Anesthesiology
2000; 92:414-24

Female Gender Associates with Increased Duration of Intubation and Length of Stay after Coronary Artery Surgery

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Background: **Females have worse outcome than do males after coronary artery bypass grafting; however, gender effects on length of stay (LOS) outcomes, such as duration of intubation or intensive care unit (ICU) LOS, have not been evaluated previously. The authors hypothesized that adjustment for pertinent preoperative covariates would eliminate any significant effect of gender on duration of intubation, LOS in the ICU after extubation, total ICU LOS, postoperative (exclusive of ICU) LOS, or total postoperative LOS.**

Methods: **Patients undergoing elective or urgent primary coronary artery bypass grafting surgery at 51 academic health centers in 1995 and 1997 were studied. Unique multivariable statistical models were developed for duration of intubation, ICU LOS after extubation, total ICU LOS, and postoperative (exclusive of ICU and total) LOS to test for independent associations with gender. Preoperative but not intraoperative or postoperative variables were included in the model. $P \geq 0.01$ was considered significant.**

Results: **All LOSs were of significantly longer duration in females than in males in both the 1995 (n = 1,064) and 1997 (n = 910) data collections. After covariate adjustment, female sex remained associated with significantly longer duration ICU LOS and total postoperative LOS in both the 1995 (female:male ratios 1.30:1 and 1.13:1, respectively) and the 1997 (female:male ratios 1.19:1 and 1.12:1, respectively) data sets. After covariate adjustment, duration of intubation and ICU LOS after extubation were of significantly longer duration in women than men in 1995 (female:male ratios 1.22:1 and 1.39:1, respectively), but the differences were not significant in 1997.**

Conclusions: **Even in the context of accelerated recovery programs, these analyses show that female sex has powerful associations with increased LOS intervals for coronary artery bypass grafting surgery, even after adjustment for preoperative covariates. These effects could result from differences in the ways in which men and women respond to coronary artery disease, anesthesia, and coronary artery bypass grafting surgery, or to bias on the part of healthcare workers. (Key words: Gender effects; length of stay.)**

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Received from the Department of Anesthesiology, Wake Forest University School of Medicine and North Carolina Baptist Hospital, Winston-Salem, North Carolina, and The University HealthSystem Consortium, Oak Brook, Illinois. Submitted for publication December 28, 1998. Accepted for publication September 21, 1999. Support for data collection was provided by the CABG Clinical Benchmarking Database Participants and the University HealthSystem Consortium, Oak Brook, Illinois. Support for analysis was provided by the Department of Anesthesiology, Wake Forest University School of Medicine, Winston-Salem, North Carolina. Presented in part at the annual meetings of the American Society of Anesthesiologists, New Orleans, Louisiana, October 23, 1996, and San Diego, California, October 21, 1997.

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A full listing of the CABG Clinical Benchmarking Database participants is provided in Appendix 1.

FOR many years, women were excluded from clinical trials of patients with coronary artery disease, in part because of the incorrect belief that this disease process was nearly exclusive to men. More recently, cardiovascular disease has been recognized as a leading cause of death in adult women in the United States. Numerous studies have shown that women with coronary artery disease tend to present at an older age and with a higher incidence of comorbid conditions than do men with coronary artery disease.[1,2] Some studies have shown women with acute myocardial infarction to have worse outcomes than do men when undergoing coronary artery bypass grafting (CABG).[3,4] Whether gender might be an independent predictor of duration of intubation or length of stay (LOS) after CABG remains unknown.

For the past 6 yr the University HealthSystem Consortium (UHC) has organized a CABG benchmarking project to help participating teaching hospitals maintain market strength in this highly competitive medical service line. Using the two most recent CABG benchmarking databases,[5,6] we compared duration of tracheal intubation, ICU LOS after extubation, total ICU LOS, postoperative (exclusive of ICU) LOS, and total postoperative LOS for CABG in men and women. Finally, we tested whether women had longer duration LOS intervals than men, adjusting for comorbid conditions and other preoperative (but not intraoperative or postoperative) covariates that could be identified and evaluated preoperatively.

Methods

During November 1995 and November 1997, 40 and 51 participating academic health centers, respectively, collected data for the CABG benchmarking project (see Appendix 1 for a listing of academic health centers that contributed data). Each institution gathered, in a standardized fashion using a common data collection form, data for 30 consecutive patients, 20 yr of age or older, undergoing their first CABGs. Patients undergoing port-access surgery, minimally invasive coronary artery bypass under direct vision, or coronary procedures in which cardiopulmonary bypass was not used were not included. "Redo" and complex valve CABG procedures were specifically excluded. Patients undergoing emergency surgery were excluded. Although data were collected for the benefit of the member institutions and condensed versions were available for their use, our study represents an ancillary analysis that was conducted retrospectively after the overall and hospital-specific raw (with no adjustment for comorbidities) results had been reported to the members.

