Gender Difference in Long- and Short-Term Outcomes of Off-Pump Coronary Endarterectomy

Abstract

Background: The role of gender in the selection of the most effective method for treatment of patients with diffused coronary artery diseases remains a matter of debate. This study thus evaluated the effect of gender on long- and short-term outcomes of off-pump coronary endarterectomy (CE). **Methods:** This was a single-center retrospective study of patients who had undergone coronary artery bypass graft (CABG). The patients were divided into two groups, the CABG and the CABG + CE group, and further stratified into male and female. Long-term survival for each group was estimated by Kaplan-Meier analysis with log-rank testing. In addition, Cox regression analyses of each gender were also carried out to identify the predictors of the primary and secondary endpoints. Results: Overall, 25.8% of the patients were female. Diseased vessels were not statistically different in the two groups - men and women. There was no significant difference in postoperative outcomes between males and females in the CABG and CABG + CE groups. There was no significant difference in hospital mortality in the two groups between males and females. Kaplan-Meier curves show that there was no significant difference in the 5-year cardiac mortality between males and females belonging to the CABG and CABG + CE groups. Conclusion: The results of this study show that there was no significant difference in the short- and long-term outcomes of off-pump CABG and CE in both genders although women tend to carry a greater risk.

Keywords: Coronary endarterectomy, females, gender difference, males, off-pump coronary artery bypass graft

Introduction

Cardiovascular disease the is most death important cause of among men and women all over the world.^[1] Over 40 years ago, coronary endarterectomy (CE) combined with coronary artery bypass grafting (CABG) was practiced in patients with coronary artery atherosclerosis.^[2] Multiple factors are involved in the pathophysiology of atherosclerosis.[3] Gender is one of them, and it has a correlation with the development of atherosclerosis and the clinical outcomes of patients with coronary artery diseases (CADs).^[4] Women present less obstructive epicardial stenosis, diffuse atherosclerosis, and microvascular dysfunction.^[5] Because of different clinical presentation, women have delay in diagnosis, so they are more often candidate for surgical treatment.^[6]

Some obvious differences in postsurgery outcomes in men and women have

attracted considerable attention.^[6] It has been reported that female gender is an independent predictor for early^[7] and late mortality after CABG.^[8,9] In addition, there is evidence that the short-term mortality rate is higher in women.^[10]

It has been demonstrated that women have a higher in-hospital mortality rate after CABG than men^[3,11] because they have risk factors such as age, small body size, small coronary arteries, more comorbidity, and more advanced disease than do their male counterparts.^[6] Previous articles discussing absolute long-term survival have shown opposing results, where most women show equal long-term survival.^[12] However, other studies report worse long-term survival in women.^[13] In contrast, female long-term absolute survival is reported to be better than that in males.^[14-16] Significant controversy exists in the literature over the effect of gender on CABG. The focus of previous investigations has been primarily on in-hospital complications and mortality^[5-10] or on long-term survival and symptoms in patients undergoing

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CABG.^[6,9,11,12] CE as an adjunct technique for CABG may affect the outcomes and survival of patients with CAD. The role of gender in the selection of the most effective method remains a matter of debate. Previous studies have compared the effect of gender in CABG, but there is not much information on the effect of gender on the long- and short-term outcomes following off-pump CE. Therefore, we aimed to examine gender difference in the long- and short-term outcomes following off-pump CE.

Patients and Methods

Study type

This was a single-center retrospective study in which patients who underwent CABG + CE in the Imam Ali Hospital of Kermanshah University of Medical Scince from March 2011 to February 2012 were analyzed.

Ethical aspect

This study was approved by the ethics committee of the Kermanshah University of Medical Science.

Sample

In this study, 473 patients underwent CABG and 69 of them had CE in addition to CABG. All the patients were operated on by the same surgeon. Any patient who had other procedures in addition to CABG, such as valve repair or replacement and left ventricular aneurysm resection, was excluded. The patients were divided into two groups, the CABG and the CABG + CE group and further stratified into male and females.

