

Coronary artery bypass in women: what is really different?

Kadınlarda koroner arter baypas: Gerçekten farklı olan nedir?

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Background: In our study, we evaluated the effects of female gender on mortality and morbidity rates of coronary artery bypass grafting (CABG).

Methods: A total of 460 patients (351 males, 109 females; mean age 60.3±11.2 years; range 16 to 83 years) who underwent CABG in our clinic between December 2006 and September 2009 were included in our study. Patients were grouped according to their gender and compared.

Results: Twenty-four percent of the patients were female and they were older than male patients (p=0.03). Diabetes mellitus (p=0.01) and hypertension (p=0.005) were found more frequently in female patients while chronic obstructive pulmonary disease (p=0.015) and peripheral artery disease (p=0.003) were found more frequently in male patients. Coronary endarterectomy (p=0.01) was performed more frequently in female patients. The rates of postoperative atrial fibrillation (p=0.04) and bleeding that required revision (p=0.02) were higher in male patients. The mortality rates were 3.6% (n=4) for female patients and 1.4% (n=5) for male patients. Coronary endarterectomy and advanced left ventricular dysfunction were statistically significant factors for mortality in female patients. The estimated survival rate of the discharged female patients at 55 months was 94.7% while the estimated survival rate of the discharged male patients at 61 months was 94.1%.

Conclusion: Based on our findings, the female patients were older and had higher rates of diabetes mellitus and hypertension. The in-hospital mortality rate of the female patients was almost two times higher than in male patients. However, there was no significant difference between the long-term survival rates of female and male patients after CABG.

Key words: Coronary artery bypass grafting; gender; survival rate; women.

Amaç: Çalışmamızda, kadın cinsiyetinin koroner arter baypas greftleme (KABG) ameliyatında mortalite ve morbidite oranları üzerindeki etkisi değerlendirildi.

Çalışma planı: Çalışmamıza Aralık 2006 ve Eylül 2009 tarihleri arasında kliniğimizde KABG ameliyatı yapılan toplam 460 hasta (351 erkek, 109 kadın; ort. yaş 60.3±11.2 yıl; dağılım 16-83 yıl) dahil edildi. Hastalar cinsiyetlerine göre gruplandırılarak kıyaslandı.

Bulgular: Hastaların %24'ü kadındı ve erkek hastalara göre daha ileri yaşlardaydı (p=0.03). Diyabet (p=0.01) ve hipertansiyon (p=0.005) kadın hastalarda daha sık bulunurken, kronik obstrüktif akciğer hastalığı (p=0.015) ve periferik arter hastalığı (p=0.003) erkeklerde daha sık olarak bulundu. Koroner endarterektominin (p=0.01) kadın hastalarda daha sık yapıldığı saptandı. Ameliyat sonrası atriyal fibrilasyon (p=0.04) ve revizyon gerektirecek kanama (p=0.02) oranları erkek hastalarda daha yüksek idi. Mortalite oranları kadın hastalarda %3.6 (n=4), erkek hastalarda ise %1.4 (n=5) idi. Koroner endarterektomi ve ileri sol ventrikül disfonksiyonu kadın hastalarda istatistiksel olarak anlamlı mortalite faktörleri idi. Tahmini sağkalım oranları taburcu edilen kadın hastalar için 55 ayda %94.7 iken, taburcu edilen erkek hastalarda 61 ayda %94.1 idi.

Sonuç: Bulgularımıza göre kadın hastalar daha ileri yaşta ve diyabet ve hipertansiyon oranları da daha yüksekti. Kadın hastaların hastane içi mortalite oranları erkek hastaların yaklaşık iki katı idi. Bununla birlikte KABG sonrası uzun dönem sağkalım oranları arasında kadınlarla erkekler arasında anlamlı bir farklılık yoktu.

Anahtar sözcükler: Koroner arter baypas greftleme; cinsiyet; sağkalım oranı; kadın.