Trained abstractors collected data, including but not limited to, age; gender; diagnosis-related group; weight; height; history (and time) of myocardial infarction; history of congestive heart failure; history of cerebrovascular accident, transient ischemic attacks, or cerebrovascular disease; history of diabetes mellitus; history of peripheral vascular disease; history of chronic obstructive pulmonary disease; history of hypertension; and duration of preoperative LOS. Duration of cardiopulmonary bypass, available only in the 1997 data set, was used in some analyses. Strict definitions were provided for each coding field to minimize ambiguity. Each data-collection form was scrutinized by University HealthSystem Consortium personnel for data entry errors and omissions. If nonsensical entries or missing data were encountered, the data-collection forms were returned to the member institutions for clarification or correction. These data were analyzed preliminarily by University HealthSystem Consortium personnel and reported to the member institutions. In our analyses, duration of intubation was measured from the end of surgery until extubation. ICU LOS after extubation included postoperative stays in the postanesthesia care unit (if any) and postoperative stays in ICU for extubated patients. Postoperative (exclusive of ICU) LOS was measured from the time of transfer from ICU until hospital discharge. These three time intervals did not overlap. Total postoperative LOS measured from end of surgery to discharge from hospital and total ICU LOS (without excluding duration of intubation) also were compared. Returns to ICU after an initial discharge from the ICU were not included in our measures of ICU LOS; these times were included in our postoperative LOS measures.

Initial analysis of the data (conducted by University HealthSystem Consortium) from 1995 and 1997 showed differences among the member institutions and between men and women regarding LOS intervals. However, this initial descriptive analysis did not incorporate adjustment for severity of illness or other covariates and, therefore, did not directly address our hypothesis.

Statistical Analysis

The data sets were analyzed using the software Proc Mixed in SAS, version 6.12 (SAS Institute, Cary, NC). Mixed-effects linear models were used to test for associations between gender and each of the LOS intervals. The mixed-effects technique allowed statistical analysis to be adjusted for the random effect of each medical center. A more complete description of the mixed-effects procedure is given elsewhere.[7] Because the LOS intervals were judged to be log-normal in distribution, the statistical analyses were performed using log-transformed LOS intervals. The decision to log-transform the data was based on inspection of raw data, regression residuals (fig. 1), and experience from a previous study.[8] Therefore, geometric rather than arithmetic means were reported for all LOS intervals. The geometric mean is the antilog of the mean of the logarithmically transformed data and is an unbiased estimator of the population median value.

Covariates were included in the models to adjust for differences in preoperative disease severity and comorbid conditions among the patients. Covariates in the

