality for women [3–7]. Attempting to reduce morbidity and mortality attributable to cardiopulmonary bypass (CPB) [8–10], surgeons in the United States performed approximately 20% of all CABG operations off-pump—without the use of CPB (OPCAB)—in 2006 [11].

Randomized trials, usually enrolling predominantly low-risk patients, have demonstrated reduced early morbidity after OPCAB compared with CABG on CPB [12–15]. However, these studies have inadequate statistical power to evaluate gender-specific outcomes or differences in infrequently occurring end points such as operative mortality. Previous retrospective reviews of large observational studies have demonstrated that OPCAB is associated with decreased early risk-adjusted morbidity and mortality compared with CABG on CPB [16–19], but few have focused on outcomes among women [20, 21]. None have examined long-term survival after OPCAB vs CABG on CPB beyond 12 months.

The present study was conducted to compare in-hospital outcomes for men and women having OPCAB vs CPB and to determine whether either gender or surgery type affect long-term survival up to 10 years after CABG.

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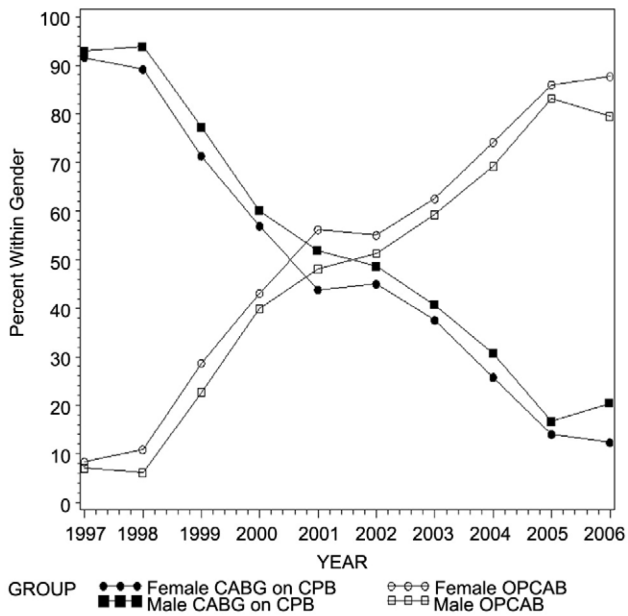

Fig 1. Longitudinal adoption of off-pump (OPCAB) procedures (clear symbols) compared with on-pump (CPB, filled symbols) procedures for coronary artery bypass grafting (CABG) between women (circles) and men (squares).

Material and Methods

Inclusions

The Society of Thoracic Surgeons (STS) National Adult Cardiac Database was queried for all patients who underwent primary isolated CABG at Emory University Hospital or Emory Crawford Long Hospital between January 1, 1997, and December 30, 2006. The study cohort consisted of 12,812 consecutive patients, including patients with emergency and urgent status. The time frame was chosen to include the entire period during which OPCAB procedures were performed at the institution, including the earliest learning curve.

Medical records from this retrospective, single-center cohort study included demographic data, preexisting comorbidities, surgeon identity, operative strategy, and clinical outcomes. The Emory University Institutional Review Board approved the study in compliance with HIPAA (Health Insurance Portability and Accountability Act) regulations and the Declaration of Helsinki and waived individual patient consent.

Interventions, Surgeons, and Surgical Technique

Each patient underwent one surgical session consisting of OPCAB or CABG on CPB, performed at the discretion of any of 17 faculty surgeons, who varied in their adoption of the off-pump procedure. Institutional adoption of OPCAB over time is displayed in Figure 1. OPCAB was performed with one of several commercially available cardiac positioning and coronary artery stabilizing devices, using techniques that have been previously described [12]. Conventional CABG on CPB 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 were converted intraoperatively from OPCAB to CABG on CPB or from CABG on CPB to OPCAB were entered into the database and analyzed according to the operation they ultimately received. Intraoperative conversion began to be routinely recorded as part of the institutional database in 2004, when a data field for conversion was introduced into the STS National Adult Cardiac Database.

