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Comparison of Early and Late Mortality in Men and Women After Isolated Coronary Artery Bypass Graft Surgery in Stockholm, Sweden, 1980 to 1989

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Objectives. **We sought to analyze early and late mortality after coronary artery bypass graft surgery (CABG) in relation to gender.**

Background. **Early mortality after CABG is generally higher in women than in men, but the causes are controversial. Few studies have investigated long-term mortality after CABG in relation to gender.**

Methods. **In all, 3,326 men and 607 women underwent isolated CABG in Stockholm from 1980 to 1989. Mortality for these patients was followed by means of the National Cause of Death Register, from the time of operation until the end of 1990. Survival was evaluated by life-table methods and by proportional hazards regression.**

Results. **Early mortality (within 30 days) was 3% in women and 1.7% in men, corresponding to a relative risk of 1.8 (95% confidence interval [CI] 1.0 to 3.0) in women compared with men. When age and body surface area were taken into account, the relative risk was 1.0 (95% CI 0.5 to 2.0), which was not markedly different but multivariate analyses that included hypertension, diabetes mellitus, previous myocardial infarction, left ventricular function and number of diseased vessels. Only small gender differences in mortality were observed for 5 years after the operation among those who survived for 30 days.**

Conclusions. **The results suggest that men and women run similar risks of early and late mortality after CABG when patient characteristics are taken into account.**

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A higher early mortality rate in women than in men after coronary artery bypass graft surgery (CABG) has been observed by several investigators (1–10). A number of factors have been suggested to explain the higher early mortality rate among women, such as older age at surgery, smaller body size, later referral to surgery in the course of the disease, more severe preoperative angina, a higher incidence of obesity, diabetes mellitus, hypertension, congestive heart failure and renal dysfunction (1–10). Women may be less likely to receive arterial grafts, and because their vessels are smaller, incomplete revascularization may occur more often in women than in men (1,9). In addition, postoperative complications such as perioperative myocardial infarction and neurologic dysfunction may be more frequent than in men (1,9). Differences between men and women regarding long-term prognosis after CABG have been studied less extensively. A similar long-term prognosis in men and women after CABG has been reported in a number of studies (1,5,9,11,12), but this needs further clarification. The aim of this study was to compare early and late mortality in men and women after CABG and to analyze possible causes of the observed differences.

Methods

Patient group. All subjects who underwent primary isolated CABG because of angina pectoris in Stockholm from 1980 to 1989 were followed with regard to mortality from the time of surgery until the end of 1990. The study comprised a total of 3,933 patients, 3,326 (85%) of whom were men and 607 (15%) were women. Most operations were performed at the Karolinska Hospital, but 611 operations were done at another hospital (Sophiahemmet) by the same operating staff.

Patient characteristics. Patient characteristics and operation variables were retrieved from medical records and computer files in the Department of Thoracic Surgery, Karolinska Hospital. Medical records were available for all but 16 patients (>99%). The collected information described body height and weight, a history of acute myocardial infarction and stroke, diabetes mellitus, smoking habits, hyperlipidemia, treatment for hypertension, intermittent claudication, number of obstructed coronary arteries, left ventricular function, number of anastomoses at surgery and use of an internal mammary graft.

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Abbreviations and Acronyms

CABG = coronary artery bypass graft surgery
CI = confidence interval

Body surface area was calculated from height and weight (13). Smoking status at the time of the operation was classified as current, former and never smokers. In many subjects, however, the distinction between a former smoker and a never smoker could not be easily made. Therefore, in the analyses we separated current smokers at the time of surgery from current nonsmokers. A history of previous myocardial infarction or stroke, diabetes mellitus, hypertension and intermittent claudication were recorded as stated in the medical record. A significant coronary obstruction was defined as >50% reduction of the lumen diameter. Patients with significant stenosis of the left main coronary artery were considered separately from those with one-, two- or three-vessel disease. The right and left anterior descending and circumflex coronary arteries, respectively, including their branches, were considered as one vessel each, whatever the number of obstructed side branches. On the basis of the angiographic findings, left ventricular function was classified as good, moderately impaired or severely impaired. Left ventricular function was classified as good if the ventricle was small with normal systolic function. In the presence of any systolic segmental wall motion abnormalities, ventricular function was classified as moderately impaired, and if there was an increased end-diastolic volume with akinetic or aneurysmal wall segments, it was classified as severely impaired.