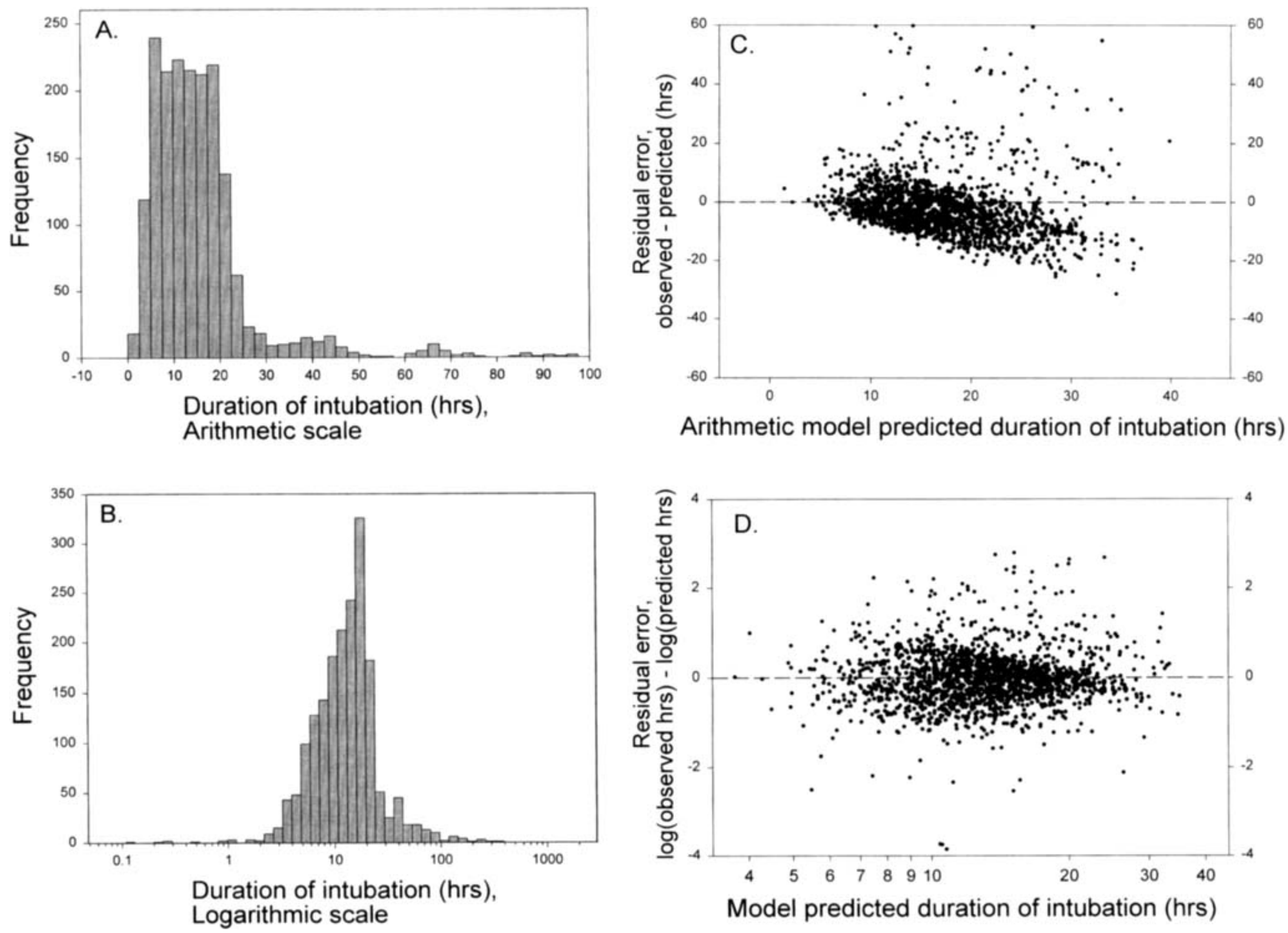

Fig. 1. Distribution of duration of intubation in the combined 1995 and 1997 data sets. (*A*) The data are presented on an arithmetic scale. (*B*) The data are presented on a logarithmic scale. Note that the data more closely resemble a normal distribution in *B* than in *A*. (*C, D*) the residual errors (differences between observed and predicted values) in duration of intubation are presented without (*C*) and with (*D*) logarithmic transformation. Notice how the plot of residuals in *C* shows a pronounced tendency toward negative values as the model predicted duration of intubation increases, whereas the residuals were distributed uniformly on either side of zero in *D*, independent of model predicted values.

models included age, weight, diagnosis-related group, chronic obstructive lung disease, congestive heart failure, renal failure, history of myocardial infarction, cerebral vascular disease, peripheral vascular disease, number of distal coronary artery anastomoses, diabetes mellitus, operative urgency, and the year of data collection (1995 or 1997). Left ventricular ejection fraction, although strongly associated with LOS, was not included in the models because values frequently were missing. The mixed-effects models excluded an observation if any covariates were missing. In a subsequent section, we report the results of a sensitivity analysis on inclusion of left ventricular ejection fraction in our models. The continuous covariates age and weight were modeled as quadratic rather than as simple linear functions, allowing for possible curvilinear relations between the LOS measures and age or weight. Adjustment was made for the use of sufentanil and fentanyl because we previously found a small association between use of sufentanil and shorter duration of intubation.[8] The interactions (diagnosis-related group × covariates and gender × year) also were included in the models. We made no corrections in *P* values. Because we were comparing men and women at five LOS intervals, we conservatively set the α level for significance at 0.01. Overall differences in preoperative demographic factors and comorbid conditions were

Table 1. Demographic Characteristics of Patients

	1995 Data (n = 1064)			1997 Data (n = 910)		
Variable	Males	Females	*P* Value	Males	Females	*P* Value
Total number	751	313	—	667	273	—
Age (yr, mean ± SD)	63 ± 11	65 ± 10	0.0005	64 ± 10	65 ± 11	0.0084
Weight (kg, mean ± SD)	86 ± 16	75 ± 18	0.0001	85 ± 16	74 ± 17	0.0001
BMI (kg/m^2; mean ± SD)	27.9 ± 5.3	29.5 ± 7.2	0.001	28.0 ± 5.6	28.9 ± 6.1	0.0274
Cerebrovascular disease (%)	9	11	0.2057	5	8	0.049
Diabetes mellitus (%)	27	45	< 0.0001	31	45	< 0.0001
History of MI (%)	51	43	0.0220	46	38	0.050
Peripheral vascular disease (%)	12	13	0.8384	12	14	0.370
Narcotic (%)						
Fentanyl	80	85	0.0460	83	83	1.000
Sufentanil	20	15		17	17	
Congestive heart failure (%)	8	21	< 0.0001	11	16	0.023
Chronic obstructive pulmonary disease (%)	10	12	0.2765	11	12	0.726
Renal failure (%)	5	7	0.4727	5	5	0.863
Left ventricular ejection fraction						
> 50 (%)	30	32	0.337*	39	47	0.043‡
35–50 (%)	29	30		37	33	
20–34 (%)	9	10		10	12	
< 20 (%)	1	0		2	0	
Missing	30	28		12	9	
Overall			0.73†			0.13†
Diagnosis-related group (%)						
106	50	58	0.013†	43	49	0.11†
107	50	42		57	51	
Operative status (%)						
Elective	70	67	0.344†	71	67	0.22†
Urgent	30	33		29	33	
Emergent*	—					
Number of distal anastomoses (%)						
1	7	7	0.619†	12	16	0.16†
2	20	24		34	37	
3	33	34		33	27	
4	27	24		16	15	
≥ 5	13	11		5	4	
Overall			0.126**			0.035**

Data are provided as incidences (N) and percent of population, or as the mean ± SD, as appropriate. Definitions of the demographic factors are provided in Appendix II. *P* values are provided for comparisons between women and men in each data set, using *t* test, unless otherwise indicated.

* Chi square test.

† Mann–Whitney test.

‡ Patients requiring emergent surgery were specifically excluded from the 1995 data collection.

BMI = body mass index; MI = myocardial infarction; SD = standard deviation.

compared using the Student *t* test, chi-square analysis, or Mann-Whitney tests, as appropriate.

