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Temporal trends in long-term mortality of patients with acute heart failure: Data from 1985–2008

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ABSTRACT

Background: Heart failure (HF) has a poor prognosis. Patients with acute heart failure in particular have a high risk of dying. However, there is a lack of data regarding their long-term mortality and changes there-in with time. The aim of our study was to describe trends in short- and long-term mortality of patients hospitalized with acute HF in the period from 1985 through 2008. In addition, we determined the prognostic worth of the aetiology of HF.
Methods and results: We included a consecutive series of 1810 patients with acute HF in this prospective registry in the period of 1985 through 2008. The cumulative one-year mortality rate of the patients was 35%. The short-term prognosis remained unchanged over the decades. However, the cumulative mortality rate ten years after admission was lowest in the last decade (73% in 2000–2008 vs. 78% in 1985–1999, p = 0.001). After multivariable adjustment, the ten-year mortality rate was lower in the last decade as compared to the first decade (hazard ratio (HR) 0.83; 95% confidence interval (CI) 0.71–0.96). Ischemic cardiomyopathy was associated with a higher mortality (HR 1.32; 95% CI 1.12–1.54) when compared to other causes of HF.
Conclusions: Patients admitted with acute HF were found to have both high short-term and long-term mortality. Long-term prognostic improvement in the last decade was observed among patients with a reduced ejection fraction. While patients with HF due to valvular heart disease had the best prognosis, an ischemic aetiology of HF was associated with the worst outcome.

1. Introduction

Worldwide, heart failure (HF) is a major public health issue. Its prevalence is 2%, but since HF increases with age, the prevalence is much higher in the elderly [1,2]. There are many different causes for HF [3], but ischemic heart disease is the most common aetiology of HF [1]. Other frequent aetiologies include HF secondary to uncontrolled hypertension as well as to valvular heart disease [4]. The cause of HF is related to prognosis [5].

Since the 2000s, several registries have investigated the short-term outcome in this population. In-hospital mortality rates range from 4% to 30% [4], whereas one-year mortality rates are reported to be as high as 20% to 30% [6–10]. One study has even reported a one-year mortality rate of almost 50% in patients with acute HF admitted to the intensive care or cardiac care unit [11]. With respect to longer-term outcome, prognosis is even worse, and five-year mortality figures in the order of 45–75% have been published [1,12].

In the last decades, several advances in the treatment of HF have taken place. Among others, angiotensin-converting enzyme (ACE) inhibitors, beta-blockers and mineralocorticoid receptor antagonists (MRAs) have been introduced in clinical practice [13–21]. Furthermore, the increasing use of implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy in the last decades may also have contributed also to a better prognosis [22–26]. Nevertheless, despite these improvements in the management and treatment of HF, the condition is and remains one with high mortality [1,2,27]. Importantly, there is no data regarding the trends in ten-year mortality in patients hospitalized with acute HF. Therefore, the aim of our study was to describe the trends in short- and long-term mortality of patients hospitalized with acute HF in the period from 1985 through 2008. In addition, we determined the impact of the aetiology of HF on long-term mortality.

2. Methods

2.1. Inclusion

This prospective registry included all consecutive patients from 18 years and older admitted with acute HF to the Intensive Coronary Care Unit (ICCU) of the Erasmus Medical Centre. The inclusion period started on 1st January 1985 and ended on 31st December

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2008. The Erasmus Medical Centre is a tertiary referral centre in the South-West of The Netherlands and the only referral centre for advanced HF with need for mechanical circulatory support or heart transplantation for almost half of The Netherlands. Following their initial hospitalization and treatment at our centre, most patients are subsequently transferred to a referring hospital after stabilization.

Patients were included when a diagnosis of acute HF or cardiogenic shock was made by the physician at admission. Both patients with a rapid, new onset of HF symptoms or patients with worsening of symptoms of chronic HF were included. Patients admitted for acute HF caused by an acute coronary syndrome without evidence of sustained systolic or diastolic dysfunction were excluded. If patients were admitted for acute HF more than once during the study period, only the first admission was included.

2.2. Ethics statement

This was a prospective cohort registry. During the enrolment of the patients, approval from the local research ethics committee to conduct this study was not required. The study was conducted according to the Helsinki Declaration [28].

2.3. Baseline variables

The baseline variables were extracted from the patient records or discharge letters. Only the variables until discharge from the ICCU were available as most patients are routinely transferred to a referring non-tertiary hospital after stabilization. The demographic variables age and gender were collected. The following clinical variables were also collected: prior myocardial infarction, coronary revascularization (coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI)), cardiac surgery other than CABG, heart transplantation or waiting for heart transplantation, rhythm or conduction disturbance, previous HF, hypertension and diabetes), aetiology of the HF, Body Mass Index (BMI), left ventricular ejection fraction (LVEF) and heart rate at moment of admission. Furthermore, the treatment at the ICCU was registered.

Diabetes mellitus was considered to be present when patients received antidiabetic therapy. The LVEF was classified into the following qualitative categories: good, moderate and poor. If quantitative outcome for the LVEF was used, we applied the following cut-offs: ≥45%, 30–44% and <30% for good, moderate and poor LVEF, respectively. The aetiology of HF was categorized into four groups: ischemic cardiomyopathy, non-ischemic cardiomyopathy, cardiac dysfunction due to valvular heart disease, and other/unknown aetiology. The non-ischemic cardiomyopathy group included patients with hypertensive cardiomyopathy, dilated cardiomyopathy, hypertrophic cardiomyopathy, immune-mediated cardiomyopathy, toxic cardiomyopathy, endocrine/nutritional cardiomyopathy, and peripartum cardiomyopathy.

2.4. End-point

The primary study endpoint was of all-cause mortality at one and ten years. Heart transplantation and implantation of a left ventricular assist device (LVAD) should be considered as equivalent to death.

