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Survival trends in men and women with heart failure of ischaemic and non-ischaemic origin: data for the period 1987–2003 from the Swedish Hospital Discharge Registry

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Aims To investigate gender-specific trends in long-term mortality in patients hospitalized for heart failure (HF).

Methods and results The Swedish hospital discharge and cause-specific death registers were used to calculate age- and gender-specific trends for long-term prognosis in patients hospitalized with a principal diagnosis of HF from 1987 to 2003. Mortality decreased, mainly during 1987–95, with no further decrease after 2001. Survival in men improved more than in women (*P*-value for interaction 0.0003), particularly among patients aged <65 years (*P*-value for interaction: age, gender, and year of hospitalization 0.0003) and more for patients with ischaemic when compared with non-ischaemic HF (*P*-value for interaction <0.0001). Among men <65 years, the hazard ratio (HR) of dying within 3 years after discharge was 0.40 (95% confidence interval 0.36–0.45) during 1999–2001 when compared with 1987–89. The corresponding HR for women was 0.58 (0.48–0.69). For those discharged during 1999–2001, almost 20% of the patients aged 35–64 years and 40% of those aged 65–84 years died within 3 years.

Conclusion Long-term mortality in HF in Sweden decreased more for men than for women and more for ischaemic than non-ischaemic HF. There was no further decrease after 2001. Long-term mortality after a first hospitalization remained high.

Keywords Heart failure • Mortality • Gender • Ischaemic • Non-ischaemic

Introduction

Heart failure (HF) is a major public health problem[1] and one that is rapidly growing, primarily because of the increasing number of elderly in the population.[2] The prevalence of chronic heart failure, a dominant cause of hospitalization in men and women >65 years,[3] is estimated to be 2% in the Western world.[4] The annual costs for treatment of HF in Sweden constitute ~2% of the Swedish health care budget,[5] where the major portion (75%) of these costs is from hospital care.[5] Hospital discharges for HF showed an increasing trend in Sweden, reaching a peak in the early 1990s, but decreasing thereafter,[6] similar to findings from other Western countries.[7,8] Overall, survival in HF is poor and 5 year survival in patients diagnosed in the late 1980s was ~40%.[9] However, from the late 1980s, and coinciding with improved treatment, a decrease in case fatality has been observed.[6]

Several factors may influence both the incidence and prognosis of HF. Improved treatment of ischaemic heart disease and hypertension, both major causes of HF, may lead to a reduction in the number of new cases.[2,8] Introduction of new treatments of HF in the last decades, including ACE-inhibitors,[10] beta-blockers,[11] angiotensin receptor blockers (ARBs),[12] and aldosterone-antagonists,[13] has been found to improve survival in selected study populations. However, most studies on treatment of HF include only patients with decreased ejection fraction (EF), i.e. those with preserved EF have largely been excluded. Partly because of this selection

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bias, women constitute only ~30% or less of many study populations.[14] Nearly half of the population hospitalized with HF has preserved systolic function,[15] a category in which women constitute ~60%.[16] With women more often having preserved left ventricular function and less coronary disease as the underlying cause of their HF,[14,16] improvement in survival in women might be expected to be less marked than for men. In addition, women with HF differ from men in several other respects, such as being older and more often exhibiting hypertension, diabetes, and atrial fibrillation.[17,18] On the other hand, men are more affected by ischaemic heart disease than women and experience an earlier onset of this disease. Consequently, there are good reasons to believe that women may respond differently than men to modern treatment of HF.

The present study had three objectives. The first objective was to study trends in long-term mortality in patients hospitalized for HF in Sweden. The second concerns investigating whether trends in long-term mortality differ between men and women, and the third objective assessed whether there are differences in long-term mortality between patients with HF of ischaemic and of non-ischaemic origin.

Methods

All Swedish hospitals register principal and contributory discharge diagnoses for all patients in the national hospital discharge register. Data from the national hospital discharge and cause-specific death registers were linked through the personal identity number (Swedish: personnummer), which is unique for all Swedish citizens. The hospital discharge register has been in operation since the 1960s and has operated on a nationwide basis since 1987. In 1984, data were available from 19 of 24 Swedish counties, comprising ~85% of the Swedish population 35–84 years old, with a mean annual population of 2.9 million.