Results

Totals of 1,164 and 1,072 CABG patient data were entered in the database during 1995 and 1997, respectively. There were 25 deaths (mortality rates: female 3.6% and male 1.4%; $P = 0.017$) recorded in the 1995 database and 31 (mortality rates: 5.4% females and 2.0% males; $P = 0.004$) in the 1997 database. After eliminating patients for whom covariate data were missing or who died perioperatively, the data were reduced to 1,064 and 910 patient records for 1995 and 1997, respectively, for a total of 1,974 patients. Further reductions of 7-213 patients from the 1,974 patients were made depending on the analysis because of missing resource-use times. The demographic characteristics of the patients are provided in table 1; women were slightly older and more frequently had diabetes mellitus and congestive heart failure. The LOS characteristics (without covariate ad-

Table 2. Differences by Gender in Durations of Intubation and Lengths of Stay after Coronary Artery Bypass Surgery in 1995 and 1997

Measurement	Year	Sex	N	Geometric Mean	95% Confidence Limits of Geometric Mean	*P* Value
Duration of intubation (h)	1995	Male	719	13.2	12.6–13.9	0.0001
		Female	297	18.0	16.5–19.6	
	1997	Male	608	10.8	10.2–11.4	0.0001
		Female	222	13.5	12.1–15.0	
ICU LOS after extubation (h)	1995	Male	661	18.3	17.0–19.6	0.0001
		Female	266	25.8	22.7–29.4	
	1997	Male	610	17.9	16.6–19.2	0.1632
		Female	221	20.0	17.6–22.8	
Total ICU LOS (h)	1995	Male	704	34.3	32.7–36.0	0.0001
		Female	291	47.7	43.7–52.1	
	1997	Male	571	33.2	31.6–34.8	0.0007
		Female	216	39.1	35.9–42.5	
Postoperative (exclusive of ICU) LOS (days)	1995	Male	665	4.7	4.5–4.9	0.0015
		Female	272	5.2	4.9–5.6	
	1997	Male	653	3.7	3.5–3.8	0.0257
		Female	242	4.0	3.8–4.2	
Total postoperative LOS (days)	1995	Male	749	5.8	5.6–6.0	0.0001
		Female	313	6.7	6.3–7.1	
	1997	Male	661	5.3	5.2–5.5	0.0003
		Female	241	5.9	5.7–6.2	

ICU = intensive care unit; LOS = length of stay; 1995 = 1995 Benchmarking study (N = 1064); 1997 = 1997 Benchmarking study (N = 968). *P* values are given testing for significant differences comparing males with females in either the 1995 or the 1997 benchmarking studies.

justments) for 1995 and 1997 are provided in table 2. It is notable that some of the differences between men and women were diminishing by the 1997 data collection. Table 3 provides effect ratios and *P* values for categoric variables that were included in the multivariable models. Each of these covariates was tested using a mixed-effects linear model with only itself, the year, and the hospital site included as factors in the statistical models.

The main effects of gender and year and their interaction from the mixed-effects linear models are described in table 4. The overall effects of gender were significant for all the resource time intervals except postoperative

Table 3. Ratios for Univariate Associations with Durations of Intubation and Length of Stay

	Duration of Intubation			ICU LOS after Extubation			Total ICU LOS			Postoperative (exclusive of ICU) LOS			Total Postoperative LOS		
Variable	*P* Value	Ratio	95% CI	*P* Value	Ratio	95% CI	*P* Value	Ratio	95% CI	*P* Value	Ratio	95% CI	*P* Value	Ratio	95% CI
CVD/none	0.0001	1.31	(1.16,1.47)	0.0008	1.29	(1.11,1.51)	0.0001	1.3	(1.18,1.45)	0.1014	1.07	(0.99,1.15)	0.0001	1.16	(1.09,1.24)
CHF/none	0.0001	1.22	(1.11,1.35)	0.0001	1.38	(1.22,1.56)	0.0001	1.3	(1.19,1.41)	0.0001	1.22	(1.15,1.30)	0.0001	1.22	(1.16,1.29)
COPD/none	0.0262	1.12	(1.01,1.23)	0.0003	1.26	(1.11,1.43)	0.0002	1.18	(1.08,1.29)	0.0001	1.15	(1.08,1.22)	0.0001	1.16	(1.10,1.23)
DM/none	0.0492	1.07	(1.00,1.14)	0.4038	1.04	(0.95,1.13)	0.0267	1.07	(1.01,1.13)	0.0389	1.05	(1.00,1.09)	0.0083	1.05	(1.01,1.09)
DA > 2/DA ≤ 2	0.0470	1.07	(1.00,1.15)	0.0003	1.18	(1.08,1.29)	0.0009	1.11	(1.04,1.18)	0.0009	1.08	(1.03,1.13)	0.0001	1.10	(1.05,1.14)
DRG 107/106	0.0010	0.90	(0.84,0.96)	0.0244	0.91	(0.84,0.99)	0.0023	0.92	(0.87,0.97)	0.8641	1.00	(0.96,1.04)	0.0532	0.97	(0.93,1.00)
MI/none	0.0090	1.09	(1.02,1.16)	0.0261	1.10	(1.01,1.19)	0.0001	1.12	(1.06,1.18)	0.4888	1.01	(0.97,1.06)	0.0498	1.04	(1.00,1.07)
Not elective/ elective	0.0053	1.11	(1.03,1.19)	0.2429	1.06	(0.96,1.16)	0.1449	1.05	(0.98,1.12)	0.8585	1.00	(0.95,1.04)	0.5224	1.01	(0.97,1.05)
PVD/none	0.7768	1.01	(0.92,1.11)	0.0037	1.19	(1.06,1.34)	0.0009	1.15	(1.06,1.25)	0.0030	1.10	(1.03,1.17)	0.0001	1.11	(1.05,1.17)
CRF/none	0.0004	1.28	(1.12,1.47)	0.0002	1.39	(1.17,1.66)	0.0001	1.36	(1.21,1.53)	0.0001	1.28	(1.17,1.40)	0.0001	1.31	(1.21,1.41)
SUF/FEN	0.0131	0.87	(0.77,0.97)	0.9586	1.00	(0.86,1.16)	0.3385	0.95	(0.86,1.05)	0.0231	0.92	(0.85,0.99)	0.0144	0.92	(0.87,0.98)