Follow-up

The primary endpoint was in-hospital mortality, and the secondary endpoints were postoperative complications and long-term all-cause mortality, which were evaluated by telephonic contact after discharge for a mean follow-up of 37.1 ± 23.8 months. The patients whose contact numbers were changed or were not responding for three times were excluded and lost to follow-up.

Data collection

It was conducted through analysis of medical records with a standardized form, including preoperative variable and consisted of the following: age, gender, body mass index, hypertension, hypercholesterolemia, mellitus, diabetes smoking history, family history of CAD, peripheral vascular disease, renal, pulmonary and hepatic failure, congestive heart failure, left ventricular ejection fraction (EF), previous myocardial infarction (MI), history of arrhythmia, angina, previous CABG and cardiopulmonary resuscitation, and left main CADs. Operative data included the number and kind of vessel diseases. Postoperative variables were MI, arrhythmia, respiratory and gastrointestinal complication, low cardiac output, bleeding, blood transfusion in the intensive care unit (ICU), total length of ICU stay, dehiscence, tamponade, arrest, reintubation, and hospital mortality.

Definitions

Bleeding was considered when patients needed reoperation. Hospital mortality was defined as death occurring before discharge from the hospital and death was classified as either cardiac or noncardiac mortality. Arrhythmia refers to postoperative tachycardia, bradycardia, atrial flutter, heart blockage that required a pacemaker, and ventricular arrhythmias. MI was defined as an elevation of the serum creatinine kinase isoenzyme MB to three times the upper limit of normal in the absence of new pathological Q-waves.

Surgical procedure

CE was carried out in severely diseased vessels where conventional CABG was impossible. Although a preoperative prediction for CE can be obtained from the coronary angiogram, the final decision is made intraoperative based on technical considerations. We did not consider complete occlusion on the angiogram as a definite indication for CE. It was considered when the vessel supplying a viable myocardium was not suitable for grafting and when multiple, discrete obstructing lesions or diffuse atherosclerosis significantly compromised the internal lumen. Surgery has improved through off-pump CABG and this was done according to internationally established techniques. The surgery was performed with Medtronic Octopus stabilizing devices for coronary stabilization and deep pericardial traction sutures for cardiac displacement and presentation. Conventional immobilization techniques such as deep pericardial sutures, Esmolol, and Octopus T-300 were used to provide better access to the lateral and posterior target vessels. Heparin 100 mg/kg was administered to keep the activated clotting time between 200 and 400 s. Before anastomosis, the target coronary artery was temporarily occluded proximally and distally by fine bulldog clamps or looped 5/0 Vilene suture. Phenylephrine was administered intravenously to keep the systolic blood pressure between 70 and 90 mmHg. In our patients, the left internal mammary artery was used as the conduit for all grafts on the LAD while a saphenous vein graft was used for all other coronary vessels.

Statistical analysis

Numerical variables are presented as mean \pm standard deviation. Discrete variables were summarized by percentages. Student's *t*-test was used to evaluate the significant differences in normal distribution between the two groups, and Mann-Whitney *U*-test was used to analyze the statistical differences between the groups since these were not normally distributed. Furthermore, the categorical variants were evaluated using Pearson's Chi-square or Fisher's absolute value Chi-square test, and the results were considered to be statistically significant with a *P* value of <0.05. Long-term survival for each group was estimated by Kaplan–Meier analysis with log-rank testing. Baseline variables with *P* value <0.01 in univariate analyses were included in multivariable analyses. In addition, Cox

regression analyses of each gender were also examined to identify the predictors of the primary and secondary endpoints. The results are expressed as odds ratios with associated 95% confidence interval. All analyses were performed in IBM SPSS Statistics, version 20.0.

Results

Baseline characteristics

A total of 473 patients were enrolled (25.8% female). Patients were divided according to procedure and gender into CABG (female: 95 and male: 309) and CE + CABG (female: 27 and male: 42) between March 2011 and February

2012 for this study. Baseline characteristics are shown in Table 1. A prevalence of hypertension, hypercholesteromia, angina, and mean left ventricular EF was higher in females in the CABG group, while smoking and left main coronary disease in the CABG group were higher in males. In the CE + CABG group, all the variables were similar, except for the history of smoking, which was higher in male patients. Diseased vessels were not statistically different between the two groups in males and females.

