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Development and course of heart failure after a myocardial infarction in younger and older people

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Abstract

Background Acute myocardial infarction (AMI) is a common cause of heart failure (HF), which can develop soon after AMI and may persist or resolve or develop late. HF after an MI is a major source of mortality. The cumulative incidence, prevalence and resolution of HF after MI in different age groups are poorly described. This study describes the natural history of HF after AMI according to age. **Methods** Patients with AMI during 1998 were identified from hospital records. HF was defined as treatment of symptoms and signs of HF with loop diuretics and was considered to have resolved if loop diuretic therapy could be stopped without recurrence of symptoms. Patients were categorised into those aged < 65 years, 65–75 years, and > 75 years. **Results** Of 896 patients, 311, 297 and 288 were aged < 65, 65–75 and >75 years and of whom 24%, 57% and 82% had died respectively by December 2005. Of these deaths, 24 (8%), 68 (23%) and 107 (37%) occurred during the index admission, many associated with acute HF. A further 37 (12%), 63 (21%) and 82 (29%) developed HF that persisted until discharge, of whom 15, 44 and 62 subsequently died. After discharge, 53 (24%), 55 (40%) and 37 (47%) patients developed HF for the first time, of whom 26%, 62% and 76% subsequently died. Death was preceded by the development of HF in 35 (70%), 93 (91%) and 107 (85%) in aged < 65 years, 65–75 years and >75 years, respectively. **Conclusions** The risk of developing HF and of dying after an MI increases progressively with age. Regardless of age, most deaths after a MI are preceded by the development of HF.

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Keywords: Myocardial infarction; Heart failure; Age

1 Introduction

Heart failure (HF) is a common complication of myocardial infarction (MI), which may develop early or late and persist, resolve or recur.[1] A growing proportion of patients with MI are aged > 65 years. Older patients are at greater risk of developing HF and have a poorer prognosis.[2–4] Surprisingly, the complex pattern and timing of the development and resolution of HF and the importance of such distinctions has not been quantified in relationship to age.[4,5] Understanding the drivers of morbidity and mortality after MI is important, given the great difference in mortality rates reported in clinical trials of MI compared to epidemiological studies. Improved understanding about which patients are at risk and the nature of the risk could help focus attention on patients at greater need, to ensure that they receive appropriate therapy and that they are targeted for recruitment into clinical trials, which currently have rather low event rates. Treatment can only help patients who are at risk of complications that the treatment aims to prevent.

2 Methods

2.1 Study population

Two hospitals in Hull and the East Riding of Yorkshire (UK) are sole providers of acute cardiac services for about 560,000 people. MI's during 1998 were identified from the Hospitals Information Department and confirmed by case note review. This research was approved by the Local Research Ethics Committee.

2.2 Follow-up

The case records of all patients were reviewed to identify use of loop diuretics and if so whether this was due to symptoms or signs of HF. Follow-up data were collected until 31st December 2005. The occurrence of major events, such as recurrent MI, and stroke were recorded.

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2.3 Definition of myocardial infarction (MI)

At least two of the following five criteria were used to confirm a diagnosis of MI: (1) prolonged cardiac chest pain; (2) increases in biomarkers (in 1998, usually creatinine kinase (CK) or CK-MB mass); (3) electrocardiographic changes of MI or new-onset left bundle branch block; (4) sudden unexpected death; and (5) autopsy evidence of MI.

2.4 Definitions

Heart failure was defined either as signs and symptoms consistent with that diagnosis (principally breathlessness and signs of fluid retention) resulting in treatment with loop diuretics. Use of loop diuretics for the treatment of hypertension or renal failure was not included in the definition of HF. Criteria for left ventricular systolic dysfunction (LVSD) were left ventricular ejection fraction (LVEF) < 40% or a qualitative report of moderate or severe LVSD. Patients were categorised into three age groups: (1) < 65 years; (2) 65–75 years and (3) > 75 years.

2.5 Resolution of heart failure

Consistent with European Society of Cardiology Guidelines,[6] resolution of heart failure was defined as the withdrawal of diuretics without the recurrence of symptoms.

2.6 Statistical analysis

Data were entered into a Microsoft Access database and analysed using SPSS Inc., version 13.0 (UK, Ltd.). Key outcomes were the proportion of patients who died and all-cause mortality. Continuously distributed data are presented as median and inter-quartile range (IQR). Categorical data are presented as percentages. Groups of patients with and without HF were compared by the Chi-squared test. Kaplan-Meier (K-M) curves were generated to illustrate patients' overall survival, and in subgroups. K-M curves were compared by the log-rank test on the appropriate degrees-of-freedom. Cox regression was used to look at mortality, from which hazard ratios (HRs) and 95%CIs were calculated. The Cox regression model is semi-parametric in the sense that no assumption concerning event-free survival times is necessary. The Cox regression model is based on the assumption that the effect of a risk factor, expressed as a HR, is constant over time. The assumption of proportionality of the Cox model covariates was tested by plotting residuals.[7,8] Linearity of continuous data was checked by including a squared term. We did not build a model using automated selection methods but rather on biological variables relevant to heart failure.[9] Hence, we adopted an epidemiological approach to model building.

Heart failure status was categorised into six groups: (1) no HF at any time (this was the reference group for statistical comparisons); (2) persistent HF (PHF), patients with HF on the index admission and persisting at follow up until death or end of follow-up; (3) late resolution HF (LRHF), patients with HF on the index admission that resolved only subsequent to discharge; (4) recurrent HF (RHF), patients with HF on the index admission that resolved prior to discharge but recurred during follow-up; (5) transient HF (THF) on the index admission that resolved prior to discharge and did not recur prior to death or end of follow-up; and (6) late-onset HF (LOHF), patients who did not develop HF on the index admission but who later developed HF during follow-up.