Operative technique. The operations were performed by means of a median sternotomy with the aid of cardiopulmonary bypass hemodilution (hematocrit 20% to 30%) and moderate hypothermia (25 to 32°C). In 1988, membrane oxygenators completely replaced previously used disposable bubble oxygenators. Myocardial protection was achieved by hypothermic, hypercalemic crystalloid cardioplegia. The distal anastomoses were constructed with a continuous running 7-0 polypropylene suture, and the proximal veins were then anastomosed to the partially clamped ascending aorta, while reperfusing the heart and rewarming the patient. Postoperative antiplatelet therapy, consisting of 160 to 250 mg of acetylsalicylic acid, was routinely used from 1983 on.

Statistical methods. Information on deaths was obtained from the National Cause of Death Register. Early mortality was defined as death within 30 days of the operation. The relative risk of death within 30 days for women compared with men was estimated by logistic regression (14). Survival over a 5-year period after operation was evaluated by life-table methods and by proportional hazards regression (15). The analyses of late mortality were carried out for subjects surviving 30 days after the operation. As a rule, the estimates were calculated together with the 95% confidence interval. In the multivariate analyses, the patients were subclassified into the age groups <49, 50–59, 60–69 and ≥70 years. Body surface area was categorized into the groups ≤1.7 m^2 and >1.7 m^2; left ventricular function into good function and moderate to severe dysfunction; and number of diseased vessels into the categories of two or less and at least three involved vessels or left main coronary artery disease. Diabetes, hypertension and previous myocardial infarction were treated as dichotomous variables (yes or no).

Results

Patient characteristics. Of the 3,933 operations, 2,508 (64%) were performed between 1985 and 1989. The proportion of women undergoing operation was similar during 1980 to 1984 and 1985 to 1989 (15% and 16%, respectively). Women were older than men (mean age 59.9 years [range 33 to 80] vs. 58.3 years [range 26 to 82], respectively). The difference in mean age between women and men was 1.6 years (95% confidence interval [CI] 0.8 to 2.3). Fifty-nine percent of the women and 48% of the men were ≥60 years of age.

Women were shorter and smaller than men, with a mean body height of 162 cm and a mean body surface area of 1.76 m^2 compared with 175 cm and 1.98 m^2 for men. The difference in mean height between men and women was 13 cm (95% CI 12 to 14) and in mean body surface area 0.22 m^2 (95% CI 0.21 to 0.23). Women were more likely than men to have diabetes mellitus, hyperlipidemia and hypertension and less likely to have a history of myocardial infarction, left ventricular dysfunction or three-vessel disease (Table 1). Although a higher proportion of men had operations involving three or more anastomoses, the proportions of patients with internal mammary grafts were similar in men and women. There were no gender differences in the proportion of current smokers or of symptoms from intermittent claudication.

Causes of death. In all, there were 322 deaths within 5 years after operation, of which 264 occurred among men and 58 among women (Table 2). Approximately three of four deaths were due to cardiac disease (International Classification of Diseases Revision 8 or 9, code 410–414) and of these, more than half were caused by acute myocardial infarction.

Early mortality. The overall early mortality rate was 3.0% in women and 1.7% in men. Accordingly, the crude relative risk was 1.8 (95% CI 1.0 to 3.0) in women compared with men (Table 3). When the influence of age was considered, the corresponding relative risk was somewhat lower, and when body surface area together with age was entered in the model, the relative risk was 1.0. This result was not altered by taking into account left ventricular function, diabetes mellitus, hypertension and previous myocardial infarction in the model. Other variables, including body mass index, were also entered into the regression analyses, without substantially changing the point estimate (not shown in Table 3). Consideration of height alone did not reduce the relative risk for women compared with men to the same extent as body surface area.

