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Influence of Cardiovascular Risk Factors on the Outcome of Coronary Artery Bypass Surgery

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Abstract

Purpose. To assess the impact of gender, age, and other cardiovascular risk factors on the outcomes of patients undergoing coronary artery bypass grafting (CABG).

Methods. A total of 5067 consecutive patients undergoing isolated CABG between 1995 and 2000 were divided into the age groups: 25–49 years, 50–59 years, 60–69 years, and 70–84 years. Data on patient age, gender, smoking, serum cholesterol, blood pressure, body mass index, diabetes, family history, morbid obesity, and renal failure were retrospectively analyzed.

Results. The percentage of women aged >60 years undergoing CABG was higher than the percentage of men aged >60 years (45.6% vs 36.6%). Most of the cardiovascular risk factors, except for smoking, were favorable in women ($P < 0.001$). The in-hospital mortality was 2.0% in women and 1.7% in men ($P = 0.409$). CABG was performed on significantly more men than women, accounting for 80.7% and 19.3% of the 5067 patients, respectively ($P < 0.001$). However, the incidence increased remarkably in women aged >60 years.

Conclusions. The risks of CABG may vary to some degree in accordance with the major cardiovascular risk factors. The risk of operative mortality was independent of gender in this study.

Key words Cardiovascular risk factors · Gender · Age · Coronary artery bypass surgery

Introduction

Coronary artery disease is the leading cause of death in most industrialized countries, and its significance as a major public health problem is also increasing in developing countries.[1] Serum total cholesterol, high-density lipoprotein cholesterol, smoking, diabetes, obesity, and blood pressure are established major risk factors for coronary heart disease.[2,3] The outcome of coronary artery bypass grafting (CABG) is known to vary with patient characteristics such as age and gender, as well as with the presence of comorbid conditions.[4–11] The risk of operative mortality and morbidity after CABG is significantly higher in women than in men,[4,7,9,10,12] which suggests that older age, diabetes, more cases of emergency surgery, or smaller body size and hence smaller coronary artery diameter, could be responsible for this.[4,9–13] There is a long-standing perception that obesity increases the risk of adverse outcomes following CABG, which could be due to the higher incidence of such comorbid conditions as diabetes, hypertension, hypercholesterolemia, and impaired respiratory function,[14–16] as well as the technical difficulties involved in the surgical and postsurgical care of obese patients.[16] Interestingly, a number of studies have reported higher operative mortality following CABG in patients with low body surface area (BSA, m^2) than in patients with normal or high BSA.[6–11]

Coronary atherosclerosis is more prevalent in diabetic patients than in non-diabetics. Diabetics with severe coronary artery disease are considered poor candidates for bypass surgery because of the related comorbidity. Furthermore, several studies have reported improved quality of life after CABG in elderly patients.[17–19] However, if the vital risk of surgery is large, then the risk-benefit ratio may be tipped toward medical therapy for the elderly.

The aim of this study was to elucidate the influence of gender, age, and other cardiovascular risk factors such as smoking, serum cholesterol, blood pressure, body mass index, diabetes, family history, morbid obesity, and renal failure on operative mortality and morbidity after isolated CABG, and to determine the

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influence of these changes on the results of coronary surgery in men and women.

Patients and Methods

Between 1995 and 2000, 5067 consecutive patients, consisting of 4090 men and 977 women aged between 25 and 84 years, underwent isolated CABG at the Florence Nightingale Hospital, Istanbul, Turkey. Patients were divided into the following age groups: 25–49 years (645 men, 68 women), 50–59 years (1347 men, 236 women), 60–69 years (1497 men, 446 women), and 70–84 years (601 men, 227 women). Patients undergoing minimally invasive direct CABG, off-pump surgery, CABG in association with heart valve repair or replacement, resection of a ventricular aneurysm, or extracardiac surgical procedure were excluded from the analysis.

Cardiopulmonary Bypass

Cardiopulmonary bypass was performed using standard techniques, and patients were cooled to 32°C under general anesthesia. While standard cardioplegia was given antegrade and retrograde, in recent years warm cardioplegia has been used more frequently. The left internal mammary artery was used to bypass the left anterior descending artery.

