Gender Differences in Outcomes After Hospital Discharge From Coronary Artery Bypass Grafting

Veena Guru, MD; Stephen E. Fremes, MD; Peter C. Austin, PhD; Eugene H. Blackstone, MD; Jack V. Tu, MD, PhD

Background—There are few comparative data regarding long-term nonfatal outcomes for women versus men after coronary artery bypass grafting (CABG). This study compares gender differences in cardiac events in a population of hospital survivors up to 11 years after isolated CABG surgery in Ontario, Canada.

Methods and Results—A population-based cohort study (n = 68,774 patients, 15,043 women) between September 1, 1991, and April 1, 2002, was assembled with linked clinical and administrative databases. Cox modeling and propensity score matching were used to compare death, cardiac readmission (angina, heart failure, myocardial infarction), repeat revascularization (angioplasty or CABG), and stroke readmission between men and women. Women were older (65 ± 17 versus 62 ± 13 years), more likely to present with urgent or emergent status (64% versus 56%), and less likely to receive arterial grafts (70% versus 78%). Women had a higher rate of cardiac readmission in the first year after surgery (hazard ratio [HR] of 1.5, 95% confidence interval [CI] 1.36 to 1.56), and this increased risk persisted after 1 year (HR 1.2, 95% CI 1.14 to 1.31). This was primarily due to readmissions for unstable angina (HR 1.3, 95% CI 1.24 to 1.38) and congestive heart failure (HR 1.1, 95% CI 1.06 to 1.21). Propensity-matched women had similar rates of death (HR 0.9, 95% CI 0.83 to 0.98) and repeat revascularization (HR 1.0, 95% CI 0.91 to 1.06).

Conclusions—Women have a more complex clinical preoperative presentation and are more likely to be readmitted with unstable angina and congestive heart failure after CABG but experience survival similar to those seen in men. Gender differences in outcomes may be improved through durable revascularization strategies and close postoperative follow-up care targeted to women. (Circulation. 2006;113:507-516.)

Key Words: bypass ■ women ■ surgery ■ epidemiology

It is recognized that the outcomes for women after coronary artery bypass grafting (CABG) are different from those of men. Specifically, in-hospital mortality is greater for women after CABG.1–4 It has been suggested this may be related to the fact that women are more likely than men to present for CABG with an acute coronary syndrome, perhaps secondary to delayed recognition of surgical coronary disease.1–5,6 Others ascribe higher in-hospital mortality to women’s smaller body and coronary artery sizes, which may lead to less durable results due to the technical constraints of bypassing smaller coronary arteries.7–10 Yet no objective evidence to date has shown a difference in graft patency for women.11 It has also been observed that women are less likely to receive evidence-based therapies such as internal mammary artery grafting.12 Despite this, long-term survival for women appears equal to or even slightly better than that for men after revascularization.13,14

There has been less research into long-term differences in gender-specific nonfatal events such as cardiac readmissions after CABG. In New York State, early readmission to the hospital was more frequent for women (n = 4635) than for men, with an odds ratio (OR) of 1.25 (95% confidence interval [CI] 1.12 to 1.39) and was especially evident in the case of wound infections (OR 1.50, 95% CI 1.24 to 1.81).15 This finding was also noted in a small study (n = 158 women) in which gender was associated with an OR of 2.45 (95% CI 1.44 to 4.20) for 30-day readmission.16 In contrast, a Swedish study involving 1588 women demonstrated no difference in readmission between men and women (OR 1.06, 95% CI 0.98 to 1.13) over a mean follow-up period of 2.1 years.17 Follow-up of CABG patients in western Sweden revealed no gender differences in rates of myocardial infarction or stroke; however, at 5 years after surgery, women complained of angina more frequently than men.8,18

The present cohort study in Ontario, Canada provides new data regarding the disparity between women and men in long-term nonfatal cardiac outcomes up to 11 years after CABG. The

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PLAD indicates proximal left anterior descending coronary artery disease. CCS Class 4a angina includes all patients admitted with UA who became pain-free with medical therapy. CCS Class 4b angina includes all patients admitted with UA who experienced pain with minimal activity despite aggressive medical therapy. CCS Class 4c angina includes all patients admitted with UA who required intravenous treatment or intra-aortic balloon pump insertion to alleviate anginal symptoms or to maintain hemodynamic stability.

All values are percentages of patients in each group.

purposes of our cohort study of CABG were to document differences between women and men in their presentation for surgery and to identify gender differences in long-term nonfatal cardiac outcomes.