Long-Term Follow-Up

The Social Security Death Index (SSDI) is a public-use national database of death records extracted from the United States Social Security Administration's (SSA) Death Master File Extract. Persons who have died since 1963 who had a Social Security Number and whose death has been reported to the SSA will be listed in the SSDI. Thus, for each patient that died before the cutoff date of March 31, 2007, a mortality date was provided, allowing construction of Kaplan-Meier long-term survival curves. Cause of death was not considered; this study sought to compare all-cause mortality between genders and between the types of operation.

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 most recent myocardial infarction (MI), if any, were reparameterized as separate nominal variables. Surgeon identity, diabetes control method (diet, oral, insulin, none), and type of unstable angina were also treated as nominal variables. Race was dichotomized to Caucasian or non-Caucasian.

The institutional database was maintained by trained and dedicated personnel; consequently, missing data were scarce. Data were 100% complete for the critical risk factors of interest (type of operation and gender) 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 = 2640, 20.6%), Canadian Cardiovascular Society Classification (n = 1654, 12.9%), ejection fraction (n = 1687, 13.2%), number of diseased vessels (n = 975, 7.6%), and STS predicted risk of mortality (n = 4, < 0.1%).

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 used both at the institutional level and before final entry into the STS National Adult Cardiac Database. Multiple imputation strategies [22, 23] were used to impute values that reflect the uncertainty surrounding the missing data.

Table 1. Preoperative Patient Characteristics by Gender and Surgery Type

					p Value	
Risk Factor[b]	F/CPB	F/OPCAB	M/CPB	M/OPCAB	Gender	OPCAB
Patients, No.	1924	1786	5221	3881		
Patient age, mean (SD), years	64.8 (11.0)	65.0 (11.9)	61.6 (10.5)	62.1 (10.9)	<0.001	0.003
Last creatinine, mean (SD) mg/dL[a]	1.10 (0.87)	1.24 (1.42)	1.24 (0.97)	1.26 (1.13)	0.004	0.043
Ejection fraction, mean (SD)[a]	0.508 (0.127)	0.528 (0.122)	0.490 (0.130)	0.499 (0.124)	<0.001	<0.001
Diseased vessels, mean (SD) No.[a]	3.57 (0.71)	3.38 (0.77)	3.65 (0.63)	3.50 (0.70)	<0.001	<0.001
STS predicted mortality, mean (SD)[a]	.030 (.036)	.033 (0.04)	.018 (.027)	.018 (.026)	<0.001	0.001
Caucasian race, No. (%)[a]	1467 (80.2)	1302 (74.9)	4324 (87.8)	3176 (85.3)	<0.001	<0.001
Cerebrovascular disease, No. (%)	279 (14.5%)	355 (19.9)	536 (10.3)	507 (13.1)	<0.001	<0.001
CVA, No. (%)	177 (9.2)	212 (11.9)	333 (6.4)	299 (7.7	<0.001	<0.001
Diabetes, No. (%)	834 (43.4)	750 (42.0)	1701 (32.6)	1269 (32.7)	<0.001	0.86
Diabetes control, No. (%)						
No control	112 (0.90)	58 (3.25)	235 (4.5)	125 (4.5)	<0.001	<0.001
Diet	62 (3.22)	63 (3.5)	154 (3.0)	104 (2.7)		
Oral	353 (18.4)	348 (19.5)	880 (16.9)	683 (17.6)		
Insulin	307 (16.0)	281 (15.7)	431 (8.3)	357 (9.2)		
Family Hx CAD, No. (%)	964 (50.1)	711 (39.8)	2386 (45.7)	1352 (34.8)	<0.001	<0.001
Hypertension, No. (%)	1535 (79.8)	1518 (85.0)	3645 (69.8)	2958 (76.2)	<0.001	<0.001
PVD, No. (%)	146 (7.6)	223 (12.5)	296 (5.7)	410 (10.6)	<0.001	<0.001
Renal failure, No. (%)	131 (6.8)	147 (8.2)	344 (6.6)	261 (6.7)	0.09	0.22
Dialysis, No. (%)	31 (1.6)	68 (3.8)	56 (1.1)	64 (1.7)	<0.001	<0.001
Current smoker, No. (%)	454 (23.6)	443 (24.8)	1324 (25.4)	1118 (28.8)	0.002	<0.001
Angina, No. (%)	1675 (87.1)	1577 (88.3)	4401 (84.3)	3196 (82.4)	<0.001	0.20
CCS class 5, No. (%)[a]	667 (40.5)	508 (32.7)	1557 (34.1)	913 (27.0)	<0.001	<0.001
CHF, No. (%)	378 (19.7)	409 (22.9)	693 (13.3)	627 (16.2)	<0.001	<0.001
MI, No. (%)	988 (51.4)	830 (46.5)	2606 (49.9)	1888 (48.7)	0.70	0.009
MI < 24 hours, No. (%)	111 (5.8)	59 (3.3)	320 (6.1)	134 (3.5)	0.45	<0.001
Medications, No. (%)						
ACE inhibitors	325 (16.9)	422 (23.6)	808 (15.5)	923 (23.8)	0.15	<0.001
Anticoagulants	701 (36.4)	713 (39.9)	1873 (35.9)	1488 (38.3)	0.21	0.001
Antiplatelets	65 (3.4)	54 (3.0)	155 (3.0)	165 (4.3)	0.38	0.015
Aspirin	1071 (55.7)	1196 (67.0)	3258 (62.4)	2757 (71.0)	<0.001	<0.001
β-Blockers	946 (49.2)	1125 (63.0)	2571 (49.2)	2443 (63.0)	0.45	<0.001
Diuretics	435 (22.6)	397 (22.2)	717 (13.7)	585 (15.1)	<0.001	0.07
Inotropes	9 (0.50)	8 (0.50)	19 (0.4)	27 (0.7)	0.73	0.07
Intravenous nitrates	355 (18.5)	342 (19.2)	760 (14.6)	627 (16.2)	<0.001	0.023
Steroid	48 (2.5)	54 (3.0)	105 (2.0)	92 (2.4)	0.048	0.11
Left main stenosis > 50%, No. (%)	400 (20.8)	397 (22.2)	1205 (23.1)	822 (21.2)	0.33	0.20
IABP, No. (%)	118 (6.1)	38 (2.1)	326 (6.2)	129 (3.3)	0.06	<0.001