There were no marked gender differences in early mortality among patients with similar body surface areas. In patients with a body surface area ≤1.7 m^2, the early mortality rate in

Table 1. Patient Characteristics in Relation to Gender

	No. (%) of Pts*		Difference Between Men and Women	
	Men (n = 3,326)	Women (n = 607)	%	95% CI
Previous myocardial infarction	1,889 (57%)	300 (50%)	7	3 to 11
Stroke	126 (4%)	14 (2%)	2	1 to 3
Diabetes mellitus	302 (9%)	84 (14%)	−5	−8 to −2
Current smoking	616 (21%)	102 (20%)	1	−3 to 5
Hyperlipidemia	275 (8%)	74 (12%)	−4	−7 to −1
Hypertension	886 (27%)	241 (40%)	−13	−17 to −9
Intermittent claudication	215 (7%)	43 (7%)	0	−2 to 2
Diseased coronary arteries				
One	338 (10%)	86 (14%)		
Two	890 (27%)	167 (28%)		
Three or more	1,556 (48%)	256 (43%)	5	1 to 9
LMCA	493 (15%)	90 (15%)		
Left ventricular function				
Moderate	1,284 (40%)	178 (30%)	11	7 to 15
Severe	130 (4%)	15 (3%)		
No. of anastomoses				
One	285 (9%)	74 (13%)		
Two	658 (20%)	154 (26%)		
Three or more	2,302 (71%)	361 (61%)	10	6 to 14
Internal mammary artery grafts	2,590 (80%)	463 (79%)	1	−3 to 5

*Patients (Pts) with missing information were not included in calculation of percentages. CI = confidence interval; LMCA = left main coronary artery.

women was 4.4% compared with 3.4% in men, corresponding to a relative risk for women of 1.3 (95% CI 0.5 to 3.5). In patients with a body surface area >1.7 m^2, the early mortality rate in women was 1.4% and in men 1.5%, and the relative risk was 0.9 (95% CI 0.3 to 2.6). The influence of body size on early mortality, irrespective of gender, was examined by comparing patients with a body surface area ≤1.7 m^2 to those with a body surface area >1.7 m^2. The early mortality rates were 4%, and 1.5%, respectively. The age-adjusted relative risk for patients with a body surface area ≤1.7 m^2, compared with patients with a larger body surface area, was 1.9 (95% CI 0.8 to 4.6) in men and 3.2 (95% CI 1.0 to 9.9) in women.

Late mortality. In patients surviving 30 days after surgery, mortality was similar in men and women over a 5-year period (Fig. 1). Among men, 1.8% of the early survivors died during the first year after surgery, and among women, this proportion was 2.2%. After 5 years ~6% of both groups had died. The crude relative risk of mortality 1 and 5 years after surgery in women versus men was 1.2 (95% CI 0.7 to 2.2) and 1.1 (95% CI 0.8 to 1.5), respectively (Table 4). Adjustment for age did not substantially alter these estimates. However, the inclusion of left ventricular function in the regression model increased the point estimate of the relative risk for women compared with men, with regard to the 1-year mortality, to 1.4 (95% CI 0.8 to 2.6), and with regard to the 5-year mortality, to 1.2 (95% CI 0.8 to 1.7). These estimates were not changed by including diabetes mellitus, number of diseased vessels and previous myocardial infarction in the model.

Separate analyses of patients with moderate or severe left ventricular dysfunction suggested a higher 1-year mortality rate in women (4.8%) than in men (2.5%). The age-adjusted relative risk was 1.8 (95% CI 0.9 to 3.8). No corresponding increase was seen in women with good left ventricular function.

Table 2. Number of Deaths According to Gender and Underlying Cause of Death During the First 5 Years of Follow-Up From Time of Coronary Artery Bypass Graft Surgery

Cause of Death	Men (n = 264) [n (%)]	Women (n = 58) [n (%)]	All Pts (n = 322) [n (%)]
Cardiac	192 (73)	39 (67)	231 (72)
Myocardial infarction	108 (41)	21 (36)	129 (40)
Noncardiac	72 (27)	19 (33)	91 (28)
Stroke	11 (4)	5 (9)	16 (5)
Cancer	28 (11)	9 (15)	37 (11)
Other	33 (12)	5 (9)	38 (12)

Discussion

The results of the present study indicated a higher early mortality in women than in men after isolated CABG. However, this increase was largely explained by differences in age and body surface area. Only small differences in late mortality were found between men and women surviving the first 30 days after surgery.

