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ORIGINAL ARTICLE

Relative survival after CABG surgery is poorer in women and in patients younger than 70 years at surgery

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Abstract

Objective. The difference in survival between genders after coronary artery bypass surgery (CABG) have been studied with varying results. We wanted to investigate gender and age specific relative survival in the CABG population. Risk factors increasing hazard of death in female patients were isolated. *Design*. Retrospectively, 6699 primary isolated CABG procedures were investigated. Long-term survival compared to expected survival in the background population was described through Kaplan-Meier plots. Two subgroups of female patients were described through baseline characteristics, t-tests, odds ratio and multivariate analysis to investigate risk factors for death within one year after surgery. *Results*. Women had significantly decreased relative long-term survival compared to men in this study. Relative survival was lower in patients below 70 years of age at surgery with about the same gender difference. Low ejection fraction, left main stem stenosis and reduced renal function were found to increase risk of death within one year after CABG in women, while body size quantified by body surface area (BSA) did not. *Conclusion*. Relative long-term survival after CABG was poorer in female compared to male patients. This tendency was kept or strengthened when only those less than 70 years of age at surgery were investigated. Lower female survival was most likely due to more comorbidity in female patients. Relative survival was lower in patients $<$70 years.

Key words: *CABG, women, relative survival, gender*

Several studies have reported worse outcome considering both early mortality (30-days mortality and in-hospital mortality) after coronary artery bypass graft surgery (CABG) in women compared to men (1–8). Only one study reports equal results comparing early mortality and morbidity in women and men (9).

Previous papers discussing absolute long-term survival have shown opposing results, where most studies show equal long-term survival (4,10–13), while other studies report worse long-term survival in women (14). In contrast, female long-term absolute survival is also reported to be better than male (15–17).

An eventually higher mortality in women going through CABG has been explained by higher age, more comorbidities and lower bypass flow due to smaller coronary vessels. The last explanation has been proposed to be due to smaller female body size, measured as body surface area (BSA) (6,18,19). However, target vessel is not found to be smaller in female patients (9).

Relative survival in CABG patients compared to expected survival in a representative Norwegian population is not well described. Expected survival curves results from calculating survival for a set of random controls, matched for sex, age and year. Precision of these expected survival curves is assumed to be higher than using other methods, like a limited number of controls (20).

We wanted to compare survival in CABG patients with expected survival in Norway, with emphasize on gender differences and age at surgery. We also wanted to isolate risk factors for death within one year after CABG in women. Specifically we were searching for answer to whether body surface area (BSA) influence one-year outcome. In addition, we wanted to investigate some perioperative values like usage of, and flow in the internal thoracic artery (ITA).

Materials

Study population and data sources

All patients having undergone isolated primary CABG at Haukeland University Hospital from 1984

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to 2008 were identified (n = 6696). These patients represented all-comers to a unit including both invasive cardiologic services and heart surgery. Time of death was received from the Norwegian Public Registry which registries every Norwegian citizens' birth and death. This registry was also the source of hazard by gender, age and year of birth.

In addition, all women who expired during the first year after CABG in the actual period were studied retrospectively (n = 52). A control group of similar size (n = 55) was constructed from women surviving the first postoperative year. Each control patient was selected from the same period as the index patient, mainly as the consecutive operated female patient.

Statistical analysis

Kaplan-Meier survival curves were generated for all patients having undergone isolated primary CABG (21). Expected survival was calculated by the so-called direct method (20,22,23), and represents the survival curve expected for a set of random population controls matched for sex, age and year.

The subgroups, dead within one year (DOY), and alive after one year (AOY), were described with baseline characteristics, t-tests, odds ratio and multivariate analysis.

Perioperative parameters were analyzed through mean, confidence intervals and multivariate analysis.

SPSS 15 and 17 have been used for statistical analysis.

Results

A total of 6699 patients mainly from the western parts of Norway underwent isolated primary CABG at Haukeland University Hospital between 01 January 1984 and 31 December 2008.

Nineteen point nine percent of the patients were female.

Early mortality (30 days and in-hospital mortality) during the whole period was 0.99% for male and 2.17% for female patients (p = 0.001).

