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Impact of gender on outcome following coronary artery bypass grafting surgery

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Background. Women experience greater complications and early mortality after both percutaneous interventions and coronary bypass surgery (CABG). Coronary artery disease is becoming more prevalent among women. The aim of the study was to determine whether gender differences in outcomes of surgical treatment persist at our institution.

Methods. A retrospective review of 3177 consecutive CABG patients operated on at our institution during a five-year period. A number of demographic and preoperative risk factors were analyzed to evaluate the risk of surgical procedure. Intraoperative variables reflected the surgical and anesthetic management of the patients. Mortality was the primary outcome, but major morbidity was also analyzed. Logistic regression analysis was performed to identify the independent predictors of postoperative mortality.

Results. The observed crude mortality rate was higher in women than in men (5.2% vs 2.8%, $p < 0.05$). Women were older (67.5 ± 8.3 vs 63.1 ± 9.4 years, $p < 0.001$) and had a greater incidence of comorbidities. The internal thoracic artery as a conduit was used with a lower rate in female patients (62.5% vs 77.8%, $p < 0.01$). Women had a higher rate of low cardiac output syndrome, were less likely to be extubated early following the procedure and required a higher rate of blood transfusions (45.2% vs 25.4%, $p < 0.01$). Logistic regression analysis revealed that age, left ventricle ejection fraction and female gender were significant independent predictors of postoperative mortality.

Conclusion. Despite advances in surgical and anesthetic techniques, female patients are operated on with an almost twice as high mortality rate as men. The risk profile of female patients differs greatly from male patients. These factors could have a negative impact on the results of surgical treatment of women.

Key words: risk assessment, mortality, gender, coronary bypass surgery

INTRODUCTION

For many years, coronary artery disease was believed to affect nearly exclusively men. However, nowadays cardiovascular disease is the leading health threat to women in the Western world, resulting in one out of two female deaths (1). Coronary artery bypass grafting (CABG) is used in women as an effective treatment for the coronary artery disease. Women now account for up to 30% of patients undergoing myocardial revascularization procedures (2). A higher mortality rate in women following CABG procedures has been observed by several investigators (3–5). The increased preoperative risk in women has been attributed to the greater incidence of comorbidities, presence of a smaller body surface area and coronary artery size, and referral patterns later in the course of coronary artery disease (6, 7). Nevertheless, when the population is adjusted for the risk factor profile, the male–female difference in mortality and morbidity tends to lose its significance (8). There have been several studies to show that over the last decade there has been a marked decrease in CABG mortality among women (9). Because of the increasing number of female patients undergoing CABG surgery in the Vilnius University Hospital Santariskiu Klinikos, the aim of the study was to determine whether gender differences in outcomes persist.

METHODS

A retrospective analysis of all consecutive CABG patients operated on in our institution between January 1, 2000 and December 31, 2004 was performed. Patients with concominant

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valve repair or replacement procedures were excluded from the investigation. Data regarding a number of variables were collected. Demographic and preoperative data were collected to describe the type and severity of the disease and to assess the risk of surgery. Intraoperative variables described the course of surgery and anesthetic management. During this time frame, there were no major changes in anesthetic or surgical technique, similar myocardial protection technique (minimally diluted tepid blood cardioplegia); uniform pathways leading to extubation, blood product transfusion or ICU discharge were applied to all patients. Median sternotomy was used in all patients. Saphenous veins, radial artery and internal mammary artery were used as conduits for myocardial revascularization. Postoperative data collection focused on mortality and morbidity, and all complications were uniformly adopted. Major postoperative cardiac complications were myocardial infarction (new Q-wave in two or more leads, new left bundle branch block, troponin higher than 10 μg/l or new regional wall motion abnormality detected by echocardiography) or low cardiac output syndrome (need for intraaortic balloon pump). Major respiratory complications were defined as need for respiratory support for more than 48 hours, pneumonia, tracheostomy or need for reintubation. The rate of stroke, coma or transient ischemic attack was used as a marker of major neurologic complications. Renal dysfunction was defined as a need for continuous renal replacement therapy.

In our analysis, we tried to determine the impact of body size on the mortality of men and women undergoing CABG surgery. Body surface area (BSA) was calculated for every patient before the cardiopulmonary bypass, and the mortality of patients following CABG surgery was analyzed in subgroups devided according to the patient body size.

Statistical analysis

All data are presented as mean ± standard deviation for continuous variables and as percentages for categorical variables. Gender differences were examined using the chi-square test for categoric variables and the Wilcoxon Rank Sum test for continuous variables. Factors showing significant gender differences at a level of p value less than 0.05 were retained for further analysis. Multivariate linear regression analysis was performed to determine the important predictors of postoperative mortality. A value less than 0.05 was considered statistically significant. Statistical analysis was carried out using the SPSS 8.0 statistical package.