The study included all men and women aged 35–84 hospitalized for the first time with a principal diagnosis of HF in the 19 counties during the period 1987–2003. Information from the register for the years 1980–86 was used to detect re-admissions for the study period 1987–2001. This introduces a possible under-detection bias for the first years of the study (in relation to the later part of the study). However, the high morbidity and mortality of HF should minimize this bias, as the left censoring within the years 1980–86 was considered as adequate to ensure that data on hospitalizations for each separate year from 1987 to 2001 were treated as uniformly as possible. Mortality from all causes within 3 years of the index admission was calculated through 31 December 2004.

The International Classification of Diseases (ICD) version 8 (ICD-8) was used until 1986, ICD-9 between 1987 and 1996, and ICD-10 from 1997 onwards. The discharge codes applied to HF were 427.00, 427.10 (ICD 8), 428A, 428B, 428X (ICD 9), and I50 (ICD 10). Because the main goal of the study was to investigate long-term mortality, we excluded patients who died during hospitalization or in the immediate post-hospitalization period, up to 28 days from admission. To ensure comparability with other studies, however, tables detailing survival from the day of admission are available in Supplementary material online, *Tables S1* to *S3*. For the present study, 3 year mortality was calculated up to 31 December 2004 in patients alive 29 days after the index admission. HF that was due to ischaemic causes was defined as having been discharged at any time before and up to 1 year after the index admission with a principal or contributory diagnosis of ischaemic heart disease [410–414 (ICD-9) and I20-I25 (ICD 10)].

A total of 179 753 first hospitalizations between 1987 and 2003 with a principal diagnosis of HF and surviving at least 28 days from admission were identified. Of these patients, 144 619 with an index hospitalization before 2001 were followed with respect to 3 year mortality. Age- and gender-specific analyses were done for each successive year, and for five fixed 3 year intervals of admission: 1987–89, 1990–92, 1993–95, 1996–98, and 1999–2001. Moreover, we investigated the 3 year mortality for HF of ischaemic and non-ischaemic aetiology separately. Survival curves for all cohorts were calculated, which included patients hospitalized from 2002 to 2003.

Other co-morbidities were defined by the use any of the following discharge codes prior to the index hospitalization: diabetes: ICD8 and ICD9 250, ICD10 E10, E11, E14; hypertension: ICD8 and ICD9 401–405, ICD10 I10–I15; atrial fibrillation: ICD8 427.92, ICD9 427D, ICD10 I48; stroke: ICD8 and ICD9 430–438, ICD10 I60–I69; valve disease ICD8 and ICD9 393–398, 424, ICD10 I05–I09, I34–I35; cardiomyopathy ICD8 and ICD9 425, ICD10 I42; pulmonary embolism ICD8 450, ICD9 415B, ICD10 I26; chronic obstructive pulmonary disease (COPD): ICD 8 and ICD9 490–496, ICD10 J44; asthma ICD 8 and ICD9 493, ICD10 J45; cancer ICD 8 and ICD9 140–239, ICD10 C00-D48.

Validity of the registers

In the period 1987–96, a primary discharge diagnosis was lacking in <1% of all admissions to Swedish departments of internal medicine, including cardiology. Heart failure and acute myocardial infarction (AMI) diagnoses in Sweden, according to the hospital discharge register, have been validated. Heart failure, as the principal diagnosis, was shown to have a validity of 95%, whereas HF in any position had a validity of 82%.[19] Similarly, validation of coronary heart disease discharge diagnoses in Sweden demonstrated high sensitivity (94%) and a high positive predictive value (86%) regarding definite AMI.[20]

Statistical methods

All rates are person-based. We calculated age- and gender-specific case fatality from day 29 until 3 years. The age- and gender-specific changes in the 3 year case fatality were calculated using 95% confidence intervals (CIs) by the proportional hazards regression procedure in SAS software version 9.1. To assess whether there were any differences between genders regarding period effect, an interaction term was used in the model as the product of period, time, and gender. The respective mortality rates were used as the dependent variable in each calculation, and a 3 year calendar year period was used as the independent variable, with the initial period of 1987–89 as reference. Age was defined as age at admission. Survival was estimated according to the Kaplan–Meier method.