3 Results

Of 1,012 patients with a death or discharge diagnosis of acute MI in 1998, 116 were excluded from further analysis because they were transferred from another region or because MI could not be confirmed. This left 896 patients for analysis, of whom 311 (35%) were < 65 years, 297 (33%) 65–75 years and 288 (32%) were > 75 years (Table 1). Survival status was known for all patients by December 2005, apart from 16, 8 and 6 from each age-group, respectively. About one third of patients were women. Older patients were less likely to be managed primarily by a cardiologist. ST-segment elevation myocardial infarction (STEMI) occurred in 193 (62%), 174 (59%) and 151 (53%) cases. About 15% had a history of HF preceding the index event, rising from 7% in those aged < 65 years to 25% in those aged > 75 years.

During the index admission, younger patients were more often treated with aspirin, statins, beta-blockers, intravenous nitrate, heparin and thrombolysis. Older patients were more likely to receive loop diuretic and digoxin ($P < 0.001$) (Table 1). Primary angioplasty was not done in this hospital group in 1998.

Overall, 75 (24%) patients < 65 years, 170 (57%) aged 65–75 years, and 235 (82%) > 75 years had died by December 2005 (Figure 1). Figure 2 shows the overall proportion of patients that developed HF at any time during follow-up and their categorisation according to persistence, remission and timing of development of HF in different age groups.

During the index hospitalization, 24 patients (8%) < 65 years, 68 (23%) patients 65–75 years, 107 patients (37%) > 75 years died with about 80% of deaths being associated with evidence of heart failure. Transient heart failure was observed in 26 (32%) patients < 65 years, in 27 (19%) patients 65–75 years, and in 21 (11%) patients > 75 years, but had resolved by discharge with cessation of diuretic therapy.

Table 1. Patients characteristics recorded during the index admission overall and treatment during index admission and any time and classified according to the three different age group: > 65 yrs, 65–75 yrs and > 75 yrs (Data are Median (inter-quartile range) and *n* (%)).

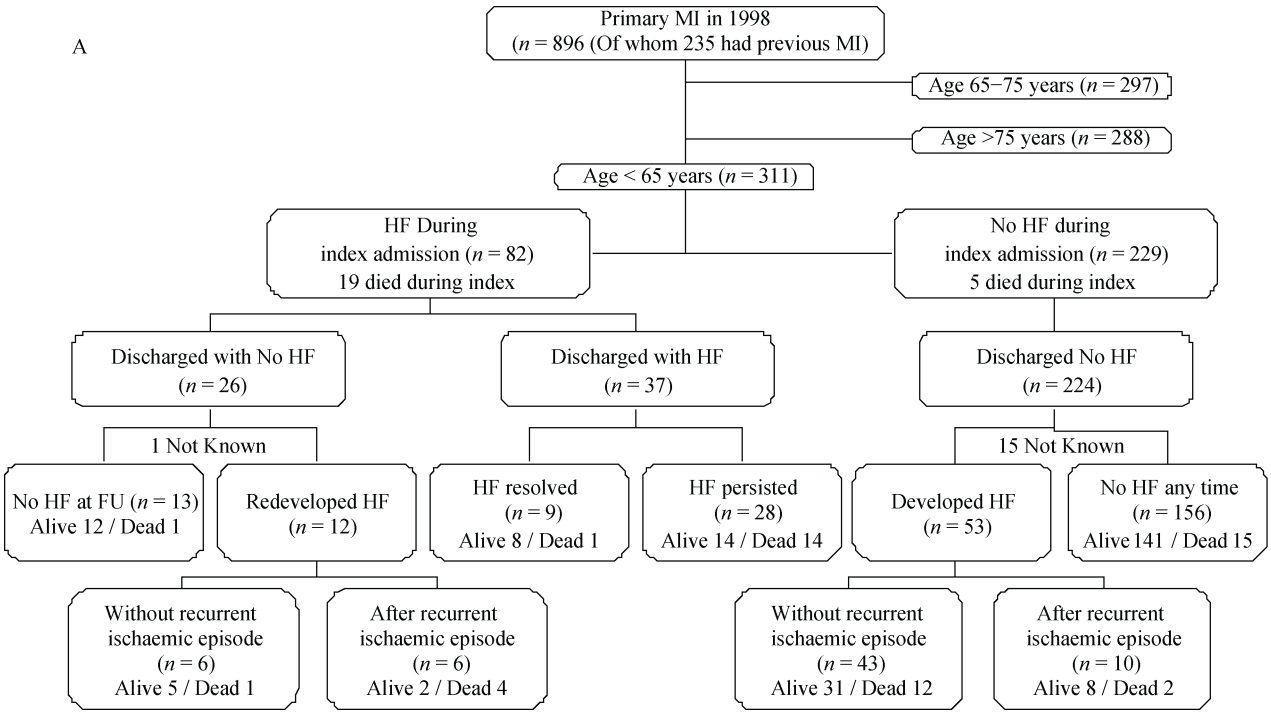
Variables	Missing data	All	< 65 yrs	65–75 yrs	> 75 yrs	*P* value
N		896	311 (35%)	297 (33%)	288 (32%)	
Age (yrs)	0	70 (61–78)	58 (51–61)	71 (68–73)	81 (78–85)	< 0.001
Women	0	333 (37%)	66 (21%)	120 (40%)	147 (51%)	< 0.001
Current smoker	87	303 (37%)	166 (55%)	97 (35%)	40 (17%)	< 0.001
Ex smoker		255 (32%)	85 (30%)	96 (35%)	74 (32%)	
History of hypertension	40	300 (35%)	81 (27%)	105 (37%)	114 (42%)	< 0.001
History of diabetes	3	82+33[a] (13%)	33 (11%)	45 (15%)	37 (13%)	0.290
Prior MI	1	235 (26%)	73 (24%)	73 (25%)	89 (31%)	0.153
History of HF	4	134 (15%)	22 (7%)	39 (13%)	73 (25%)	< 0.001
Prior CABG		39 (4%)	19 (6%)	14 (5%)	6 (2%)	0.051
Prior PTCA		14 (2%)	10 (3%)	4 (1%)	0	< 0.001
Managed primarily by cardiologist		558 (62%)	233 (75%)	186 (63%)	139 (48%)	< 0.001
Index admission ECG						
ST segment elevation[b]	10	518 (58%)	193 (62%)	174 (59%)	151 (53%)	< 0.001
Chest X-ray						
Pulmonary oedema	227	160 (24%)	33 (14%)	54 (24%)	73 (33%)	< 0.001
Physical examination						
Heart rate	9	78 (64–97)	73 (61–88)	76 (64–98)	85 (68–101)	< 0.001
Atrial fibrillation (yes/no)	2	153 (17%)	19 (6%)	56 (19%)	78 (27%)	< 0.001
Systolic blood pressure	5	140 (120–160)	132 (121–142)	140 (120–160)	140 (120–160)	0.610
Blood tests (on admission)						
Peak CK	49	828 (376–1901)	1062 (418–2262)	767 (369–1779)	684 (318–1651)	0.018
Creatinine	127	105 (89–129)	95 (83–108)	108 (90-132)	117 (96–149)	< 0.001
Anaemia in 1st available Hb[e]	41	206 (24%)	34 (11%)	67 (24%)	105 (38%)	< 0.001
Revascularisation during admission						
Thrombolysis	0	372	159 (51%)	127 (43%)	86 (30%)	< 0.001
PCI	0	20	16 (0.05%)	4 (0.01%)	0(%)	< 0.001
CABG	0	8	4 (0.01%)	3 (0.01%)	1 (0%)	0.459
Treatment at any time during admission						
Selected parenteral agents						
Loop diuretic	7	262	49 (16%)	91 (31%)	122 (42%)	< 0.001
Nitrates	3	309	125 (40%)	103 (35%)	81 (28%)	0.019
Inotropic therapy	2	94	22 (0.07%)	34 (11%)	38 (13%)	0.121
Oral						
Aspirin	2	792	302 (97%)	251 (85%)	239 (83%)	< 0.001
Statin	2	406	214 (69%)	141 (48%)	51 (18%)	< 0.001
ACE inhibitors	2	354	126 (41%)	120 (41%)	108 (38%)	0.782
ARBs	2	8	2 (1%)	2 (1%)	4 (1%)	0.689
Beta-blockers	2	497	236 (76%)	163 (55%)	98 (34%)	< 0.001
Loop diuretic	3	297	58 (19%)	94 (32%)	145 (50%)	< 0.001
Digoxin	2	68	6 (2%)	22 (7%)	40 (14%)	< 0.001
Revascularisation at any time[c]						
PCI	0	94	72 (23%)	20 (8%)	2 (1%)	< 0.001
CABG	0	98	58 (19%)	35 (12%)	5 (2%)	< 0.001

