Original Article

Early and Mid-term Outcomes in Female Patients Undergoing Isolated Conventional Coronary Surgery

Kazim Erguneş*, Levent Yilik, Ufuk Yetkin, Banu Lafcı, Serdar Bayrak, Berkan Ozpak, Ali Gurbuz

Izmir Katip Celebi University Ataturk Training and Research Hospital, Department of Cardiovascular Surgery , Izmir, Turkey

Abstract

Introduction: Several observational studies comparing outcomes between female and male patients after coronary artery bypass grafting (CABG) have shown that operative mortality rate is higher among female patients than in male patients. However, some conflicting studies report that early mortality among female patients is equivalent to that among male patients. We investigated predictive factors of morbidity, mortality and survival in female patients undergoing isolated conventional CABG.

Methods: Between January 2002 and December 2009, 1657 patients underwent isolated conventional CABG in our clinic. 21.8% (n=361) of patients were female and 78.2% (n=1296) males.

Results: Advanced age (P<0.0001), hypertension (P<0.0001), diabetes (P<0.0001), and hyperlipidemia (P<0.0001) were the independent predictive factors among female patients. Mean in-hospital mortality rates were 5.8% and 3.2%; for females and males, respectively (P=0.029). Prolonged ventilatory support (P=0.009) and postoperative atrial fibrillation (P=0.049) were the independent predictive factors of in-hospital mortality in female patients. Cardiopulmonary bypass time (P=0.041), prolonged ventilatory support (P<0.0001), and postoperative atrial fibrillation (P=0.031) were the independent predictive factors of in-hospital mortality in male patients. Mean follow-up was 47.51±25.06 months and 48.42±25.21 months among female and male patients (P=0.820). In follow-up, mortality rate was 6.1% (n=22) among female patients and 4.6% (n=60) among male patients (P=0.272). Left internal thoracic artery (LITA) usage (P=0.001) was the independent predictive factor of survival in female patients.

Conclusion: In-hospital mortality rate was higher in female patients. Length of ICU and hospital stay, and mid-term survival was similar between female and male patients.

Introduction

Despite the decrease in operative mortality and morbidity rate in patients undergoing isolated on-pump coronary artery bypass grafting (CABG) in recent years, several observational studies comparing outcomes between female and male patients after CABG have shown that operative mortality rate is higher among female patients than in male patients.[1-4] However, some conflicting studies report that early mortality among female patients is equivalent to that among male patients.[5,6]

Conflicting results among published studies with regard to the influence of gender on postoperative morbidity and mortality after CABG are influenced by a number of factors: dissimilar study designs and data collection method, different study sample sizes, and variable application of statistical methods to analyze the data sets.

In our study, we investigated predictive factors of morbidity, mortality and survival in female patients undergoing isolated conventional CABG.

Materials and methods

Between January 2002 and December 2009, 1657 patients underwent isolated CABG in our clinic. 21.8% (n=361) of patients were female and 78.2% (n=1296) male.

Cases of redo-CABG surgery, off-pump CABG surgery, simultaneous cardiac valve surgery, simultaneous carotid endarterectomy, simultaneous ventricular aneurysm surgery and simultaneous peripheral vascular surgery were not included in the study.

Perioperative management

Anesthetic, surgical, and CPB techniques were similar for all patients. The method of anesthesia was equally applied to all cases. Induction of anesthesia was provided through titration of 2 mg of midazolam I.V, 2-5 μg/kg of fentanyl I.V and 2-5 mg/kg of thiopental sodium I.V. Muscle

*Corresponding author: Kazım Ergüneş, Email: kazimergunes@yahoo.com

relaxation was achieved by 0.1 mg/kg pancuronium bromide and anesthesia was maintained by high dose fentanyl. Cardiopulmonary bypass was undertaken using a standardized extracorporeal circulation utilizing non-pulsatile flow, and an alpha-stat management protocol.

The systemic perfusion was performed using hypothermic bypass strategy of systemic cooling between 28 ̊C and 32 ̊C. Isothermic blood cardioplegia was initially administered antegradely and retrogradely, and thereafter continuously retrogradely. After the surgery, patients were transported to the intensive care unit and followed up according to the unit protocol. Prolonged CPB time was defined as CPB time >3 hours. Prolonged inotropic drug support was defined as use of inotropic drug for >24 hours.