There was no significant difference in the postoperative outcome in males and females in either of the CABG and CE + CABG groups [Table 2].

Table 1: Baseline characteristics by gender in patients undergoing CABG and CABG + CE						
Variables	CABG (<i>n</i> =404)		Р	CABG +	CABG + CE (<i>n</i> =69)	
	Male (<i>n</i> =309)	Female (n=95)		Male (<i>n</i> =42)	Female (n=27)	
Age	58.7±9.6	59.3±9.1	0.274	58.19±10.97	60.59±9.72	0.357
Cardiac risk factors						
BMI	26.9±3.7	27.05±4.8	0.821	26.96±4.16	28.84 ± 4.84	0.197
Diabetes mellitus	75 (24.3%)	30 (31.6%)	0.706	13 (31%)	9 (33.3%)	1
Hypertension	123 (39.8%)	54 (56.8%)	0.004	20 (47.6%)	18 (66.7%)	0.143
Hypercholesterolemia	90 (29.1%)	38 (40%)	0.032	14 (33.3%)	13 (48.1%)	0.314
Smoking history	155 (50.2%)	24 (25.3%)	0<001	19 (45.2%)	2 (7.4%)	0.001
Family history of CAD	89 (28.8%)	31 (32.6%)	0.521	9 (21.4%)	6 (22.2%)	1
Noncardiac morbidities						
Peripheral vascular disease	2 (0.6%)	1 (1.1%)	0.554	0	0	1
Renal failure	4 (1.3%)	0	0.577	3 (7.1%)	1 (3.7%)	1
Pulmonary failure	7 (2.3%)	3 (3.2%)	0.706	1 (2.4%)	0	1
Hepatic failure	0	1 (1.1%)	0.235	0	0	1
Cardiac profile						
Congestive heart failure	34 (11%)	5 (52%)	0.114	1 (2.4%)	2 (7.4%)	0.556
Left ventricular EF	43.6±11.59	46.8±9.9	0.009	44±10.42	44.7±11.50	0.768
Previous myocardial infarction	34 (11%)	6 (6.3%)	0.239	4 (9.5%)	3 (11.1%)	1
History of arrhythmia	3 (1%)	0	1	2 (4.8%)	1 (3.7%)	1
Prior PCI	7 (22%)	2 (21%)	1	2 (4.8%)	0	0.517
Angina	79 (25.6%)	39 (37.9%)	0.027	8 (19%)	6 (22.2%)	0.767
Previous CABG				1 (2.4%)	1 (3.7%)	1
Previous CPR	1 (0.3%)	1 (1.1%)	0.415	0	0	1
Left main coronary diseases	72 (23.5%)	13 (13.7%)	0.044	8 (19%)	2 (7.4%)	0.296
Diseased vessel						
LAD	305 (99.3%)	93 (97.9%)	0.238	39 (92.9%)	27 (100%)	0.275
RCA	219 (71.3%)	61 (64.2%)	0.203	35 (83.3%)	20 (74.1%)	0.374
PLV	4 (1.3%)	0	0.577	4 (9.5%)	3 (11.1%)	1
PDA	16 (5.2%)	10 (10.5%)	0.091	7 (16.7%)	5 (18.5%)	1
Diagonal	35 (11.4%)	13 (13.7%)	0.587	1 (2.4%)	1 (3.7%)	1
OM1	221 (72%)	69 (72.6%)	1	33 (78.6%)	20 (74.1%)	0.772
OM2	17 (5.5%)	7 (7.4%)	0.468	6 (14.3%)	1 (3.7%)	0.233
OM3	1 (0.3%)	0	1	1 (2.4%)	0	1
R.V Branch	4 (1.3%)	1 (1.2%)	1	0	0	1
Number of vessels diseased						
Ι	22 (7.1%)	7 (7.4%)	0.978	1 (2.4%)	0	0.121
II	71 (23.1%)	21 (22.1%)		5 (11.9%)	4 (14.8%)	
III	196 (63.6%)	60 (63.2%)		26 (61.9%)	22 (81.5%)	
IV	19 (6.2%)	7 (7.4%)		10 (23.8%)	1 (3.7%)	

BMI: Body mass index, EF: Ejection fraction, PCI: Percutaneous coronary intervention, CABG: Coronary artery bypass graft, CE: Coronary endarterectomy, CPR: Cardiopulmonary resuscitation

There were three (0.6%) in-hospital deaths in our study. The mortality rate of female patients was 1.6% (n = 2).

