Turk Gogus Kalp Dama 2014;22(3):534-539
doi: 10.5606/tgkdc.dergisi.2014.8997

*Original Article / Özgün Makale*

# Effect of sex on early surgical outcomes of isolated coronary artery bypass grafting

*Cinsiyetin izole koroner arter baypas greftlemenin erken cerrahi sonuçları üzerine etkisi*

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***Background:*** In this study, we investigated possible effects of sex on early surgical outcomes of isolated coronary artery bypass grafting (CABG).

***Methods:*** In this retrospective review of existing database including patients with heart disease, 1,390 consecutive cases (393 males, 997 females; mean age 58.7±10.1 years; range 23 to 87 years) who underwent isolated CABG in Shariati Hospital, Tehran Iran between August 2007 and March 2011 were recruited. Male and female sexes were compared for preoperative characteristics. A stepwise multivariate logistic regression analysis was performed to evaluate possible effects of sex on postoperative mortality and morbidity.

***Results:*** Female patients were older with a higher prevalence of diabetes mellitus, hypertension, hypercholesterolemia and hyperlipidemia. The mortality rate was significantly higher in women compared to men (6.9% vs. 2.3%; p<0.001). Female sex was an independent predictor of postoperative mortality, septicemia, prolonged mechanical ventilation, leg infection, and renal complications.

***Conclusion:*** Our study results show that female sex is an independent predictor of postoperative mortality and some of morbidities. Therefore, specific attention should be warranted to female patients undergoing isolated CABG.

*Keywords:* Coronary artery bypass grafting; morbidity; mortality; postoperative; sex.

***Amaç:*** Bu çalışmada cinsiyetin izole koroner arter baypas greftlemenin (KABG) erken cerrahi sonuçları üzerindeki muhtemel etkileri araştırıldı.

***Çalışma planı:*** Kalp hastalarını kapsayan mevcut veri tabanının retrospektif incelemesine, Ağustos 2007 ve Mart 2011 tarihleri arasında İran, Tahran Shariati Hastanesi'nde izole KABG yapılan 1390 ardışık olgu (393 erkek, 997 kadın; ort. yaş 58.7±10.1 yıl; dağılım 23-87 yıl) alındı. Erkek ve kadın cinsiyetleri ameliyat öncesi özellikler açısından karşılaştırıldı. Cinsiyetin ameliyat sonrası mortalite ve morbidite üzerindeki muhtemel etkilerini değerlendirmek üzere basamaklı çok değişkenli lojistik regresyon analizi yapıldı.

***Bulgular:*** Kadın hastaların yaşı daha ileriydi ve diabetes mellitus, hipertansiyon, hiperkolesterolemi ve hiperlipidemi prevalansı daha yüksekti. Mortalite oranı, erkeklere kıyasla, kadınlarda anlamlı düzeyde daha yüksekti (%2.3'e kıyasla %6.9; p<0.001). Kadın cinsiyeti ameliyat sonrası mortalite, septisemi, uzamış mekanik ventilasyon, bacaklarda enfeksiyon ve renal komplikasyonların bağımsız bir öngördürücüsüydü.

***Sonuç:*** Çalışma bulgularımız, kadın cinsiyetinin ameliyat sonrası mortalite ve bazı morbiditelerin bağımsız bir öngördürücüsü olduğunu göstermektedir. Bu nedenle, izole KABG yapılan kadın hastalara özel ihtimam gösterilmelidir.

*Anahtar sözcükler:* Koroner arter baypas greftleme; morbidite; mortalite; ameliyat sonrası; cinsiyet.