In order to estimate the independent and combined effect of the main factor (year with the co-variates: gender, age group, and ischaemic/non-ischaemic cause of HF on mortality risk), we used a Cox regression model. Interactions between the co-variates were also entered in the model in order to increase the fit and possibly find statistical evidence for the observed varying effect of the period of time on risk of death across different group categories. In addition, separate simpler Cox models were used to estimate hazards within different combinations of age group, gender, and ischaemic/non-ischaemic cause of HF ($2 \times 2 \times 2$ models) where the period of time was adjusted for age measured in years. These results were calculated to provide a more detailed analytic and descriptive information on the structure of the association between period of time and risk of

death and guided us to adapt and estimate the final main model as mentioned earlier (which included all the data).

In our Cox regression model, we included additionally time-dependent variables corresponding to year, sex, and age, to resolve the tentative problem of non-proportionality of the hazards for these variables. The estimates remained more or less unchanged. Accordingly, the assumption of proportional hazards was not essential to our conclusions.

The significance level for testing whether the model parameters are different from zero (two-sided test) was on the 5% level. No corrections were made for multiple testing in the separate models for each age group and sex category. These can be regarded as a step towards the final model. Also, Kaplan–Meier survival estimates were calculated and presented in diagrams for the different periods to provide a more intuitive feeling of the gradual risk reduction across the period time scale.

Results

The mean age of the study population was 74.1 [standard deviation (SD) 8.4] years [men 72.9 (SD 8.7) and women 75.6 (SD 7.6)], with no difference in age between patients with ischaemic and non-ischaemic HF; 44.3% were women. Co-morbidities (*Table 1*) among men and women with non-ischaemic and ischaemic HF were broadly similar.

Survival curves showed an overall improvement in long-term prognosis over time (*Figures 1–4*) for both men and women and in older and younger patients. However, most of the reduction in mortality occurred in the beginning of the study period. After 1995, only smaller reductions were observed, with no further decrease in mortality noted in the last period studied (2002–03).

Gender differences

Among younger patients (i.e. 35–64 years), prognosis among men improved more than for women (*Table 2*). Among men aged 35–64 years, the hazard ratio (HR) of dying within 3 years after discharge was 0.40 (95% CI 0.36–0.45) during the period 1999–2001 when compared with the period 1987–89. In women aged 35–64 years, the corresponding HR was 0.58 (0.48–0.69). Still, for those discharged from 1999 to 2001, 17% of the men and 19% of the women aged 35–64 years died within 3 years, which corresponds to an annual mortality of ∼6%.

Among older patients (>64 years), HRs of dying within 3 years in 1999–2001 (compared with 1987–99) were practically identical in men and women, i.e. 0.61 (0.58–0.69) in men and 0.62 (0.59–0.65) in women. After 3 years, 41% of the men and 36% of the women had died, corresponding to annual mortality rates of almost 14% among men and 12% among women.

Further, we calculated 3 year mortality from the first day of hospitalization (day 0) to investigate whether the exclusion of patients who died during hospitalization and up to 28 days from admission displayed the same trends. While the absolute 3-year mortality was higher, the relative decrease remained more or less the same (Supplementary material online, *Tables S1–S3*).