Survival analysis

After a mean follow-up of 37.1 ± 23.8 months in total, of 29 deaths, 17 were cardiac and 12 noncardiac. Twenty-four deaths were in the males, of which 21 of them were in the CABG and 3 of them in the CABG + CE group. Long-term survival rates, as estimated by Kaplan–Meier curves in two groups, are shown in Figure 1. There was no significant difference in hospital mortality in the two groups between males and females. Kaplan–Meier curves showed that there was no significant difference in the 5-year cardiac mortality in the CABG and CABG + CE groups between male and females [Figures 1 and 2].

Kaplan–Meier survival analysis showed that the mean survival was 1660.52 ± 24.47 days in males compared with 1721.56 ± 28.63 days in female patients in the CABG group. Log-rank analysis showed that there was no significant difference between the two genders (P = 0.201). The mean survival in the CABG + CE group was 1663.28 ± 55.07 days in males and 1622.31 ± 61.33 days in female patients. The result of log-rank analysis showed that there was no significant difference between the two genders (P = 0.960). Life table presented in Table 3 displays the cumulative proportion of survival rate by gender in each year interval. Multivariate Cox regression analysis for the overall study revealed that age, EF, and reintubation are the predictors of mortality [Table 4].

Discussion

The main finding of this analysis is that despite differences in the baseline, short- and long-term outcomes were similar in males and females in both the CABG and CABG + CE groups. In fact, performing CE is a safe technique and better incomplete revascularization for both genders.

In the CABG and CABG + CE groups after a mean 37.1 ± 23.8 months of follow-up, there was no significant

difference in long-term survival in male and female patients. In fact, female gender is not a risk factor for mortality. Previous studies reported that among patients undergoing CABG, women have a higher mortality rate and complication after surgery.^[17,18] Although women have different risk factor profiles and anatomical characteristics such as the smaller size of coronary arteries, in our study there was no significant difference in short- and long-term survival.

In-hospital mortality in CABG and CABG + CE groups among male and female patients was similar. Several studies have reported worse outcome, considering 30 days and in-hospital mortality after CABG in women compared with men.^[19,20]

In our study, women made up 25.8% of the overall sample, and the average age between males and females was similar. In most of the other studies, women were older,^[21-25] which was associated with higher risk of postoperative complications, including short-term mortality.^[15,26] Consistent with other studies,^[25,27] prevalence of hypercholesteromia, hypertension, and angina was found to be higher in female patients, but smoking was higher in males.

In our study, no difference was observed between male and female patients with regard to the number and kind of diseased vessel. Aldea *et al.* reported that the number of grafts is greater in men.^[28] In addition, it has been reported that three-vessel disease has a high prevalence in men.^[15,29,30] Our data demonstrated that gender does not statistically have a significant impact on long-term all-cause mortality for the CE + CABG and CABG groups.

In our study, the rate of CE was higher in males. It is consistent with the study of Abramov *et al.*,^[15] but Amato *et al.*,^[27] reported similar rates of CE in both genders.