Prolonged ventilatory support was defined as pulmonary insufficiency requiring ventilatory support >24 hours postoperatively. Prolonged ICU stay was defined as ICU stay of >48 hours, while normal ICU stay was defined as ICU stay lasting ≤48 hours. Prolonged hospital stay was defined as hospital stay of >5 days. Preoperative, operative, and postoperative data of the patients were collected prospectively and entered into our cardiac surgery registry. Data of death and cause of death were obtained through hospital records and physician records. Information was obtained through phone calls with patient families, or the patient's family physician or cardiologist.

Statistical Analysis

Following data accumulation, statistical models were formed and analysed using SPSS 15 (SPSS Inc, Chicago, The United States). Non-categorical data were analysed with t-test and categorical data with Chi-Square or Fisher's Exact test where appropriate. Mann-Whitney was used in analysing duration of intensive care unit stay and hospitalization periods. Survival analysis was performed using the Kaplan-Meier method. Log-Rank test was used in analysis of risk factors affecting survival. Variables with a P value equal or less than 0.05 were entered into the multivariate regression model. Independent predictors of duration of ICU and hospital stay were analyzed using a multivariate linear regression analysis. Independent predictors of postoperative mortality were analyzed using a multivariate logistic regression analysis. In multivariate analysis, independent predictors of survival were analyzed using Cox-regression analysis.

Results

Advanced age, hypertension, diabetes, and hyperlipidemia were more common among female patients. Smoking and peripheral vascular disease were more common among male patients (Table 1).

Chronic obstructive pulmonary disease (COPD), Left main coronary artery disease (LMCAD), preoperative renal disease, preoperative atrial fibrillation, previous stroke or trancient ischemic attack, previous PTCA, preoperative ejection fraction rates were similar between female and male patients (Table 1).

The mean cardiopulmonary bypass was 98.84 ± 31.82 minutes and 100.81 ± 33.91 minutes among male and female patients, respectively (P=0.304). The mean cross-clamp time was 42.23 ± 12.99 minutes and 42.60± 12.77 minutes among male and female patients, respectively (P=0.623). Postoperative blood transfusion (≥3 units) requirement and renal insufficiency were more common

Table 1. Preoperative data for female and male patients

	Male	Female	P value
	(N=1296)	(N=361)	
Age (yrs)	57.71±10.74	63.18±9.53	<0.0001
Smoking	69.1 % (896)	16.3% (59)	< 0.0001
Diabetes	32.3% (418)	47.9 % (173)	<0.0001
Hyperlipidemia	42.8 % (555)	53.2 % (192)	<0.0001
Hypertension	40.2% (521)	67.3% (243)	<0.0001
COPD	4.6% (59)	4.2% (15)	0.885
LMCAD	6 % (78)	5 % (18)	0.525
Renal failure or creatinine ≥2 mg/dl	1.1% (14)	1.9%(7)	0.191
Peripheral vascular disease	5.6 % (73)	0.8% (3)	<0.0001
Preoperative AF	1.3% (17)	1.7 % (6)	0.612
Previous PTCA	5.6% (72)	4.7% (17)	0.599
Previous stroke or TİA	0.7% (9)	1.1% (4)	0.497
Aort calcification	3.1% (40)	3.9 % (14)	0.502
Ejection fraction (%)			
<30	6.6 % (85)	5% (18)	0.139
30-50	40.7% (523)	46.1% (166)	
>50	52.7% (678)	48.9 % (177)	

AF: Atrial fibrillation, COPD: Chronic obstructive pulmonary disease, LMCAD: Left main coronary artery disease, TIA: Transient ischemic attack

among female patients (Table 2).

The independent predictive risk factors among female patients were shown in Table 3. The independent predictive factors of length of ICU stay among female patients were shown in Table 4. The independent predictive factors of length of hospital stay among female patients were shown in Table 5. Mean in-hospital mortality rates were 5.8% and 3.2%; for females and males, respectively which was statistically significant (P=0.029).