[a] Contains some missing data.

[b] Surgeon, year of surgery (see Fig 1), and six indicators of missingness are also included in the propensity score.

ACE = angiotensin-converting enzyme; CAD = coronary artery disease; CCS = Canadian Cardiovascular Society; CHF = congestive heart failure; CPB = on-pump coronary artery bypass; CVA = cardiovascular accident; F = female; Hx = history; IABP = intraaortic balloon pump; M = male; MI = myocardial infarction; OPCAB = off-pump coronary artery bypass; PVD = peripheral vascular disease; SD = standard deviation; STS = Society of Thoracic Surgeons.

This was not performed in an effort to recreate the truth; rather, the goal of the imputation was to avoid selection bias that can occur by deleting cases with missing variables of interest. Data were assumed to be missing at random.

Patients were classified according to gender and the type of operation (OPCAB or CABG on CPB) they received. To control for potential selection bias, propensity scores (PS), described by Blackstone [24] and D'Agostino [25], were calculated for each patient based on 40 risk factors (including surgeon identity and year of operation) available preoperatively. For the PS calculation, a multiple logistic regression model was used nonparsimoniously to model OPCAB (yes or no) as a function of all 40 risk factors (Table 1). The resulting conditional probability of a patient receiving OPCAB is the PS.

Table 2. Unadjusted Outcomes by Gender and Surgery Type

Outcome	F/CPB (n = 1924)	F/OPCAB (n = 1786)	M/CPB (n = 5221)	M/OPCAB (n = 3881)	*p* Value	
					Gender	OPCAB
Mortality	78 (4.1)	29 (1.6)	94 (1.8)	49 (1.3)	<0.001	<0.001
Stroke	60 (3.1)	28 (1.6)	82 (1.6)	41 (1.1)	<0.001	<0.001
MI	27 (1.4)	15 (0.8)	27 (0.5)	21 (0.5)	<0.001	0.42
MACE	87 (4.5)	43 (2.4)	108 (2.1)	61 (1.6)	<0.001	<0.001

CPB = on-pump coronary artery bypass; F = female; M = male; MACE = major adverse cardiac event; MI = myocardial infarction; OPCAB = off-pump coronary artery bypass.

