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Risk and predictors of readmission for heart failure following a myocardial infarction between 2004 and 2013: A Swedish nationwide observational study☆,☆☆

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A B S T R A C T

Background: Data are scarce regarding the risk, temporal trends and predictors of late-onset heart failure (LOHF) after acute myocardial infarction (AMI). We aimed at studying the risk and predictors of LOHF and the composite event of LOHF or death after AMI.
Methods: AMI patients first entered in the nationwide SWEDEHEART registry between 2004 and 2013 were included. Patients with a prior history of heart failure (HF) and those who died in-hospital were excluded. Dates and ICD-codes for LOHF in the national patient and death registries were used to determine time to first readmission due to LOHF and/or death.
Results: A total of 150,566 AMI patients were included in the analysis. The 1-year, 2-year and 5-year cumulative risk of developing LOHF were 11.4%, 14.6% and 21.8% respectively. The risk of LOHF within 2 years decreased from 15.5% to 14.4% (2004–2005 vs 2010–2011), $p < 0.001$. Calendar year was protective of LOHF/death after adjustment (HR 0.96, 95% CI 0.94–0.98, $p < 0.001$). In-hospital HF, age, diabetes mellitus, chronic kidney disease, peripheral arterial disease, chronic obstructive pulmonary disease and atrial fibrillation, were strong predictors of LOHF. Risk profile improved and use of evidence based therapies increased during the time period.
Conclusions: Survivors of AMI remain at a continued risk of LOHF. However, the overall risk of LOHF shows a decreasing trend after an index AMI over time. Lower risk of LOHF may relate to decreasing burden of comorbidities and increasing use of evidence based treatments.

1. Introduction

Ischemic heart disease is a common cause of heart failure (HF) [1–3]. Studies have shown decreases in the incidence and severity of acute myocardial infarction (AMI) which are partly ascribed to the growing use of coronary artery revascularization procedures and better medical treatment [4–6] though mainly attributable to a reduction in major risk factors [7]. Similarly, a decreasing incidence of HF irrespective of etiology has been shown during recent years [8,9]. HF ranks as the most frequent cause of hospitalization among older individuals [10, 11]. Although there is some evidence that the incidence of HF hospitalizations may be declining [5,11–14], others claim that improving survival after AMI has made a major contribution to the reported epidemic of HF [15–17]. HF that occurs post AMI is particularly serious because of its association with a considerable increase in the risk of death. In a nationwide study we have shown a marked decrease of in-hospital HF during the reperfusion era, in particular in ST-elevation MI (STEMI) patients and a subsequently lower short and long-term mortality risk for those who developed in-hospital HF in the later years [18]. There is still a lack of contemporary studies examining time trends and predictors of late-onset heart failure (LOHF).

Using a nationwide coronary care registry we aimed at analyzing the incidence of late-onset heart failure, its predictors and temporal trends among patients admitted for an index AMI and followed over time.

2. Methods

The nationwide Swedish Web-system for Enhancement and development of Evidence-based care in Heart disease evaluated according to recommended Therapies (SWEDEHEART) [19,20] registry enrolls consecutive patients with symptoms suggestive of an acute coronary syndrome admitted to a coronary intensive care unit or coronary catheterization lab in Sweden. Information on baseline characteristics such as age, BMI, smoking status, ECG findings as well as other examinations, interventions, complications, discharge

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medications and diagnoses are prospectively collected and entered into the registry. Data on comorbidities were also collected from the National Patient Register, which includes all hospital diagnoses or specialized outpatient diagnoses. In-hospital clinical outcomes, such as ECG findings, type of AMI, cardiogenic shock (CS), and left ventricular ejection fraction (LVEF) before discharge were obtained from SWEDEHEART. Data on death (up to 31-Dec-2013) were obtained from the National Population Register. A hospital diagnosis of HF in Sweden has been validated against ESC criteria for the definition of HF, with a validity of 95% for a principal diagnosis and 82% irrespective of position [21]. Data on hospitalization for HF after discharge from the index AMI admission (up to 31-Dec-2013) were obtained from the national patient register and defined as a new hospitalization for HF (WHO's ICD-10 coding). Data from the above mentioned registers were merged into a single database using a unique personal identification number. Late onset HF was defined prospectively if the patient was rehospitalized and diagnosed as having HF as principal or secondary diagnosis.

