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

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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. 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.

Materials and 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) male.

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).

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

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.
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 antegrade 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 analyzed using SPSS 15 (SPSS Inc, Chicago, The United States). Non-categorical data were analyzed with t-test and categorical data with Chi-Square or Fisher’s Exact test where appropriate. Mann-Whitney was used in analyzing 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).

|                              | Male (N=1296) | Female (N=361) | P value |
|------------------------------|--------------|---------------|---------|
| 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 TIA       | 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

106  | J Cardiovasc Thorac Res, 2014, 6(2), 105-110
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, 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.

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

|                          | Male         | Female       | P  |
|--------------------------|--------------|--------------|----|
| 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)    | 0.892 |
| 2                        | 35.5% (460)  | 36.8% (133)  |    |
| ≥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)  | 0.037 |
| ≥3-4 hour                | 51.9% (672)  | 44.3% (160)  |    |
| >4 hour                  | 8.8% (114)   | 9.4% (34)    |    |
| Prolonged intropo 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 fibrillation | 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 multivariate 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 |
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.\(^4\) Previous studies showed that the rate of female gender in patients undergoing CABG surgery was between 19.3% and 30.6.\(^5\) 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,\(^4,9,12,15\) and had a higher prevalence of hyperlipidemia.\(^4,5,11,12\)

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 higher inotropic support.\(^4\) and had longer length of hospital stay,\(^4\) 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.\(^4,6\)

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.\(^4\) 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\(^12\)\(^-\)\(^24\) have concluded that female patients had equally or better late survival than 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.

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**Ethical issues**

This study was approved by our local Ethics Committee.

**Competing interests**

Authors declare no conflict of interest in this study.

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