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Decreasing trends in the incidence of heart failure after acute myocardial infarction from 1993–2004: a study of 175 216 patients with a first acute myocardial infarction in Sweden

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Aims To investigate temporal trends in the risk of heart failure (HF) complicating acute myocardial infarction (AMI) and to determine whether these trends differ by gender or age.

Methods and results The national Swedish hospital discharge and death registries from 1993 to 2004 were used to calculate age- and gender-specific trends for a first episode of HF within 3 years in 175 216 patients aged 35–84 and hospitalized with a first AMI. Overall, 14.4% of patients aged 35–64 and 31.5% of those aged 65–84 with AMI in 1993–1995 had a hospital diagnosis of HF within 3 years (including the index admission). Corresponding figures for patients with AMI from 2002 to 2004 were 11.5 and 28.0%, respectively. In multivariable analyses, the risk of HF decreased by 4% per year. Having had a stroke before admission increased HF risk by 37%, diabetes increased the risk by 76% and atrial fibrillation by 80%. Patients with any kind of valvular disease had a more than doubled risk. Women had a 6% higher incidence of HF than men, whereas men with an index admission for AMI who did not develop HF had higher mortality than women.

Conclusions In this national sample, we observed a steady decrease in the risk of being hospitalized with HF after an AMI. However, the 3-year risk of HF remains high, with nearly one-third of AMI patients aged 65–84 developing HF within 3 years.

Keywords Acute myocardial infarction • Heart failure • Epidemiology • Incidence

Introduction

Heart failure (HF) is a health problem worldwide with a prevalence of ~2% in the Western world.[1] Although modern treatment modalities have improved the prognosis and decreased hospitalizations for HF, the prognosis is still poor[2] with frequent re-admissions and high mortality.[2,3] The annual costs for treatment of HF in Sweden constitute ~2% of the Swedish healthcare budget, with the major part (75%) of these costs derived from hospital care.[4]

In the Western world, coronary artery disease (CAD) is the most common cause of HF, with HF often developing after an AMI.[5] Despite the decline in CAD in many European countries and in North America, AMI remains a serious clinical problem.[6] During the past few decades, introduction of new medical and interventional treatments, such as thrombolytic strategies,[7] antiplatelet agents,[8] β-blockers,[9] angiotensin-converting enzyme inhibitors (ACE-inhibitors),[10] statins,[11,12] and percutaneous coronary intervention,[13] have improved prognosis in patients with AMI.

The development of HF after AMI is serious because patients manifesting HF after AMI have a dramatic increase in the risk of death when compared with other AMI survivors.[14] Several studies have investigated changes over time in the risk of

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developing HF after AMI. Although some studies found a decrease in the incidence of HF after AMI,[15–17] two recent studies reported increasing incidence, thought to be partly due to increased survival.[18,19] Accordingly, there is a need of further studies in this area.

The present study had three objectives. The first objective was to investigate age- and gender-specific long-term risk of HF in 175 216 patients with a first AMI using the Swedish national hospital discharge and death registries. The second objective was to determine whether the risk of developing HF after AMI changed over time. The third objective was to explore the potential predictors of hospitalizations for HF complicating AMI.

Methods

Sweden has a universal healthcare system that provides low-cost health care (including hospital care) to the Swedish population (population ranging from 8.6 to 9.0 million people during the period 1993–2004). Registration of principal and contributory discharge diagnoses for all patients is mandatory in the hospital discharge register. Diagnosis at discharge is coded with the International Classification of Diseases (ICD) system (ICD 9th revision until December 1996, ICD 10th revision thereafter). Each patient is given a principal diagnosis and up to five secondary diagnoses. For the purpose of the present study, data from the national hospital discharge and cause-specific death registers were linked through the personal identification number, which is unique for all Swedish citizens. The hospital discharge register has been in existence since the 1960s and operating on a nationwide basis since 1987.

In Sweden, the number of secondary diagnoses per case in inpatient care increased during the 1990s after the introduction of DRG-based prospective payment systems.[20] Most of this increase took place in the early 1990s. To ensure a sufficiently long period of observation while minimizing the potential bias from the increase in secondary diagnoses, the starting point for the present study was set at 1993.