Available online at
www.tgkdc.dergisi.org
doi: 10.5606/tgkdc.dergisi.2014.8997
QR (Quick Response) Code

*Received:* July 08, 2013 *Accepted:* October 06, 2013

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Although women make up only about one-third of all patients who undergo coronary artery bypass grafting (CABG), they experience a higher incidence of postoperative mortality and morbidities.[1-10] Furthermore, several studies have identified female gender as an independent predictor of postoperative mortality and complications.[8-10] Pre-existing comorbid conditions such as diabetes mellitus (DM), hypertension (HT), dyslipidemia, peripheral vascular diseases (PVD), and congestive heart failure (CHF) also occur more often in women than men.[1,2,11,12]

These differences in the preoperative clinical characteristics between men and women make it hard to interpret how gender affects postoperative outcomes after CABG, and except for some recent studies,[8,10,13,14] most of the existing literature provides unadjusted outcomes with regard to this issue. In this study, we conducted multivariate logistic regression analyses using an extensive database containing more than 200 different variables to investigate the effects of sex on postoperative mortality and complications associated with CABG.

## PATIENTS AND METHODS

In this retrospective review of existing data banks of patients with heart disease, all consecutive cases who underwent isolated CABG in Shariati Hospital, Tehran, Iran between August 2007 and March 2011 were included in this study while those for whom additional concomitant procedures were performed, such as a valve operation and a carotid endarterectomy, were excluded. A total of 2,333 patients were initially recruited for our study, but 613 were not eligible for inclusion because had undergone previous valve surgery or an operation for coronary heart disease (CHD). An additionaly 330 patients were also excluded because of incomplete data. In the end, our study was comprised of 1,390 patients (393 males, 997 females; mean age 58.7±10.1 years; range 23 to 87 years) who underwent isolated CABG and were followed up for postoperative outcomes and complications. We compared the pre-, peri-, and postoperative characteristics, including age, DM, HT, hypertriglyceridemia, hypercholesterolemia, PVD, cerebrovascular disease (CVD), renal function, intraoperative findings [average units of packed red blood cells (PRBCs) transfused, perfusion time, aortic cross-clamp time (ACCT), and mechanical ventilation time, inotropic support], and postoperative mortality and morbidities of the male and female study participants. We also evaluated which patients had required an intra-aortic balloon pump (IABP), with the indications being a low left ventricular ejection fraction (LVEF), difficulty in weaning from cardiopulmonary bypass (CPB), and intractable arrhythmia. Furthermore, we examined the patients regarding whether or not they had a family history of coronary artery disease (CAD). A written consent form was filled out by each patient prior to being enrolled in the study, and anyone who did not complete this was also excluded. The study protocol was approved by the ethics committee of the Tehran University of Medical Sciences (TUMS).

A primary outcome was defined as an early mortality rate within the first 30 postoperative days while a secondary outcome was signified by morbidities that happened during hospitalization. Additionally, patients with deep or superficial sternal, leg, or urinary tract infections, were recorded as having an infection complication, and when a pulmonary embolism, pneumonia, pleural effusion, or a pneumothorax occurred, these were categorized as having pulmonary complications. Furthermore, patients who suffered a stroke within the first 72 hours, had a transient ischemic attack (TIA), or were in a coma were classified as having neurological complications.

### Statistical analysis

The results were reported as mean ± standard deviation (SD) for quantitative variables and percentages for categorical variables, and the two groups were compared using Student's t-test for continuous variables and a Chi-square test (or Fisher's exact test, if required) for categorical variables. Statistical significance was based on two-sided, design-based tests with a level of significance set at 0.05.

The potential confounding effects of risk factors on surgical outcomes was first tested using univariate analyses for each dependent variable. When it was significant at $p<0.2$, the variables were entered into the stepwise multivariable logistic regression analyses, with the male gender being the reference group. All of the statistical analyses were performed using the SPSS for Windows version 16.0 software program (SPSS Inc., Chicago, IL, USA).

## RESULTS

The patients' baseline characteristics are summarized in Table 1. Compared to the men, the women were older and had a higher prevalence of DM, HT, hypercholesterolemia, and hyperlipidemia, whereas more of the men were smokers and opium addicts. Furthermore, previous myocardial infarction (MI) was less present in the women, and they also showed a lower mean clearance of creatinine than the men.