Table 1 Co-morbidity at discharge in patients with heart failure of ischaemic and non-ischaemic origin

		Non-ischaemic heart failure			Ischaemic heart failure		
		Gender		All	Gender		All
		M	F		M	F	
Diabetes	*n*	8288	7123	15 411	8980	7637	16 617
	%	17	17	17	22	25	23
Hypertension	*n*	9003	8375	17 378	8503	7684	16 187
	%	18	20	19	20	26	23
Stroke	*n*	9158	6795	15 953	8428	5654	14 082
	%	18	16	17	20	19	20
Valve disease	*n*	4536	4564	9100	3752	3463	7215
	%	9	11	10	9	12	10
Atrial fibrillation	*n*	15 013	12 632	27 645	10 478	7868	18 346
	%	30	30	30	25	26	26
Cardiomyopathy	*n*	1810	737	2547	792	329	1121
	%	4	2	3	2	1	2
Pulmonary embolism	*n*	1376	1430	2806	1201	1140	2341
	%	3	3	3	3	4	3
COPD	*n*	5913	4395	10 308	4724	2975	7699
	%	12	10	11	11	10	11
Asthma	*n*	1871	2067	3938	1677	1541	3218
	%	4	5	4	4	5	4
Cancer	*n*	6163	4615	10 778	4559	2837	7396
	%	12	11	12	11	9	10

COPD, chronic obstructive pulmonary disease.

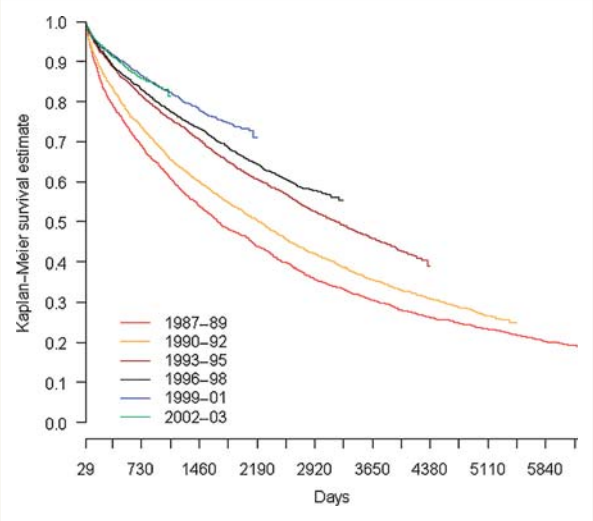

Figure 1 Men, age 35–64.

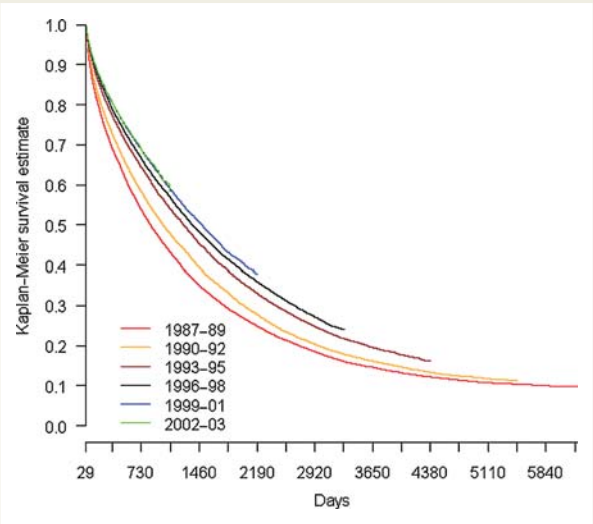

Figure 2 Men, age 65–84.

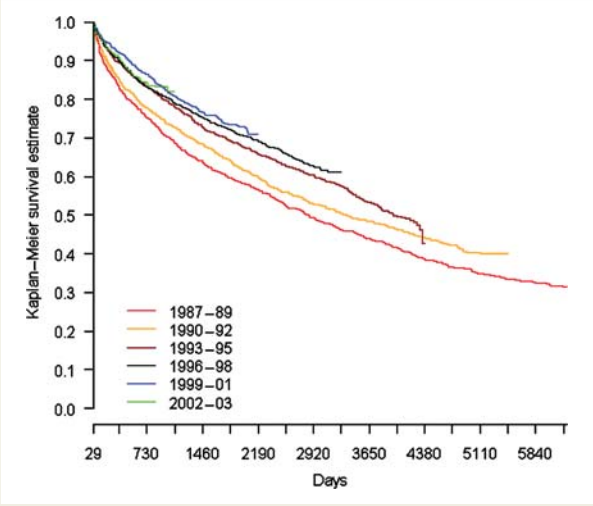

Figure 3 Women, age 35–64.