To statistically evaluate the main effects of gender and operation type, a multivariable logistic regression model was constructed that related each binary outcome as a function of gender and surgery type (OPCAB vs CABG on CPB), adjusted for the PS. Adjusted odds ratios (AOR) associated with OPCAB and female gender, along with 95% confidence intervals (CI), were computed for each adverse outcome. After this, interaction terms were added to test whether OPCAB modified the effect of gender with respect to the outcomes. When significant interactions existed, comparisons of group/surgery combinations were made and AORs examined.

Long-term survival comparisons were made using Cox proportional hazards regression models for each outcome, which modeled the hazard of each outcome as a function of gender, operation type, and their interaction, adjusted for the PS and patient age. Hazard ratios (HRs) and 95% Cis were generated for each model term, Kaplan-Meier curves were generated that provide survival estimates at postoperative points in time. These estimates include operative deaths.

The data were managed and analyzed using SAS 9.1 (SAS Institute Cary, NC) and Stata 9.0 (StataCorp LP, College Station, TX) software. All statistical tests were two-sided using an $\alpha = 0.05$ level of significance. No adjustments for multiple tests were made.

Results

Preoperative Patient Characteristics

Table 1 reports preoperative patient characteristics for all surgical combinations and gender for the 12,812 consecutive patients. Female patients older (64.9 vs 61.8, $p < 0.001$), had a higher STS predicted risk of mortality (0.032 vs 0.018, $p < 0.001$), and generally were burdened with more comorbidities than male patients. Similarly, OPCAB patients were older (63.0 vs 62.4, $p = 0.003$), had a higher STS predicted mortality risk (0.023 vs 0.021, $p = 0.001$), and had more comorbidities than patients treated with CABG on CPB. Women treated with OPCAB had a higher STS risk of mortality than women treated with CABG on CPB (0.033 vs 0.030, $p = 0.021$).

Table 3. Observed to Expected Society of Thoracic Surgeons Expected Risk of Mortality by Gender and Surgery Type

Group	Patients	Observed (O), %	Expected (E), %[a]	O/E Ratio
F/CPB	1924	4.05	3.02	1.34
F/OPCAB	1786	1.62	3.31	0.49
M/CPB	5221	1.80	1.80	1.00
M/OPCAB	3881	1.26	1.84	0.68

[a] Expected mortality is the mean of Society of Thoracic Surgeons predicted risk of mortality for each group.

CPB = on-pump coronary artery bypass; F = female; M = male; OPCAB = off-pump coronary artery bypass.

Unadjusted Outcomes

Women in this study had higher rates than men of death (2.9% vs 1.6%, $p < 0.001$), stroke (2.4% vs 1.4%, $p < 0.001$), MI (1.1% vs 0.5%, $p < 0.001$), and the combined end point major adverse cardiac events (MACE; 3.5% vs 1.9%, $p < 0.001$) within 30 days postoperatively. Compared with CPB patients, OPCAB patients had lower rates of death (1.4% vs 2.4%, $p < 0.001$), stroke (1.2% vs 2.0%, $p < 0.001$), and overall MACE (1.8% vs 2.7%, $p < 0.001$), but MI rates were not statistically different (0.6% vs 0.8%, $p = 0.42$; Table 2). Observed/expected [26] mortality ratios were highest among women treated with CABG on CPB (1.34) and lowest among women treated with OPCAB (0.49; Table 3).

Risk-Adjusted Comparisons of Short-Term Outcomes

The C index for the propensity model was 0.916, indicating that the PS has excellent ability to discriminate between OPCAB and CABG on CPB. OPCAB was associated with statistically lower rates of death (AOR, 0.68; 95% CI, 0.46 to 0.99; $p = 0.045$), stroke (AOR, 0.48; 95% CI, 0.32 to 0.71; $p < 0.001$), and overall MACE (0.66; 95% CI, 0.47 to 0.93; $p = 0.018$) but rates of MI that were not statistically different (AOR, 1.58; 95% CI, 0.85 to 2.94; $p = 0.15$). Female gender was associated with statistically higher rates of death (AOR, 1.93; 95% CI, 1.49 to 2.48; $p < 0.001$), stroke (AOR, 1.82; 95% CI, 1.38 to 2.40; $p < 0.001$), MI (AOR, 2.19; 95% CI, 1.45 to 3.33; $p < 0.001$), and overall MACE (AOR, 1.97; 95% CI, 1.56 to 2.48; $p < 0.001$; Table 4).

