

Do Women Currently Receive the Same Standard of Care in Coronary Artery Bypass Graft Procedures as Men? A Propensity Analysis

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Background. The purpose of this study was to determine whether, in recent years, sex differences in the type of care during coronary artery bypass graft surgery procedures occurred.

Methods. Between 1995 and 2004, 5,935 consecutive patients (4,867 men and 1,068 women) underwent isolated coronary artery bypass graft surgery; propensity score matching was used to investigate whether sex adversely impacts standard care and early outcomes of coronary revascularization.

Results. Of the 1,068 women undergoing isolated coronary artery bypass graft surgery, only 280 (26.2%) were matched on propensity scores with men. Distribution of preoperative variables among matched pairs was, on average, equal. Propensity-matched women received similar number of distal anastomoses as men (2.70 ± 0.89 versus 2.82 ± 0.97 ; $p = 0.13$), had similar rates of complete revascularization (82.5% versus 81.6%; $p = 0.78$), and of off-pump procedures (24.3% versus 27.5%; $p = 0.39$); also,

the rate of utilization of arterial grafts (left internal mammary artery 98.5% versus 98.2%; $p = 0.73$; right internal mammary artery 3.2% versus 3.2%; $p > 0.99$; radial artery 8.2% versus 9.6%; $p = 0.55$), as well as the number of distal anastomoses performed with arterial grafts (1.11 ± 0.36 versus 1.13 ± 0.39 ; $p = 0.47$), were similar in women and men. No differences were detected in major complications (in-hospital mortality, perioperative myocardial infarction, and stroke) in propensity-matched pairs, whereas women had lower reexploration for bleeding and blood transfusion rates.

Conclusions. The preoperative profiles of women and men were markedly different, as only one fourth of women could be matched. In the current era, after adjustment for preoperative variables, female patients received the same standard of care as men, with improved results in some minor early outcomes.

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Coronary artery disease is the leading cause of mortality in women, and more women than men die each year of heart disease [1, 2]. Numerous studies have shown that women suffer higher mortality and major complications rates after coronary artery bypass grafting (CABG) than men, although the increased risks for women undergoing CABG is substantially reduced once adjustment for preoperative risk factors is performed [3–7].

Several US studies have also shown that women in the late 1980s and early 1990s were less likely to receive diagnostic and therapeutic cardiac procedures, especially soon after myocardial infarction, and that this difference has become smaller in recent years, when women and men were as likely to receive a catheter-based revascularization procedure, but not CABG, which was still more frequent in men [8]; the trend to undertreat women with

coronary disease and myocardial infarction has also been documented by recent European studies [9]. About CABG, some studies have suggested that female sex is associated with substantial differences in care, with mammary arteries [4, 10, 11] and radial arteries [12] used less frequently in women, and the number of distal anastomoses being performed lower in women [3, 4, 11, 13], but the results of these studies concerning possible differences in care were not usually adjusted for baseline preoperative features that usually markedly differ between men and women.

We therefore assessed whether the standard of CABG care differs in men and women by applying propensity-modeling techniques to adjust for different risk profiles related to sex.

Patients and Methods

Patients

From January 1995 through December 2004, 5,935 patients underwent isolated CABG at Centro Cardiologico

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Monzino IRCCS, University of Milano. Of these patients, 1,068 (18.0%) were women and 4,867 (82.0%) were men. All patients underwent revascularization through a median sternotomy, and patients undergoing coronary revascularization through a thoracotomy were excluded. Patients were operated both on-pump in 4,623 (77.9%) cases and off-pump in 1,312 (22.1%) cases, respectively.

In operations done on-pump, conduits were harvested and prepared, and patients were fully heparinized. Standard cannulation for cardiopulmonary bypass was performed with ascending aortic cannulation and dual-stage cannulation of the right atrium. A nonpulsatile roller or centrifugal pump, hollow-fiber oxygenator with integrated heat exchanger, arterial filter, open cardiotomy reservoir, and polyvinyl tubing system were used in all cases. Each operation was performed with moderate or tepid hypothermia and hemodilution. Blood flow during cardiopulmonary bypass was kept at greater than $2.0 \text{ L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$, and hematocrit at 18% to 25%. Myocardial protection was achieved by the administration of cold, multidose crystalloid or blood cardioplegia infused either antegrade or retrograde or in combination on induction and every 20 minutes. Distal anastomoses were usually constructed first, and the proximal anastomoses were constructed to the ascending aorta with a tangential clamp. After the patient was weaned from cardiopulmonary bypass and the cannulas were removed, heparin was reversed with protamine in a 1:1 ratio.