All patients aged 35–84 with a first-time admission for AMI as a principal diagnosis from 1993 to 2004 were included. Of 193 460 patients, 175 216 (64% men) had no prior diagnosis of HF or CAD before admission and therefore form the study population for this investigation. We divided the patients into two age groups: 35–64 and 65–84 years. The study period was divided into four 3-year intervals of admission: 1993–1995, 1996–1998, 1999–2001, and 2002–2004.

The discharge codes used to define AMI were 410 (ICD-9) and I21 (ICD-10) and to define HF were 428A, 428B, 428X (ICD-9), and I50 (ICD-10). Heart failure was defined by these diagnostic codes, irrespective of whether it was a principal or secondary diagnosis. Codes used to define CAD were 412, 414 (ICD-9), I22, I23, I24, and I25 (ICD-10). Other co-morbidities were defined by the following discharge codes prior to and including the index hospitalization: diabetes: 250 (ICD-9), E10, E11, E14 (ICD-10); hypertension: 401– 405 (ICD-9), I10–I15 (ICD-10); atrial fibrillation: 427D (ICD-9), I48 (ICD-10); stroke: 430–438 (ICD-9), I60–I69 (ICD-10); valvular disease: 393–398, 424 (ICD-9), I05–I09, I34–I35 (ICD-10); chronic obstructive pulmonary disease: 490–496 (ICD-9), J44 (ICD-10); and asthma: 493 (ICD-9), J45 (ICD-10).

Validity of the registers

Heart failure and AMI diagnoses according to the hospital discharge register have been validated in Sweden.[21,22] Heart failure as the principal diagnosis was shown to have a validity of 95%, whereas HF in any position had a validity of 82%.[22] In 2001, the biochemical criteria for AMI were revised in accordance with the ESC/ACC consensus document[23] with more sensitive and specific biomarkers, and accordingly, potentially more patients were diagnosed with smaller infarcts during the later years of data collection. A recent small Swedish single-centre study[24] demonstrated that at least 95% of cases discharged with an AMI diagnosis fulfilled the criteria; in the rest, there was insufficient data but AMI could not be excluded. This uncertainty pertained particularly to patients older than 80 years and to those where AMI was a secondary diagnosis.

Statistical methods

All analyses were carried out using the Statistical Analysis System (SAS), version 9.1, and the R statistical computing system, version 2.9.0. Means and proportions for continuous and categorical variables were calculated. Estimates of the conditional probability of HF within 30 days, 30 days–1 year, and 1–3 years are presented for each period of AMI admission, gender, and age group. The estimates are calculated through the cumulative incidence function for HF with death as a competing risk.[25] Additionally, the cumulative incidence functions for HF and death from any other cause than HF are illustrated graphically for the whole population, from AMI admission and up to each time point within the 3-year interval. Different curves are presented for each period of AMI admission. Additionally, a graph illustrating age-adjusted cumulative incidence functions for men and women is presented. Age adjustment was done implicitly through comparison of subsets of men and women with exactly the same age structure. The average annual change in HF incidence within different time intervals was estimated through the Poisson regression while controlling for age, gender, and differences in co-morbidity.

Results

Of the 175 216 patients included in the study, 43 034 (25%) had a diagnosis of HF within 3 years from admission (58.5% men). Almost 70% of all HF cases were registered either concomitantly with the index AMI admission or within the first 30 days after admission. Descriptive data for the study population are provided in *Table 1*.

Table 2 shows the probability of developing HF within 30 days, 30 days–1 year, and 1–3 years by age separately for men and women, while taking the issue of competing risk into consideration (see the 'Methods' section). There were decreasing trends in both genders for each time interval up to 3 years after admission. Overall, 14.4% of patients aged 35–64 and 31.5% of those aged 65–84 with AMI in 1993–1995 developed HF within 3 years. Corresponding figures for patients with AMI in 2002–2004 were 11.5% (patients aged 35–64) and 28.0% (patients aged 65–84).

Figure 1 demonstrates a decreasing trend in developing HF up to 3 years after an index admission for AMI. Additionally, the figure shows that the mortality of patients admitted for AMI who did not develop HF decreased during all time periods up to 3 years.