To be contin.

Table 1. Contin.

Variables	Missing data	All	< 65 yrs	65–75 yrs	> 75 yrs	*P* value
Treatments at any time[c]						
ACE-inhibitors (seven cases prior to index were on ACE-inhibitors)	2	496	197 (63%)	170 (57%)	129 (45%)	< 0.001
ARBs	2	44	26 (8%)	11 (4%)	7 (2%)	< 0.001
Beta-blockers	2	541	256 (82%)	173 (58%)	99 (35%)	< 0.001
Loop diuretic	2	539	130 (42%)	187 (63%)	222 (77%)	< 0.001
Thiazide diuretic	2	68	30 (10%)	20 (8%)	18 (6%)	0.287
Spironolactone	2	64	28 (9%)	20 (8%)	17 (6%)	0.301
Digoxin	2	110	16 (5%)	38 (13%)	56 (20%)	< 0.001
Insulin	1	92	33 (11%)	39 (13%)	20 (7%)	0.083
Oral hypoglycaemic agent	2	67	26 (8%)	24 (8%)	17 (6%)	0.499
Aspirin	2	805	304 (98%)	256 (86%)	245 (85%)	< 0.001
Statin	2	530	269 (86%)	189 (64%)	72 (25%)	< 0.001
Imaging[d]						
N		**861**	**296**	**284**	**281**	
Echocardiography		**283**	**96**	**100**	**87**	
Major LVSD	4	141	44 (46%)	51 (51%)	46 (55%)	0.029
Moderate or severe mitral regurgitation	12	39	9 (9%)	14 (14%)	16 (18%)	0.519
Moderate or severe other valve disease	6	11	1 (1%)	5 (5%)	5 (6%)	0.329
Radionuclide		**357**	**176**	**123**	**58**	
LVEF 35%–40%		42	46 (26%)	39 (32%)	25 (43%)	0.087
LVEF < 35%		110	18 (10%)	18 (15%)	6 (10%)	
Major LVSD/Survived and did not develop HF[e]		38	20 (20%)	11 (11%)	7 (9%)	
No major LVSD/Survived and did not develop HF[f]		142	92 (67%)	44 (45%)	6 (17%)	
No LV function report/Survived and did not develop HF[g]		44	26 (53%)	13 (16%)	5 (3%)	