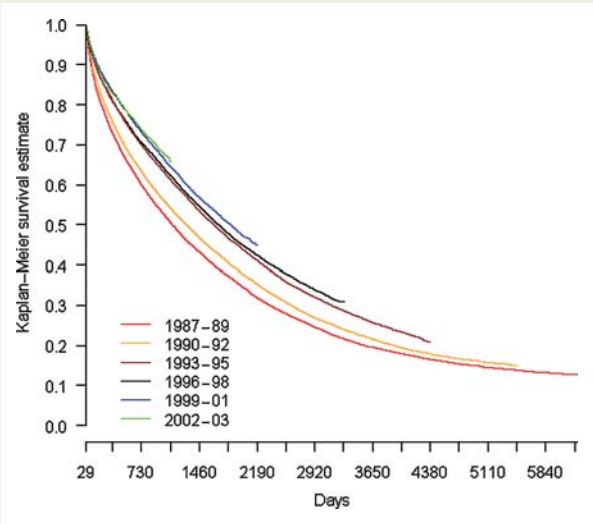

Figure 4 Women, age 65–84.

Heart failure with and without ischaemic origin

Of the 144 619 patients who survived the first 28 days, 61 586 (42.6%) were diagnosed with ischaemic heart disease, either before or within 1 year of being admitted with HF. The most marked decrease in 3 year mortality was observed among men aged 35–64 years with HF of ischaemic origin, with a mortality reduction from 46 to 19% (HR 0.36, 0.31–0.43) (*Table 3*). Reductions in mortality were less marked in men with HF of non-ischaemic origin and in women, particularly in women with HF of non-ischaemic origin, where the reduction in mortality was from 27 to 18% (HR 0.63, 0.50–0.79). In the 65–84-year patient group (*Table 4*), the reduction in mortality was more pronounced among those with HF of ischaemic origin when compared with patients with HF of non-ischaemic origin, but with no gender differences.

Interactions

In a final model, where we specifically tested for statistical interactions between the predictors of survival, we found that the association between year of hospitalization and survival was significantly different in the two sexes, with a stronger association among men ($P = 0.0004$) and among younger patients (*P*-value for interaction between age and year of hospitalization <0.0001). Moreover, the difference between men and women became significantly weaker with increasing age (*P*-value for interaction between the effects of age, gender, and year of hospitalization 0.0003). In addition, there was a significant interaction between year of hospitalization and ischaemic vs. non-ischaemic HF ($P < 0.0001$). These model-based findings for the whole material are in accordance with the results found separately for the combination of gender and age groups and provide a formal statistical justification for the observed interactions of our results mentioned earlier.

Table 2 Three year mortality for men and women after a first hospitalization with a diagnosis of heart failure in 19 Swedish counties from 1987 to 2001 as a function of gender and age (*n*, number of deaths)

	Period	Three year mortality in men				Three year mortality in women			
		n	%	HR	95% CI	*n*	%	HR	95% CI
Age 35–64 years	87–89	2205	39	1.00		930	31	1.00	
	90–92	2475	34	0.85	0.77–0.94	1027	27	0.86	0.73–1.02
	93–95	2895	24	0.57	0.51–0.62	1318	22	0.67	0.57–0.79
	97–99	2709	22	0.52	0.47–0.58	1150	21	0.64	0.54–0.76
	99–01	2480	17	0.40	0.36–0.45	1101	19	0.58	0.48–0.69
		Mean decline per year, % (95% CI)			7.5 (6.7–8.2)	Mean decline per year, % (95% CI)			4.7 (3.5–6.0)
		P-value			<0.0001	*P*-value			<0.0001
Age 65–84 years	87–89	13 007	57	1.00		11 546	50	1.00	
	90–92	14 004	52	0.87	0.85–0.90	12 136	46	0.89	0.86–0.92
	93–95	15 437	46	0.72	0.70–0.75	13 456	39	0.70	0.68–0.73
	97–99	13 811	43	0.66	0.64–0.68	11 665	38	0.68	0.66–0.71
	99–01	11 568	41	0.61	0.58–0.63	9699	36	0.62	0.59–0.65
		Mean decline per year, % (95% CI)			4.3 (4.0–4.5)	Mean decline per year, % (95% CI)			4.1 (3.8–4.4)
		P-value			<0.0001	*P*-value			<0.0001