Methods

All patients who underwent isolated coronary artery bypass surgery in the province of Ontario between September 1, 1991, and March 31, 2002, were identified with the Cardiac Care Network (CCN) database. Their data were linked to 4 administrative databases through the use of unique encrypted identifiers. The Canadian Institutes for Health Information (CIHI) database provided each patient’s discharge disposition, which allowed us to identify patients discharged alive from hospital and their subsequent cardiovascular hospital readmissions for acute myocardial infarction (AMI), congestive heart failure (CHF), unstable angina (UA), and stroke. The Registered Persons Database (RPDB) was used to identify deaths that occurred outside of hospitals. The Canadian Census database from 1996 was used to estimate each patient’s income quintile based on linkage to postal code of primary residence (enumeration area). Finally, the Ontario Health Insurance Plan (OHIP) database was used to determine type of grafts used and repeat revascularization procedures (angioplasty or repeat CABG).

Data Analysis

Statistical significance was defined as a probability value less than 0.01. χ² Tests and t tests were used to compare categorical and continuous variables, respectively, between genders in terms of both clinical variables and outcomes. We completed an unadjusted survival analysis using Kaplan-Meier curves stratified by gender to understand its influence on each outcome of interest, including death, cardiac readmission (MI, CHF, or UA), stroke readmission, and repeat revascularization.

Cox proportional hazards models were used to identify the impact of gender after adjustment for age; triage status; era of surgery; income quintile; left ventricular function; Canadian Cardiovascular Society (CCS) angina class; coronary anatomy, defined categorically from angiographic data as either (1) left main disease with a stenosis ≥50%, (2) proximal left anterior descending artery stenosis in conjunction with either or both circumflex and right coronary stenoses ≥70%, (3) triple-vessel coronary disease without proximal left anterior descending stenoses ≥70%, or (4) other coronary anatomy, ie, single-vessel disease involving proximal left anterior descending coronary artery and single- or double-vessel disease not involving the proximal left anterior descending coronary artery; CHF; previous CABG; cerebrovascular disease; peripheral vascular disease (PVD); chronic obstructive pulmonary disease (COPD); dialysis; diabetes mellitus; body size (subset of patients operated on from fiscal years 1998 to 2001 from which quartiles of body surface area were calculated); and arterial graft number (subset of patients at 8 of the 9 participating hospitals for which we had billing data).19 To test the proportional hazards assumption for the gender effect in the Cox model, a time-varying gender covariate was included to understand the interaction between sex and survival time. The proportionality assumption was violated for 1 outcome, cardiac readmission. For this outcome, separate early (<1 year) and late (>1 year) models were created. Risk-adjusted survival curves for each outcome were constructed by methods previously described to understand the relative impact of gender when all other differing clinical characteristics were taken into account, including separate models for patient subsets (ie, those with body size data, arterial graft number).20

A propensity-matched analysis was used as a sensitivity analysis to test robustness of the results. Outcomes were compared between males and females who closely matched on propensity scores. The propensity score was calculated for each patient on the basis of a logistic regression analysis of the probability of being female, using age, triage status, era of surgery, income quintile, left ventricular function, CCS class, coronary anatomy, CHF, previous CABG, cerebrovascular disease, PVD, COPD, dialysis, and diabetes mellitus. A greedy matching algorithm was used to match patients on the logit of the propensity score with a caliper width of 0.2 of the standard deviation of the logit of the propensity score.21

A total of 14,378 of 14,393 women were matched on propensity score to men (99.9% efficiency). McNemar’s test was used to assess
Patients did not demonstrate a gender-versus-age interaction on variables included in the propensity model except in the case of CHF, which remained significantly different, although only by 1 percentage point between groups (Table 3); however, matched patients did not differ statistically on left ventricular ejection systolic grade. Furthermore, matched patients did not demonstrate a gender-versus-age interaction that measured variables were balanced between women and men in the propensity-matched cohort. To take into account the time-sensitive nature of the outcomes, stratified Cox models were constructed for each outcome of interest by this method. The gender effect was then further evaluated in subsets of patients that excluded those presenting with the outcome of interest (ie, the Cox analysis of readmission for CHF excluded those admitted with CHF at the time of surgery, and the Cox analysis of readmission for UA excluded those admitted with CCS 3 or greater angina). The statistical analyses were completed with SAS software (version 8.2; SAS Institute Inc). The authors had full access to the data and take full responsibility for its integrity. All authors have read and agreed to the manuscript as written.