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Although coronary artery disease (CAD) may be thought of as a male disease, statistical data from the World Health Organization shows that CAD is the leading cause of mortality in women as well as men.^[1] Coronary artery bypass graft (CABG) surgery has been the gold standard for the treatment of CAD for 30 years. In fact, it is one of the most common surgeries performed in the United States with just below 500,000 procedures per year. Of that number, about one third are women.^[2] As awareness of heart disease in women has expanded and more women are referred for surgical treatment, some obvious differences in outcomes between men and women have attracted considerable attention.

Recent studies have shown that female patients have increased mortality and morbidity rates after CABG according to the EuroSCORE and STS (The Society of Thoracic Surgeons) scoring systems.^[3,4] For years, cardiac surgeons and researchers have been puzzling over the differences between men and women related to CABG surgery.

Much of the research on gender differences related to CABG was conducted in the 1990s, and the answers were somewhat disconcerting. It has been demonstrated that women had a one and a half to two times higher in-hospital mortality rate after CABG than men.^[5] The most accepted theory for this difference is that women undergoing the operation are higher-risk patients than men. They tend to be older and have a smaller body size, smaller coronary arteries, more co-morbidity (other conditions such as diabetes, kidney disease, and high blood pressure), and more advanced disease than do their male counterparts.

In this current study, we evaluate the early results of CABG operations in women compared with men in our institution.

PATIENTS AND METHODS

This is a retrospective study conducted in a tertiary care teaching university hospital. A total number of 460 patients (351 males, 109 females; mean age 60.3±11.2 years; range 16 to 83 years) who underwent isolated on-pump CABG in our clinic between December 2006 and September 2009 were included. Patients were grouped according to gender and compared according to their perioperative risk factors, associated morbidity, and mortality rates. All patients were operated on by the same surgical team.

Study endpoints

The primary endpoint of our study was postoperative in-hospital death. Secondary endpoints were duration of intensive care unit (ICU) stay, duration of hospitalization,

and any complication that might be related to the operation.

Surgical technique

Following endotracheal intubation and administration of appropriate anesthetic agents, radial arterial, central venous, and Swan-Ganz catheters (Edward Lifesciences, Irvine, Ca, USA) were introduced per routine. Median sternotomy was performed followed by arterial and venous cannulations. Standard cardiopulmonary bypass (CPB) technique was carried out using membrane oxygenators. Mean arterial blood pressure was kept between 50 and 70 mmHg during CPB. Myocardial protection was achieved by combined antegrade and retrograde isothermic blood cardioplegia. Proximal anastomoses were performed during the aortic cross-clamping period. A single internal mammary artery was used to revascularize the left anterior descending coronary artery, and all remaining targets were bypassed with saphenous vein grafts harvested by open technique. Mild hypothermia was applied to all patients. Heparin was administered to achieve an activated clotting time >480 seconds. This was neutralized with the appropriate use of protamine administered within 10 minutes after the end of CPB.

Definitions

Inotropic support was defined as the need for any inotropes, except for dopamine, lower than 4 mcg/kg/min. Infection was defined as any reason to continue, restart, or rewrite antibiotics beyond 48 hours. Perioperative myocardial infarction was defined as having biomarker values of more than five times the 99th percentile of the normal reference range during the first 72 hours following CABG when associated with the appearance of new pathological Q-waves or new left bundle branch block (LBBB).^[6] Urgent operation was defined as any need for operation before the next morning.

Statistical analysis

Demographic, peri- and intraoperative continuous variables were compared using either the unpaired or paired t-test. Accordingly, dichotomous variables were compared using either the Fisher's exact test or chi-square tests. Predictors of mortality were then entered into a forward and backward stepwise multivariate logistic regression model to identify the risk factors of mortality. Survival analysis was conducted with the Kaplan-Meier test according to gender.

Values were expressed as mean ± standard deviation and percentage per variables. All analyses were performed with Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, USA) 13.0 version software.