In off-pump operations, conduits were harvested and prepared first, then patients were fully heparinized. Coronary artery exposure was achieved with stay sutures applied on the left lateral side of the pericardium or with deep pericardial stay sutures placed above the entry of the left lower pulmonary vein and lateral to the entry of the inferior vena cava. Distal anastomoses were constructed before proximal anastomoses. The left internal thoracic artery to left anterior descending coronary artery anastomosis was constructed first. Mechanical stability of the distal anastomosis area was achieved with a mechanical or a suction (Medtronic Octopus, Medtronic Inc, Minneapolis, MN) stabilizer; target vessel hemostasis was obtained with proximal and distal vessel coronary

Table 2. Comparison of Patient Characteristics in the Whole Patient Population

Variable	Males (n = 4,867)	Females (n = 1,068)	p Value
Age (y)	64 ± 9.1	68 ± 8.1	<0.001
Weight (kg)	77 ± 10.9	65 ± 10.8	<0.001
Body surface area (m ²)	1.86 ± 0.15	1.65 ± 0.16	<0.001
Urgent or emergent surgery	163 (3.3%)	51 (4.8%)	0.024
Hypertension	2,846 (58.5%)	782 (73.2%)	<0.001
Diabetes	1,046 (21.5%)	271 (25.4%)	0.006
Redo operation	186 (3.8%)	27 (2.5%)	0.040
Previous stroke	107 (2.2%)	16 (1.5%)	0.146
Carotid artery disease	354 (7.3%)	120 (11.2%)	<0.001
Smoke	2,106 (43.3%)	241 (22.6%)	<0.001
Chronic obstructive pulmonary disease	495 (10.2%)	99 (9.3%)	0.374
Previous myocardial infarction	2,080 (42.7%)	333 (31.2%)	<0.001
Previous myocardial infarction, less than 6 months	664 (13.6%)	164 (15.0%)	0.252
Atrial fibrillation	87 (1.8%)	15 (1.4%)	0.383
Dialysis	15 (0.3%)	4 (0.4%)	0.728
Preoperative intraaortic balloon pump	15 (0.3%)	4 (0.4%)	0.764
New York Heart Association functional class	2.0 ± 0.66	2.3 ± 0.62	<0.001
Echocardiographic ejection fraction	0.56 ± 0.11	0.59 ± 0.11	<0.001
Serum creatinine (mg/dL)	1.1 ± 0.50	1.0 ± 0.55	<0.001
Tuman score	1.6 ± 1.7	3.7 ± 1.6	<0.001
Number of diseased vessels	2.7 ± 0.57	2.6 ± 0.64	<0.001
Triple-vessel disease	3,495 (71.8%)	684 (64.0%)	<0.001
Significant left main trunk stenosis	998 (20.5%)	185 (17.3%)	0.018
Discontinuation of antiplatelet drugs occurring less than 5 days before surgery	2,343 (48.1%)	549 (51.4%)	0.053
Preoperative therapy with anticoagulant drugs (vitamin K antagonists)	18 (0.4%)	1 (0.1%)	0.229

Table 1. Patient Characteristics Associated With Female Sex

Variable	p Value
Age	<0.0001
Weight	<0.0001
Urgent or emergent surgery	<0.0001
Hypertension	<0.0001
Diabetes	<0.0001
Redo operation	<0.0001
Previous stroke	<0.0001
Carotid artery disease	<0.0001
Smoke	<0.0001
Echocardiographic ejection fraction	<0.0001
Serum creatinine	<0.0001
Tuman score	<0.0001
Triple-vessel disease	<0.0001

occlusion with a single 4-0 polypropylene stitch or with a soft plastic coronary flow shunt. Proximal anastomoses were constructed to the aorta with a tangential clamp. After completion of all anastomoses, heparin was reversed with protamine in a 1:1 ratio.