Percentages are shown are of those in whom measurements were made. Example interpretation: older patients had high creatinie levels compare to younger patients. Many of these associations show dose-response. The differences for Na are exaggerated because of the relative large sample sizes between the three groups, and the relatively low standard deviations (in other words, this is a statistical quirk). [a]Thirty-three cases newly diagnosed as diabetic on index admission; [b]*P*-value for ST calculated between three groups (STE, No STE and other (LBBB) and pace); [c]Treatment any time until 31st December 2005; [d]Evidence of left ventricular function during index admission or shortly after; [e]Three patients age < 65 years and one 65–75 years lost follow-up; [f]Eight patients age < 65 years, two with 65–75 years and two in those > 75 years lost follow-up; [g]Three patients age < 65 years, two with 65–75 years lost follow-up. ARB: angiotensin receptor blockers; CABG: coronary artery bypass grafting; CK: creatine kinase; ECG: electrocardiogram; HF: heart failure; LBBB: Left bundle branch block; LVEF: left ventricular ejection fraction; LVSD: left ventricular systolic dysfunction; MI: myocardial infarction; STE: ST- segment elevation; PTCA: percutaneous transluminal coronary angioplasty.



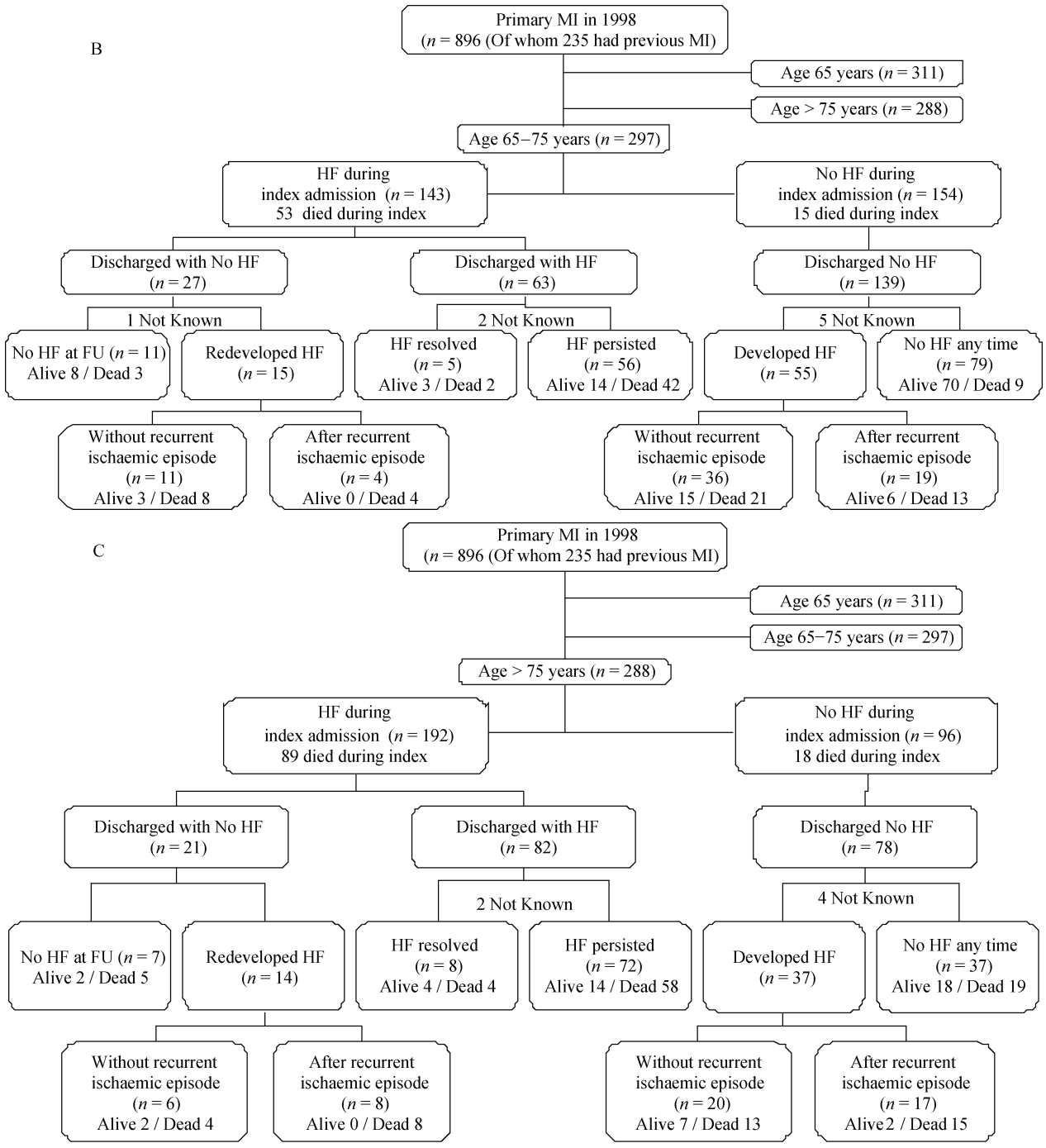


Figure 1. The sequence of events leading to the development of HF and/or death. (A): Flow diagram showing the sequence of development of HF and relationship with recurrent ischemic episodes and mortality over approximately 6 years in patients less than 65 years old which admitted with an acute MI during 1998. Follow-up data were incomplete in 16 patients. (B): Flow diagram showing the sequence of development of heart failure and relationship with recurrent ischemic episodes and mortality over approximately 6 years in patients 65–75 years old which admitted with an acute MI during 1998. Follow-up data were incomplete in 8 patients. (C): The sequence of development of heart failure and relationship with recurrent ischemic episodes and mortality over approximately 6 years in patients more than 75 years old which admitted with an acute MI during 1998. Follow-up data were incomplete in 6 patients. HF: heart failure; MI: myocardial infarction.