Data Collection

Clinical, operative, and outcome data were collected prospectively in a computerized database (summit program), for the 5067 consecutive patients who underwent isolated CABG between 1995 and 2000. Clinical variables were used to compare men and women. For statistical analysis, data were divided into four age cohorts: 25–49 years, 50–59 years, 60–69 years, and 70–84 years. Gender, age, and cardiovascular risk factors such as smoking, serum cholesterol, blood pressure, body mass index, diabetes, family history, morbid obesity, and renal failure were recorded for each patient by researching extensive historic, physical, and laboratory information.

Obesity was defined by the body mass index (BMI, kg/m^2), which was used as a measure of relative body weight. BSA and BMI were calculated by the standard formulas[11]

$$\mathrm{BSA} = \left[\frac{\mathrm{Height} \times \mathrm{weight}}{3600}\right]^{1/2}$$

and

$$\mathrm{BMI} = \left[\frac{\mathrm{Weight}}{\mathrm{Height}^2}\right]$$

Five-year Kaplan-Meier survival plots were calculated for all patients combined and for four patient size subgroups; namely, small (BMI $\leq 24\,kg/m^2$), normal ($30 \geq \mathrm{BMI} > 24$), obese ($34 \geq \mathrm{BMI} > 30$), and grossly obese ($\mathrm{BMI} > 34$).

Priority of surgery was assessed by the cardiothoracic surgeons and defined as:

1. Emergency-salvage, meaning medical factors relating to the patient's coronary catheterization necessitated immediate surgery
2. Emergency, meaning medical factors relating to the patient's cardiac disease dictated that surgery should be performed within hours to prevent morbidity or death
3. Urgent, meaning medical factors required the patient to stay in hospital for an operation before discharge, ideally within 24–48 h of coronary catheterization
4. Elective, meaning medical factors indicated the need for surgery, but the clinical situation allowed for discharge from hospital with readmission at a later date

Operative mortality was defined as any death that occurred during the hospital stay or within the first 30 postoperative days if patients died after discharge.

Statistical Analysis

Statistical analysis was done with the univariate and multivariate linear and regression analyses and stepwise manipulations, using a Statistical Package for the Social Sciences (Table 4) (SPSS Base System User's Guide). All results are expressed as the mean ± standard deviation (SD). Cardiovascular risk factors of the gender differences were assessed using chi-squared tests. Continuous data were analyzed using two-tailed *t*-tests. Differences in BMI between men and women were analyzed using two-tailed *t*-test. Differences between men and women in the four age groups for postoperative mortality and morbidity were analyzed using chi-squared tests.

Logistic regression analysis and stepwise manipulations were used to assess the relationships among age, gender, risk factors, BMI, and hospital mortality. A P value of less than 0.05 was considered significant.

Results

The 5067 consecutive isolated CABG patients included 4090 men (80.7%) and 977 women (19.3%). The overall incidence of CABG was significantly higher in men than

Table 1. Clinical characteristics of men and women who underwent coronary artery bypass grafting

Risk factor	Women		Men		*P* value (χ^2)[a]
	Patients	Percent	Patients	Percent	
Age 25–49 years	68	7.0	645	15.8	0.001
Age 50–59 years	236	24.2	1347	32.9	0.001
Age 60–69 years	446	45.6	1497	36.6	0.001
Age 70–84 years	227	23.2	601	14.7	0.001
Smoking history	241	24.7	2974	72.7	0.001
Family history	481	49.2	1801	44.0	0.01
Diabetes	343	35.1	928	22.7	0.001
Morbid obesity	224	22.9	349	8.5	0.001
Hypercholesterolemia	502	51.4	1779	43.5	0.001
Renal failure	45	4.6	244	6.0	0.10
Hypertension	608	62.2	1662	40.6	0.001
Mortality	20	2.0	68	1.7	0.409
BMI (kg/m^2)		29.4		30.1	0.001

BMI, body mass index
[a] Difference between women and men, adjusted for age

in women (4090/977 = 4, χ^2 test, $P < 0.001$). The mean age ± standard error of the mean (SE) in men was 60.08 ± 9.35 (range: 25–84) years.