Over the observation period, the proportion of AMI patients with diabetes, valvular disease, and atrial fibrillation increased somewhat, whereas there was little change with respect to stroke and other co-morbidities (data not shown). In a multiple regression model, the mean incidence of HF after AMI decreased by 4% per year between 1993 and 2004, independently of age, gender, and co-morbidities (*Table 3*). The risk increased markedly

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Table 1 Characteristics of 175 216 men and women with a first acute myocardial infarction at their index admission

	Men (n = 112 373)	Women (n = 62 843)	Total (n = 175 216)
Age at MI (years), mean (SD)	67.1 (11.1)	72.0 (9.8)	68.9 (10.9)
Angina pectoris	15 334 (13.6)	9103 (14.5)	24 437 (13.9)
Diabetes	13 270 (11.8)	8880 (14.1)	22 150 (12.6)
Hypertension	17 134 (15.2)	12 270 (19.5)	29 404 (16.8)
Atrial fibrillation	8657 (7.7)	5920 (9.4)	14 577 (8.3)
Valvular disease	2312 (2.1)	1898 (3.0)	4210 (2.4)
Prior stroke	9179 (8.2)	6154 (9.8)	15 333 (8.8)
Asthma	1463 (1.3)	1338 (2.1)	2801 (1.6)
COPD	3497 (3.1)	2489 (4.0)	5986 (3.4)

COPD, chronic obstructive pulmonary disease.

with age, with every additional year increasing the 3-year incidence by 6%. Women had a 6% higher incidence of HF than men (*Figure 2*), whereas men with an index admission for AMI who did not develop HF had higher mortality than women (*Figure 2*). Having had a stroke before admission increased the risk of HF by 37%, diabetes increased the risk by 76%, and atrial fibrillation by 80%. Patients with any kind of valvular disease had a more than doubled risk (*Table 3*).

Discussion

We investigated all patients without prior HF and admitted with a first AMI in Sweden between 1993 and 2004. Our findings indicate a steady decrease in the risk of developing HF after AMI, regardless of gender or age. However, the 3-year risk of HF remains high, with nearly a third of AMI patients aged 65–84 developing HF within 3 years and more than 1 in 10 of patients aged <65.

During the past few decades, the introduction of new pharmacological and interventional treatments has reduced in-hospital mortality for patients with AMI.[7–14] Simultaneously, the introduction of several new treatments for HF has been demonstrated to improve morbidity and mortality in selected study populations.[26–30] In keeping with these developments, epidemiological studies have shown that the long-term mortality in patients who are diagnosed with HF has decreased markedly during the past two decades.[31,32]

Overall, we found that 25% of the patients with a first AMI developed HF within 3 years. This figure varies in the literature from 30 up to 75%, depending on the population studied and the time of follow up (3 or 5 years follow-up).[19,33,34] However, studies consistently show that most HF cases develop either in relation to the AMI or within the first few months after the AMI.[15,16,19]

Table 2 Probability of developing heart failure within defined time periods after an acute myocardial infarction while considering death from other causes as competing risk

Period	AMI (n)	HF within 30 days (n)	Percentage	AMI surviving 30 days without HF (n)	HF 31 days to 1 year (n)	Percentage	AMI surviving 1 year without HF (n)	HF 1–3 years (n)	Percentage	AMI Surviving within 3 years without HF (n)	HF within 3 years (n)	Percentage
Men (35–64 years)												
1993–1995	10 950	938	8.57	9520	302	2.75	9033	263	2.40	8588	1502	13.72
1996–1998	10 475	885	8.45	9208	238	2.27	8819	176	1.68	8448	1299	12.40
1999–2001	10 437	844	8.09	9298	210	2.01	8935	176	1.69	8579	1230	11.78
2002–2004	10 957	865	7.89	9810	208	1.90	9490	145	1.32	9178	1218	11.12
P-value			0.020			0.000			0.000			0.000
Women (35–64 years)												
1993–1995	3022	336	11.09	2507	115	3.81	2355	61	2.02	2253	512	16.91
1996–1998	2984	287	9.62	2592	92	3.05	2452	68	2.31	2333	447	14.98
1999–2001	3389	300	8.82	2937	90	2.69	2796	71	2.10	2668	461	13.60
2002–2004	3490	312	8.94	3075	67	1.92	2958	68	1.95	2819	447	12.81
P-value			0.005			0.000			0.370			0.000