Heart failure was present at discharge in 37 (12%) patients < 65 years, 63 (21%) patients 65–75 years and 82 (28%) patients > 75 years, which had preceded admission in approximately one third of cases in each age group.

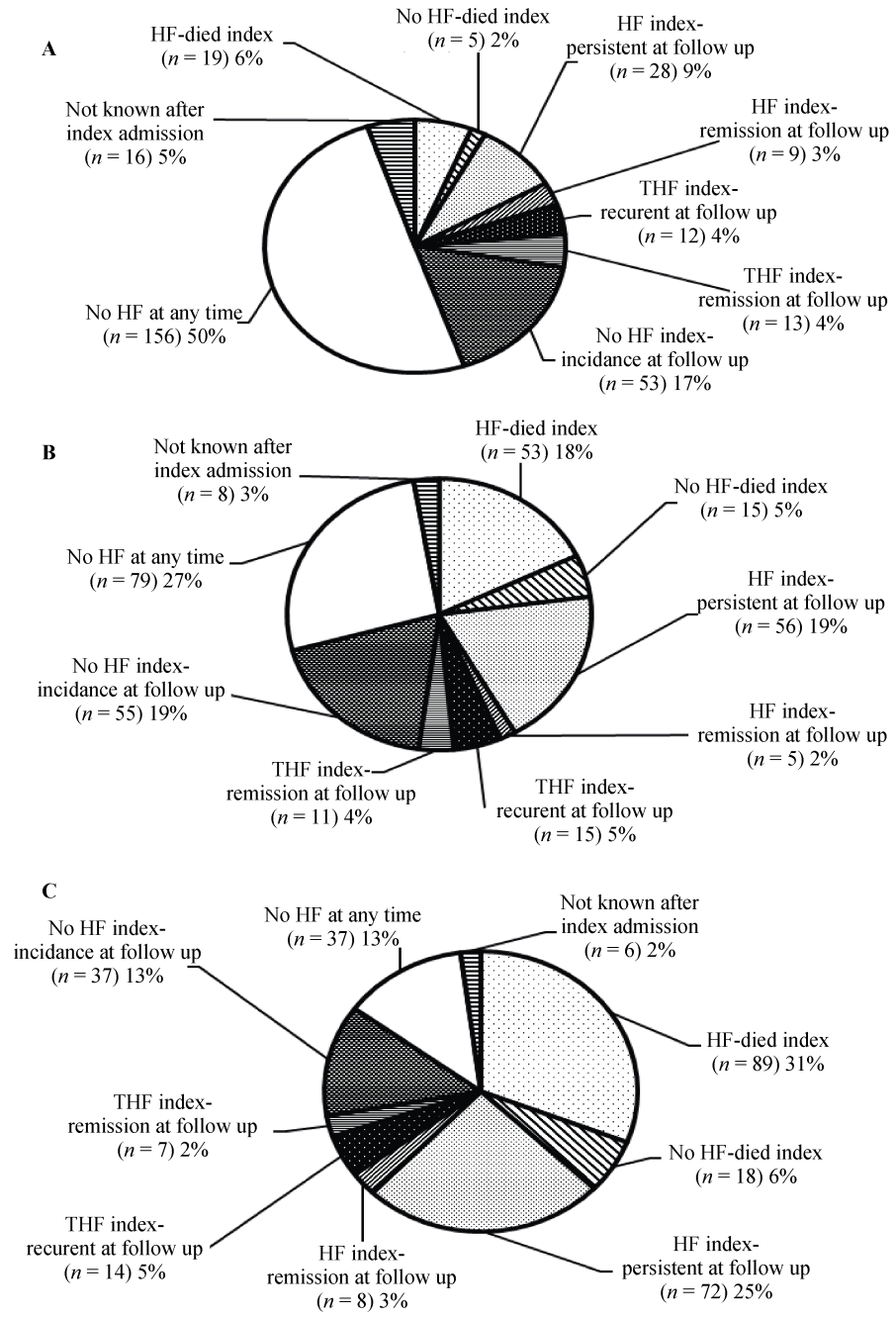


Figure 2. The proportions of patients developing different categories of heart failure according to early mortality, timing of onset and persistence according to different age group. (A): > 65 years; (B): 65–75 years and (C): > 75 years. See methods for definitions of transient, persistent, remission and recurrence. HF: heart failure; MI: myocardial infarction; THF: transient heart failure.

3.1 Long-term follow-up

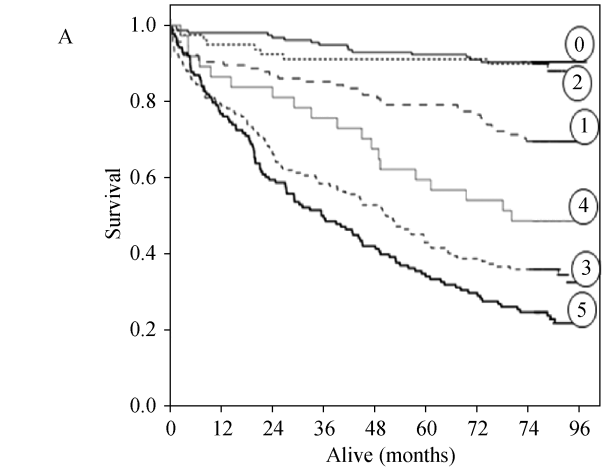
Amongst patients aged < 65 years, 65–75 years and > 75 years with persistent heart failure at discharge, crude mortalities at six years were 41%, 70% and 76%, respectively. Amongst patients with transient heart failure during the index admission, it recurred in 46%, 56% and 67% and of these 23%, 56% and 81% died in each age group, respectively. Amongst patients who did not have heart failure at discharge, 25%, 41% and 50% subsequently developed HF and of these 26%, 62% and 76% died in each age group, respectively. Thus of 271, 221 and 175 patients aged < 65 years, 65–75 years and > 75 years who survived to discharge and were not lost to follow-up, 50 (18%), 102 (46%) and 126 (72%) subsequently died, of whom 35 (70%), 93 (91%) and 107 (85%) first developed HF (Figures 3A, 3B).