The study comprised a complete series of patients under-

Table 3. Relative Risk of Early Mortality With 95% Confidence Interval in Women Versus Men

	Men		Women	
Variable	RR	95% CI	RR	95% CI
Gender	1.0	–	1.8	1.0–3.0
Gender and age	1.0	–	1.5	0.9–2.6
Gender, age and body surface area	1.0	–	1.0	0.5–2.0
Gender, age, body surface area, left ventricular function, diabetes, hypertension, previous myocardial infarction	1.0	–	1.0	0.5–2.1

CI = confidence interval; RR = relative risk.

going isolated CABG in Stockholm during the period 1980 to 1989. The indications for myocardial revascularization were wider during the later years of the period, with more elderly patients and a higher proportion of patients with triple-vessel disease. However, the indications for surgery were similar for men and women throughout the period.

Methodologic considerations. There is essentially no loss of deaths in the National Cause of Death Register (16), and it is likely that all deaths occurring among the patients during the follow-up period were identified. Medical records were found for >99% of the patients, and information on all variables used in this study were available for at least 90% of the patients. However, some of the variables obtained from medical records may have been misclassified. Body surface area was computed from height and weight and any misclassification was very small. For some other variables, the misclassification may have been greater, but it seems reasonable to assume that the misclassifications in general were not related to gender and mortality (nondifferential misclassification). The probable effect would be some remaining confounding effects from these variables. Although this study comprised almost 4,000 patients, the number of deaths among women was small in some of the analyses. Thus, the size of the study was not large enough to exclude the presence of prognostic differences in small subgroups such as in women with severely impaired left ventricular function. Neither was it possible to evaluate the potential effect of changes in surgical technique on the association between gender and mortality.

Body size of importance for early mortality. Our results indicate that small persons rather than women per se are at an increased risk of early mortality when undergoing CABG. This increased risk is in agreement with the previous findings by O'Connor et al. (10) and by the Coronary Artery Surgery Study (17). Our findings also are in accordance with analyses of patients operated on at the Cleveland Clinics, demonstrating that body surface area was the strongest predictor of operative risk (11).

The diameter of the epicardial arteries is proportional to cardiac mass, and patients who die shortly after CABG have been shown to have smaller hearts than those who die later (18). The mean cross-sectional areas of proximal coronary artery segments obtained at necropsies of women are significantly smaller than the corresponding vessel segments in men (19). It seems likely that the increased early mortality after CABG among persons of smaller physical size is due, at least in part, to technical operative factors. The small size of the coronary arteries makes suturing of the distal anastomoses more demanding, particularly if the vessel wall is thin and the lumen collapses. Small lumen size, as estimated with probes during operations, correlates to poor early and late patency rates of vein grafts (20). Tyras et al. (21) pointed out that women receive fewer grafts and have lower patency rates than