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Table 2 *Continued*

Period	AMI (*n*)	HF within 30 days (*n*)	Percentage	AMI surviving 30 days without HF (*n*)	HF 31 days to 1 year (*n*)	Percentage	AMI surviving 1 year without HF (*n*)	HF 1–3 years (*n*)	Percentage	AMI Surviving within 3 years without HF (*n*)	HF within 3 years (*n*)	Percentage
Men (65–84 years)												
1993–1995	19 045	3651	19.17	12 672	1085	5.70	10 799	931	4.89	8832	5667	29.76
1996–1998	16 983	3271	19.26	11 602	954	5.62	9926	725	4.27	8377	4950	29.15
1999–2001	16 754	3236	19.31	11 779	838	5.00	10 199	750	4.48	8611	4824	28.79
2002–2004	16 772	2989	17.82	12 267	809	4.82	10 689	679	4.05	9085	4477	26.69
P-value			0.000			0.000			0.000			0.000
Women (65–84 years)												
1993–1995	13 309	2959	22.23	8157	867	6.51	6806	695	5.22	5600	4520	33.96
1996–1998	11 815	2633	22.29	7573	696	5.89	6424	553	4.68	5344	3882	32.86
1999–2001	12 324	2680	21.75	8223	665	5.40	7041	544	4.41	5869	3889	31.56
2002–2004	12 510	2467	19.72	8813	670	5.36	7616	573	4.58	6369	3710	29.66
P-value			0.000			0.000			0.000			0.000
Overall (35–64 years)												
1993–1995	13 972	1273	9.11	12 027	416	2.98	11 387	324	2.32	10 840	2013	14.41
1996–1998	13 459	1172	8.71	11 797	329	2.44	11 270	245	1.82	10 779	1746	12.97
1999–2001	13 826	1143	8.27	12 234	301	2.18	11 730	247	1.79	11 247	1691	12.23
2002–2004	14 447	1177	8.15	12 885	275	1.90	12 447	213	1.47	11 997	1665	11.52
P-value			0.001			0.000			0.000			0.000
Overall (65–84 years)												
1993–1995	32 354	6610	20.43	20 829	1951	6.03	17 605	1626	5.03	14 432	10 187	31.49
1996–1998	28 798	5904	20.50	19 175	1650	5.73	16 350	1278	4.44	13 720	8832	30.67
1999–2001	29 078	5916	20.35	20 002	1503	5.17	17 239	1294	4.45	14 479	8713	29.96
2002–2004	29 282	5456	18.63	21 080	1479	5.05	18 305	1252	4.28	15 454	8187	27.96
P-value			0.000			0.000			0.000			0.000

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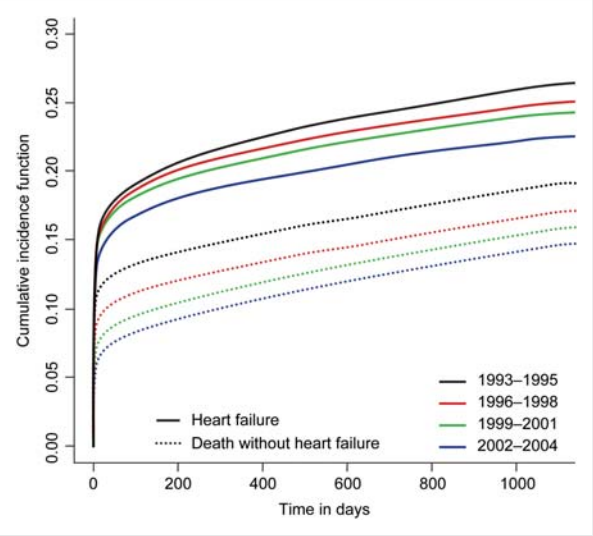

Figure 1 Probability of developing heart failure after acute myocardial infarction for the whole population during different time-periods between 1993 and 2004 and mortality in patients with acute myocardial infarction without concomitant heart failure.