We also discovered that a higher proportion of the women were referred in the late stages of the Canadian

Cardiovascular Society (CCS) angina classification system and the New York Heart Association (NYHA) functional classification system (class III and IV). However, there were no significant differences between the two genders regarding a family history of CAD, chronic obstructive pulmonary diseases (COPD) and cerebrovascular accidents (CVAs).

Additionally, we determined that there were no significant differences related to operative factors, including the mean perfusion time, ACCT, average number of PRBCs transfused, and mechanical ventilation, but a higher proportion of women did undergo the insertion of an IABP. However, the two groups did not differ significantly with regard to inotropic support (Table 1).

The results of the study outcomes related to the male and female patients is shown in Table 2. The mortality rate was significantly higher in the women compared with the men (6.9% vs. 2.3%, respectively; p<0.001), and there was a significant association between female gender and postoperative mortality [odds ratio (OR)=1.58; 95% confidence interval (CI)=1.17-2.14; p<0.001].

In the unadjusted analyses, female gender generally was associated with a higher incidence of postoperative complications than the men (36.4% vs. 30.3%, respectively; OR=1.08; 95% CI=1.01-1.17; p=0.028). For instance, we detected a significant correlation between female gender and ventricular and supraventricular arrhythmia [including atrial fibrillation (AF)], prolonged mechanical ventilation, and postoperative septicemia. However, we were not able to confirm any significant relationship between female gender and vascular, renal, pulmonary, neurological, or gastrointestinal complications, leg site infections, deep sternal infections, or the need for a reoperation due to bleeding.

As shown in Table 3, in order to correct the confounding variables, the effects of gender on early surgical outcomes were measured using multivariable logistic regression analyses in the presence of other gender-specific characteristics such as, DM, HT, smoking status, opium addiction, hypertriglyceridemia, hypercholesterolemia, previous MI, and renal dysfunction as well as being over the age of 65. This revealed that female gender continued to be an

**Table.1. The patients' baseline characteristics**

| Variables | Females (n=393) | | | Males (n=997) | | | |
|---|---|---|---|---|---|---|---|
| | n | % | Mean±SD | n | % | Mean±SD | *p* |
| Mean age (years) | | | 60.3±9.3 | | | 58.0±10.3 | <0.001 |
| Over (>65 years old) | 126 | 32.1 | | 271 | 27.2 | | 0.070 |
| Smokers | 9 | 2.3 | | 250 | 25.1 | | <0.001 |
| Opium addiction | 13 | 3.3 | | 194 | 19.5 | | <0.001 |
| Family history of coronary artery disease | 32 | 8.1 | | 72 | 7.2 | | 0.557 |
| Previous myocardial infarction | 102 | 26.0 | | 376 | 37.7 | | <0.001 |
| Canadian Cardiovascular Society class III and IV | 94 | 23.9 | | 126 | 12.6 | | <0.001 |
| New York Heart Association class III and IV | 126 | 32.1 | | 193 | 19.4 | | <0.001 |
| Diabetes mellitus | 181 | 46.1 | | 298 | 29.9 | | <0.001 |
| Hypertension | 284 | 72.8 | | 405 | 40.6 | | <0.001 |
| Hypercholesterolemia | 246 | 62.6 | | 437 | 43.8 | | <0.001 |
| Hypertriglyceridemia | 242 | 61.6 | | 437 | 43.8 | | <0.001 |
| Renal failure | 9 | 2.3 | | 13 | 1.3 | | 0.187 |
| Clearance of creatinine | | | 62.3±21.0 | | | 76.9±24.6 | <0.001 |
| Clearance of creatinine (<30 ml/minutes) | 15 | 3.8 | | 13 | 1.3 | | 0.003 |
| Peripheral vascular disease | 0 | 0.0 | | 1 | 0.1 | | 0.530 |
| Chronic obstructive pulmonary disease | 2 | 0.5 | | 6 | 0.6 | | 0.410 |
| Cerebrovascular accident | 12 | 3.1 | | 33 | 3.3 | | 0.778 |
| Packed red blood cells transfused | | | 2.3±2.1 | | | 2.4±2.1 | 0.754 |
| Perfusion time (minutes) | | | 80.2±30.5 | | | 81.3±24.3 | 0.576 |
| Aortic cross-clamp time (minutes) | | | 44.3±24.5 | | | 44.7±24.4 | 0.887 |
| Mechanical ventilation (minutes) | | | 171.6±41.1 | | | 173.4±45.4 | 0.495 |
| Inotropic support | 78 | 19.8 | | 158 | 15.8 | | 0.074 |
| Intraaortic balloon pump | 37 | 9.4 | | 63 | 6.3 | | 0.037 |