Data Collection

Data for this study were retrieved from our prospective hospital database whose use for research had been approved by the Centro Cardiologico Monzino Institutional Review Board; in addition, the Institutional Review Board approved this study and waived the requirement for informed consent on the condition that the subjects' identities were hidden. Preoperative, operative, and

Table 3. Comparison of Intraoperative and Postoperative Events in the Whole Patient Population

Variable	Males (n = 4,867)	Females (n = 1,068)	p Value
Left internal mammary artery use	4,770 (98.0%)	1,038 (97.2%)	0.105
Right internal mammary artery use	346 (7.1%)	41 (3.8%)	<0.001
Radial artery use	434 (8.9%)	70 (6.6%)	0.012
Number of distal anastomoses	2.9 ± 0.95	2.6 ± 0.64	<0.001
Complete revascularization	4,079 (83.8%)	872 (81.6%)	0.103
Off-pump revascularization	1,056 (21.7%)	256 (24.0%)	0.105
Number of distals with arterial grafts	1.2 ± 0.43	1.1 ± 0.36	<0.001
In-hospital mortality	35 (0.7%)	7 (0.7%)	0.822
Perioperative myocardial infarction	137 (2.8%)	31 (2.9%)	0.876
Perioperative stroke	40 (0.8%)	10 (0.9%)	0.711
Composite outcome of death and serious morbidity	199 (4.1%)	45 (4.2%)	0.887
Perioperative atrial fibrillation	500 (10.3%)	111 (10.4%)	0.907
Reoperation for bleeding	211 (4.3%)	41 (3.8%)	0.466
Artificial ventilation time (h)	11 ± 16.3	12 ± 15.4	0.061
Number of units of red blood cells	0.9 ± 1.9	1.7 ± 2.1	<0.001

postoperative variables that were collected are reported in the Appendix.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation, categorical variables as percentage. To minimize selection bias before comparing male and female patients, propensity score matching was used to create equivalent treatment groups [14]. Our propensity scores were computed from a logistic regression model with forward stepwise selection analyzing the association with sex of 26 preoperative variables (collected from our database, see Appendix); Table 1 reports the 13 variables that were found to be significantly associated with female sex at logistic regression analysis. These variables were used to develop the propensity score for each patient of the database. The C-statistic of this model was 0.92. Using only the propensity score, female patients were matched to male patients by using a greedy matching strategy. For this, matching to 5 decimal points was initially performed, followed by 4-, 3-, 2-, and 1-decimal-point matching. Female patients whose propensity scores deviated more than 0.10 from those of male patients were considered unmatched. This resulted in 280 matches (26% of women and 6% of men).

Group differences in clinical variables in unmatched and in propensity-matched female and male patients were assessed by analysis of variance, Mann-Whitney (in

case of nonnormal distribution), χ^2 , or Fisher's exact tests as indicated.

A probability value of less than 0.05 was considered significant.

Results

Whole, Unmatched Patient Population

Female patients differed in many clinical characteristics from male patients (Table 2). Female patients were older