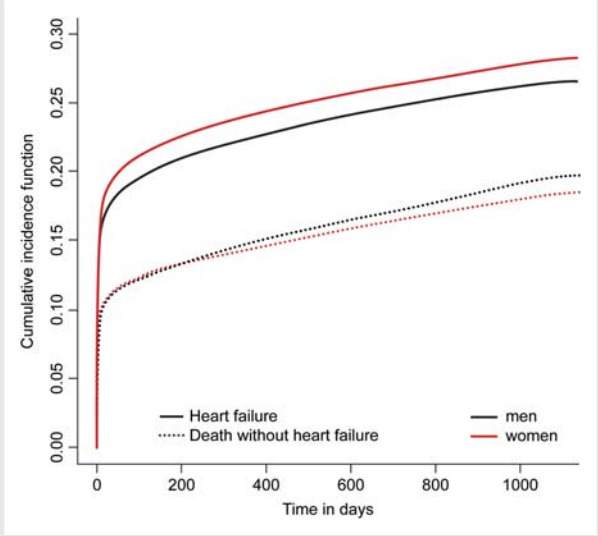

Figure 2 Probability of developing heart failure after acute myocardial infarction in men and women up to 3 years after admission between 1993 and 2004 and mortality for both genders after acute myocardial infarction without concomitant heart failure.

Table 3 Factors associated with the risk of developing heart failure within 3 years in 175 216 patients with a first acute myocardial infarction in Sweden 1993–2004

	Risk ratio (95% confidence interval)
Calendar year of onset	0.96 (0.95–0.96)
Age (year)	1.06 (1.06–1.06)
Gender (male/female)	1.06 (1.04–1.08)
Diabetes (yes/no)	1.76 (1.70–1.81)
Atrial fibrillation (yes/no)	1.80 (1.75–1.84)
Valvular disease (yes/no)	1.22 (1.12–1.32)
Stroke (yes/no)	1.37 (1.33–1.41)

During the past decade, the majority of registry studies have shown a decline in the incidence of HF after AMI,[15–17] but in one Canadian study,[19] which investigated the incidence of HF after a first AMI among patients aged >65 from 1994 to 2000, the incidence increased, with 76% of the patients developing HF after AMI within 5 years. In our study, we investigated the incidence of HF after AMI during the period 1993–2004, which is approximately the same period as in the Canadian study and, in contrast to their findings, we observed a decline in the incidence of HF after AMI. The reason for this discrepancy is unclear, given that their sample, like ours, probably included milder infarctions during the latter part of the study. One reason for the discrepancy could be that in the Canadian study all incident HFs were registered, including patients managed in primary health care as well as in hospital, whereas our study included only hospitalized HF patients. A hospital diagnosis of HF in Sweden has been validated against the European Society of Cardiology criteria for the definition of HF,[21] with a validity of 95% for a principal diagnosis of HF. Although admission criteria might have varied over the period, we probably captured the majority of severe HF cases with reasonable accuracy. However, we were unable to capture milder cases managed on an outpatient basis or in primary care. In patients with stable chronic HF, a hospital admission for worsening HF would markedly increase the risk of subsequent death.[35]

Velagaleti *et al.*[18] observed an increase over time in the incidence of HF after AMI in 676 Framingham Heart study participants with a first AMI from 1970 to 1999, 165 of whom developed HF. The authors divided the study period into three decades (1970–1979, 1980–1989, and 1990–1999). In our study, we investigated the incidence of HF after AMI from 1993 to 2004, coincident to their last time period. The careful case-finding method of the Framingham Heart study is obviously different to that of the present study, but the limited size of their study population, as well as differences in identification of HF cases makes it difficult to draw conclusions concerning the discrepancies between our study and theirs.