Prolonged ventilatory support (Beta 4.69, S.E 1.79, P=0.009, OR 109.50, 95% CI for OR 3.24 - 3694.45) and postoperative atrial fibrillation (Beta 4.09, S.E 2.07, P=0.049, OR 60.03, 95% CI for OR 1.02 - 3510.10) were the independent predictive factors of in-hospital mortality in female patients.

Cardiopulmonary bypass time (Beta 1.55, S.E 0.76, P=0.041, OR 4.73, 95% CI for OR 1.06 – 20.98), prolonged ventilatory support (Beta 2.95, S.E 0.83, P<0.0001, OR 19.27, 95% CI for OR 3.79 – 98.04), and postoperative atrial fibrillation (Beta 1.87, S.E 0.87, P=0.031, OR 6.49,

Table 2. Intraoperative, and postoperative data for female and male patients

	Male	Female	P
	(N=1296)	(N=361)	
Urgent and emergent operations	1.2 % (15)	-	0,052
CPB time			
< 3 hour	96.2% (1247)	93.9% (339)	0.076
>3 hour	3.8% (49)	6.1% (22)	
Number of bypass grafts			
1	6.3% (82)	6.1% (22)	
2	35.5% (460)	36.8% (133)	0.892
≥3	58.2% (754)	57.1% (206)	
Cross-clamp time			
< 1 hour	93.1% (1207)	91.7% (331)	0.357
> 1 hour	6.9% (89)	8.3 % (30)	
Duration of surgery			
<3 hour	39.4% (510)	46.3% (167)	
≥ 3-4 hour	51.9% (672)	44.3% (160)	0.037
>4 hour	8.8% (114)	9.4% (34)	
Prolonged intrope use	15.5% (201)	15.5% (56)	1.000
Intra-aortic balloon support	7.6% (98)	10% (36)	0.155
Prolonged ventilatory support	3.1% (40)	5% (18)	0.104
Postoperative renal failure	2.8% (36)	5.8% (21)	0.008
Postoperative dialysis	1.2% (15)	2.5% (9)	0.078
Postoperatif atrial fibrilasyon	16.3% (211)	16.9% (61)	0.810
Hemorrage-related reexploration	2.5% (32)	2.8% (10)	0.708
Postoperative blood transfusion			
Requirement ≥3 unite	4.8% (62)	7.5% (27)	0.048
Postoperative stroke	1% (14)	0.5% (2)	0.503
Mean ICU length of stay (days)	2.67±3.44	2.69.±2.07	0.879
Mean hospital length of stay (days)	6.40±2.16	6.34.±1.40	0.224
In-hospital mortality	3.2% (42)	5.8 % (21)	0.029

AF: Atrial fibrillation, CPB: Cardiopulmonary bypass, ICU: Intensive care unit

Table 3. Independent predictive factors by multivariete regression analysis of female patients undergoing CABG

Variable	Beta	Std. Error	OR	95% CI for OR	P value
Age	0.038	0.007	1.09	1.02 – 1.05	<0.0001
Diabetes	0.64	0.13	1.91	1.47 – 2.46	<0.0001
Hyperlipidemia	0.68	0.13	1.98	1.53 – 2.56	<0.0001
Hypertension	0.95	0.13	2.60	2.01 – 3.37	<0.0001

Table 4. Independent predictive factors of length of ICU stay by multivariete regression analysis in female patients

Variable	Beta	Std. Error	P value
COPD	1.33	0.44	0.003
Cross-clamping time	0.88	0.36	0.016
Prolonged inotropic support	1.42	0.39	<0.0001
Prolonged ventilatory support	3.00	0.48	<0.0001
Hemodialysis	2.07	0.72	0.004
Postoperative blood transfusion (≥3 unite)	1.39	0.41	0.001
Postoperative stroke	2.59	1.18	0.029

COPD: Chronic obstructive pulmonary disease

Table 5. Independent predictive factors of length of in-hospital stay by multivariete regression analysis in female patients