Both 5- and 10 year absolute survival was higher for males than females (p = 0.0079 and p = 0.0097). However, 15- and 20 year absolute survival were higher for females than males (p = 0.0364 and p = 0.0491).

Main results

Relative long-term survival

Figure 1 shows the survival curves for the complete material represented as a Kaplan-Meier plot with confidence intervals and the expected survival. We observe that the CABG population had a higher survival than the expected survival the first 16 years postoperatively.

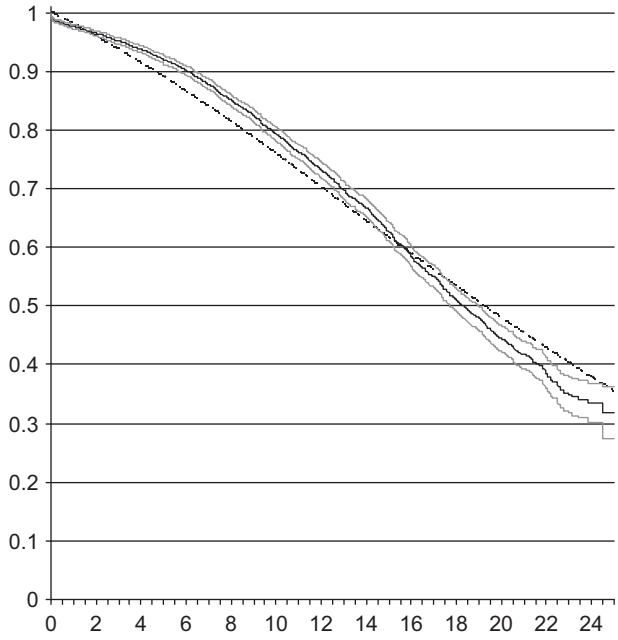

Figure 1. Survival of all CABG patients (black continuous) with 95% confidence intervals (grey). Expected survival (black fragmented). X-axis represents years after surgery.

Figure 2 shows that female patients had poorer outcome than male patients. Except from the first year postoperatively, men had higher survival compared to the background population. Female patients did not achieve this higher survival at any point through the study period.

In order to reduce possible effects from women's older age at surgery, and to reduce the effect of selection, we also selectively examined patients of age younger than 70 years (Figure 3). Ratio male/female patients then was 4099/890, which gives 17.8% women. Average age was 58.7 for male and 61.1 years for female patients. This investigation showed a slightly larger difference in relative survival between the genders in disfavor of female patients. In addition, the relative survival in these patients was lower for both genders compared to the complete CABG material.

Other results

ITA was used in 91.4% in male versus 90.1% in female patients (p = 0.201).

Number of venous anastomoses in male patients were an average of 2.58, in female 2.43 (p < 0.0001). ITA flow was measured to an average of 29.0 ml/min in 2170 male, and 22.4 ml/min in 553 female patients (p < 0.0001).

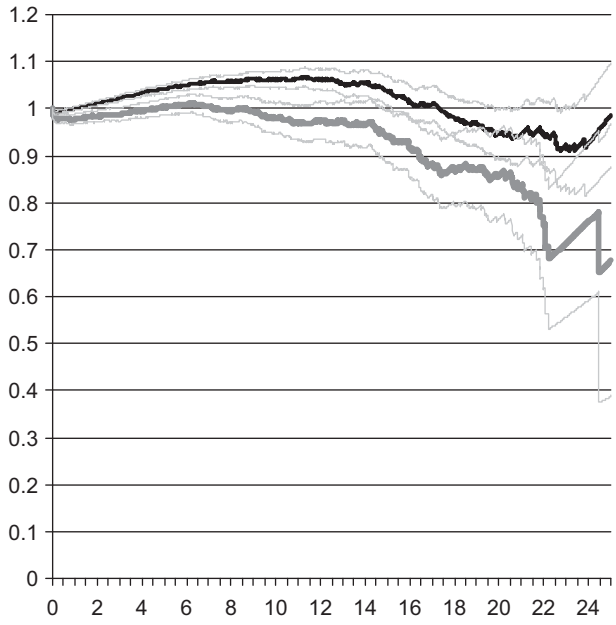

Figure 2. Relative survival curves for men and women, respectively black and grey with confidence intervals. Y-value "1" represents equal to expected survival. X-axis represents years after surgery.