The explanation for the decrease in hospitalizations for HF found in the present study is concomitant with better treatment in the acute stage of AMI with rapid revascularization/lysis in ST elevation AMI and in improved secondary prevention.[36,37] According to data from the Swedish registry of heart intensive care (RIKS-HIA; available in English at http://www.ucr.uu.se/rikshiaint/document/RiksHia_Report_2004_EN1.pdf) report in 2005, the use of reperfusion treatment in eligible patients remained steady at 60% between 1995 and 2004, but with a shift from almost no acute percutaneous interventions in 1995 to more than half of all reperfusion treatment in 2004. Use of β-blockers and aspirin at discharge was already high in 1995, but there was increasing

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use of combination aspirin–clopidogrel therapy in 2004. Statin use increased very markedly from 10 to 80%, as did the use of ACE-inhibitors/angiotensin receptor blockers (from 40 to 60%). The report also found a slight increase in the age of AMI patients, by 1–2 years, and the proportion of women increased.

These developments may have reduced long-term complications, including HF. Additionally, the introduction of several new HF treatments over the past three decades has been shown to improve morbidity and mortality in selected populations of HF patients.[26–30] Some of these treatments, notably ACE-inhibitors, angiotensin receptor blockers and β-blockers, may also have helped to prevent the development of HF in some patients with AMI.

During the past two decades, the incidence of AMI has decreased in Sweden, this is probably partly due to a reduction in risk factors.[38] In contrast to a diagnosis based solely on history and electrocardiography findings, AMI diagnosis based on serial biomarker measurements has substantially increased the detection of AMI cases.[39] At the same time, the size of AMIs is becoming smaller,[40] which could contribute to a reduced risk of subsequent HF and potentially to reduced severity. This in turn might partly explain the declining incidence of HF after AMI. However, even though the new criteria have resulted in a substantial increase in the diagnosis of AMI, patients diagnosed by these criteria may not have a better prognosis. In one study, patients identified with the new criteria who would have been missed by the old criteria had more co-morbidities and worse 6-month outcomes, suggesting that additional patients identified by the new diagnostic criteria may not necessarily have a better outcome.[41]

The most common predictors for HF after AMI in previous studies were age, diabetes, previous AMI, history of hypertension, and reduced renal function.[42–44] In our study of patients, all of whom had a first MI, the most important predictors were age, valvular disease, atrial fibrillation, diabetes, and previous stroke. Hypertension did not predict HF, possibly because hypertension as a co-morbid condition will not be adequately captured by a hospital diagnosis.[31] We additionally observed that women had higher incidence of HF after AMI than men, which can partly be explained by the fact that men had higher mortality after AMI than women and may have died before they could develop HF (*Figure 2*).

Limitations

There are several limitations to this study. First, the diagnosis of HF was taken from administrative registers without formal internal validation. Obviously, a study using administrative databases cannot rival the meticulous detail of the Framingham study. However, our findings may be more applicable to the unselected patients of today. Additionally, both HF and AMI diagnoses have been validated demonstrating good accuracy.[21,22] A second limitation is that the diagnostic criteria for AMI changed over the study period, with the adoption of new and sensitive markers in 2001.[23] As diagnostic criteria for AMI have changed during the period of interest, it is not clear whether the observations are related to a true trend of disease development or just due to the fact that smaller infarcts were included in the analysis within the latter years. Even so, the fact that nearly one in eight younger patients and more than one quarter of older patients with AMI develop HF within 3 years deserves attention. In addition, as already discussed, the decline in the risk of HF after AMI started in the mid-1990s, and the fact that smaller infarctions were captured may not necessarily mean that these patients had an overall better prognosis. Third, there was a lack of additional clinical data, such as infarct size and echocardiography measurements, which would have helped to put these data into a better context.

Conclusion

In this national sample, investigating all patients admitted with a first AMI in Sweden from 1993 to 2004, we observed a steady decrease in the risk of hospitalization for HF in patients with an index AMI, regardless of gender and age. Factors associated with a higher risk of developing HF include diabetes, atrial fibrillation, prior stroke, and valvular disease. Women had a slightly higher incidence rate than men, independently of age, year of AMI, and co-morbidities. Improved treatment in the acute phase of an AMI has probably contributed to the decreasing subsequent risk for HF. The risk of HF hospitalization after a first AMI remains high, with nearly one-third of patients with an AMI aged 65–84 developing HF within 3 years and more than 1 in 10 patients aged 35–64.

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