The cardiovascular risk factors according to gender are listed in Table 1. Here a comparison of cardiovascular risk factors for men and women shows that there were significant differences in the two populations. In general, women were older, had a higher incidence of diabetes, morbid obesity, hypercholesterolemia, hypertension ($P < 0.001$), and positive family histories of coronary artery disease ($P < 0.01$), but more men had a history of smoking ($P < 0.001$). The incidence of renal failure was similar in men and women (($P < 0.10$). Operative mortality was similar, being 2.0% (20/977) for women and 1.7% (68/4090) for men. Mortality was not significant for either gender ($P = 0.409$, Table 1).

Table 2 shows the comparative CABG incidence and mortality, and cardiovascular risk factor differences between genders according to age group. The incidence of isolated CABG was highest in the 60–69-year age group (36.6% for men and 45.6% for women; Fig. 1). Operative mortality increased significantly in the 70–84-year age group in men and women (Table 2). BMI ranged between 22.1 and 42.7 kg/m^2, with near normal distribution (mean 29.9 kg/m^2, Fig. 2). There was no positive correlation between BMI and age in men or women (Table 2) (correlation coefficient: $r = -0.137$, $P < 0.001$ for men; $r = -0.08$, $P < 0.05$ for women). Table 3 shows the timing of surgery and the incidence of reoperation.

Discussion

The role of major cardiovascular risk factors in the development of coronary artery disease was similar in men and women. In the younger age groups, the overall risk factor level was more favorable in women; however, this advantage of women diminished remarkably with aging. Coronary artery disease was significantly more common in men than in women, and the incidence increased with age, especially in women. In this study, the CABG incidence among men was about 4-fold, but mortality was 1.2-fold greater in women. The isolated CABG incidence was greatest in the 60–69-year age group.

The higher risk of hospital mortality and morbidity among women who undergo CABG is attributed to multifactorial risk factors. The most common explanations center around the fact that women have smaller, more technically challenging coronary vessels, internal mammary artery grafting is used less frequently, and a referral bias causes them to present for surgical intervention at a more advanced stage of disease. Khan and colleagues[13] and Weintraub and associates[7] reported that women were older with a higher prevalence of hypertension, diabetes, unstable angina, need for urgent operation, and single-vessel disease. The role of estrogen is logically implicated in attempts to explain these observations.[6,20] It is possible that the higher mortality in women is in fact attributable to diabetes. The reported prevalence of diabetes among patients undergoing CABG ranges from 7% to 20%.[4,6–9,11] Cohen and colleagues[21] reported that operative mortality was 5.0% in diabetic patients ($n = 1034$) and 2.5% in nondiabetics ($n = 3350$), and suggested that female gender may not be a risk factor for CABG mortality among nondiabetic patients. Conversely, other reports indicate that there is no real difference in CABG operative mortality between genders when these factors are normalized.[4,6,9] In our patients, operative mortality was 2.0% for women and 1.7% for men, with no significant

Table 2. Incidence of cardiovascular risk factors and mortality after CABG in men and women in the four age groups

Cardiovascular risk factor	25–49 years			50–59 years			60–69 years			70–84 years	
	Women (n = 68) Mean	Men (n = 645) Mean	P^a	Women (n = 236) Mean	Men (n = 1 347) Mean	P^a	Women (n = 446) Mean	Men (n = 1 497) Mean	P^a	Women (n = 227) Mean	Men (n = 60) Mean
Smoking (%)	42.6	83.4	0.001	30.1	76.6	0.001	20.6	68.3	0.001	21.6	63.6
Family history (%)	54.4	50.5	0.05	52.5	45.1	0.05	47.3	40.1	0.01	48.0	44.4
Diabetes (%)	29.4	16.1	0.01	36.9	21.8	0.001	36.5	25.5	0.001	32.2	24.8
Morbid obesity (%)	19.1	8.7	0.01	22.9	9.5	0.001	25.8	8.5	0.001	18.5	6.3
Hypercholesterolemia (%)	42.6	45.6	0.05	55.1	44.2	0.01	49.1	41.0	0.01	54.6	45.8
Renal failure (%)	2.2	0	0.05	6.4	4.2	0.05	3.6	6.7	0.01	6.2	12.1
Hypertension (%)	41.2	29.5	0.05	58.1	36.5	0.001	63.9	45.9	0.001	69.6	48.9
Mortality (%)	1.5	0.3	0.05	1.3	1.3	0.59	2.5	1.6	0.05	2.2	4.2
BMI (kg/m^2)	26.6	27.1	0.001	31.8	32.1	0.001	30.7	31.4	0.001	28.4	29.8