SD: Standard deviation.

**Table 2. Between-gender comparison with regard to early mortality and morbidities after coronary artery bypass grafting**

| Variables | Females (n=393) | | Males (n=997) | | |
|---|---|---|---|---|---|
| | n | % | n | % | *p* |
| Mortality | 27 | 6.9 | 23 | 2.3 | <0.001 |
| Postoperative complications | 143 | 36.4 | 303 | 30.3 | 0.028 |
| Ventricular arrhythmia | 75 | 19.1 | 188 | 18.9 | 0.92 |
| Ventricular tachycardia | 9 | 2.3 | 15 | 1.5 | 0.34 |
| Ventricular fibrillation | 8 | 20 | 8 | 0.8 | 0.052 |
| Supraventricular arrhythmia | 61 | 15.5 | 103 | 10.3 | 0.007 |
| Atrial fibrillation | 57 | 14.5 | 97 | 9.7 | 0.011 |
| Postoperative myocardial infarction | 2 | 0.51 | 2 | 0.2 | 0.318 |
| Renal complications | 4 | 1.0 | 16 | 1.6 | 0.408 |
| Renal failure | 1 | 0.3 | 1 | 0.1 | 0.486 |
| Pulmonary complications | 8 | 2.0 | 19 | 1.9 | 0.894 |
| Neurological complications | 8 | 2.0 | 25 | 2.5 | 0.603 |
| Vascular complications | 0 | 0.0 | 2 | 0.2 | 0.374 |
| Infection complications | 7 | 1.8 | 7 | 0.7 | 0.07 |
| Leg infections | 2 | 0.5 | 2 | 0.2 | 0.318 |
| Deep sternal infections | 4 | 1.0 | 6 | 0.6 | 0.482 |
| Septicemia | 3 | 0.7 | 0 | 0.0 | 0.006 |
| Prolonged mechanical ventilation | 21 | 5.3 | 20 | 2.0 | 0.074 |
| Need for reoperation due to bleeding | 12 | 3.1 | 41 | 4.1 | 0.353 |

independent risk factor for postoperative mortality. Furthermore, the association between female gender and postoperative septicemia along with prolonged mechanical ventilation remained significant, but we found no significant relationship between female gender and ventricular and supraventricular arrhythmia after these analyses were performed. In the unadjusted analyses, there were no significant associations between gender and renal (protective) and infection complications (including leg infection), although there was a significant correlation once we applied the logistic regression analyses.

**Table 3. Between-gender multivariate logistic regression results for early mortality and morbidities after coronary artery bypass grafting**