Variable	Beta	Std. Error	P value
Diabetes	0.027	0.10	0.009
Previous stroke	2.25	0.55	<0.0001
Cardiopulmonary bypass time	1.22	0.47	0.010
Cross-clamping time	0.70	0.27	0.010
Prolonged inotropic support	1.41	0.27	<0.0001
Prolonged ventilatory support	2.26	0.58	< 0.0001
Postoperative AF	0.66	0.16	<0.0001
Postoperative renal insufficiency	1.28	0.38	<0.001
Hemodialysis	2.31	0.60	<0.0001
Postoperative blood transfusion (≥3 unite)	1.38	0.33	<0.0001
Postoperative stroke	2.52	0.78	<0.001

AF: Atrial fibrillation

95% CI for OR 1.18 – 35.75) were the independent predictive factors of in-hospital mortality in male patients. Causes of in-hospital death among female patients were arrhythmia (n=2, 0.6%), arrhythmia and pneumonia (n=1, 0.3%), pneumonia (n=1, 0.3%), myocardial infarction (n=2, 0.6%), multiorgan failure (n=14, 3.9%), and renal insufficiency (n=1, 0.3%). Mean follow-up was 47.51±25.06 months and 48.42±25.21 months among female and male patients (P=0.820). LITA usage (B -0.39, S.E 0.11, OR 1.48, 95% CI for OR 1.17 – 1.88, P=0.001) was the independent predictive factor in multivariate cox-regression analysis of survival in female patients. Calcification of ascending aorta (Beta 0.55, S.E 0.18, OR 1.73, 95% CI for OR 1.21 – 2.48, P=0.002), LITA usage (Beta -0.35, S.E 0.06, OR 0.70, 95% CI for OR 0.61 – 0.80, P<0.0001), operation time (Beta 0.22, S.E 0.06, OR 1.25, 95% CI for OR, 1.10 – 1.43, P=0.001), prolonged inotropic support (Beta 0.85, S.E 0.13, OR 2.35, 95% CI for OR 1.81 – 3.06, P<0.0001), and use of IABP (Beta -0.44, S.E 0.16, OR 0.64, 95% CI for OR 0.46 – 0.89, P=0.009) were the independent predictive factors in multivariate cox-regression analysis of survival in male patients. In follow-up, mortality rate was 6.1% (n=22) among female patients and 4.6% (n=60) among male patients (P=0.272).

Causes of death in follow-up among female patients were myocardial infarction (n=6), multiorgan failure (n=14), multiorgan failure and colon carcinoma (n=1), multiorgan failure and larynx carcinoma (n=1).

Causes of death in follow-up among male patients were myocardial infarction (n=14), multiorgan failure (n=43), multiorgan failure and colon carcinoma (n=1), multiorgan failure and larynx carcinoma (n=1), multiorgan failure and bronchial carcinoma (n=1).

Discussion

Previous studies suggested that female were more likely to present late for diagnosis, interventional cardiology procedures or surgery than males.[4,7] Previous studies showed that the rate of female gender in patients undergoing CABG surgery was between 19.3% and 30%.[4,8-10] In our study, 21.8% of patients were female.

Advanced age, hypertension, diabetes, and hyperlipidemia are recognized risk factors for early and late adverse outcome in patients undergoing CABG. It was stated in the literature that female patients undergoing CABG were older,[4,9,12,13] and had a higher prevalence of diabetes,[4,6,14,15] hypertension,[10,12,13] and hyperlipidemia.[9,12]

We stated that advanced age, hypertension, and diabetes were more common among female patients. In our study, the preoperative lipid profiles for female patients were distinctly different from male patients. Hyperlipidemia rate was higher among female patients. We also stated that these risk factors were independent predictive factors among female patients. Previous studies showed that female patients undergoing CABG had higher prevalence of peripheral vascular disease,[9,12,15] low ejection fraction[12,15] and had longer CPB time,[4] cross-clamping time[4] and had higher inotropic support,[4,5] and had longer length of hospital stay,[4,9] but these factors could not be confirmed in our study. Several studies showed that compared with male patients, female patients undergoing coronary surgery were less likely to receive vessel grafts.[4,16]

Some studies showed that rate of use vessel grafts was similar between female and male patients.[13,17]

We found that rate of use of vessel grafts was similar between female and male patients. Several studies showed that risk of morbidity and mortality after coronary artery bypass grafting was higher for women than for men.[1-3,9,18]

Several studies showed that in-hospital mortality rate was between 3.6% and 5.6% among female patients and between 1.4% and 2.9% among male patients.[11,13,19,20]

Some studies showed that incidence of in-hospital mortality was not statistically different between women and men.[6,9] Our investigation of 1657 patients undergoing coronary surgery found that female patients was so distinctly different from male patients in their preoperative and postoperative profiles.