From the investigation of the two groups: dead within one year (DOY) and alive after one year (AOY) we observe that ejection fraction (EF), left main stem stenosis and estimated glomerular filtration rate (eGFR) differs between the groups, consistent while applying multivariate methods. There were no difference in BSA between the groups ($p = 0.822$).

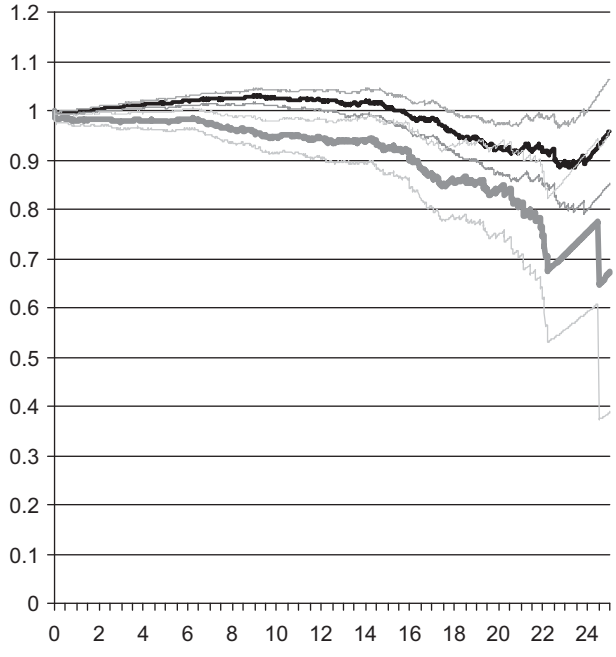

Figure 3. Male relative survival <70 (black), and female $<(70$ grey) with 95% C.I. X-axis represents years after surgery.

Discussion

Early mortality is higher among female than male CABG patients (1–7,10–12,16,18,19,24–26). This is assumed to be related to higher age and more comorbidity among the female patients. In addition, different relative influence from a specific risk factor may exist between the genders (7,17, 27). This study supports higher female early mortality.

Investigations so far have seemed to be inconclusive to whether gender is an independent risk factor for long-term mortality after CABG, though most researchers seem to conclude with equal survival between the genders after adjusting for comorbidities (4,11,12,14–16,25,26). Our study shows higher unadjusted absolute male survival patients the first 10 postoperative years. Female patients tend to have higher absolute survival when investigating 15 and 20 years of survival. Length of study period may be of importance to what result is achieved.

Main agenda – Gender specific relative survival

Relative long-term survival after CABG is not well established. This insufficiency of investigation is due to lacking complete registries in most countries. Our study shows extended periods of increased survival in the CABG population compared to the background population. Secondary prophylaxis through surgery, medical intervention and a favorable change in lifestyle may be some of the factors behind improved long-term survival. Patient selection, however, is probably the main reason for this higher survival. Patients with coronary disease are not necessarily accepted for CABG surgery if severe comorbiditiy exists. Among relative contraindications we find severely impaired lung function, active malignant disease and dementia. These non-cardiac diseases are known to reduce life length, and lack of such diseases will tend to give higher survival in the group accepted for CABG surgery.

Impact of age

Selection criteria are not static. Younger patients, here defined as <70 years at surgery, tend to be accepted for surgery with more severe comorbidity. This practise is probably the main reason why younger patients show poorer relative long-term survival after CABG. Earlier onset of coronary disease also suggests more aggressive coronary disease and may also explain shortened relative life-length expectancy in younger patients.

Table I. Perioperative variables for total CABG (n = 6696) population.

	Males (n = 5363)	Females (n = 1336)	P-value
ITA-usage	91.4%	90.1%	=0.201
Number venous anast	2.58	2.43	<0.0001
Flow ITA (ml/min)	29.0	22.4	<0.0001
Extracorporeal circulation (min)	84.16	83.03	0.28
Aorta crossclamping time (min)	50.4	49.1	0.044

ITA, Arteria thoracica interna.