Ratios are provided for the effect of having the indicated variable divided by the effect of not having the indicated variable (unless otherwise indicated).

Note that for simplicity, we report distal anastomoses here in only two classes (> 2 or ≤ 2), whereas in the multivariable model we included, for completeness, additional classes.

CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CRF = chronic renal failure; CVD = cerebrovascular disease; DA > 2 = more than two distal coronary anastomoses; DM = diabetes mellitus; DRG = diagnosis-related group; FEN = fentanyl; MI = myocardial infarction; Not elective = emergent or urgent surgery; PVD = peripheral vascular disease; SUF = sufentanil.

(exclusive of ICU) LOS. The year of data collection significantly affected duration of intubation, postoperative (exclusive of ICU) LOS and total postoperative LOS, confirming that these LOS intervals were decreasing progressively. The mixed-effects linear models provide estimates of the gender differences in the log-transformed time intervals and LOS measures. These gender differences then become female:male LOS ratios as the measures are transformed back to an arithmetic scale using the antilog. These estimates of the female:male LOS intervals ratios are shown in figure 2, with the 95% confidence intervals. All female:male LOS ratios were estimated to be greater than 1. When the lower bound of the ratios' 95% confidence interval exceeded 1, women had a significantly longer LOS than did men. The gender × year interactions in table 4 were not significant for any of the LOS intervals, indicating that, overall, the female:male ratios did not change significantly between 1995 and 1997.

To be certain that the differences between men and women were not the result of site-to-site variability, we undertook an additional analysis. Using the full, covariate-adjusted model, we tested for an effect of medical center for each of the LOS intervals. Medical center had a highly significant association ($P < 0.0,001$) with every LOS interval. Conversely, interaction between medical center and gender had no significant association ($P \geq 0.01$) with LOS interval. Duration of cardiopulmonary bypass was available only for the 1997 data set, and a separate analysis that incorporated this value as a covariate yielded male:female ratios that were nearly identical to those in figure 2.

Table 4. Interacting Effects of Gender and Year on LOS Intervals from Mixed-effects Regression Analysis

LOS Interval	N	Factor(s)	*P* Value
Duration of intubation	1849	Gender	0.0005
		Year	0.0001
		Gender*year	0.5480
ICU LOS after extubation	1761	Gender	0.0002
		Year	0.2904
		Gender*year	0.1032
Total ICU LOS	1785	Gender	0.0001
		Year	0.1054
		Gender*year	0.1461
Postoperative (exclusive of ICU) LOS	1835	Gender	0.0773
		Year	0.0001
		Gender*year	0.7959
Total postoperative LOS	1967	Gender	0.0001
		Year	0.0001
		Gender*year	0.7890

ICU = intensive care unit; LOS = length of stay.

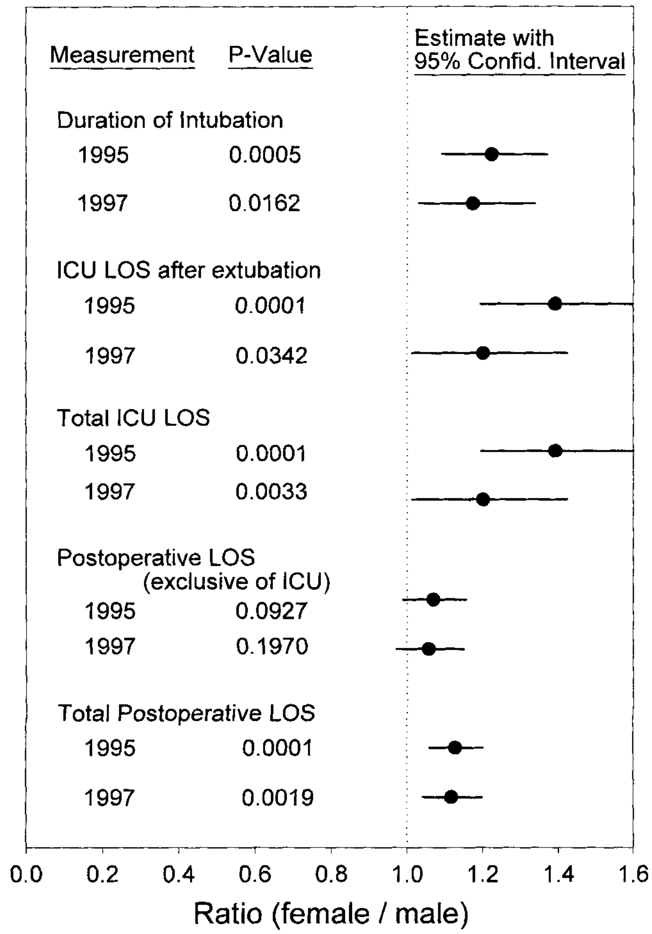

Fig. 2. Ratios of female:male length of stay (LOS) after CABG surgery. Covariate-adjusted multivariable models yielded estimates (with 95% confidence intervals) for ratios of female:male values for each of five LOS intervals. Ratios greater than unity denote an association of increased LOS with female sex. Note that $\alpha = 0.01$ for significance in this study even though 95% confidence intervals were provided on this figure.