A statistically significant interaction was found between gender and surgery type for death ($p = 0.041$); thus, this outcome merits special consideration and direct comparisons were made between combinations of gender and surgery types. Odds of death for women on CPB were statistically higher than for women treated with OPCAB (AOR, 2.07; 95% CI, 1.24 to 3.44; $p = 0.005$).

Table 4. Adjusted Odds Ratios for Surgery Type and Gender

Variable	OPCAB vs CABG on CPB AOR (95% CI)	Surgery Type *p* Value	Female vs Male AOR (95% CI)	Gender *p* Value
Death	0.68 (0.46–0.99)	0.045	1.93 (1.49–2.48)	<0.001
Stroke	0.48 (0.32–0.71)	<0.001	1.82 (1.38–2.40)	<0.001
MI	1.58 (0.85–2.94)	0.15	2.19 (1.45–3.33)	<0.001
MACE	0.66 (0.47–0.93)	0.018	1.97 (1.56–2.48)	<0.001

AOR = adjusted odds ratio; CABG = coronary artery bypass grafting; CPB = on-pump coronary artery bypass; MACE = major adverse cardiac events; MI = myocardial infarction; OPCAB = off-pump coronary artery bypass.

However, the same comparison in odds of death between men on CPB and men treated with OPCAB was not statistically significant (AOR, 1.16; 95% CI, 0.75 to 1.80; $p = 0.51$; Table 5).

Risk-Adjusted Comparisons of Long-Term Survival

Overall, 2308 (18%) of the original sample of 12,812 patients died during the study period. Survival curves were generated for each gender and surgery type combination (Fig 2). An unadjusted log-rank test revealed that the four Kaplan-Meier curves were not all equal ($p < 0.001$). The survival curves clearly showed that women had poorer postoperative long-term survival than men, regardless of surgery type. Estimates of 1, 3, 5, and 10-year survival are summarized in Table 6. The number of patients left at risk at the beginning of each year is summarized by surgery type and gender in Table 7.

After verifying the proportional odds assumption, the adjusted effects of surgery type and gender were assessed by using a Cox proportional hazards regression model. After adjustment for PS and patient age, female gender was significantly associated with an increased hazard of death (HR, 1.15; 95% CI, 1.03 to 1.28; $p = 0.011$), but OPCAB was not associated with hazard of death (HR, 1.09; 95% CI, 0.95 to 1.25; $p = 0.23$). No interaction was found between gender and surgery type ($p = 0.49$) in long-term survival.

Comment

In an earlier review [20] of this large institutional database, preoperative risk factors and postoperative outcomes were analyzed for consecutive patients who underwent isolated, primary CABG either by OPCAB or on CPB. Overall, even when adjusted for 30 preoperative risk factors, female patients had a significantly increased early incidence of death, stroke, MI, or MACE than male patients. Most striking was the finding that female patients benefited more than male patients from the avoidance of CPB during CABG. The present analysis includes statistical adjustment for 40 preoperative risk factors, updates the sample through 2006, and examines long-term survival up to 10 years after OPCAB vs CPB for male and female patients by cross-referencing the institutional database with the NSSDI.

Risk-adjusted analysis of 30-day outcomes showed that female patients fared less well than male patients with similar preoperative risk factors. Overall, OPCAB was associated with 32% lower risk-adjusted odds of death than CABG on CPB ($p = 0.045$). Much of this mortality benefit was found in outcomes among women; compared with CABG on CPB, OPCAB reduced risk-adjusted mortality by 52% for women, but by only 14% for men. These results are similar to those found in a larger sample of the contemporary STS National Cardiac Database, analyzed by intention-to-treat, in which OPCAB reduced risk-adjusted operative mortality by 17% overall ($p = 0.03$), by 24% ($p < 0.05$) for women and 12% ($p = 0.24$) for men [21]. A definitive explanation for these differences remains elusive [18, 20, 21].