Table 1. Preoperative characteristics of the patients

	Female (n=109)			Male (n=351)			p
	n	%	Mean±SD	n	%	Mean±SD	
Age (year)			64.2±9.9			58.4±10.2	0.03
Preoperative urea (mg/dL)			42.2±20			43.1±24	0.98
Preoperative creatinine (mg/dL)			0.9±0.3			0.9±0.2	0.4
Diabetes mellitus	49	44.9		124	35.4		0.01
Chronic obstructive pulmonary disease	8	7.3		54	15.3		0.015
Hypertension	85	79.9		144	41		0.005
Hyperlipidemia	18	16.5		56	15.9		0.34
Peripheral arterial disease	4	3.6		85	24.2		0.003
Mild LVD (EF<45%)	23	21.1		74	21		0.66
Severe LVD (EF<30%)	13	11.9		25	7.1		0.72
Mild mitral regurgitation	8	7.3		25	7.1		0.92
Three vessel CAD	88	80.7		270	76.9		0.09
Chronic renal failure	1	0.1		4	1.1		0.45
Body surface area (m ²)			1.63±0.1			1.83±0.2	0.001
EuroSCORE			2.9±6.4			2.8±6.1	0.73

SD: Standard deviation; CAD: Coronary artery disease; LVD: Left ventricular dysfunction.

RESULTS

Female patients were older than male patients (64.2±9.9 and 58.4±10.2, $p=0.03$; Table 1). Diabetes mellitus ($p=0.01$) and hypertension ($p=0.005$) were found more frequently in female patients while chronic obstructive pulmonary disease ($p=0.015$) and peripheral artery disease ($p=0.003$) were found more frequently in male patients. Hyperlipidemia, mild to severe left ventricular dysfunction, the incidence of three-vessel CAD, and chronic renal failure did not show any difference among the groups (Table 1).

The mean number of distal anastomosis in our study was 2.87±0.9 per patient. Female patients received a mean of 2.81±1.03, and male patients received 2.94±0.94 distal anastomosis ($p=0.98$). The internal mammary artery was used in 107 (98.1%) patients in the female group and 342 (97.45%) patients in the male group ($p=0.6$). Coronary endarterectomy ($p=0.01$) was performed more frequently in female patients (Table 2). Aortic cross-clamp and total

perfusion times were similar among the groups ($p=0.09$ and $p=0.07$).

Postoperative atrial fibrillation (AF) ($p=0.04$) and bleeding that required revision ($p=0.02$) rates were higher in male patients (Table 3). Forty-eight patients required temporary inotropic support following surgery, 14 (12.8%) in the female group and 36 in the male group ($p=0.42$). Perioperative myocardial infarction was observed in three (2.7%) patients in the female group and in 12 (2.5) patients in the male group ($p=0.86$). Sixty-five of the females (59.6%) and 214 of the males (60.1) received at least one unit of packed red blood cells (PRBC) ($p=0.44$). Stroke was observed in one female patient (0.9%) and two male patients (0.5%; $p=0.62$). The mean hospitalization time of the patients was similar among groups (6.5±6.4 and 6.6±8.2, $p=0.94$, respectively).

There were nine (1.9%) in-hospital deaths in our study. The mortality rate of female patients was 3.6% ($n=4$). There were five in-hospital deaths in the male

Table 2. Operative variables

	Female (n=109)			Male (n=351)			p
	n	%	Mean±SD	n	%	Mean±SD	
Aortic cross clamp time (min)			72.7±30			74.5±28.2	0.65
Total perfusion time (min)			103.9±36.9			108±29.2	0.74
Number of distal anastomoses (n)			2.81±1.03			2.94±0.94	0.98
Urgent operation	4	3.6		12	3.4		0.97
Internal mammary artery graft	107	98.1		342	97.4		0.6
Coronary endarterectomy	16	14.6		24	6.8		0.01

SD: Standard deviation.