Results

Gender-Specific Clinical Characteristics

A total of 66,193 patients were discharged alive after CABG in Ontario during the study time period. Of these, 14,393 (22%) were females, and 51,800 (78%) were males. Women tended to be older and of lower socioeconomic status (Table 1). Women possessed more comorbid illness, including diabetes mellitus, COPD, PVD, cerebrovascular disease, and CHF (Table 1). The triage status and CCS class were more severe in women (Table 1). A lower proportion of women had a previous CABG or poor left ventricular systolic function (Table 1). Women were less likely to receive arterial grafts and received fewer total grafts regardless of presenting coronary anatomy (Table 2). We further noted that those with the lowest quartile of body surface area were significantly more likely to receive no arterial grafts (18%) compared with those in the remaining 3 quartiles (range from 10% to 11%).

Propensity matching resulted in 14,378 females matched (99.8%) to males in the cohort. Matched groups were similar on variables included in the propensity model except in the case of CHF, which remained significantly different, although only by 1 percentage point between groups (Table 3); however, matched patients did not differ statistically on left ventricular ejection systolic grade. Furthermore, matched patients did not demonstrate a gender-versus-age interaction that would explain the gender gradient in socioeconomic status that was observed in the entire cohort.

Death

Propensity matching revealed that females were less likely to die (hazard ratio [HR] 0.9, 95% CI 0.83 to 0.98) after being discharged alive after CABG surgery (Table 4). We have included the frequency of outcomes for both the entire cohort and propensity-matched patients by gender at 1, 5, and 10 years after surgery in Table 5.

Cardiac Readmission

Women were more likely than men to be readmitted both early and late after CABG (Figure 1). After risk adjustment for patient characteristics in the entire cohort with a Cox model, this difference narrowed but remained statistically significant (Figure 2). In response to this finding, the model was segmented into early cardiac readmission (≤1 year) and late cardiac readmission (>1 year) models. The largest HR (1.4; 95% CI 1.32 to 1.47) was early after CABG. This model was then further altered to include body surface area and arterial graft number, which were only available on a subset of patients (25,662; 4268 females); however, this did not alter female risk (HR 1.4, 95% CI 1.31 to 1.59). The gender difference in late cardiac readmissions was only slightly lower (HR 1.2, 95% CI 1.14 to 1.24) and remained elevated with further risk adjustment using body surface area and arterial graft number (HR 1.3, 95% CI 1.11 to 1.44).

Stratified Cox models with patients matched on propensity score also revealed that females were more likely to be admitted for cardiac readmissions. Females had an HR of 1.3 (95% CI 1.28 to 1.41) for all cardiac readmissions, including AMI, CHF, and UA, compared with men (Table 4). This composite outcome was further broken down into separate Cox models to reveal the difference was mainly due to readmissions for UA (HR 1.3, 95% CI 1.24 to 1.38) and CHF (HR 1.1, 95% CI 1.06 to 1.21), whereas AMI readmissions were similar (HR 1.0, 95% CI 0.93 to 1.07) between men and women (Table 4).
To further understand the gender differences for UA readmissions in the propensity-matched cohort, patients with preoperative angina greater than CCS class II were excluded; however, this did not change the female HR for UA readmission (HR 1.3, 95% CI 1.23 to 1.38). The number of arterial grafts was significantly protective against UA readmission; however, this did not change the female HR for UA readmissions when added to the model (HR 1.3, 95% CI 1.23 to 1.38).

To further understand the gender differences for CHF readmissions in the propensity-matched cohort, patients with preoperative CHF were excluded, and it was found the HR did not change for females (HR 1.1, 95% CI 1.03 to 1.21). Similarly, the female HR for CHF readmissions remained the same even after arterial graft number was added to the model (HR 1.1, 95% CI 1.03 to 1.19).

Repeat Revascularization
The crude freedom from repeat revascularization appeared to be less for women than for men (Figure 3); however, when we used risk adjustment with a Cox model in the entire cohort, this difference was not statistically significant (Figure 4). Propensity-matched Cox models of repeat revascularization indicated women had a similar composite rate of repeat angioplasty and CABG (HR 1.0, 95% CI 0.91 to 1.06), which did not change if each of those individual outcomes were analyzed separately (Table 4).

Stroke
Stroke readmissions occurred more frequently for women, both early and late after CABG (Figure 5), but with risk adjustment in the entire cohort, the risk actually became slightly higher for men (Figure 6). Propensity matching revealed that females were less likely to be readmitted to the hospital with a stroke (HR 0.9, 95% CI 0.84 to 0.97) after being discharged alive after CABG surgery (Table 4).

Composite End Point
The composite HR for females including all of the above outcomes was similar to the HR for cardiac readmission at 1.3 (95% CI 1.25 to 1.38).