Table 4. Comparison of Patient Characteristics in Propensity-Matched Pairs

Variable	Males (n = 280)	Females (n = 280)	p Value
Propensity score	-1.31 ± 1.898	-1.33 ± 1.888	0.907
Age (y)	65 ± 10.6	66 ± 7.6	0.571
Weight (kg)	71 ± 8.8	72 ± 10.7	0.289
Body surface area (m ²)	1.79 ± 0.14	1.78 ± 0.16	0.437
Urgent or emergent surgery	9 (3.2%)	6 (2.1%)	0.432
Hypertension	184 (65.7%)	183 (65.4%)	0.929
Diabetes	62 (22.1%)	70 (25.0%)	0.426
Redo-operation	7 (2.5%)	6 (2.1%)	0.779
Previous stroke	6 (2.1%)	6 (2.1%)	>0.99
Carotid artery disease	29 (10.4%)	34 (12.1%)	0.504
Smoke	96 (34.3%)	107 (38.2%)	0.334
Chronic obstructive pulmonary disease	33 (11.2%)	27 (9.6%)	0.495
Previous myocardial infarction	122 (43.6%)	103 (36.8%)	0.101
Previous myocardial infarction, less than 6 months	32 (11.4%)	34 (12.1%)	0.932
Atrial fibrillation	3 (1.1%)	4 (1.4%)	>0.99
Dialysis	2 (0.7%)	1 (0.4%)	>0.99
Preoperative intraaortic balloon pump	3 (1.1%)	1 (0.4%)	0.624
New York Heart Association functional class	2.1 ± 0.77	2.3 ± 0.60	0.565
Echocardiographic ejection fraction	0.56 ± 0.118	0.56 ± 0.109	0.610
Serum creatinine (mg/dL)	1.14 ± 0.49	1.10 ± 0.64	0.322
Tuman score	2.9 ± 1.7	2.9 ± 1.2	0.409
Number of diseased vessels	2.57 ± 0.59	2.63 ± 0.62	0.295
Triple-vessel disease	181 (64.6%)	195 (69.6%)	0.242
Significant left main trunk stenosis	58 (20.7%)	48 (17.1%)	0.281
Discontinuation of antiplatelet drugs occurring less than 5 days before surgery	135 (48.2%)	121 (43.2%)	0.270
Preoperative therapy with anticoagulant drugs (vitamin K antagonists)	2 (0.7%)	0	0.499

Table 5. Comparison of Intraoperative and Postoperative Events in Propensity-Matched Pairs

Variable	Males (n = 280)	Females (n = 280)	p Value
Left internal mammary artery use	266 (98.2%)	269 (98.5%)	0.728
Right internal mammary artery use	9 (3.2%)	9 (3.2%)	>0.99
Radial artery use	27 (9.6%)	23 (8.2%)	0.553
Number of distal anastomoses	2.82 ± 0.97	2.70 ± 0.89	0.131
Complete revascularization	226 (81.6%)	231 (82.5%)	0.779
Off-pump surgery	77 (27.5%)	68 (24.3%)	0.385
Number of distals with arterial grafts	1.13 ± 0.39	1.11 ± 0.36	0.466
In-hospital mortality	4 (1.4%)	2 (0.7%)	0.686
Perioperative myocardial infarction	11 (3.9%)	9 (3.2%)	0.649
Perioperative stroke	2 (0.7%)	0	0.499
Composite outcome of death and serious morbidity	16 (5.7%)	11 (3.9%)	0.324
Perioperative atrial fibrillation	33 (11.8%)	26 (9.3%)	0.335
Reoperation for bleeding	19 (6.8%)	7 (2.5%)	0.016
Artificial ventilation time (h)	12 ± 14.7	11 ± 13.3	0.404
Number of units of red blood cells	1.3 ± 1.1	1.1 ± 0.9	0.018

than men, had lower weight and body surface area, were more likely to undergo urgent or emergent surgery, were more frequently hypertensive and diabetics, were less likely to be redo operations, be smokers, and to have had a previous myocardial infarction, and were more likely to have carotid artery disease. In addition, women presented with higher New York Heart Association class and Tuman score, lower serum creatinine levels, and lower number of diseased vessels, and were less likely to be affected by triple-vessel disease. Concerning intraoperative variables and postoperative events (Table 3), women less frequently received right internal mammary artery and radial artery conduits, and had a lower total number of distal anastomoses done with arterial grafts. Also, female patients received fewer grafts per patient, although the complete revascularization (incomplete revascularization was defined as failure to graft a coronary artery system with a 50% or greater stenosis or lack of grafts to both the left anterior descending and circumflex coronary artery systems with a 50% or greater left main coronary artery stenosis [15, 16]) rates were similar in men and women (please note that women showed a lower number of diseased coronary vessels than men), as were the off-pump coronary bypass surgery adoption rates. In-hospital mortality, perioperative myocardial infarction, stroke, atrial fibrillation, reoperation for bleeding rates, and mechanical ventilation time were similar in the two groups, whereas the units of red blood cell transfusions were higher in female patients when considering the whole, unmatched patient population. Finally, the composite outcome of death and serious mor-

bidity (stroke and perioperative myocardial infarction) was very similar in unmatched women and men (4.2% versus 4.1%; $p = 0.89$).