Table 3 Three year mortality after a first hospitalization with a diagnosis of heart failure in men and women aged 35–64 years in relation to ischaemic and non-ischaemic origin (*n*, number of deaths)

		Three year mortality in men				Three year mortality in women			
	Period	*n*	%	HR	95% CI	*n*	%	HR	95% CI
35–64 years, ischaemic	87–89	1178	46	1:00		357	38	1:00	
	90–92	1122	39	0.83	0.73–0.94	402	36	0.92	0.73–1.17
	93–95	1287	27	0.52	0.45–0.59	501	26	0.65	0.51–0.82
	97–99	1101	25	0.47	0.40–0.54	434	25	0.59	0.46–0.76
	99–01	882	19	0.36	0.31–0.43	371	22	0.53	0.40–0.67
		Mean decline per year, % (95% CI)			8.4 (7.3–9.4)	Mean decline per year, % (95% CI)			5.7 (3.9–7.6)
		P-value			<0.0001	*P*-value			<0.0001
35–64 years, non-ischaemic	87–89	1027	30	1:00		573	27	1:00	
	90–92	1353	30	0.96	0.83–1.11	625	22	0.81	0.64–1.02
	93–95	1608	22	0.68	0.58–0.79	817	19	0.69	0.55–0.86
	97–99	1608	20	0.64	0.55–0.75	716	19	0.68	0.54–0.86
	99–01	1598	16	0.50	0.42–0.59	730	18	0.63	0.50–0.79
		Mean decline per year, % (95% CI)			5.8 (4.7–6.9)	Mean decline per year, % (95% CI)			3.8 (2.1–5.5)
		P-value			<0.0001	*P*-value			<0.0001

Discussion

In the present study, we investigated trends over time after a first hospitalization for HF as the principal diagnosis among patients in Sweden between 1987 and 2003. We observed a substantial reduction in 3 year mortality during the period studied, particularly among male patients aged <65 years and among patients with HF of ischaemic origin. Most of the decrease was observed in the first periods, levelling out successively, and among those admitted during the last period (i.e. 2002–03), there was no further reduction.

A decrease in mortality among patients diagnosed with HF was first observed in the USA and in Scotland in the 1980s and first half of the 1990s.[21,22] We have previously reported that the 30 day and 1 year mortality after a first hospitalization for HF decreased markedly in Sweden during the 1990s, particularly in younger patients (45–64 years).[6] In the present study, in which we extended this observation to 3 years, we found that the positive trend continued

Table 4 Three year mortality after a first hospitalization with a diagnosis of heart failure in men than and women aged 65–84 years in relation to ischaemic and non-ischaemic origin (*n*, number of deaths)

		Three year mortality in men				Three year mortality in women			
	Period	*n*	%	HR	95% CI	*n*	%	HR	95% CI
65–84 years ischaemic	87–89	6607	65	1:00		5085	61	1:00	
	90–92	6469	60	0.86	0.83–0.90	4993	55	0.84	0.80–0.89
	93–95	6805	52	0.67	0.64–0.70	5581	45	0.63	0.60–0.67
	97–99	5805	49	0.61	0.58–0.64	4634	44	0.61	0.58–0.65
	99–01	4376	46	0.55	0.53–0.58	3596	42	0.56	0.53–0.60
		Mean decline per year, % (95% CI)			5.2 (4.8–5.5)	Mean decline per year, % (95% CI)			5.1 (4.6–5.5)
		P-value			<0.0001	*P*-value			<0.0001
65–84 years non-ischaemic	87–89	6400	48	1:00	0.88–0.97	6461	41	1:00	0.91–1.01
	90–92	7535	46	0.93	0.78–0.86	7143	40	0.96	0.75–0.83
	93–95	8632	42	0.82	0.72–0.80	7875	34	0.79	0.73–0.82
	97–99	8006	39	0.76	0.68–0.76	7031	34	0.78	0.67–0.75
	99–01	7192	38	0.72		6103	32	0.71	
		Mean decline per year, % (95% CI)			2.8 (2.4–3.2)	Mean decline per year, % (95% CI)			3.0 (2.6–3.4)
		P-value			<0.0001	*P*-value			<0.0001

until 2001, but that no further improvement was noted among patients with a first admission in 2002–03.