To further clarify the effects of gender and year, covariate-adjusted (least-squares) geometric-mean LOS intervals by gender and year are provided in table 5. Assuming a patient age of 65 yr, a weight of 80 kg, and elective surgery, for comparison purposes, we calculated the least-squares geometric means. As noted, in both the 1995 and the 1997 data sets, female gender was associated with longer durations of intubation, longer duration ICU LOSs, and longer duration total postoperative LOSs, even after adjustment for multiple covariates, including age, weight, diabetes, myocardial infarction,

Table 5. Effects of Gender on Covariate-adjusted LOS Intervals

Outcome	Year	Sex	Covariate-adjusted Geometric Means	95% Confidence Limits of Geometric Mean	*P* Values
Duration of intubation (h)	1995	Male	12.3	11.0–13.7	0.0001
		Female	15.1	13.3–17.2	
	1997	Male	10.63	9.3–12.2	0.783
		Female	12.47	10.6–14.7	
ICU LOS after extubation (h)	1995	Male	16.6	13.9–19.8	0.0001
		Female	19.9	16.4–24.3	
	1997	Male	16.5	13.5–20.2	0.305
		Female	19.8	15.7–25.0	
Total ICU LOS (h)	1995	Male	31.6	28.2–35.3	0.0001
		Female	37.8	33.3–42.9	
	1997	Male	31.2	27.3–35.7	0.054
		Female	37.1	31.8–43.2	
Postoperative (exclusive of ICU) LOS (days)	1995	Male	4.6	4.3–4.9	0.0330
		Female	4.9	4.5–5.3	
	1997	Male	3.5	3.2–3.8	0.0023
		Female	3.7	3.3–4.1	
Total postoperative LOS (days)	1995	Male	5.5	5.2–5.9	0.0002
		Female	5.9	5.5–6.4	
	1997	Male	5.1	4.7–5.4	0.0001
		Female	5.6	5.2–6.2	

See text for details. *P* values are given for comparisons between men and women after adjustment for other covariates. Covariate-adjusted geometric means were calculated assuming age = 65 yr and weight = 80 kg.

ICU = intensive care unit; LOS = length of stay.

renal failure, chronic obstructive pulmonary disease, peripheral vascular disease, congestive heart failure, left ventricular ejection fraction, cerebrovascular disease, number of distal anastomoses, diagnosis-related group, operative urgency, and medical center in which the surgery was performed.

Discussion

A medical center must be capable of predicting resource use and LOS accurately to competitively bid with insurers and simultaneously avoid excessive financial risk. Many factors that influence costs are controlled by the medical center and its staff; other factors, such as the gender of patients, are dependent on the demographic characteristics of the insured pool. It is important for an institution to adjust for both classes of factors, so that appropriate global fees can be determined. We confirmed that, even after adjusting for comorbid conditions and other covariates, female gender remained associated with prolonged LOS. Therefore, it is likely that the costs of providing CABG surgery to a patient population increase as the fraction of females in that population increases.

Evidence supports[2,3,9–11] and refutes[1,12] worse outcomes in women (compared with men) with coronary artery disease. Multiple studies have shown that women, even after covariate adjustment, have a greater frequency of complications and of death after myocardial infarction.[2,3,9–11] Conversely, two large trials that measured outcome after acute coronary syndromes found that, although women tended to be older and had a higher incidence of diabetes and hypertension, rates of myocardial infarction and death were similar to those of men.[1,12]

Other studies evaluated the influence of gender on outcome after coronary revascularization procedures. Edwards *et al.*[4] used the Society of Thoracic Surgeons database of 344,913 patients undergoing CABG surgery to determine that women had a significantly higher risk of mortality than did men, even after adjustment for multiple covariates. Christakis *et al.*,[13] studying 7,025 patients undergoing CABG surgery, found that after adjustment for body size, older age, diabetes, and other risk factors, women still had a higher incidence of mortality. Conversely, several smaller studies found that covariate adjustment removes the adverse outcome association with female sex. Koch *et al.*[14] and Hammar *et al.*[15] found no significant gender-related differences in ICU LOS or morbidity or mortality rate after covariate adjustment. Jacobs *et al.*,[16] studying 1,829 patients in the Bypass Angioplasty Revascularization Investigation, reached the surprising and contrary conclusion that after covariate adjustment women had a significantly lower risk of mortality compared with men. In summary, most studies show that women have worse outcomes than men with acute coronary ischemia and after coronary revascularization.