RESULTS

A total of 3177 patients were operated on during the study period. Women constituted 25.5% of all patients undergoing CABG at our institution. The proportion of female patients undergoing myocardial revascularization procedure increased slightly from 23% in 2000 to 27% in 2004. The preoperative variables were compared between women and men and are presented in Table 1. The preoperative risk profile was significantly different between the genders. Women undergoing surgery were older and had more comorbidities, including hypertension, previous cerebrovascular accident, diabetes mellitus, obesity and left ventricle dysfunction. Men were more likely to have peripheral vascular disease, left main coronary disease and have a prior CABG, however, women were more often operated on emergency basis. There were no significant differences in the operative time, CPB time or aortic cross clamp time, however, women received fewer internal mammary artery grafts as compared to men (Table 2). Emergency resumption of CPB during surgery was also more often in female patients. The unadjusted operative mortality for the entire study group was 4.06%. Women's operative mortality was almost twice as high as men's (5.2% vs 2.8%, $p < 0.05$). Although the rate of perioperative myocardial infarction was similar in both groups, women were more likely to develop

Table 1. **Preoperative characteristics of patients**

Characteristics	Women (n = 801)	Men (n = 2376)	P value
Age	67.5 ± 8.3	63.1 ± 9.4	<0.001
Age >75 years	161(20.1%)	245(10.3%)	<0.001
BMI >30	280(34.9%)	606(25.5%)	<0.001
Left main disease	203(25.3%)	725(30.5%)	<0.01
LV EF <30%	26(3.2%)	150(6.3%)	<0.05
MI <90 days	119(14.9%)	347(14.6%)	n. s.
Hypertension	666(83.1%)	1703(71.7%)	<0.001
Diabetes	145(18.8%)	261(11.0%)	<0.001
Previous CVA	59(7.4%)	95(4.0%)	<0.01
Peripheral vascular disease	35(4.4%)	216(9.1%)	<0.001
Creatinin >200 zmol/l	10(1.2%)	38(1.6%)	n. s.
Preoperative IABP	6(0.75%)	19(0.8%)	n. s.
Emergency surgery	109(13.6%)	216(9.1%)	<0.01
Previous cardiac surgery	11(1.4%)	102(4.3%)	<0.001

BMI – body mass index, LV EF – left ventricle ejection fraction, MI – myocardial infarction, IABP – intraaortic balloon pump.

Table 2. **Intraoperative data**

Characteristics	Women (n = 801)	Men (n = 2376)	P value
ITA used	501(62.5%)	1849(77.8%)	<0.01
No of distal anostomosis	3.7 ± 1.1	3.9 ± 1.1	n. s.
Operative time (min)	215 ± 72	214 ± 68	n. s.
CPB time (min)	104 ± 38	106 ± 41	n. s.
Aortic cross clamp (min)	61 ± 21	63 ± 21	n. s.
Reinstitution of CPB	42(5.3%)	47(2.0%)	<0.01

ITA = internal thoracic artery, CPB – cardiopulmonary bypass.

Table 3. **Postoperative outcomes**

Characteristics	Women (n = 801)	Men (n = 2376)	P value
Hospital mortality	42(5.2%)	67(2.8%)	<0.05
Perioperative MI	23(2.8%)	50(2.1%)	n. s.
IABP	50(6.2%)	102(4.3%)	<0.05
CMV <8 h	303(37.8%)	1086(45.7%)	<0.01
Stroke	14(1.74%)	42(1.77%)	n. s.
Delirium	10(1.2%)	67(2.8%)	<0.05
Resternotomy	42(5.2)%	38(5.8%)	n. s.
Blood products used	362(45.2%)	604(25.4%)	<0.001
ICU stay (days)	2.4 ± 2.4	2.2 ± 2.5	n. s.

MI – myocardial infarction, IABP – intraaortic balloon pump, CMV – continuous mechanical ventilation, ICU – intensive care unit.

Table 4. **Body surface area and mortality following CABG surgery**

BSA	Women n = 801 Died / total / %	Men n = 2376 Died / total / %
BSA ≤1.7 m^2	14/208 (6.7%)	2/98 (2.0%)
BSA 1.7–1.8^2	15/316 (4.7%)	19/472 (4.0%)
BSA 1.85–2 m^2	10/197 (5.0%)	24/722 (3.32%)
BSA >2 m^2	3/80 (3.75%)	22/1080 (2.03%)

low cardiac output postoperatively (Table 3). They also had a higher rate of unsuccessful extubation early after surgery, a higher rate of blood transfusions. Men were more likely to develop delirium following surgery. Underweight women had a higher mortality rate (Table 4) than women with bigger body surface area. Logistic regression analysis showed that age, low left ventricle ejection fraction and gender are the only independent predictors of postoperative mortality (Table 5).