In the present analysis, the risk-adjusted odds of stroke and MACE—but not of MI—were lower for patients who had OPCAB than CABG on CPB. This finding is somewhat less consistent with the larger national experience, in which adjusted risk of death, stroke, MI, and MACE were all significantly reduced after OPCAB compared with CABG on CPB [21].

Kaplan-Meier curves showed that female patients had poorer long-term survival than male patients during up to 10 years of follow-up. Proportional hazards regression analysis showed that female gender was associated with an increased adjusted risk of death. Despite a significant early risk-adjusted mortality advantage of OPCAB, long-term survival was not different between surgery types. Moreover, although a strong interaction was found between gender and surgery type for early risk-adjusted mortality, no such interaction existed for long-term survival.

Numerous possible explanations for the gender-based disparity in outcomes after cardiac operations have been

Table 5. Adjusted Odds Ratios of Death for Gender and Surgery Type Combinations

Outcome	Comparison	AOR (95% CI)	*p* Value
Death[a]	F/CPB vs F/OPCAB	2.07 (1.24–3.44)	0.005
	M/CPB vs M/OPCAB	1.16 (0.75–1.80)	0.51
	F/CPB vs M/CPB	2.31 (1.70–3.13)	<0.001
	F/OPCAB vs M/OPCAB	1.29 (0.82–2.06)	0.27
	F/OPCAB vs M/CPB	1.12 (0.68–1.84)	0.67

[a] A significant interaction between surgery type and gender existed for this end point.

AOR = adjusted odds ratio; CI = confidence interval; CPB = on-pump coronary artery bypass; F = female; M = male; OPCAB = off-pump coronary artery bypass.

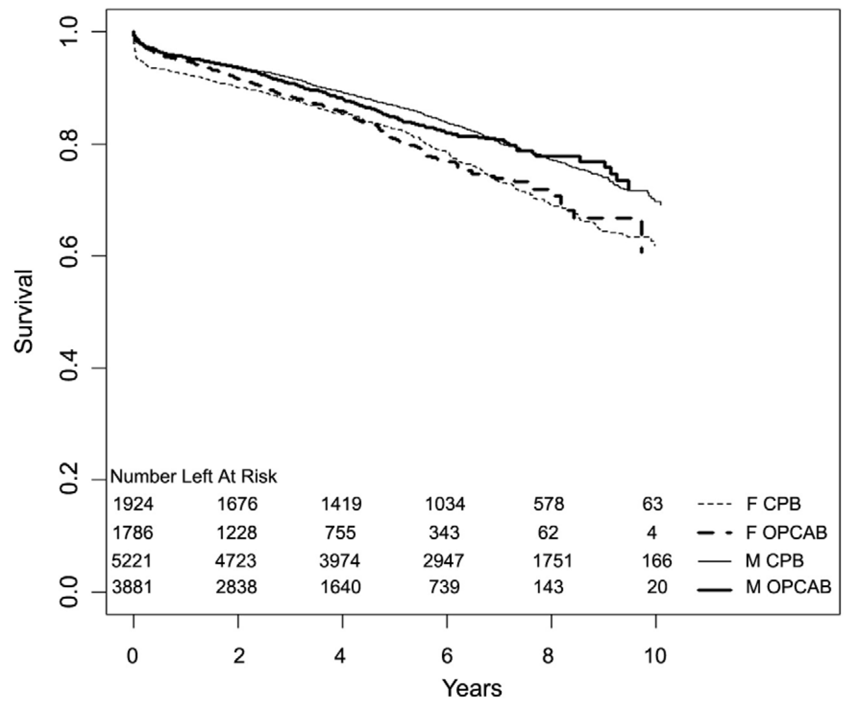

Fig 2. Kaplan-Meier 10-year survival curve by gender and coronary artery bypass (CAB) grafting procedures with cardiopulmonary bypass (CPB) or off-pump (OPCAB). (F = females—small dashed line, CPB; large dashed line, OPCAB. M = males—thin line, CPB; thick line, OPCAB.)

presented [27–32]. None of these have been proved. Forty risk factors, including indices of body habitus, completeness of revascularization, surgeon identity, and year of surgery were included in the present PS analysis. Thus, these possible confounders cannot explain the differences observed nor invalidate the effect of gender and surgery type on outcomes. It is not within the scope of this study to elucidate the physiologic mechanisms by which OPCAB reduces morbidity and mortality after CABG or by which gender affects outcomes or interacts with CPB to further influence risk-adjusted outcomes. Nonetheless, the present findings suggest that in the modern era, female gender remains a risk factor for negative outcomes after CABG and that OPCAB significantly reduces that gender-based risk.