Why do females appear to have a worse outcome after CABG surgery? There are several potential reasons. As noted previously, women generally have worse outcomes associated with coronary artery disease itself, with or without myocardial infarction. For instance, women appear to have less of a reduction in mortality risk than do men in response to atenolol, nitrates, captopril, aspirin, and streptokinase.[7,17-19] Women and men have differing autonomic responses to acute coronary occlusion, and patients with angina pectoris, particularly those older than 50 yr, show significant gender differences in multiple laboratory assessments of coagulation.[20,21] Recently, and most pertinently, Fontes *et al.*[22] studied patients undergoing CABG surgery at a single site and confirmed that women had longer durations of intubation and longer LOSs. Nevertheless, most investigators have assumed that, but for the older age and incidence of comorbid conditions and smaller size of women, they and men would have similar outcomes. In our study population, women were significantly older, more frequently afflicted with diabetes and congestive heart failure, and consistently associated with longer durations of intubation, ICU LOS, and total postoperative LOS compared with men. Longer LOS intervals with women were present whether we adjusted for weight or body mass index. It is particularly notable that some of the gender differences we identified in the 1995 data set remained significant in the 1997 data set, despite significant reductions over 2 yr in all LOS intervals (tables 4 and 5). This suggests that these gender differences may not disappear even as medical centers gain greater success and efficiency at streamlining the recovery process after CABG surgery.

These differences between men and women could result from subtle biases on the part of healthcare workers in the ways that they care for women *versus* men, or from biologic differences. Perhaps women are more sensitive than men to opioid-induced respiratory depression after cardiopulmonary bypass, or they may receive more postoperative opioid analgesics. The latter would be consistent with studies showing differing male and female responses to pain and to opioids and other analgesics.[23-26] Perhaps the data showing that women have a worse outcome than men after CABG surgery resulted in a widespread reluctance of healthcare workers to "push" women as hard as men to meet accelerated recovery goals. Alternatively, women may experience more emboli during or more brain edema after CABG surgery or be more susceptible to postoperative complications.[25,27]

Analysis of our database presents inevitable limitations and challenges. The design of our study permitted us to test for associations, but we could not test for causality in the way that a randomized, controlled trial could; this limitation must be emphasized. Conversely, it would be difficult to blind clinicians to the gender of patients during and after CABG surgery and impossible to assign gender on a random basis. Each member institution was responsible for collecting its own data, and, despite extensive efforts to ensure that a common set of definitions was used at each site, there was no external mechanism for confirming that the data had been gathered and recorded in exactly the same way in every institution. The University HealthSystem Consortium personnel responsible for collecting and collating data had no vested interest in the outcome of the analysis we report herein; therefore, these personnel would be an unlikely source of bias. Perioperative medical management of patients in this database was not standardized among institutions and undoubtedly varied widely among institutions. We previously showed marked variations among the participating institutions in the LOSs we report herein.[8] Standardized intraoperative and postoperative management protocols might have provided a clearer context in which to interpret our findings. We did not include intraoperative or postoperative factors in the analyses, and there is no question that postoperative complications have a profound effect on LOS.

There were relatively few deaths ($n = 25$ and 31, respectively, for the 1995 and 1997 data sets) in the study population. Had large numbers of patients died during or immediately after CABG (and had we included these patients in our LOS analyses), our estimates of LOS might have been skewed. In any case, the decision to exclude perioperative deaths from our LOS analyses was made before the data were collected. We found significant differences in mortality rates between men and women, but that was not the focus of the study. Although we tested for medical center differences and found significant variations, the data did not identify individual physicians; therefore, we could not draw conclusions about the role of individual physicians in controlling the outcome variables.[8] Nevertheless, gender × site interactions did not show statistical significance. Smith *et al.*[28] have shown marked differences in costs among surgeons at a single center. It is unlikely that the physicians caring for the patients in this database made equivalent efforts to minimize duration of intubation, ICU LOS, and hospital LOS. Therefore, our results and conclusions should be interpreted with caution. Conversely, medical centers participated in this project for the stated purpose of comparing their resource use with that of other comparable academic medical centers. Compared with the 1995 data, the unadjusted geometric mean postoperative LOS decreased by 0.5 days in the 1997 data. This is strong evidence that physicians at the participating centers were attempting, some more successfully than others, to reduce LOS for CABG surgery for men and women. It could be considered a strength of this study that 51 different centers contributed data. It is likely that this data set more completely represents current practice in US academic health centers than would the same-size database collected from a single site. One strength of the mixed-effects technique that we used in this study relative to other statistical techniques is that we could adjust for the random effects of the different medical centers.

We assume that we studied LOS intervals that relate to resource consumption, but we have not calculated resource consumption or costs directly. We assume that a patient who has a longer duration LOS has greater costs, but this may depend on staffing practices at each medical center, whether patients discharged after shorter duration LOS are more likely to be sent to rehabilitation facilities, and the extent of postoperative follow-up care.[28-30]

In summary, we found that women had longer LOSs than men at every milestone in recovery from CABG surgery, even after adjusting for greater incidence of comorbid conditions and more advanced age. Our analyses suggest that institutions may wish to account for the fraction of women in a referral population in estimating the costs of providing CABG surgery. Future studies should address whether these gender-based differences in LOS intervals result from specific, preventable complications, bias, or inadequate appreciation for differences in how men and women respond to treatment for coronary artery disease.