CABG, coronary artery bypass grafting
[a]Difference between women and men, adjusted for age

Table 3. Timing of surgery and reoperation

Timing of surgery	Patient (n)	Percent
Elective	4258	84.0
Urgent	628	12.4
Emergency	69	1.4
Emergency-salvage	19	0.4
Reoperation	93	1.8
Total	5067	100.0

Table 4. Relationship between body mass index and gender, age, and cardiovascular risk factors

Risk factors	Coefficients			
	Beta	SE	t	P
BMI	46.946	0.518	90.559	0.000
Gender	−1.427	0.073	−19.671	0.000
Age	−0.284	0.031	−9.272	0.000
Hypercholesterolemia	−0.302	0.056	−5.354	0.000
Hypertension	−0.291	0.058	−5.030	0.000
Morbid obesity	−3.109	0.089	−34.977	0.000
Renal failure	0.337	0.120	2.811	0.05
Mortality	0.462	0.212	2.181	0.029

	Excluded variables		
	Beta	t	P
Smoking	−0.018	−1.348	0.178
Diabetes	0.019	1.519	0.129
Family history	0.007	0.603	0.547
	r	F	P
Regression (total)	0.497	236.999	0.000

Dependent variable: BMI

difference between genders (P = 0.409). However, operative mortality significantly increased in the 70–84-year age group in both men and women.

Previous reports investigating the role of patient body size on the outcome of coronary revascularization surgery have focused primarily on comparisons of in-hospital mortality and postoperative complications between obese and nonobese patients.[10,16] Obesity is a well-defined risk factor for the development of coronary artery disease, type II diabetes mellitus, hypertension, and many other diseases. Various studies have also shown reduced life expectancy in obese patients.[15,22] On the other hand, Loop et al.[4] suggested that patients with low body weight might actually be at higher risk when undergoing coronary artery surgery. Koshal et al.[23] and Prasad et al.[14] found no increase in operative mortality in obese patients undergoing CABG.

BSA has been shown to correlate with the diameter of the coronary arteries.[9,12,24,25] However, this study did not examine coronary artery size, but rather focused on the independent influence of body size on postoperative

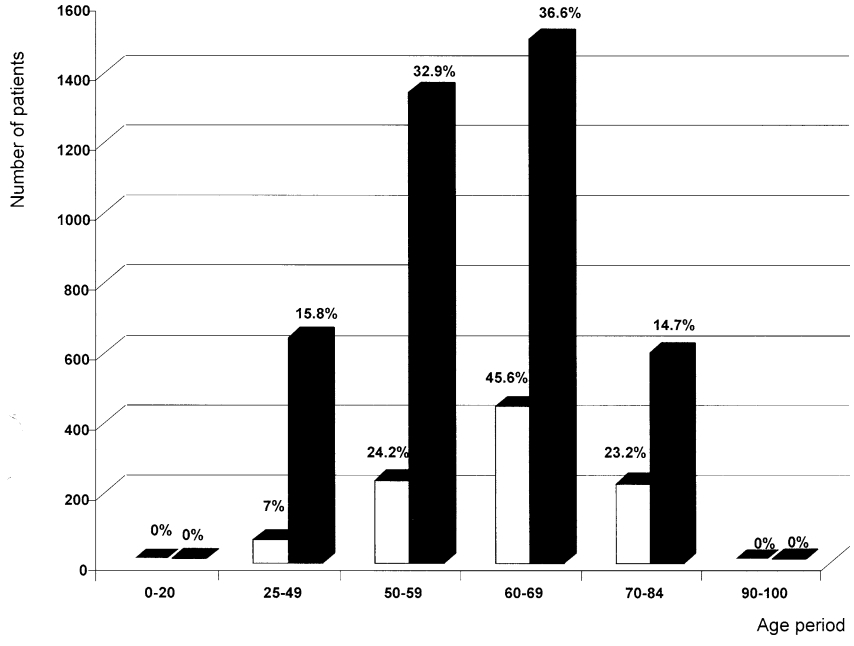

Fig. 1. Distribution of isolated coronary artery bypass grafting ($n = 5067$) in the four age groups. *Black bars*, men; *white bars*, women