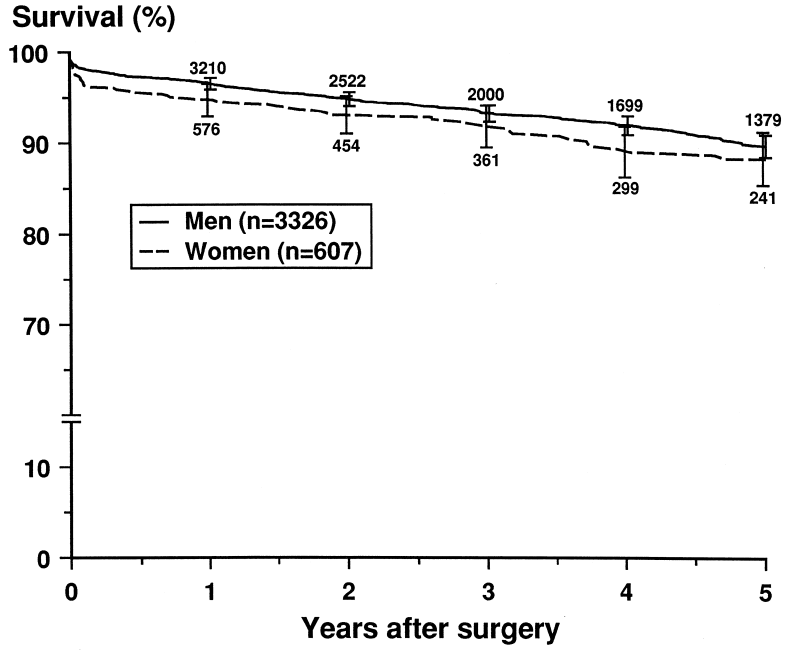

Figure 1. Survival of 3,933 patients 5 years after primary isolated CABG in relation to gender. The yearly 95% confidence limits are slightly displaced laterally and the numbers of patients at risk are indicated.

Table 4. Relative Risk of Mortality With 95% Confidence Interval 1 and 5 Years After Coronary Artery Bypass Graft Surgery in Male and Female Patients Surviving 30 Days After Operation

	1 Year				5 Years			
	Men		Women		Men		Women	
Variable	RR	95% CI	RR	95% CI	RR	95% CI	RR	95% CI
Gender	1.0	–	1.2	0.7–2.2	1.0	–	1.1	0.8–1.5
Gender and age	1.0	–	1.2	0.6–2.1	1.0	–	1.0	0.7–1.4
Gender, age and left ventricular function	1.0	–	1.4	0.8–2.6	1.0	–	1.2	0.9–1.7
Gender, age, left ventricular function, diabetes, number of diseased vessels and previous myocardial infarction	1.0	–	1.4	0.8–2.6	1.0	–	1.2	0.8–1.7

CI = confidence interval; RR = relative risk.

men. They assumed that these findings may be explained by the smaller coronary arteries in women.

Weintraub et al. (7) concluded that it is essential to identify women who will benefit from CABG. Some groups of women may not run a greater risk of early mortality, but because of the expected excess risk in women, they may be less likely to be referred for CABG. Our results indicate that women with a body surface area of at least 1.7 m^2 do not run a greater risk of early mortality than men of similar size. The increased risk of early mortality among small subjects should be considered when patients are referred to surgery, irrespective of gender. However, in absolute terms the mortality was very low even in this group of patients.

Kahn et al. (4) concluded that women undergoing CABG have more severe disease and are referred later in the stage of the disease process than men. In a review of the published data, women were consistently more symptomatic and had more risk factors, although with less coronary artery disease and better preserved cardiac function, than men (8). In recent studies, women's coronary artery disease is more advanced and their ventricular function poorer, and there seems to be underreferral for angiography (8). We found no indication of more severe coronary artery disease in women than in men; in fact, it may have been less. Women had hypertension more frequently and tended to have diabetes mellitus more often, but these factors did not seem to contribute substantially to the increase in early, but not late, mortality.

Small gender differences in late mortality. Our finding of only small gender differences in late mortality among early survivors is consistent with a number of previous studies. Thus, in a few large studies taking major risk factors into account, there were no substantial differences in the long-term survival of men and women after CABG (1,5,9,11,12). Rahimtoola et al. (5) concluded that, although early and late mortality were higher in women, the differences were small and could be predicted from the patient characteristics. However, Richardsson and Cyrus (6) found that the 5-year survival and event-free survival rates were lower in women, and recently Carey et al. (2) reported that the 5- to 15-year survival rate was lower in women, possibly due to a higher incidence of diabetes. These results were based on analyses of all patients and not only on the early survivors, and the lower long-term survival rate seen in women was in part due to a higher early mortality. In addition, the estimates of long-term survival in these studies were not adjusted for age and other factors of importance for prognosis.

Although there seem to be only small differences overall in late mortality after CABG between men and women, there may be greater differences in subgroups of patients. We observed a possibly increased late mortality in women with left ventricular dysfunction, which is in agreement with analyses by Rahimtoola et al. (5).

Conclusions. Our results indicate that the higher early mortality in women versus men after isolated CABG is largely explained by differences in age and body size. The mortality among early survivors appears to be similar in men and women over a 5-year period. These results imply that age and body size rather than gender should be considered when deciding on CABG.