Propensity-Matched Pairs

Of 1,068 female patients undergoing CABG at our hospital, only 280 (26.2%) could be propensity-matched with men. This reflects the vast sex difference in preoperative profiles resulting in important differences in baseline characteristics among women and men, as described in the previous paragraph.

Preoperative characteristics of on-pump and off-pump propensity-matched patients were well matched (Table 4), including a similar extent of major risk factors and of coronary artery disease (2.63 ± 0.62 diseased coronary vessels in women versus 2.57 ± 0.59 in men; $p = 0.30$) and similar involvement of the left main trunk.

About intraoperative and postoperative features (Table 5), matched female patients had very similar rates of left and right internal mammary artery utilization as men, as well as comparable use of radial artery grafts. Women received a similar number of distal anastomoses, and of distal anastomoses with arterial grafts; also the rates of complete revascularization and of off-pump coronary surgery were comparable in men and women.

Major postoperative complications rates were similar in female and male patients. However, women experienced lower reoperation for bleeding rates, and lower red blood cell use than men.

Comment

Several studies have assessed sex differences in procedure use for ischemic heart disease; most of these have shown that women are less likely to have diagnostic, interventional, or surgical procedures than men [4]. For CABG, even when female patients are referred for it, there are substantial differences in the quality of care, as they less frequently receive the conduits with better long-term patency such as internal mammary [4, 10, 11] and radial arteries [12]. In addition, the recently published sex-specific practice guidelines for CABG of The Society of Thoracic Surgeons confirm that internal mammary arteries are severely underutilized in women, who receive an internal mammary conduit in only 60% to 75% of cases [17]. Also, many studies examining sex differences in therapeutic strategies and outcomes after CABG report a higher postoperative morbidity and mortality, and usually less aggressive therapeutic strategies, for women compared with men who undergo CABG [3, 4, 6, 8, 9, 12].

It is still unclear whether previously described sex differences in outcome and, especially, in type of care provided to women are attributable to female sex per se or to a higher prevalence of unfavorable risk factors in women that might affect the choice of a different (eg, less aggressive or less complete) surgical strategy. Although the majority of investigations report that sex has no influence on adverse postoperative outcomes after CABG when adjustment for sex dissimilarities in preoperative risk is performed [17-21], some studies report an increase

in postoperative risk for women, despite application of risk-adjustment strategies [7, 22–24]. Finally, a few investigations report no difference in operative mortality even with statistically significant sex differences in the preoperative risk profiles [3, 4, 13, 25]. The results of our study are in line with these latter experiences; when we consider the whole unmatched population, although there are several differences in clinical presentation of women and men candidates to CABG, the results in term of hard outcomes (mortality, stroke, myocardial infarction, and the composite end point) and of some minor ones (perioperative atrial fibrillation, reoperation for bleeding, and ventilation time) are remarkably similar. And the incredible closeness of the findings suggests that regardless of the many differences in presenting characteristics, the variables most determining of comparable outcome are meticulous conduct of surgery with use of left internal mammary artery and completeness of revascularization; in our 10-year experience, both left internal mammary artery use and completeness of revascularization were remarkably similar in women and in men, even in the unmatched patients.

In recent years, although sex disparities in some aspects of the cardiac care process appear to have progressively and substantially narrowed, especially in the treatment of acute myocardial infarction and in the adoption of interventional cardiology procedures [8, 9], the reported differences in the rates of coronary surgery seem to be, however, still relatively large, with women 22% less likely to undergo CABG after an acute myocardial infarction [8]. A recent paper has confirmed this progressive narrowing during the years of the previously documented sex disparities in cardiac care, but only in the field of diagnostic procedures and of interventional cardiology and not in CABG [26].

In addition, common opinion on this topic still suggests that besides the fact that lower percentages of female patients affected by coronary disease are being considered to undergo CABG, there are still substantial differences in the type of care that is provided to women who have been considered good candidates. In fact, an editorial concerning sex disparities in cardiac care published in 2003 still warned that "...sex should no longer be a significant factor in decisions regarding revascularization" [27].