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Appendix 1: Academic Health Centers Contributing to the 1995 and 1997 CABG Clinical Benchmarking Databases

**Clarion Health Partners, Inc., Indianapolis, Indiana; Crawford Long Hospital of Emory University, Atlanta, Georgia; Emory University Hospital, Atlanta, Georgia; **Fairview University Medical Center, Minneapolis, Minnesota; Froedtert Memorial Lutheran Hospital, Inc., Milwaukee, Wisconsin; **Georgetown University Hospital, Washington, DC; Hermann Hospital at the University of Texas Health Science Center, Houston, Texas; ††Indiana University Medical Center, Indianapolis, Indianapolis; John Dempsey Hospital, The University of Connecticut Health Center, Farmington, Connecticut; Louisiana State University Medical Center, New Orleans, Louisiana; Loyola University Medical Center, Maywood, Illinois; **Massachusetts General Hospital, Boston, Massachusetts; Medical College of Georgia Hospital and Clinics, Augusta, Georgia; Medical College of Ohio Hospital, Toledo, Ohio; Medical College of Virginia Hospital, Virginia Commonwealth University, Richmond, Virgina; Medical University of South Carolina, Charleston, South Carolina; New York University Medical Center, New York, New York; The Ohio State University Medical Center, Columbus, Ohio; Oregon Health Sciences University Hospital and Clinics, Portland, Oregon; Pennsylvania State University/Milton S. Hershey Medical Center, Hershey, Pennsylvania; Robert Wood Johnson University Hospital, New Brunswick, New Jersey; Stanford University Hospital, Stanford, California; State University of New York Medical Center of Stony Brook, Stony Brook, New York; **State University of New York Health Science Center at Syracuse, Syracuse, New York; Thomas Jefferson University Hospital, Philadelphia, Pennsylvania; **University Hospital, Inc., Cincinnati, Ohio; **University Hospitals of Cleveland, Case Western Reserve University, Cleveland, Ohio; University Medical Center Corporation, Arizona, Tucson, Arizona; University of Alabama Hospital, Birmingham, Alabama; University of California Irvine Medical Center, Irvine, California; University of California Los Angeles Medical Center, Los Angeles, California; **University of California San Francisco Medical Center, San Francisco, California; The University of Chicago Hospital and Health System, Chicago, Illinois; **University of Colorado Hospital, Denver, Colorado; The University of Illinois at Chicago Medical Center, Chicago, Illinois; The University of Kansas Hospital, Kansas City, Kansas; University of Kentucky Hospital, Lexington, Kentucky; **The University of Maryland Medical System, Baltimore, Maryland; University of Massachusetts Medical Center, Worcester, Massachusetts; The University of Medicine and Dentistry of New Jersey, University Hospital, Newark, New Jersey; ††University of Minnesota Hospital and Clinics, Minneapolis, Minnesota; University of Missouri Hospital and Clinics, Columbia, Missouri; University of Nebraska Medical Center, Omaha, Nebraska; University of North Carolina Hospitals, Chapel Hill, North Carolina; **University of Texas Medical Branch, Galveston, Texas; University of Virginia Health Science Center, Charlottesville, Virginia; University of Washington Academic Medical Center, Seattle, Washington; **University of Wisconsin Hospital and Clinics, Madison, Wisconsin; Vanderbilt University Hospital and Clinic, Nashville, Tennessee; Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina; West Virginia University Hospitals, Morgantown, West Virgina; Yale-New Haven Hospital, New Haven, Connecticut; **Zale Lipshy University Hospital, University of Texas Southwestern Medical Center, Dallas, Texas.

** Participated in 1997 only.

†† Participated in 1995 only.

Appendix 2: Definitions of Covariates

Diagnosis-related group

Tested whether patients who underwent cardiac catheterization during the same hospital admission as for CABG had differing outcomes from patients who did not undergo cardiac catheterization during the same hospital admission as for CABG.

Diabetes

Indicated that the patient was treated with drugs or diet therapy for a diagnosis of either type I or type II diabetes mellitus.

Vascular disease

Indicated that the patient had a history of intermittent claudication or had previous infrainguinal vascular surgery.

Cerebrovascular disease

Indicated that the patient had previous stroke or transient ischemic attacks or previous carotid thromboendarterectomy or was known to have more than 70% stenosis in at least one carotid artery.

Renal failure

Indicated a documented fasting serum creatinine level of more than 2.0 mg/dl preoperatively, or a preoperative need for dialysis.

Left ventricular ejection fraction

Generally calculated during cardiac catheterization using the Dodge formula but sometimes obtained echocardiographically or through use of radiocontrast ventriculography.

Myocardial infarction

Indicated that the patient was as having a myocardial infarction at some time before CABG. No attempt was made to determine whether history, electrocardiography, or biochemical studies were used to make the initial diagnosis.

Congestive heart failure

Indicated that the patient was diagnosed with congestive heart failure at some time before CABG surgery, based on at least three factors from among dyspnea, rales thought to represent pulmonary congestion, peripheral edema, cardiomegaly seen on chest radiograph, and pulmonary interstitial edema seen on chest radiograph.

Distal anastomoses

Recorded the number of graft connections to native coronary arteries that were performed intraoperatively, regardless of the type of conduit.

Operative status

Compared patients who were undergoing elective, urgent, or emergent surgery. Elective cases were scheduled at least 1 day before the surgical procedure. Urgent surgery was necessary within 24 h to minimize the risk of further deterioration. Emergent surgery was necessary immediately.

Site

Refers to the specific medical center in which CABG surgery was performed.

Preoperative duration of stay

Measured from the time of hospital admission until the day of CABG surgery.

Opioid

Referred to whether fentanyl or sufentanil was used during anesthesia.