Table 3. Postoperative morbidities of the patient groups

	Female (n=109)			Male (n=351)			p
	n	%	Mean±SD	n	%	Mean±SD	
CK-MB / CK (IU/L)			83.2±86.1			79.2±94.3	0.84
Postoperative urea (mg/dL)			49.8±24.7			54.4±34.9	0.67
Postoperative creatinine (mg/dL)			1.1±0.5			1.2±0.6	0.84
Extubation time (hour)			4.4±6.9			4.7±8.7	0.85
Intensive care unit stay (hour)			15.5±24.3			14.7±18.8	0.89
Atrial fibrillation	28	25.6		144	41.1		0.04
Bleeding	1	0.9		12	3.4		0.02
Intra-aortic balloon pump	8	7.3		18	5.1		0.7
Inotropic support	14	12.8		36	10.2		0.42
Perioperative myocardial infarction	3	2.7		9	2.5		0.86
Infection	6	5.5		22	6.2		0.56
Use of blood products	65	59.6		214	60.1		0.44
Transient ischemic attack	4	3.6		12	3.4		0.74
Stroke	1	0.9		2	0.5		0.62
Discharge day (day)			6.5±6.4			6.6±8.2	0.94
Mortality	4	3.6		5	1.4		0.73

SD: Standard deviation; CK-MB: Creatine kinase-myocardial band; EF: Ejection fraction; CK: Creatine kinase.

group (1.4%). Three female patients died later, and six were lost to follow-up. The estimated survival rate of the discharged female patients at 55 months was 94.7%. Among male patients, nine died and 22 were lost to follow-up. The estimated survival rate of the discharged male patients at 61 months was 94.1% (Figure 1).

Stepwise multivariable logistic regression according to gender analysis showed that coronary endarterectomy [odds ratio (OR): 3.2, 95% confidence interval (CI): 1.1-26.6] and severe left ventricular dysfunction (OR: 1.4, 95% CI: 1.1-12.2) were the factors of mortality in female patients while left ventricular dysfunction (OR: 1.8, 95%

CI: 1.4-14.4), coronary endarterectomy (OR: 1.4, 95% CI: 1.2-2.4), chronic obstructive lung disease (OR: 1.2, 95% CI: 1.0-2.4), and chronic renal failure (OR: 1.08, 95% CI: 1.01-2.0) were the factors of mortality in male patients (Table 4).

DISCUSSION

A multicenter study evaluating gender difference in CAD treatment found that while 27.3% of male patients underwent angiography, only 15.4% of female patients were catheterized ($p=0.001$).^[7] A total of 12.7% of male patients compared with only 5.9% of female patients underwent CABG ($p=0.001$). Several studies showed that doctors manage CAD in women in a more noninvasive way.^[7,8] Our results also showed that female patients were older than male patients when they underwent CABG procedures in our institution ($p=0.03$; Table 1).

Risk factors showed some differences among genders. It has been reported that female patients tend to have higher rates of diabetes mellitus and hypertension while the five-year mortality rates following operations were similar.^[9] Diabetes mellitus is a more evident risk factor of CAD in female patients while hyperlipidemia has a poor relationship.^[10,11] Our study showed that female patients had higher rates of diabetes mellitus ($p=0.01$) and hypertension ($p=0.005$) while male patients had higher rates of chronic obstructive pulmonary disease (COPD; $p=0.015$) and peripheral artery disease ($p=0.003$).

Postoperative AF was higher in male patients in our study ($p=0.04$). Although the mean age of the

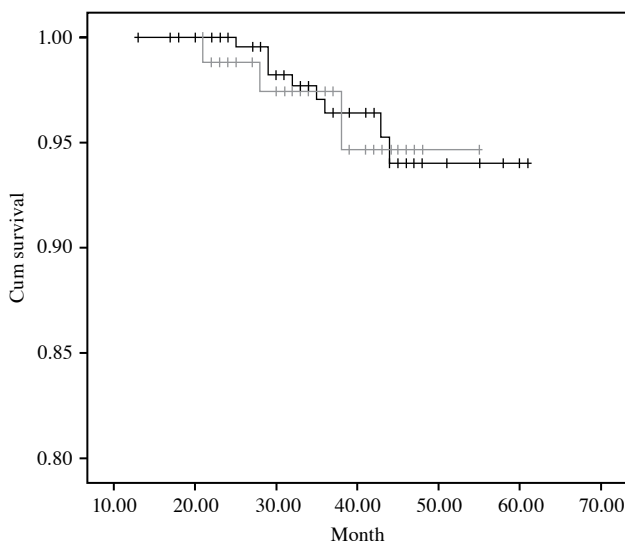


Figure 1. Survival rate of the female and male patients.