To the best of our knowledge, however, no reports have focused on sex disparities in CABG care after adjustment for preoperative baseline risk profile, and only unadjusted retrospective reports are available, unanimously showing that women receive a type of surgical care that differs in several aspects from that usually provided to men [3, 4, 10–13, 28, 29]; this occurs not only for standard CABG performed on-pump but even when off-pump techniques are chosen [29].

Our study shows that once adjustment for preoperative clinical features is performed, there are no substantial differences in the type of care provided during hospitalization for CABG to male and female patients in recent years. Arterial conduit usage, as well as the extent and completeness of revascularization are remarkably similar in women and men.

Data from our study confirm and extend previous evidence concerning the progressive narrowing of the

"sex gap" in cardiac care; in fact, based on the results shown, even the last gap (CABG), which has been previously documented to remain in clinical practice, has faded out, and women now appear to receive the same standard of care as men once they are referred for surgical myocardial revascularization, and, actually, the sex difference is mainly in presentation, not in quality of care. Another potential implication of our data is that the current apparently restricted policy of some centers of providing fewer services for female compared with male patients should be reviewed. Because of the similar outcomes in both groups, the indications for women having CABG should be similar to those used in men.

Finally, the analysis of perioperative complications in propensity-matched pairs has shown that similar to unmatched patients, there are no substantial differences in major and some minor postoperative complications between women and men, with in-hospital mortality, perioperative stroke, myocardial infarction, and atrial fibrillation rates, as well as mechanical ventilation times, very similar in both groups. This further supports the proof of concept that careful surgery with the use of the left internal mammary artery and complete revascularization may be the key to erase the apparent sex discrepancy in outcomes. On the other hand, when considering propensity-matched pairs, women are less likely to undergo reexploration for bleeding and to receive red blood cell transfusions perioperatively than men; we have no clear explanation as to why women are at reduced risk for postoperative bleeding and for subsequent blood transfusions, and further studies are warranted to clarify this issue.

In conclusion, this study shows that compared with men, women are actually as likely as men to receive the same standard of care during CABG procedures, with similar early outcomes. With contemporary surgical techniques, female sex itself does not seem to pose an independent risk for adverse early postoperative outcomes or for undertreatment. The decision to surgically treat women affected by ischemic heart disease and especially the revascularization strategies chosen during surgery are now made without the unsupported bias of higher complications and with expectations of comparable results to those noted in men. Further studies are encouraged to support these findings.

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Appendix

Patient Variables Collected in Database

Preoperative

- Age (y)
- Weight (kg)
- Body surface area (m²)
- Year of surgery (1995-2004)
- Urgent or emergent surgery (y/n)
- Hypertension (y/n)
- Diabetes (insulin-treated, oral hypoglycemic [y/n])
- Redo operation (y/n)
- Previous stroke (y/n)
- Carotid artery disease (y/n)
- Current smoker (y/n)
- Chronic obstructive pulmonary disease (y/n)
- Previous myocardial infarction (y/n)
- Previous myocardial infarction, less than 6 months (y/n)
- Atrial fibrillation (y/n)
- Dialysis (y/n)
- Preoperative intraaortic balloon pump (y/n)
- New York Heart Association functional class (1-4)
- Echocardiographic ejection fraction
- Serum creatinine (mg/dL)
- Tuman score
- Number of diseased vessels (1-3)
- Triple-vessel disease (y/n)
- Significant left main trunk stenosis (y/n)
- Discontinuation of antiplatelet drugs occurring less than 5 days before surgery (y/n)
- Preoperative therapy with anticoagulant drugs (vitamin K antagonists) (y/n)

Intraoperative

- Left internal mammary artery use (y/n)
- Right internal mammary artery use (y/n)
- Radial artery use (y/n)
- Number of distal anastomoses
- Complete revascularization (y/n)
- Number of distal anastomoses with arterial grafts

Postoperative

- In-hospital mortality (y/n)
- Perioperative myocardial infarction (y/n)
- Perioperative stroke (y/n)
- Composite outcome of death and serious morbidity (stroke and myocardial infarction) (y/n)
- Perioperative atrial fibrillation (y/n)
- Reoperation for bleeding (y/n)
- Artificial ventilation time (h)