It is clear that this study is limited by its retrospective nature, and that despite advanced statistical methodology, unknown sources of bias may possibly confound these results. Moreover, much of the data reviewed predates the introduction in 2004 of the STS database field for intraoperative conversions; thus, this study analyzed surgical cases according to the final type of procedure that was performed. Eighty patients were converted intraoperatively from OPCAB to CPB. Of these, 3 patients (3.8%) died and 3 (3.8%) had strokes. The incidence of these two outcomes was not significantly different between the converted group and the nonconverted OPCAB group. An intention-to-treat analysis of the STS National Cardiac Database since the introduction of the conversion field demonstrated that intraoperative conversion could not account for the significant benefit of OPCAB on risk-adjusted outcomes, especially among women [20].

Finally, it is possible that the 17 Emory University faculty surgeons in the present study may have average experience with OPCAB that exceeds the national norm, limiting generalizability of these results. Further, the long-term survival end point is "all-cause" mortality and not mortality that is directly attributable to their surgical characteristics.

In conclusion, women undergoing CABG procedures are at increased risk of death, stroke, MI, and the composite end point of death/stroke/MI compared with men. Although both men and women have superior risk-adjusted outcomes after OPCAB than after CABG on CPB, women may benefit more than men from avoidance of CPB. Long-term survival after CABG is worse for women than for men. This disparity is not affected by

Table 6. Long-Term Survival by Gender and Surgery Type

Survival Group	Patients, No.	1 Year (95% CI)	3 Years (95% CI)	5 Years (95% CI)	10 Years (95% CI)
F/CPB	1924	.924 (.911–.935)	.879 (.863–.893)	.827 (.809–.844)	.618 (.581–.652)
F/OPCAB	1786	.947 (.935–.956)	.884 (.866–.899)	.810 (.785–.832)	.606 (.468–.718)
M/CPB	5221	.955 (.949–.961)	.918 (.910–.925)	.868 (.858–.877)	.696 (.673–.718)
M/OPCAB	3881	.954 (.947–.960)	.908 (.898–.918)	.848 (.833–.862)	.718 (.656–.770)

CPB = on-pump coronary artery bypass; F = female; M = male; OPCAB = off-pump coronary artery bypass.

Table 7. Number Left at Risk at the End of Each Year by Surgery Type and Gender

	Number Left at Risk			
Year	F/OPCAB	F/CABG on CPB	M/OPCAB	M/CABG on CPB
1	1515	1748	3363	4884
2	1228	1676	2838	4723
3	965	1581	2175	4414
4	755	1419	1640	3974
5	539	1243	1141	3486
6	343	1043	738	2947
7	172	801	364	2351
8	62	578	143	1751
9	30	315	72	936
10	4	63	20	166
Mean follow-up, years	3.7	6.2	3.8	6.3

CABG = coronary artery bypass grafting; CPB = on-pump coronary artery bypass; F = female; M = male; OPCAB = off-pump coronary artery bypass.

surgery type; overall, OPCAB and CABG on CPB are associated with similar long-term survival.

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DISCUSSION

DR JOHN S. IKONOMIDIS (Charleston, SC): John, in the on-pump coronary artery bypass group, what do you think the effect is when you include current strategies to reduce the morbidity associated with bypass, such as elimination of cardiotomy suction and retrograde autologous priming?

DR PUSKAS: Of course over these 10 years, both techniques—both off-pump and on-pump techniques—evolved. At the beginning, of course, cardiotomy suction was routine. Towards the end, cardiotomy suction is infrequent, replaced by various cell-scavenging techniques for the most part. Retrograde autologous prime has been something we have done for more than 10 years, and of course, each generation of membrane oxygenators gets a little better, and, of course, each generation of coronary stabilizers gets better for the off-pump group.