Discussion
Women discharged after CABG surgery in Ontario were more complex and at higher risk than their male counterparts.
Women received fewer arterial grafts during surgery and were more likely to be readmitted to the hospital with UA. Paradoxically, women were less likely to have poor ventricular function preoperatively; however, they had higher rates of postoperative hospital readmission for CHF. This finding was apparent even for those women who did not have preoperative CHF. In the long term, women had better or equivalent rates of death, readmission for myocardial infarction, and readmission for stroke.

The observed difference in long-term cardiac outcomes that existed despite extensive risk adjustment for women is puzzling. This finding is important because it supplements our knowledge of the long-term results of CABG surgery for women, which for the most part has been derived from randomized trials that mainly included male patients. We hope the present study helps to more accurately describe the long-term results of a surgical revascularization strategy, especially in an era where there may be other evolving treatment options for women, and also hint at how we might improve the differences observed in CABG results.

One hypothesis that could explain these differences in outcomes is that women may be subject to delayed referrals or impaired access to care for coronary disease. This may explain the differences observed in age and comorbidity status between men and women. There is evidence to demonstrate that timeliness of invasive management with revascularization when presenting with an acute coronary syndrome has an effect on downstream outcomes for women, as it does for men. The fact that the female patients in the present study were more likely to present with urgent and emergent status may indicate delayed referral compared with their male counterparts, as described in other patient cohorts. This is debatable, because current clinical data measuring the referral patterns from the time of coronary catheterization onward do not show a gender bias in access to revascularization procedures. It has also been suggested that women may be less likely to recognize they are having acute myocardial ischemia for 2 reasons. First, their symptoms are less typical of those classically reported and studied in men. Second, women have a higher pain threshold than men. This theory could be supported by the Framingham Study observation that women demonstrated higher percentages of silent or unrecognized AMI than men, which may explain why their presentation at surgery carries more urgency.

As demonstrated in the present study, women were less likely than men to receive arterial grafts. In our region of Canada, use of multiple arterial grafts has increased steadily in recent years, although we suspect not all eligible patients are receiving at least 2 arterial grafts. However, regardless of this fact, women have lagged behind in receiving arterial grafts each year. It is not surprising, then, that women had higher rates of readmission for unstable angina in the long term, indicative of their receiving less-durable grafts (that is, nonarterial). In addition, because they receive fewer grafts, revascularization may be incomplete; unfortunately, we do not have information on graft targets to verify this inference.

It is interesting to note that in a matched study of women and men who had received bilateral internal mammary artery grafting at a mean 9-year follow-up, there was no difference in mortality or freedom from angina, reoperation, and angioplasty. Despite this optimal grafting strategy, women still experienced a statistically significant higher rate of late myocardial infarction. The conclusion was that bilateral internal mammary artery grafting in women ameliorated the gender disparity in outcomes. Even in that study, in which all patients had bilateral mammary arteries, women on average received fewer grafts than men.

Another study (n=412 matched pairs of men and women) found that women received fewer distal anastomoses, which led to less complete revascularization. At 21 months, anginal status was not improved for 8% of women compared with 4% of men, and women having a repeat angiogram had worse saphenous vein graft patency than men (74% versus 86%, $P=0.001$). It was suggested this may be related to smaller native coronary arteries in women, which leads to a more technically difficult anastomosis and poor runoff. Another graft patency study with internal mammary artery grafts also observed a nonsignificant lower vein graft patency for women that was similar as for men at 1 year after CABG.
surgery. The present findings along with others indicate that at surgical revascularization, we need to ensure that women receive more arterial grafts and complete revascularization to optimize their postoperative outcomes to rates comparable to those observed for men. The Bypass Angioplasty Revascularization Investigation (BARI) trial observed that women had a much higher rate of repeat revascularization (relative risk 1.74, \( P = 0.04 \)). In that trial, it was also noted that female gender was an independent predictor of decreased internal mammary artery use. In the present study, we did not find any indirect evidence of decreased graft patency for women reflected through long-term rates of readmission for myocardial infarction and repeat revascularization.

We did find women were much more likely to be readmitted with UA after CABG surgery. In the Coronary Artery Surgery Study (CASS), gender predicted anginal status at 1

**Figure 1.** Crude survival with freedom from cardiac readmission for patients discharged alive after CABG surgery in Ontario (1991–2001) by gender.

**Figure 2.** Risk-adjusted survival with freedom from cardiac readmission for patients discharged alive after CABG surgery in Ontario (1991–2001) by gender.
year of follow-up. Conversely, the BARI trial found that women after CABG surgery did not differ from men with respect to anginal status or myocardial infarction rate at 5 years. The opposite was found in a small study that reported a much higher proportion of women (60%) experiencing angina than men (40%) at 5 years after CABG surgery.