We stated that in-hospital mortality rate was 5.8% and 3.2% in female and male patients and these findings were significant statistically. Risk factors affecting in-hospital mortality in female patients in a study that could not be confirmed in our study were advanced age, peripheral

vascular disease, postoperative blood transfusion, abnormal left ventricular function.[5]

Reasons for increased in-hospital mortality in female patients compared to male patients remain unclear. Conflicting results among published studies with regard to the influence of female gender on postoperative morbidity and mortality after coronary surgery are influenced by a number of factors: associated comorbidities, dissimilar study designs, different study sample sizes, and variable application of statistical methods to analyze the data sets. We stated that prolonged ventilatory support and postoperative atrial fibrillation were the independent predictive factors of in-hospital mortality in both male and female patients. We also stated that cardiopulmonary bypass time was the independent predictive factors of in-hospital mortality in male patients.

Several studies showed that length of hospital stay was longer among female patients undergoing coronary surgery.[4,9] We stated that length of ICU and hospital stay was not significantly different between female and male patients. Additionally, we investigated factors affecting length of ICU and hospital stay in female patients. COPD, prolonged cross-clamping time, prolonged inotropic support, prolonged ventilator support, hemodialysis, postoperative blood transfusion (≥3 units), and postoperative stroke were the independent predictive factors in multivariate regression analysis of length of ICU stay in female patients.

Diabetes, previous stroke, prolonged cardiopulmonary bypass time, prolonged cross-clamping time, prolonged inotropic support, prolonged ventilator support, postoperative atrial fibrillation, postoperative renal insufficiency, hemodialysis, postoperative blood transfusion (≥3 units), and postoperative stroke were the independent predictive factors in multivariate regression analysis of length of hospital stay in female patients.

Several authors[13,21-24] have concluded that female patients had equally or better late survival then compared with male patients. Abramov et al. stated that 5-year survival was longer in female patients than male patients (93.1% versus 90%).[9] In our study, mid-term survival rate revealed no significant differences between female and male patients (93.9% versus 95.4%). The LITA usage were the independent predictive factors of survival in female patients. Calcification of ascending aorta, LITA usage, operation time, prolonged inotropic support, IABP usage were the independent predictive factors of survival in male patients. We hope the present study helps to more accurately describe postoperative and mid-term results of a surgical revascularization strategy, especially in an era where there may be other evolving treatment options for women, and also hind at how we might improve the differences observed in CABG results.

Conclusions. Advanced age, hypertension, diabetes, and hyperlipidemia were the independent predictive risk factors among female patients. Postoperative mortality was higher in female patients. Length of intensive care unit and hospital stay, and mid-term survival was similar between female and male patients.

Ethical issues
This study was approved by our local Ethics Committee.

Competing interests
Authors declare no conflict of interest in this study.

References

1. Ennker IC, Albert A, Pietrowski D, Bauer K, Ennker J, Florath I. Impact of gender on outcome after coronary artery bypass. **Asian Cardiovasc Thorac Ann** 2009;17:253-8.

2. Guru V, Fremes SE, Tu JV. Time-related mortality for women after coronary artery bypass graft surgery: A population-based study. **J Thorac Cardiovasc Surg** 2004;127:1158-65.

3. Al-Alao BS, Parissis H, McGovern E, Tolan M, Young VK. Gender influence in isolated coronary artery bypass graft surgery: a propensity match score analysis of early outcome. **Gen Thorac Cardiovasc Surg** 2012;60:417-24.

4. Aldea GS, Gaudiani JM, Shapira OM, Jacobs AK, Weinberg J, Cupples AL, et al. Effect of gender on postoperative outcomes and hospital stays after coronary artery bypass grafting. **Ann Thorac Surg** 1999;67:1097-1103.

5. Koch CG, Khandwala F, Nussmeier N, Blackstone EH. Gender and outcomes after coronary artery bypass grafting:a propensity-matched comparison. **J Thorac Cardiovasc Surg** 2003;126:2032-43.