A report on LV function during or shortly after the index admission was available in 228 (83%), 175 (81%) and 104 (60%) surviving patients in the three age groups and in 16, 24 and 31 patients who died during the index admission (Table 1). LVSD was associated with a greater likelihood of developing heart failure and a worse prognosis.

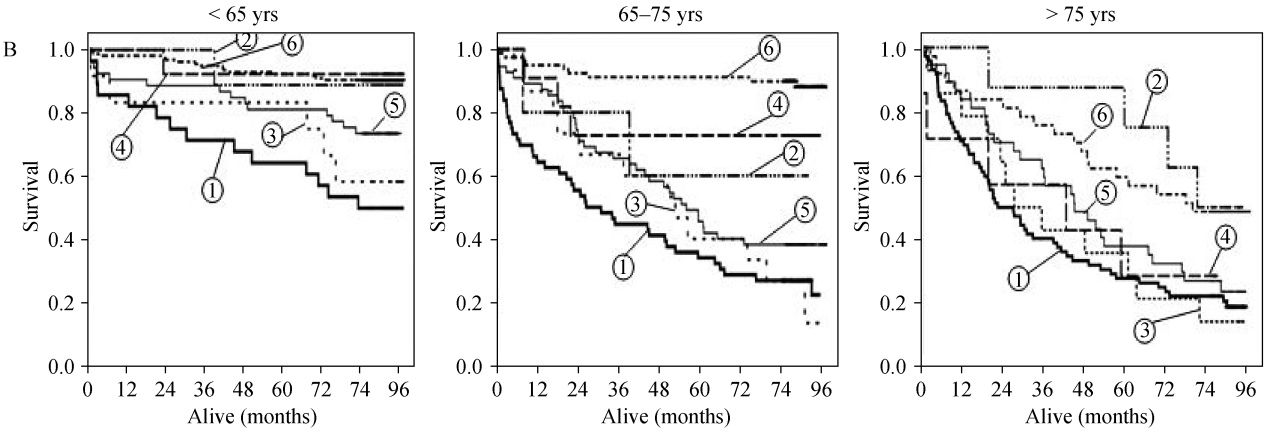
Of patients who died after the index admission, 23 (45%), 67 (66%) and 78 (61%) patients died during a re-admission to hospital in each of the three age groups (Table 2). Little detailed information was available for out-of-hospital deaths but review of existing data suggested that most were unexpected and probably sudden.

3.2 Cox model

Patients with HF during the index admission had the poorest survival across all age groups (Figure 3A and B) particularly if PHF. The increased risk conferred by PHF was marked for patients aged 65–75 years and less pronounced for patients aged > 75 years, most of whom developed HF and had a poor outcome even if they were not reported to develop HF (Table 3).



Group ID	0	1	2	3	4
	sig	sig	sig	sig	sig
1	<0.001				
2	0.650	<0.001			
3	<0.001	<0.001	<0.001		
4	<0.001	0.019	<0.001	0.88	
5	<0.001	<0.001	<0.001	0.49	<0.001



KEY:		< 65 yrs	65–75 yrs	> 75 yrs
①	HF at Index- Persistent at follow-up	28	56	72
②	HF at Index- Remission at follow-up	9	5	8
③	Transient HF at Index- Recurrent at follow-up	12	15	14
④	Transient HF at Index- Remission at follow-up	13	11	7
⑤	No HF at Index- Incident at follow-up	53	55	37
⑥	No HF at any time	156	79	37

Figure 3. The prognosis of patients discharged after the index MI according to different age groups with and without any HF. (A): Prognosis amongst patients discharged after the index myocardial infarction in different age groups (> 65 years, 65–75 years and > 75 years) with any HF (persistent or transient) and those who never developed HF; (B): Kaplan-Meier curves showing prognosis amongst patients discharged after the index myocardial infarction with and without transient or persistent heart failure according to different age group (> 65 years, 65–75 years and > 75 years). For statistical comparisons see Table 3. HF: heart failure; MI: myocardial infarction.

Table 2. Mode of death in patients who died during index admission (*n* = 199) and subsequent to discharge (*n* = 281).

	All	Age < 65 years	Age 65–75 years	Age > 75 years
	896	**311 (35%)**	**297 (33%)**	**288 (32%)**
Died during index admission	**199**	**24**	**68**	**107**
SCD	55	6	18	31
HF	114	16	38	60
Stroke	2	0	0	2
Cardiac procedures related	4	0	1	3
Other cardiac	8	1	3	4
Infection	4	0	2	2
Cancer	1	0	0	1
Other non cardiac	11	1	6	4
Died after the index admission	**281**	**51**	**102**	**128**
Died during a re-admission	**168**[a]	**23**	**67**	**78**
SCD	9	2	3	4
HF	68	8 (35%)	30 (45%)	30 (39%)
Stroke	11	1	4	6
Cardiac procedures related	2	0	2	0
Other cardiac	4	1	1	2
Infection	22	2	7	13
Cancer	24	6	8	10
Other non cardiac	27	3	12	12
Died out of hospital[b]	**113**	**28**	**35**	**50**
Severe HF[c]	16	7	5	4
Advanced cancer	9	2	2	5
Stroke	2	1	0	1
Any transient or persistent HF	**83**	**17**	**29**	**37**
Any HF with LVSD prior to death[d]	48	12	20	16
Any HF with no LV assessment	16	2	3	11
Any HF with No LVSD	19	3	6	10
Never HF	**30**	**11**	**6**	**13**
Never HF with LVSD prior to death	7	5	2	0
Never HF with no LV assessment	10	2	2	6
Any HF with No LVSD	13	4	2	7