Figure 1: Kaplan–Meier survival curve in CABG group

For both the CE and CABG groups, gender did not have a statistically significant impact on long-term all-cause mortality. In the CABG group, we saw the same situation



Figure 2: Kaplan–Meier survival curve in CABG + CE group

Table 2: Postoperative outcome							
Variables	CABG (<i>n</i> =404)		Р	CABG + CE (n=69)		Р	
	Male (n=309)	Female (n=95)		Male (<i>n</i> =42)	Female (n=27)		
MI	10 (3.3)	7 (7.4%)	0.086	0	0	1	
Arrhythmia	21 (6.8%)	2 (2.1%)	0.125	3 (7.3%)	3 (11.5%)	0.67	
Atrial fibrillation	7 (2.3%)	3 (3.2%)	0.705	1 (2.4%)	0	1	
Ventricular fibrillation	7 (2.3%)	3 (3.2%)	0.705	1 (2.4%)	0	1	
Pleural effusion	0	1 (1.1%)	0.234	0	0	1	
Renal failure	5 (1.6%)	2 (2.1%)	0.668	1 (2.4%)	1 (3.8%)	1	
Gastrointestinal system complications	2 (0.7%)	0	1	2 (4.8%)	0	0.521	
Respiratory complications	3 (1%)	2 (2.1%)	0.334	2 (4.8%)	0	0.521	
Intra-aortic balloon pump insertion	1 (0.3%)	0	1	0	1 (3.8%)	0.382	
Low cardiac out put	14 (4.6%)	7 (7.4%)	0.291	3 (7.1%)	4 (15.4%)	0.415	
Dehiscence	0	0	1	2 (4.8%)	0	0.521	
Reintubation	3 (1%)	0	1	1 (2.4%)	0	1	
Bleeding leading to reoperation	25 (8.1%)	5 (5.3%)	0.502	3 (7.3%)	0	0.277	
Arrest	1 (0.3%)	2 (2.1%)	0.138	1 (2.4%)	0	1	
Tamponade	1 (0.3%)	0	1	0	0		
Total blood transfusions (packed red cells)	337.4±449	289.8±447	0.369	754.5±945	465.7±772.2	0.198	
ICU stay (hours)	36.7±18	39.2±16.7	0.241	54.5±56.5	46.2±20.2	0.466	
Hospital mortality	1 (0.3%)	2 (2.1%)	0.139	0	0	1	
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CABG: Coronary artery bypass graft, CE: Coronary endarterectomy; MI: Myocardial infarction; ICU: Intensive care unit

	Table 3: Life	e table of 5-ye	ar survival rat	e by gender:	cumulative sur	vival rate and	l hazard rate	
Interval	CABG (<i>n</i> =404)				CABG + CE (n=69)			
	Male (<i>n</i> =309)		Female (<i>n</i> =95)		Male (<i>n</i> =42)		Female (<i>n</i> =27)	
	Survival	Hazard	Survival	Hazard	Survival	Hazard	Survival	Hazard
1 year	0.97	0.01	1	0	0.97	0.03	1	0
2 year	0.94	0.02	0.97	0.0.2	0.97	0.03	0.95	0.0.4
3 year	0.94	0.02	0.97	0.02	0.95	0.04	0.95	0.04
4 year	0.92	0.02	0.95	0.03	0.91	0.05	0.90	0.07
5 year	0.91	0.02	0.95	0.03	0.91	0.05	0.90	0.0.7

CABG: Coronary artery bypass graft, CE: Coronary endarterectomy

Table 4: Results of multivariate Cox regression						
analysis						
Variables	Р	Hazard ratio	95% CI			
Age	0.011	1.061	1.014-1.110			
EF	0.016	0.945	0.903-0.989			
Reintubation	0.024	0.017	0-0.584			

CI: Confidence interval, EF: Ejection fraction

as for the CE group. Age, comorbidities, postoperative outcomes, and the survival curves in males and females were similar in the CABG group.

The strengths of our study are as follows: the study was conducted in a single center by a single surgeon, and all the procedure was done off-pump. The data were related to complications that could be caused by gender difference, particularly the incidence of bleeding complications.

The limitations of our study are retrospective design and low number of woman present in each group, which may influence outcome. A propensity-matched analysis would be a better way to assess gender differences in clinical outcomes in such a study where the population was unbalanced in the sample size and had different patient backgrounds.

The results of this study show that there is no significant difference in short- and long-term outcomes of patients undergoing off-pump CABG and CABG + CE in both genders, although women tend to have a greater risk factor.

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Conflicts of interest

There are no conflicts of interest.

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