Survival status was obtained from the Municipal Civil Registries in January 2016. The survival status was available for 98% of all included patients.

2.5. Statistical analysis

The population was divided into the following time periods: 1985–1989, 1990–1999 and 2000–2008. Categorized variables are presented as frequencies and percentages. Continuous variables are presented as mean values and standard deviation. The categorized variables were compared with the χ^2 test or the Fisher–Freeman–Halton exact test. The continuous variables were compared by using one-way ANOVA.

Data for LVEF was not complete in 28% of the patients: 51% missing in the 1980s, 23% in the 1990s and 18% in the 2000s. Therefore, multiple imputation was applied using baseline characteristics as predictors. Pooled means were given for LVEF.

Cumulative mortality curves are presented by the Kaplan–Meier method. For comparing the mortality curves, the log-rank test was used. As a secondary analysis, landmark analyses were performed for the 30-day survivors. The Cox proportional hazard model was used for comparing ten-year mortality rates, adjusted for period of admission, age, gender, history of HF, prior rhythm- or conduction disorder, diabetes in history, aetiology of HF and LVEF.

All tests were two-tailed and p-values < 0.05 were considered statistically significant. Results of the Cox proportional hazard model were reported in hazard ratios (HRs) with their corresponding 95% confidence interval (95% CI). All data were analysed using SPSS software (SPSS 21.0, IBM Corp., Armonk, NY, USA).

3. Results

3.1. Baseline characteristics

In total, 1810 patients were included, all hospitalized for acute HF in the period between 1985 and 2008. Over these periods, their baseline characteristics slightly changed (Table 1). Over time, the mean age remained stable although the percentage of patients older than 75 years increased. In addition, the proportion of male patients decreased, although male sex still represented the majority in each decade. Also, with time, patients less often had a history of prior myocardial infarction. Still, they were more likely to have undergone coronary revascularization, and to have rhythm- or conduction disorders, hypertension and diabetes mellitus. The aetiology of HF changed over time: the number of patients with ischemic cardiomyopathy decreased, while the number of patients with a non-ischemic cardiomyopathy increased. Valvular heart disease became a less common cause of HF. The distribution of LVEF did not change over time.

The median length of stay at the ICCU was 2 days (interquartile range: 1 to 4 days) and did not differ between the three decades ($p = 0.28$). The heart rate at admission was 106 ± 26 beats per minute and was similar in all periods ($p = 0.68$). Therapy during ICCU hospitalization changed over time (Table 2). For instance, more patients received mechanical ventilation in the most recent decade. In the period 1990–1999, inotropic drugs and nitrates were more often prescribed than in the other decades, while the use of mechanical circulatory support increased. The use of beta-blockers and ACE-inhibitors or angiotensin receptor blockers (ARBs) increased over time, while therapy with digitalis decreased.

3.2. Mortality over time

During the whole follow-up time, 1555 (86%) patients reached the primary endpoint: 1474 (81%) patients died, 77 (4%) patients underwent heart transplantation and 4 (0.2%) LVAD implantation. The cumulative mortality rate at one and ten years was 35% and 76%, respectively. The ten-year cumulative mortality curve of the three periods is depicted in Fig. 1. Early mortality rates at 30 days and 1 year after admission were similar in all decades. In contrast, the cumulative mortality rate ten years after admission was lowest in the last decade (73% in

Table 1
Baseline characteristics.

	1985–1989	1990–1999	2000–2008	p-value
No. of patients	389	842	579	
Baseline				
Age (mean, y)	62 ± 13	64 ± 15	64 ± 15	0.24
Age categories				0.008
18–54 years	100 (26%)	209 (25%)	142 (25%)	
55–64 years	102 (26%)	170 (20%)	127 (22%)	
65–74 years	129 (33%)	258 (31%)	171 (30%)	
75 years and older	58 (15%)	205 (24%)	139 (24%)	
Male	273 (70%)	510 (61%)	370 (64%)	0.005
BMI	24 ± 5.2	25 ± 4.4	26 ± 5.4	0.01
Medical history				
Myocardial infarction	185 (48%)	332 (39%)	197 (34%)	<0.001
Coronary revascularization*	78 (20%)	150 (18%)	162 (28%)	<0.001
Heart surgery (not CAGB)	52 (13%)	103 (12%)	82 (14%)	0.56
Heart transplantation	1 (0.3%)	5 (0.6%)	3 (0.5%)	0.83
Waiting for heart transplantation	9 (2%)	14 (2%)	12 (2%)	0.68
Heart failure	188 (48%)	403 (48%)	297 (51%)	0.42
Rhythm- or conduction disorder	90 (23%)	183 (22%)	173 (30%)	0.001
Hypertension	91 (23%)	275 (33%)	224 (39%)	<0.001
Diabetes	56 (14%)	174 (21%)	154 (27%)	<0.001
Heart failure				
Aetiology of heart failure				0.02
Ischemic cardiomyopathy	171 (44%)	332 (39%)	237 (41%)	
Non-ischemic cardiomyopathy	61 (16%)	198 (24%)	143 (25%)	
Valvular heart disease	91 (23%)	178 (21%)	101 (17%)	
Other/unknown	66 (17%)	134 (16%)	98 (17%)	
Atrial fibrillation at admission	79 (20%)	181 (22%)	131 (23%)	0.69
Left ventricular ejection fraction				NS
Good	112 (29%)	255 (30%)	159 (27%)	
Moderate	83 (21%)	208 (25%)	139 (24%)	
Poor	195 (50%)	379 (45%)	281 (49%)	

BMI, body mass index; CABG, coronary artery bypass graft; NS, non-significant *percutaneous coronary intervention and/or CABG.