| Variables | OR (95% CI) | *p* |
|---|---|---|
| Mortality | 1.03 (1.01-1.05) | 0.039 |
| Ventricular arrhythmia | 1.03 (0.97-1.09) | 0.224 |
| Ventricular tachycardia | 1.01 (0.98-1.02) | 0.973 |
| Ventricular fibrillation | 1.02 (0.99-1.03) | 0.077 |
| Supraventricular arrhythmia | 1.01 (0.97-1.09) | 0.594 |
| Atrial fibrillation | 1.01 (0.99-1.02) | 0.269 |
| Postoperative MI | 1.00 (0.99-1.01) | 0.440 |
| Renal complications | 0.97 (0.96-0.99) | 0.006 |
| Pulmonary complications | 1.03 (0.99-1.04) | 0.215 |
| Neurological complications | 0.98 (0.96-1.01) | 0.215 |
| Vascular complications | 0.99 (0.98-1.00 | 0.543 |
| Infection complications | 1.02 (1.01-1.03) | 0.018 |
| Leg infections | 1.02 (1.01-1.03) | 0.017 |
| Deep sternal infections | 1.01 (0.97-1.02) | 0.225 |
| Septicemia | 1.02 (1.01-1.05) | 0.004 |
| Prolonged mechanical ventilation | 1.03 (1.01-1.05) | 0.025 |
| Need for reoperation for bleeding | 0.99 (0.96-1.01) | 0.456 |

Male gender was considered to be the reference; MI: Myocardial infarction.

## DISCUSSION

In the current study mortality rate in women was significantly higher than the men. However, the observed mortality rates in both genders in our study were comparatively higher than in those identified in recent investigations.[8-10]

In consistence with most recent investigations, comorbid conditions including older ages, lower creatinine clearance levels, diabetes mellitus, hypertension, hypercholesterolemia and hypertriglyceridemia were observed higher in women in our study[15-20] and a higher proportion of them referred in late stages of CCS and NYHA class III and IV.[4,21,22] More men smoked and were addicted to opium, and they also had a higher prevalence of previous MI. A number of recent studies have found that female gender is an independent risk factor for postoperative mortality,[8-10,23] but there are a few studies that do not agree with this conclusion.[24-26]

Some issues have been proposed to explain the higher postoperative mortality in female patients. As confirmed by our findings, different baseline risk factors in men and women may to some extent explain the observed differences in outcomes.[27-29] Furthermore, being diagnosed with CCS and NYHA class III and IV would increase the number of urgent surgeries, thus offering an explanation for the poorer outcomes.[21,22] Moreover, although we made an adjustment for all of the different gender-based factors via multivariate regression analyses, female gender was still significantly related to postoperative mortality.

Similar to our findings, Alam et al.,[8] in a study involving 13,115 patients who underwent isolated CABG, found that female gender was an independent risk factor for postoperative wound infection. They also determined that women had a lower risk of postoperative AF. The female patients in our study also had higher rates of AF, but the between-gender difference was not significant. Some authors believe that the observed differences in postoperative outcomes between males and females can be attributed to the varied distribution of the preoperative risk factors[5] and that some of these factors may even be more important predictors for postoperative mortality and morbidity than gender alone.[30-32]

Furthermore, in agreement with our findings, several studies have noted an increased risk for postoperative morbidities in females, including prolonged mechanical ventilation,[13,14] surgical site infection, sepsis,[14] and renal complications;[8] however, not all studies have been able to confirm this risk.[5] In addition, our data did not always correspond to that found in other studies. Hence, the existing literature seems to provide no consensus opinion regarding the relationship between morbidities and gender as they relate to the early surgical outcomes of patients who undergo isolated CABG.

The retrospective nature of our study was a limitation. In addition, our study was conducted at a tertiary care referral center, which could lead to referral bias. We also applied a stepwise multivariate logistic regression model to correct for baseline gender-specific differences, but there may have been other confounding factors that were not accounted for in this model. In addition, we excluded 330 (14.1%) of our initial sample size due to incomplete data.

### Conclusion

In our retrospective study involving patients who underwent isolated CABG, we determined that female gender was an independent predictor of postoperative mortality and some morbidities. Therefore, careful attention should be paid to women scheduled for this type of surgery.

### Acknowledgement

The authors would like to thank the Farzan Institute for Research and Technology for their technical support.

### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

### Funding

The authors received no financial support for the research and/or authorship of this article.

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