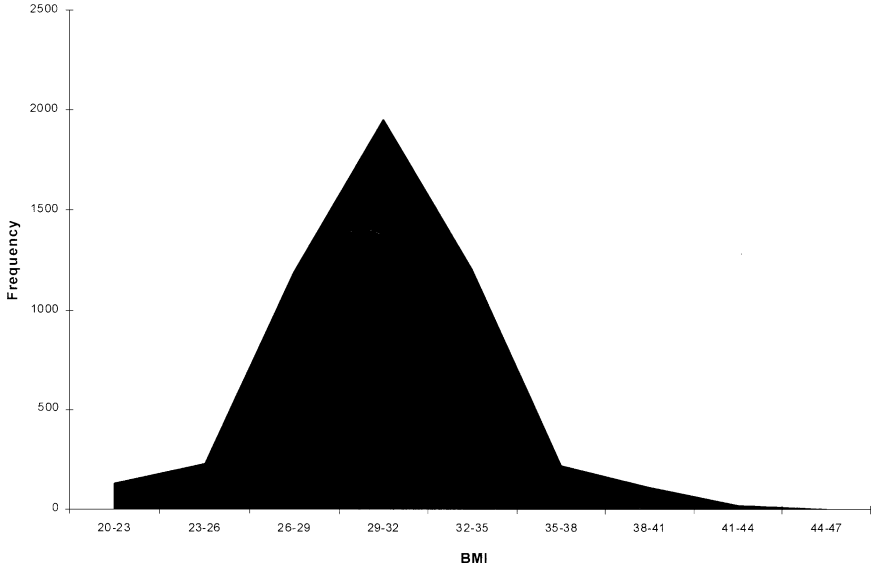

Fig. 2. Histogram of the distribution of body mass index in the 5067 patients who underwent coronary artery bypass grafting

outcomes. Assessing the influence of body size on postoperative outcomes is difficult when comparing men and women. Grover and associates[26] studied 12712 patients and identified height, weight, and BSA as significant unvaried, but not multivariable, predictors of operative mortality. Moreover, Khan and associates[13] did not find a significant association between mortality and BSA. In our study, obesity was defined by the BMI, which has several advantages over other methods of measuring obesity.[2] We did not find a positive correlation between BMI and age in men or women; however, all of the cardiovascular risk factors, apart from smoking, family history, and diabetes, were affected by the BMI (Table 4).

Using the National Medicare administrative data, Peterson and colleagues[27] reported an 18% reduction in risk-adjusted 30-day mortality after CABG surgery in the United States between 1987 and 1990. Recent studies from New York,[28] northern New England,[29] and Massachusetts[30] have reported trends of decreasing mortality after CABG surgery. In New York, in-hospital mortality decreased from 3.5% to 2.8% between 1989 and 1992, with a 41% decrease in adjusted mortality.[28,31]

In this study, incremental risk factors for operative mortality and morbidity were determined in 5067 patients undergoing isolated CABG surgery in our hospital between 1995 and 2000. Operative mortality, defined as either in-hospital or out of our entire study population, was low, at 1.7% and 2.0%, in men and women, respectively. Table 2 shows the rate of each comorbid condition in men and women, confirming that men and women present with different risk factors. Following CABG, not only do women have higher immediate postoperative mortality, but they also have higher postoperative morbidity and worse long-term survival.[6] In this study, the women who underwent CABG were older than the men, less women had a history of smoking, but the women had a higher incidence of diabetes, morbid obesity, hypercholesterolemia, hypertension, and positive family histories of coronary artery disease. This may suggest that the mechanisms of atherogenesis could also be different in men and women.

Although advancing age remains a consistent predictor of operative mortality after isolated CABG, a variety of reports in the literature have demonstrated that elderly patients previously thought to be at very high risk for adverse events can now undergo this beneficial procedure with acceptable postoperative risk.[19] Our findings confirm that there has been not only a time-related increase in the prevalence of older patients undergoing isolated CABG at our center, but also an increase in the severity of the preoperative risk profile of those patients. In this study, operative mortality significantly increased between 70 and 84 years in men and women.

In conclusion, the influence of gender, age, and cardiovascular risk factors on the outcome of CABG is multifactorial. In both men and women, coronary artery disease, and operative mortality and morbidity can be effectively prevented or decreased by reducing these risk factors. Therefore, further studies are necessary to identify the influence of individual risk factors on the outcomes of CABG.

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