[a]One patient with age > 75 years had missing data during last admission; [b]with age 65–75 years one patients died of self-poisoning, with age < 65 years one patient had three vessel disease and was waiting for CABG, one patient had three vessel disease and was waiting for PTCA and another had LAD disease but were not suitable for surgery and one patient 65–75 year old had severe pulmonary hypertension; [c]Severe HF during one month prior to death of whom two had missed HF (chest X-rays report were pulmonary oedema after death); [d]LVSD in last cardiac imaging prior to death P-values not calculated owing to small cell numbers. CABG: coronary artery bypass grafting; HF: heart failure; LAD: left anterior descending; LVSD: left ventricular systolic dysfunction; PTCA: percutaneous transluminal coronary angioplasty; SCD: Sudden cardiac death.

4 Discussion

This analysis shows that the development of heart failure after a MI increases steeply with age, that most patients who die subsequent to a MI will first develop heart failure and that heart failure is a powerful adverse prognostic factor. Patients aged < 65 years were least likely to get heart failure but half developed it over the subsequent six years and 70% of deaths in this age group occurred subsequent to the onset of heart failure. For patients aged 65–75 years, 73% developed heart failure during follow-up and 91% of deaths

Table 3. Cox-regression models, unadjusted and multivariate-adjusted procedures of mortality in patients subsequent to discharge (*n* = 667).

Variable	*n*	Univariate			Multivariable adjusted		
			HR	*P* value		HR	*P* value
< 65 years old	**271**						
Heart failure status*	156	**30.559**			**24.632**		
PHF-persistent at follow up	28	26.103	6.701 (3.230–13.902)	< .001	20.904	5.889 (2.754–12.593)	< 0.001
PHF-resolved at follow up	9	0.618	0.450 (0.061–3.301)	0.432	0.436	0.507 (0.068–3.802)	0.509
THF-redevelop HF	12	2.667	2.543 (0.830–7.793)	0.102	2.378	2.420 (0.787–7.439)	0.123
THF-remission at follow up	13	1.203	0.319 (0.042–2.456)	0.273	1.160	0.326 (0.042–2.508)	0.281
No HF-developed HF	53	1.035	1.512 (0.682–3.351)	0.309	0.915	1.478 (0.664–3.287)	0.339
Re-admission with MI	39	9.474	2.638 (1.422–4.893)	< .001	2.607	1.747 (0.888–3.437)	< 0.106
Re-admission with angina	51	0.019	0.950 (0.462–1.955)	0.890	0.027	0.938 (0.435–2.022)	< 0.870
65–75 years old	**221**						
Heart failure status*	79	49.172			46.855		
PHF-persistent at follow up	56	44.738	11.798 (5.724–24.315)	< .001	42.600	11.408 (5.492–23.697)	< 0.001
PHF-resolved at follow up	5	0.136	1.309 (0.313–5.483)	0.712	0.225	1.416 (0.337–5.960)	0.635
THF-redevelop HF	15	6.317	2.683 (1.243–5.791)	0.012	4.199	2.143 (1.036–4.856)	0.040
THF-remission at follow up	11	0.796	0.578 (0.173–1.929)	0.372	1.089	0.526 (0.157–1.758)	0.297
No HF-developed HF	55	4.398	1.753 (1.037–2.962)	0.036	2.433	1.525 (0.897–2.592)	0.119
Re-admission with MI	47	21.711	2.660 (1.763–4.015)	< .001	3.718	1.522 (0.993–2.334)	0.054
Re-admission with angina	39	11.348	0.267 (0.124–0.576)	< .001	8.644	0.305 (0.138-0.673)	< .001
> 75 years old	**175**						
Heart failure status*	37	14.914			12.452		
PHF-persistent at follow up	72	11.415	2.452 (1.457–4.127)	< .001	7.580	2.114 (1.241–3.603)	< 0.001
PHF-resolved at follow up	8	1.572	0.523 (0.190–1.441)	0.210	2.580	0.434 (0.157–1.202)	0.108
THF-redeveloped HF	14	3.293	1.872 (0.951–3.684)	0.070	3.266	1.869 (0.948–3.682)	0.071
THF-remission at follow up	7	0.463	1.381 (0.545–3.504)	0.496	1.184	1.689 (0.657–4.338)	0.277
No HF-developed HF	37	0.335	1.152 (0.713–1.861)	0.563	0.328	1.151 (0.711–1.863)	0.567
Re-admission with MI	59	7.351	1.641 (1.147–2.349)	< .001	1.516	1.269 (0.868–1.855)	0.218
Re-admission with angina	21	9.641	0.321 (0.157–0.658)	< .001	7.531	0.357 (0.171–0.745)	< 0.001

*With reference to No HF any time (index admission and follow up). HF: heart failure; HR: hazard ratio; MI: myocardial infarction; PHF: persistent heart failure during the index admission; THF: transient HF during the index admission.

in this group occurred subsequent to the development of HF. In patients aged > 75 years, 87% developed heart failure but the prognosis was poor whether or not overt heart failure developed. Few of those with documented substantial LVSD after a myocardial infarction escaped death or the development of heart failure over the subsequent six years. However, about half of patients in whom substantial LVSD had been excluded still went on to develop heart failure, of whom a large proportion died. Thus the prevention and management of heart failure rather than LVSD may be the most important therapeutic target in patients with heart failure.