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References

1. Brandrup-Wognsen G, Berggren H, Hartford M, Hjalmarson Å, Karlsson T, Herlitz J. Female sex is associated with increased mortality and morbidity after coronary artery bypass grafting. Eur Heart J 1996;17:1426–31.
2. Carey JS, Cukingnan RA, Singer LKM. Health status after myocardial revascularization: inferior results in women. Ann Thorac Surg 1995;59: 112–7.
3. Kennedy JW, Kaiser GC, Fischer LD, et al. Multivariate discriminant analysis of the clinical angiographic predictors of operative mortality from the Collaborative Study in Coronary Artery Surgery. J Thorac Cardiovasc Surg 1980;80:876–87.
4. Khan SS, Nessim S, Gray R, Czer LS, Chaux A, Matloff J. Increased mortality of women in coronary artery bypass surgery: evidence for referral bias. Ann Intern Med 1990;112:561–7.
5. Rahimtoola SH, Bennett AJ, Grunkemeier GL, Block P, Starr A. Survival at

15 to 18 years after coronary artery bypass surgery for angina in women. Circulation 1993;88(Pt 2):71–8.
6. Richardsson JV, Cyrus RJ. Reduced efficacy of coronary artery bypass grafting in women. Ann Thorac Surg 1986;42 Suppl:16–21.
7. Weintraub WS, Wenger NK, Jones EL, Craver JM, Guyton RA. Changing clinical characteristics of coronary surgery patients: differences between men and women. Circulation 1993;88(Pt 2):79–86.
8. Finlay IN. Coronary bypass surgery in women. Curr Opin Cardiol 1994;9: 650–7.
9. Babir M, Lazem F, Ilsley C, Mitchell A, Khaghani A, Yacoub M. Coronary artery surgery in women compared with men: analysis of coronary risk factors and in-hospital mortality in a single center. Br Heart J 1994;71:408–12.
10. O'Connor GT, Morton JR, Diehl MJ, et al. Differences between men and women in hospital mortality associated with coronary artery bypass graft surgery. Circulation 1993;88(Pt 1):2104–10.
11. Loop FD, Golding LR, MacMillan JP, Cosgrove DM, Lytle BW, Sheldon WC. Coronary artery surgery in women compared with men: analysis of risk and long-term results. J Am Coll Cardiol 1983;1:383–90.
12. Johnson D, Brenowitz J, Kayser KL. Factors influencing long-term (10–15 year) survival after successful coronary artery bypass operation. Ann Thorac Surg 1989;49:19–25.
13. DuBois D, DuBois EF. Clinical alorimetry: a formula to estimate the appropriate surface area if height and weight to be known. Arch Intern Med 1916;17:963–71.
14. Breslow N, Day N. Statistical Methods in Cancer Research, Vol. 1. Lyons (France): IARC Scientific Publications No. 32, 1980.
15. Cox DR, Oakes D. Analysis of Survival Data. Cambridge (UK): Chapman & Hall, 1984.
16. Causes of death 1990: official statistics of Sweden. Stockholm: Statistics Sweden, 1992.
17. Fischer LD, Kennedy JW, Davis KB, Maynard C, Fritz JK, Kaiser G. Association of sex, physical size and operative mortality after coronary artery bypass in the Coronary Artery Surgery Study. J Thorac Cardiovasc Surg 1982;84:334–41.
18. Kalan JM, Roberts WC. Significance of cardiac weight in patients having coronary bypass grafting for angina pectoris. Am J Cardiol 1988;62:36–40.
19. Roberts CS, Roberts WC. Cross-sectional area of the proximal portion of the three major epicardial coronary arteries in 98 necropsy patients with different coronary events. Circulation 1980;62:953–9.
20. Björk VO, Ekeström S, Henze A, Ivert T, Landou C. Early and late patency of aortocoronary vein grafts. Scand J Thorac Cardiovasc Surg 1981;15:11–21.
21. Tyras DH, Barner HB, Kaiser GC, Codd JE, Laks H, Willman VL. Myocardial revascularization in women. Ann Thorac Surg 1978;25:449–53.