Introduction of several new treatments over the past three decades has been demonstrated to improve morbidity and mortality of HF in selected study populations.[10–13,23] The use of ACE-inhibitors and beta-blockers became widespread in the beginning of the 1990s and increasingly so during the past decade, leading to improved survival in patients with HF.[18] In several studies from the late 1990s, the use of aldosterone antagonists and ARBs, in addition to ACE-inhibitors and beta-blockers, has been found to improve survival further.[12,13,23,24] Moreover, small studies of nurse-led HF clinics have shown that structured follow-up of patients with HF improves mortality and morbidity.[25,26] However, whether it is the titration of medication or other aspects of improved care that increases survival has yet to be investigated.

Hypertension and myocardial infarction are major causes of HF.[27–29] The treatment of myocardial infarction improved dramatically during the study period,[30,31] which may have reduced long-term complications, including HF. During the past two decades, the incidence of myocardial infarction has decreased in Sweden, probably partly because of a reduction in risk factors.[29,32] Furthermore, there are indications that the size of the myocardial infarctions is becoming smaller,[33] which could contribute to less risk of subsequent HF and, potentially, to less severe cases. A decline in the prevalence of hypertension in the population and the increased use of antihypertensive drugs may have also reduced the severity of HF.[34–36]

The frequency of hypertension in non-ischaemic and ischaemic HF reported from different studies[2,17] ranged from 50–70%. We observed very low frequency of hypertension among non-ischaemic HF patients (~20%) in our material. Hypertension as co-morbidity may be underestimated in our material because many cases are undetected or may be obscured by medication and/or a failing myocardium.

Because men are more affected by ischaemic heart disease and experience an earlier onset of it than women,[37] improved treatment of ischaemic heart disease could explain the more prominent decrease in case fatality among men. This may also be a contributing factor to the more pronounced reduction in mortality found among patients with HF of ischaemic aetiology. Women with HF differ from men in several respects: women are generally older and they have more hypertension, diabetes, and atrial fibrillation but less ischaemic heart disease. Furthermore, HF with preserved systolic function is more prevalent in women, with accompanying lower mortality.[14,16–18] Some studies have suggested that women with HF receive poorer quality of care than men,[37] but findings have been inconsistent. A recent European multi-centre survey of the quality of care in patients admitted to hospital with HF found that fewer women with evidence of left ventricular systolic dysfunction were treated with drugs, with a documented impact on survival, but were more often treated with cardiac glycosides.[37] Conversely, in an international survey of treatment in primary care settings, women were similarly likely to receive ACE-inhibitors/ARBs or beta-blockers.[38] In two US studies, gender differences in quality of care were minimal or non-existent.[39,40]

So far, most investigations of interventions aimed at the reduction of mortality in HF have been performed in patients with reduced systolic function, a strategy that excludes a large proportion of women with HF. In the large mortality trials, only 20–30% of the patients have been female.[12,14] There is limited experience from trials and available guidelines for the optimal treatment of HF with preserved systolic function. A proportion of patients with preserved systolic function will instead have diastolic dysfunction, a condition that has been reported to be associated with increased mortality.[3] Accordingly, lack of knowledge concerning treatment of HF with preserved systolic function may have contributed to our finding that mortality of women decreased less than that of men during the study period.