Table 4. Factors that effects the in-hospital mortality after operation

	Male patients		Female patients	
	OR	%95 CI	OR	%95 CI
Coronary endarterectomy	1.4	(1.2-2.4)	3.2	(1.1-26.6)
Severe LVD (EF<30%)	1.8	(1.4-14.4)	1.4	(1.1-12.2)
Chronic obstructive lung disease	1.2	(0.9-2.4)		
Chronic renal failure	1.08	(1.01-2.0)		

OR: Odds ratio; CI: Confidence interval; LVD: Left ventricular dysfunction; EF: Ejection fraction.

female patients was higher, it seems that AF was not associated with advanced age in our study. However, COPD was higher in male patients ($p=0.015$), which is a well-known risk factor for postoperative AF.^[12] Further studies are needed to clarify these findings.

Since women usually have a smaller body surface area (BSA), there is a natural tendency to have smaller coronary arteries.^[13,14] A study that was made with intravascular ultrasound (IVUS) which compared the left main coronary artery (LMCA) diameter between the two genders found that both lumen areas of coronary arteries, areas of external elastic lamina, and minimum diameters were significantly narrower in females ($p<0.001$).^[14] It is also a well-known fact that the relationship between coronary artery diameter and early mortality in CAD is inversely proportional.^[15] A study found that patients with a coronary artery diameter of 2.0-3.5 mm had a mortality rate of 1.5%, those with a 1.5-2.0 mm diameter had a mortality rate of 4.6%, and those with 1 mm diameter had a mortality rate of 15.8%.^[16] Smaller coronary arteries may lead females to have a more occlusive and complex disease and increase the rate of endarterectomy as well as result in possibly higher in-hospital mortality rates. In our retrospective analysis, we found that female patients have a tendency to undergo endarterectomy procedures more than men [16 (14.6%) vs. 24 (6.8%), respectively] ($p=0.01$; Table 2).

The mortality rate among female patients was almost double the rate than that of males (3.6% vs. 1.4%). This may be related to smaller coronary arteries, higher endarterectomy rates, and increased age. However, the mortality rates of male and female patients did not correlate with the endarterectomy rates. Female gender is an independent risk factor of morbidity and mortality of CABG in the EuroSCORE and STS scoring systems.^[3,4] It has been reported that the first-month mortality rate was 1.9-3.6% for male and 2.0-2.7% for female patients.^[17,18] Despite females having more risk factors and higher in-hospital mortality rates, the similar long-term survival rates are similar for both genders. This suggests that once female patients underwent the CABG procedure, the CAD progression did not affect long-term results. Females may benefit from CABG

more than men in the long-term when they have the diagnosis of CAD, although they have more complex risk factors.

The need for revision for bleeding according to gender was different among groups. However, only one patient required a second operation for bleeding in the female group. The small number of patients with this complication created the difference. Moreover, the use of blood and blood products was similar, so we believe there is no objective difference in terms of postoperative bleeding between genders.

In our study, multivariate logistic regression analysis showed that the factors for in-hospital mortality for women are endarterectomy and severe left ventricular dysfunction (Table 4). In addition to these factors, the mortality rate in male patients is also affected by COPD and chronic renal failure.

Our study has several limitations. First, the design was retrospective, so it shares the same bias as other retrospectively designed studies. Second, this study was conducted in only one center which may contribute to a lack of variety. Third, the time period for follow-up was limited to five years. Longer follow-up periods with large volumes of patients, including multi-center studies, may lead to more accurate data.

In conclusion, based on our findings, the major differences between females and males were preoperative risk factors such as high age, higher rate of diabetes mellitus, and hypertension in women. It was also found that PAD and COPD were lower in females. Female patients were more likely to have endarterectomy procedures during the operation, and in-hospital mortality rates among female patients were almost two times higher than those of men. However, there was no significant difference between long-term survival rates of CABG in female and male patients.

Declaration of conflicting interests

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