One of the benefits of off-pump bypass is it has spurred innovation in on-pump technologies that have improved outcomes for on-pump patients and reduced systemic inflammatory response. On the other hand, while all those improvements seek to limit systemic inflammatory response in the manipulation of the aorta caused by cannulation and cardiopulmonary bypass, none of those improvements can expect to eliminate those negative effects of the heart-lung machine. However, eliminating the heart-lung machine can be rationally expected to eliminate those negative effects.

DR JUERGEN CARL ENNKER (Lahr, Germany): Dr Puskas, congratulations on this very fine series. I have a couple of questions. First of all, what was the impact of learning curves through these 10 years? What was the conversion rate at the beginning of your series? What is it right now? And I am sure that you are pursuing the aim of complete arterial revascularization. What was the percentage of complete arterial revascularization at the beginning, 10 years ago, what is it now, and what was the impact on the follow-up and those results of venous versus complete arterial revascularization? Thank you very much and congratulations.

DR PUSKAS: Thank you for those interesting questions. The conversion rate is an important consideration. Early on, the conversion rate was about 2%. As you know, the Society of Thoracic Surgeons National Database introduced a data field in 2004 to account for intraoperative conversions. Prior to 2004, we have to go back to the operative notes, and they are not always clear. After 2004, that data set of 13,000 patients includes 80 patients who were converted from off-pump to on-pump. Among those 80 patients, 3 had a stroke and 3 died. So it is clear that intraoperative conversions since 2004 cannot in any way explain these outcomes, because the number of conversions and the negative events in those patients converted are simply far too small to impact such a large data set.

Your comments about arterial grafting are well taken. I can tell you that in 2000 we randomized 200 patients in our off-pump trial, comparing off-pump and on-pump. In those patients, 41% of all grafts were arterial and they did not differ between groups. I do not have those data for the overall data set, nor have we examined longer-term survival yet on the basis of number of arterial grafts. We do not believe that choice of on-pump surgery vs off-pump surgery does or should have any impact on choice of conduits.

DR DAVID J. UNDERHILL (Hartford, CT): We know that heterologous blood transfusions are associated with early short-term mortality and also long-term survival. One of the benefits of OPCAB surgery is supposedly decreased blood transfusion. Have you been able to show in your database that women really got benefit from this just because they got less transfusions?

DR PUSKAS: In a previous analysis we did include rate of transfusion, and, as well, we included body mass index, body surface area, weight and height, and various indices of body mass and red cell mass. Those things do have an impact, but they have an impact independent of gender. Gender, in addition, has an incremental impact, and I can't explain to you exactly why. But as you well know, for 30 years that people have noticed a difference in gender-related outcomes. Transfusion rates and body mass and red cell mass have been suspect as confounders in that analysis, and a few studies have suggested that they do confound and more studies have suggested they do not. Our analyses with this large database suggest that they do not account for the gender-base difference entirely.

DR JOHN FEHRENBACHER (Indianapolis, IN): Was this adjusted for individual surgeons? Or asked another way, did certain surgeons do OPCABs and certain surgeons do on-pump?

DR PUSKAS: A very important question. There were a total of 17 surgeons on faculty during that 10-year period. Surgeon identity was one of the 40 covariants in each of the multivariable logistic regression models. So that was accounted for within the statistical adjustment. It is true that the rate of adoption of off-pump bypass has differed among our faculty members, much more in the past than recently. Institution-wide we do about 80% of all bypasses off-pump. In 1998, a smaller number of surgeons accounted for the large bulk of the off-pump bypass cases.

DR FAYYAZ HASHMI (Oklahoma City, OK): Dr Puskas, do you think the difference is because you are converting a cardiac operation into a vascular operation?

DR PUSKAS: I think the difference is because we avoid the heart-lung machine, and I think that extracorporeal circulation seems to be more poorly tolerated by female humans than by male humans. Why, I cannot tell you. But we have been unable to tease out what preoperative predictor or intraoperative variable can explain this away, just as we have been unable in the medical profession to explain why women have more rheumatoid arthritis and systemic lupus erythematosus than men. I can't explain that to you, but I see that it is the case in our data set.