Limitations

There are several limitations to this study that deserve consideration. First, the diagnosis of HF was taken from administrative registers, with no formal internal validation. However, the diagnosis of HF in the Swedish patient register from which our data were derived has been validated in one study, showing that HF as primary diagnosis in the hospital discharge register used has a validity of $\geq$90%.[19] Likewise, a diagnosis of AMI has been validated,[20] suggesting quite reasonable accuracy. Even so, we have no validation for other ischaemic diagnoses. Still, in comparison with other studies,[18] an unexpectedly low proportion of the patients had ischaemic heart disease, indicating that the disorder is underdiagnosed. If this were the case, the difference in mortality trends between patients with HF of ischaemic and non-ischaemic aetiology would likely have been underestimated. Another limitation is that we had no information about left ventricular function, prescribed medication, or the use of structured follow-up. Accordingly, the reasons why trends in men and women differ remain a matter of speculation.

Conclusion

Long-term mortality after a first hospitalization for HF has decreased dramatically in Sweden during the past two decades, particularly in younger patients, in men, and more for ischaemic than for non-ischaemic HF. However, in comparison with 1999–2001, there was no further improvement in 2002–03. Mortality in all groups remains high. Our findings indicate a need for new strategies in the treatment of HF, potentially more so in patients with preserved left ventricular systolic function, a group representing almost 50% of the HF population with larger proportions of women and older patients.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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CARDIOVASCULAR FLASHLIGHT

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Obstructive thrombosis of a bileaflet mitral valve assessed with real-time three-dimensional transoesophageal echocardiography

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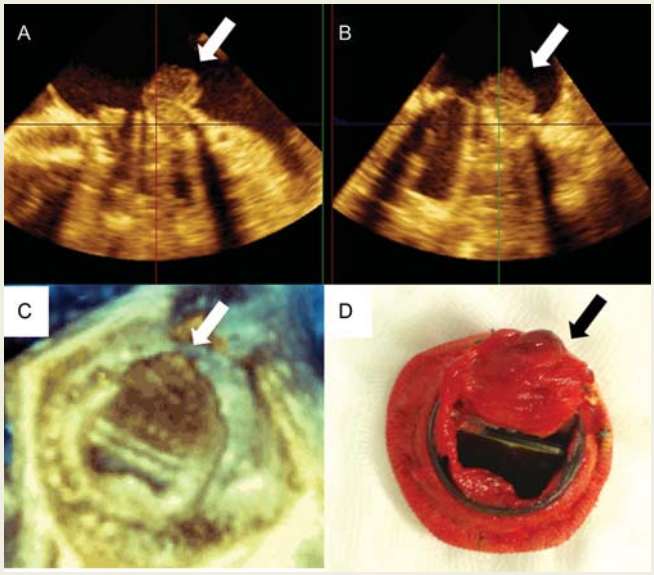
A 55-year-old woman was admitted for sub-acute ischaemia of the left leg. Three years earlier, the patient underwent a mitral replacement with a bileaflet valve for a symptomatic rheumatic mitral valve disease. Two months before admission, she presented a non-severe acute biliary pancreatitis associated with a time interval with international normalized ratio lower than 2.5.

Lower limb angiography confirmed the occlusion of the left common femoral artery. Transoesophageal echocardiography (TEE) using a fully sampled 3D matrix TEE probe (Philips Medical Systems, Andover, MA, USA) showed a large obstructive thrombus appended to the mitral valve and restricting the movement of one of the leaflets (*Panels A–C*). Mean mitral gradient and pressure half time were measured with continuous Doppler at 16 mmHg and 240 ms, respectively. The patient underwent urgent mitral valve replacement. Images obtained with real-time 3D TEE matched closely to per-operative view of the thrombus obstructing the mitral prosthesis (*Panel D*).



Supplementary material is available at *European Heart Journal* online.

Panels A–C. Transoesophageal echography with multi-planar simultaneous 2D views (*Panels A* and *B*), real-time volume rendering 3D view (*Panel C*), and movie (Supplementary material online) from the left atrial side showed an obstructive thrombus (white arrows) appended to the bileaflet mitral valve.

Panel D. Per-operative view after removal of the prosthetic mitral valve confirmed the presence of a large thrombus (black arrow) restricting the movement of the upper leaflet.