Smaller studies have found much higher 30-day to 2-year all-cause readmission rates for females; however, this was attributed in part to a higher occurrence of surgical wound infections. In contrast, in Sweden, a study with 1588 female patients found no gender difference in all-cause readmission rates with multivariable adjustment. The pres-
ent study based on a large population of women after CABG with complete long-term follow-up indicates that cardiac readmission specifically for UA is much higher for women than for men. A major goal of CABG surgery is to improve anginal status, and this finding suggests fewer benefits for women. Perhaps there is a differential threshold for women who present with chest pain to receive a hospital admission because the diagnosis is less clear.

In the present study, despite the fact that women had less systolic ventricular dysfunction at presentation for surgery, they were more likely to present with a history of CHF and then be readmitted for CHF after CABG. In contrast, women in New York State were not found to be at higher risk of 30-day readmission for CHF after CABG.\(^{13}\) We may have observed this because the present study included much longer follow-up, up to 11 years after surgery. However, this is

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**Figure 5.** Crude survival with freedom from stroke readmission for patients discharged alive after CABG surgery in Ontario (1991–2001) by gender.

**Figure 6.** Risk-adjusted survival with freedom from stroke readmission for patients discharged alive after CABG surgery in Ontario (1991–2001) by gender.
consistent with data from other smaller studies that have also found higher early readmission rates for CHF between 2 and 6 months after surgery for women.31,34

There is evidence to suggest that women with known ischemic heart disease tend to be older and have more comorbidity when they develop CHF but surprisingly continue to have preserved left ventricular function compared with their male counterparts.35 Furthermore, women with CHF, when matched by age and comorbidity, do better as measured by further deterioration of ventricular function and mortality.35 In the present study, this is consistent with the observation that women had improved long-term survival compared with men despite the gender difference in readmission rates for CHF. This highlights the need for further research measuring quality of life in the long term for women compared with men after CABG surgery.

Late mortality after CABG surgery has been shown in previous work to be comparable and even lower than for men.13,14,23 In the present study cohort, there was a slight survival advantage for women who had survived their hospital stay after surgery. In addition, stroke readmissions were slightly lower for women in the present study, similar to findings of a smaller study with only 2 years of follow-up.8

Limitations of the present study include lack of detailed operative, echocardiographic follow-up, graft-patency, or cause-of-death data. These parameters could have differed between women and men. Such detailed data may have helped us explain the difference in outcomes experienced by women. We also did not have available other adverse in-hospital postoperative outcomes, such as neurological complications or renal insufficiency, that may have differed by gender and could have affected long-term outcomes. Our outcomes did not include quality-of-life measures. However, symptomatic status has an effect on quality of life, and smaller studies indicate that as early as 2 months after discharge, women have a much higher rate of physical decline and depressive symptoms than men.31,36 Women appear to derive fewer benefits from CABG surgery, and it has been shown that their health-related quality-of-life scores are lower than men postoperatively.37 Another limitation of the present study is that it was conducted in the setting of a public healthcare system, and thus, our conclusions may not be generalizable to other healthcare systems in other regions.

Conclusions
The present study data highlight the fact that despite equivalent or improved survival for women after CABG surgery, nonfatal cardiac event rates for women are inferior to men. There are operative disparities in the type of bypass grafts that women receive, which could partially explain this difference. Delayed referral or, conversely, the optimal timing of CABG surgery in women may need further exploration to explain this finding. New evidence also indicates that certain women have genetic predispositions to developing ischemic heart disease.38 It is possible genetics may play a role in the gender disparity we observe in outcomes after CABG surgery. In the current era of angioplasty with drug-eluting stents, genetic typing, and improved medical therapies for ischemic heart disease, there is a need to understand the best revascularization strategy for women. Despite a paucity of trial evidence for women for surgical revascularization, we need to create an optimal management plan that helps to close this gender gap in nonfatal outcomes.

Acknowledgments
The authors wish to acknowledge the cooperation of the Cardiac Care Network of Ontario. Dr Guru is supported by a salary fellowship from the Canadian Institutes of Health Research (CIHR), a TACTICS training grant, and a grant from the Tanna-Schulich fellowship fund of Sunnybrook and Women’s College Health Sciences Centre. Dr Austin is supported by a new investigator award from the CIHR. Dr Tu is supported by a Canada Research Chair in Health Services Research and a Career Investigator award from the Heart and Stroke Foundation of Ontario.

Disclosures
None.

References
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Circulation. 2006;113:507-516
doi: 10.1161/CIRCULATIONAHA.105.576652
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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