DISCUSSION

Despite a few studies showing a marked decrease in the adverse outcome in women undergoing cardiac surgery, our results with respect to gender differences to in-hospital mortality are consistent with those of most studies (4, 5, 10). The mortality and morbidity of women undergoing coronary revascularization surgery remains much higher than of men. Some investigators reported diminishing the differences in adverse outcomes between men and women. However, despite the improvement in short-term mortality of women undergoing coronary artery bypass grafting, the authors had found that women were by 42% more likely to die within the 30 days after CABG compared to men (11). The smaller size of a woman was assumed by several investigators as a risk factor increasing mortality rates of female patients. The smaller size of coronary vessels could contribute to incomplete revascularization or graft failure following surgery. Body surface area is considered a surrogate marker of coronary artery size. When cardiopulmonary bypass is used, there is an evidence that on-pump

Table 5. **Independent predictors of postoperative mortality**

Variable	Coef. (SE)	Sig	Odds ratio	95% CI
Age	0.073(0.024)	0.003	1.076	1.026–1.128
LV EF	–0.08(0.02)	0.000	0.923	0.888–0.959
Gender	–0.343(0.23)	0.056	0.649	0.416–1.012

LV EF – left ventricle ejection fraction.

hemodilutional anemia is particularly prevalent in smaller patients and might be a major cause of morbidity and mortality (12, 13). Worse averse outcomes in underweight women undergoing CABG procedures were found in our investigation. Our study showed that CABG was also associated with an increased morbidity of female patients. Although the rate of perioperative myocardial infarction was similar in both genders, female patients had a higher incidence of low cardiac output syndrome, more often failed the early extubation protocol, recieved more blood transfusions. Butterworth et al. (14) in a multicenter study showed that female gender was associated with a longer duration of intubation and stay in the ICU and in the hospital. Female gender was found to be associated with prolonged intubation times and longer postoperative stay in the hospital in a study by Capdeville et al. (15). The higher number of adverse outcomes in women might be explained partly by their worse preoperative risk profile. Data in the literature and our results show that women undergoing cardiac surgery are older, with a higher rate of cerebrovascular disease, diabetes, with a lower left ventricle ejection fraction and are more often operated on emergency basis. This might contribute to a higher mortality and increased morbidity in female patients. Some operative factors, such as a smaller body surface area as a marker of smaller coronary arteries and a lower use of the internal thoracic artery might have an impact on adverse outcomes in female patients. Specific pharmacologic and therapeutic considerations, such as the role of estrogen replacement therapy, need to be clarified, as they might have a positive impact the outcome in female patients. More research is needed to evaluate the appropriate utilization of treatment procedures that might reduce the mortality and morbidity of female patients undergoing cardiac surgery.

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LYTIES ĮTAKA MIOKARDO REVASKULIARIZAVIMO OPERACIJŲ REZULTATAMS

S a n t r a u k a

Darbo tikslas. Vis dažniau moterys serga širdies ir kraujagyslių ligomis. Vis dėlto joms taikomą miokardo revaskuliarizaciją lydi didesnė operacinė rizika. Mūsų darbo tikslas buvo įvertinti lyties įtaką chirurginio gydymo rezultatams mūsų klinikoje.

Tyrimo medžiaga ir metodai. Retrospektyviai išanalizuoti 3 177 ligonių, operuotų Vilniaus universiteto ligoninės Santariškių klinikoje per penkerius metus, gydymo rezultatai. Surinkti duomenys atspindi priešoperacinę ligonių būklę bei rizikos veiksnius, galinčius turėti įtakos chirurginio gydymo rezultatams. Analizuotas ligonių mirštamumas ir komplikacijos pooperaciniu laikotarpiu. Regresine analize nustatyti mirties rizikos veiksniai.

Rezultatai. Tiriamuoju laikotarpiu moterų hospitalinis mirštamumas ligoninėje buvo didesnis lyginant su vyrais (5,2 % vs 2,8 %, $p < 0,05$). Moterys buvo vyresnės (67,5 ± 8,3 vs 63,1 ± 9,4 m, $p < 0,001$), dažniau sirgo kitomis ligomis. Operacijos metu moterims rečiau taikyta vidinė krūtinės arterija apeinamosios jungties suformavimui (62,5 % vs 77,8 %, $p < 0,01$), po operacijos joms dažniau pasireiškė širdies silpnumas, ilgiau taikyta mechaninė plaučių ventiliacija, dažniau atliktos donorinio kraujo transfuzijos (45,2 % vs 25,4%, $p < 0,01$). Regresinė analizė atskleidė, kad amžius, kairiojo skilvelio išstūmimo tūris ir lytis yra nepriklausomi veiksniai, lemiantys pooperacinį mirštamumą.

Išvados. Nepaisant chirurginės ir anesteziologinės technikos pasiekimų, po miokardo revaskuliarizavimo operacijos pooperaciniu laikotarpiu moterų miršta beveik dvigubai daugiau.

Raktažodžiai: rizikos įvertinimas, mirštamumas, lytis, miokardo revaskuliarizavimo operacijos