Gender specific differences

Our study shows significantly reduced relative long-term survival in female compared to male patients. More comorbidity in female patients is the most likely main reason. Whether this should result in any change in admission to surgery is doubtful as we know that CABG is a useful treatment if comorbidity like diabetes and others exist (28).

Other topics

In our material usage of ITA is not significantly different between the genders. Number of venous anastomoses is on the other hand lower in women compared to men ($p < 0.0001$). The reason for this might be less extensive disease, and therefore less need for extensive revascularization (25). Smaller recipient vessel diameter might also be an explanation.

ITA flow was significant lower in female patients in our material. Although low perioperative graft-flow have been found to increase risk of adverse outcome (29–32), the actual difference in our material is not necessarily of prognostic value since female patients generally have less myocardial mass.

Low ejection fraction, left main stem stenosis and impaired renal function are all well known as factors determining prognosis after CABG. This study confirms that these are significant factors in determining one-year mortality in female patients. Since it has been proposed to be of importance, it is noticeable that body surface as a possible indicator of coronary vessel size does not seem to influence one-year mortality in female patients.

The limitation of this study is a lack of extensive baseline characteristics of the patients investigated. This is well described in other papers, and described thoroughly in a most likely similar population to ours (25).

Conclusion

Relative long-term survival after CABG was poorer in female compared to male patients. This tendency was more pronounced in younger patients. Lower female survival was most likely due to more comorbidity. Survival was lower in patients less than 70 years at surgery. This was most likely due to acceptance of

Table II. Preoperative variables in subgroups (n = 52, n = 55).

	DOY (n = 52)	AOY (n = 54)	p-value/OR (95%)
Age (years)	68.3	64.9	p = 0.212
Body surface (m^2)	1.72	1.71	p = 0.822
Ejection fraction (%)	53.5	65.4	p = <0.001
eGFR	59.1	72.8	p = <0.001
Hypercholesterolemia	23/52 = 44.2%	31/54 = 57.4%	OR = 0.59(0.3–1.3)
Diabetes non insulin	4/50 = 8%	3/54 = 5.6%	OR = 1.47(0.32–6.78)
Diabetes insulin	6/50 = 12%	3/54 = 5.6%	OR = 2.24(0.57–8.75)
Diabetes total	10/50 = 20%	6/54 = 11.2%	OR = 0.5(0.17–1.50)
Myocardial infarction			
>21 days prior to CABG	27/52 = 51.9%	19/54 = 35.2%	OR = 1.96(0.91–4.22)
<21 days prior to CABG	10/52 = 19.2%	7/54 = 13.0%	OR = 1.58(0.56–4.45)
One-vessel disease	2/51 = 3.9%	5/54 = 9.3%	OR = 0.31(0.08–1.24)
Two-vessel disease	7/51 = 13.7%	15/54 = 27.8%	OR = 0.43(0.17–1.10)
Three-vessel disease	42/51 = 82.3%	34/54 = 63.0%	OR = 2.61(1.12–6.13)
Disseminated vasc. dis	10/50 = 20.0%	13/54 = 24.1%	OR = 0.79(0.31–2.00)
COLS Gold I	5/52 = 9.6%	3/54 = 5.6%	OR = 1.77(0.42–7.47)
COLS Gold II	1/52 = 1.9%	1/54 = 1.9%	OR = 1.04(0.06–16.84)
COLS Gold III	0	0	
COLS Gold IV	0	0	
LITA	40/48 = 83.3%	47/54 = 87%	OR = 0.75(0.25–2.23)
Previous PCI	3/52 = 5.8%	6/54 = 11.1%	OR = 0.49(0.12–2.07)
LMS	27/52 = 51.9%	10/53 = 18.7%	OR = 4.20(1.89–9.31)

AOY, alive after one year after CABG; DWOY, death within one year after CABG; eGFR, estimated glomerular filtration ratio; ITA, internal thoracic artery; LMS, left main stenosis; Previous PCI, percutan coronary intervention prior to coronary surgery.

patients with more comorbidity among the younger patients and more aggressive coronary disease. Low ejection fraction, left main stem stenosis and reduced renal function were among the factors that increased hazard of death within one year in women. BSA did not influence one year mortality in female patients.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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