6. Woods S, Noble G, Smith J, Hasselfeld K. The influence of gender in patients undergoing coronary artery bypass graft surgery: an eight-year prospective hospitalized cohort study. **J Am Coll Surg** 2003;196:428-34.

7. Lawton JS, Brister SJ, Petro KR, Dullum M. Surgical revascularization in women: unique intraoperative factors and considerations. **J Cardiovasc Surg** 2003;126:936-8.

8. Hamulu A, Ozbaran M, Atay Y, Posacioglu H, Aras I, Buket S, et al. Evaluation of risk factors related to morbidity and mortality in patients undergoing coronary artery grafting. **Turkish J Thorac Cardiovasc Surg** 1995;3:245-52.

9. Abramov D, Tamariz MG, Sever JY, Christakis GT, Bhatnagar G, Heenan AL, et al. The influence of gender on the outcome of coronary bypass surgery. **Ann Thorac Surg** 2000;70:800-5.

10. Mandegar MH, Marzban M, Lebaschi AH, Ghaboussi P, Alamooti AR, Ardalan A. Gender influence on

hospital mortality after coronary artery bypass surgery. **Asian Cardiovasc Thorac Ann** 2008;16:231-5.

11. Vaccarino V, Abramson JL, Veledar E, Weintraub WS. Sex differences in hospital mortality after coronary artery bypass surgery . Evidence for a higher mortality after coronary artery bypass surgery. **Circulation** 2002;105:1176-81.

12. Ahmed WA, Tully PJ, Psych M, Knight JL, Baker RA. Female sex as an independent predictor of morbidity and survival after isolated coronary artery bypass grafting. **Ann Thorac Surg** 2011;92:59-67.

13. Goksedef D, Omeroglu SN, Balkanay O, Talas Z, Arabi B, Ipek G. Coronary artery bypass in women:wath is really different? **Turkish J Thorac Cardiovasc Surg** 2012;20:8-13.

14. Cihan HB, Erdil N, Nisanoğlu V, Colak C, Erdil F, Ege E, Battaloglu B. Does type II diabetes mellitus increase mortality and morbidity in coronary artery bypass surgery? **Turkish J Thorac Cardiovasc Surg** 2005;13:93-8.

15. Guru V, Fremes SE, Austin PC, Blacstone EH, Tu JV. Gender differences in outcomes after hospital discharge from coronary artery bypass grafting. **Circulation** 2006;113:507-16.

16. Hammar N, Sandberg E, Larsen FF, Ivert T. Comparison of early and late mortality in men and women after isolated coronary artery bypass greft surgery in Stockholm, Sweden, 1980 to 1989. **J Am Coll Cardiol** 1997;29:659-64.

17. Parolari AP, Dainese L, Naliato M, Polvani GL, Loardi C, Trezzi M, et al. Do women currently receive the same standard of care in coronary artery bypass graft procedures as men? A propensity analysis. **Ann Thorac Surg** 2008;85:885-90.

18. Wenger NK. Is what's good for the gander good for the goose? **J Thorac Cardiovasc Surg** 2003;126:929-31.

19. Czech B, Kucewicz-Czech E, Pacholewicz J, Wojarski J, Puzio J, Przybylski R, et al. Early results of coronary bypass graft surgery in women. **Kardiol Pol** 2007;65:627-33.

20. Perek B, Jemielity M, Dyszkiewicz W. Why are the results of coronary artery bypass grafting in women worse? **Asian Cardiovasc Thorac Ann** 2003;11:293-8.

21. Eagle KA, Guyton RA, Davidoff R, Edwards FH, Ewy GA, Gardner TJ, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Surgery). **Circullation** 2004;110:e 340-437.

22. Mikail GW. Coronary revascularization in women. **Heart** 2006;92: 19-23.

23. Lansky AJ. Outcomes of percutaneous and surgical revascularization in women. **Prog Cardiovasc Dis** 2004;46:305-19.

24. Guru V, Fremes SE, Tu JV. Time-related mortality for women after coronary artery bypass graft surgery: a population-based study. **J Thoracic Cardiovasc Surg** 2004;127:1158-65.