This cohort of patients was enrolled prior to the widespread adoption of primary angioplasty and before national audits were introduced to improve the quality of care. Treatments to restore coronary perfusion were suboptimal. Studies show that thrombolysis and primary percutaneous angioplasty can reduce myocardial damage[10–12] leading to improved long-term recovery of cardiac function[13–15] and reduced mortality.[16–19] This should reduce the incidence of heart failure, although evidence in support of this hypothesis is scant. ACE inhibitors,[20] angiotensin receptor blockers,[21,22] aldosterone receptor antagonists,[23] beta-blockers[24] and statins[25] were not used optimally by contemporary

standards. Greater use might have assisted recovery in ventricular function, reduced the development of heart failure and improved prognosis. Thus, our data should not be perceived as an accurate description of outcome in contemporary patients but rather likely outcome if modern standards are not applied. Further cohorts should be enrolled to assess contemporary populations, recognising these must still be many years out of date if 5-year outcome is to be reported. Great care should be taken in case-ascertainment. Those lucky enough to reach the catheter laboratory probably have a better prognosis than those who do not, partly due to case-selection.

Hopefully, improvements in care have improved the prognosis of patients with myocardial infarction.[26] However, a repeat survey in our hospital conducted in 2005, with much higher uptake of guideline-indicated therapy, revealed a three year mortality which was still in excess of 30%, suggesting that the prognosis of MI in epidemiologically representative cohorts of patients, not just those who get to the catheter laboratory, remains poor.[27] Overall, our cohort of patients was most unlike that observed in clinical trials. The median age in our cohort in 1998 was 70 years and 35% were women.[1] This had changed little by 2005 and is similar to that reported by the Myocardial Infarction National Audit Programme (MINAP) in the UK in 2003–2005 (mean age 69 years and 36% women).[28] The Euro Heart Survey of Acute Coronary Syndromes reported a mean age of just 63 years and 29% women amongst patients with an ST elevation MI and 66 years and 36% in those with MI but no ST elevation.[29] In contemporary clinical trials of acute MI, such as the Platelet Inhibition and Patient Outcomes (PLATO) study, the median age was only 62 years, only 15% were ≥ 75 years old and 28% were women.[30] One year mortality, including in-patient deaths, was only 6%. The mean age of these patients was 61 years and only 11% were aged ≥ 75 years.[31] In the TRITON-TIMI 38 study, the median age was 61 years and only 13% of patients were aged > 75 years.[32] Overall mortality was 3% over a median follow-up of 15 months, patients aged > 75 years were more likely to reach the primary end-point (cardiovascular death, MI or stroke) (18.3% *vs*. 10.6% in those assigned to clopidogrel). These outcomes compare to in-patient and one year mortalities in our epidemiological cohorts of 22% and 31% in 1998 and 11% and 19% in 2005.[1,27] The difference in outcome between observational and trial data-sets could reflect differences in care but may also reflect differences in case ascertainment and selection. Old, frail patients with multiple comorbidities may be excluded by the protocol or may decline to participate in trials. Alternatively, investigators, for a variety of reasons including compassion and the fact that managing such cases consumes more research time and resources, may avoid enrolling frail, elderly patients. A low threshold for the detection of MI with the use of more sensitive troponin assays may also lead to an apparent improvement in prognosis, as small MIs will generally have a better prognosis than large ones. The quality of care may also be inferior in older patients. However, it is also possible that compassionate clinicians decide that palliative care is appropriate and that it is no longer appropriate to try to modify the prognosis in some older patients. The rights and wrongs must be argued on an individual case basis.

The prognosis of younger patients enrolled in many contemporary trials of acute coronary syndrome is now so good it may be difficult to improve. Clinical trials specifically amongst older patients would be valuable as they are at high risk, both in terms of prognosis and side effects of treatment. The balance of risk and benefit may differ from younger patients.[33,34] However, disease in older patients may be more resistant to modification by therapy.

The problem may not be so much chronological as biological age. Older patients have more co-morbid conditions such as AF, conducting system disease, respiratory disease, renal dysfunction, anaemia and, worst of all, heart failure. In a sense, age is a surrogate for the drivers of an adverse outcome. Identification and effective management of these co-morbidities might improve outcomes. Patients aged 65–75 years are at intermediate risk and this may be where the greatest therapeutic gains occur. It may be difficult to reduce risk in a group already at low risk, whereas in patients aged > 75 years, an effective therapy may still not be effective enough to make a meaningful difference in outcome.[35] Identifying and managing modifiable risk is key and it may be best to target intermediate risk to achieve the greatest benefit.

4.1 Study limitations

Substantial changes in management have occurred since 1998 as discussed above. Systematic attempts were not made to withdraw diuretics, therefore we may have overestimated the persistence of HF. A simple, robust definition of HF remains elusive. However, patients who receive loop diuretics and who have cardiovascular disease clearly have a poor prognosis whether or not they have a low ejection fraction.[36] Ultimately, the diagnosis of HF relies on a doctor's skill in assessing patients in the light of appropriate investigations. It is probably under- rather than over-diagnosed.

4.2 Conclusions

The development of HF precedes death in the great majority of patients who die within six years of an MI, espe-

cially amongst patients aged > 65 years. Improved prevention and management of HF and its important co-morbidities may improve outcome.

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