In-hospital HF was defined by the presence of pulmonary rales or use of i.v. diuretics or i.v. inotropic drugs during hospitalization for the index AMI. Based on echocardiographic LVEF data during hospitalization patients were categorized into four groups: Those with signs of HF and normal EF (≥50%) (HFNEF), those with signs of HF and reduced EF (<50%) (HFREF), those with normal EF ≥50% (NEF) and no signs of HF and those with reduced EF <50% (REF) and without signs of HF. EF is registered as a category and not as a digit in the registry and we are therefore unable to present EF as a digit. The study design is an observational cohort study with prospectively collected data. The regional ethics committee in Stockholm approved this study.

2.1. Study population

A total of 177,645 AMI patients were entered in the SWEDEHEART registry for the first time between 2004 and 2013. Among these 19,483 were excluded from the study because of prior history of HF. Additionally 7416 patients were excluded due to in-hospital mortality. The study population comprised a total of 150,566 AMI patients.

2.2. Statistical analysis

Baseline characteristics by LOHF and the composite event of LOHF/death status, are presented as numbers and percentages for categorical variables. Continuous parametric variables are expressed as means (±standard deviation) and medians (IQR). Qualitative data were compared using Pearson's Chi-square test while quantitative data were compared using independent student *t*-test. Chi-square test for trend was used to test changes in temporal trends. Factors predicting the risk of LOHF and the composite of LOHF/death were explored in a univariable and multivariable cox-regression model with LOHF or LOHF/death as the outcome (dependent) variable and all covariates described below as predictor (independent) variables. In the multivariable model, all variables associated with the evaluated endpoint at the 0.05 level in the univariable analysis were entered in the model and removed using a backward stepwise likely-hood ratio selection process for determination of predictors of late onset HF. For each covariate, HR, 95% CI and p-value are reported.

Covariates included in the multivariable analysis were age, sex, comorbidities (diabetes mellitus (DM), hypertension, chronic kidney disease (CKD), peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), previous MI, previous stroke, previous cancer diagnosis, newly diagnosed atrial fibrillation (AF) on electrocardiogram (ECG) during admission), type of AMI (STEMI/LBBB vs Non-STEMI) and calendar year (2004–2008 vs 2009–2013), and in-hospital HF (AHF). In-hospital HF (AHF) was defined by the presence of crepitations or use of i.v. diuretics and/or iv inotropes during admission as in previous studies [18,22]. The cumulative probability of HF readmission and HF readmission or death was illustrated with Kaplan-Meier time to event curve estimates. To handle the competing risk of death, predictive models predictive of LOHF/death and death are calculated and presented together with Kaplan-Meier curve for LOHF as outcome variables. Statistical analyses were performed using SPSS 23.0 for Macintosh (IBM).

3. Results

3.1. Baseline characteristics and in-hospital management

Out of 150,566 AMI survivors without prior HF entered in the registry for the first time between 2004 and 2013, 19.4% (n = 29,194) were readmitted because of HF during the study period, with a median follow up of 4 years. Patients with LOHF and those with LOHF or death were older, more often women and with higher burden of comorbidities such as DM, hypertension and CKD compared to patients who did not develop late-onset HF (Table 1). Previous illnesses such as stroke, PAD, prior MI, and COPD were also more prevalent in patients who developed LOHF and LOHF or death during follow-up. The proportion of STEMI patients was fairly similar in patients with and without LOHF. In-hospital HF (AHF), cardiogenic shock (CS), pathological ECG changes, reduced left ventricular ejection fraction (LVEF) and newly diagnosed AF during hospitalization for AMI were more prevalent in patients with LOHF. The proportion of patients treated by PCI was lower in those who developed LOHF during follow up compared to those who did not develop LOHF.

3.2. Changes in traditional risk factors and treatment patterns

Comparing the cohorts of 2004–2005 and 2012–2013, mean age was relatively unchanged (69.9 vs 69.7), prevalence of DM remained unchanged and comorbidities such as CKD, prior stroke, prior AMI, PAD and in-hospital HF decreased, while the proportion of hypertension, COPD and NSTEMI increased. The use of revascularization treatment (PCI and CABG) and evidence based pharmacologic treatments increased progressively and substantially over the study period (Supplemental material, Table S1).

3.3. Late-onset HF

The 1-year, 2-year and 5-year cumulative risk of developing LOHF were 11.4%, 14.6% and 21.8% respectively. The, 1-year, 2-year and 5-year cumulative risk of the composite event of LOHF/death were 16.6%, 22.4% and 35.8% respectively (Fig. 1).

The risk of developing LOHF within 2 years after discharge decreased from 15.5% to 14.4% between the cohorts included in 2004–2005 and 2010–11, $p < 0.001$. Among patients who did not develop in-hospital HF during the index admission 9.0% developed late-onset HF within 2 years for the cohort 2004–2005 while 9.4% developed late-onset HF within 2 years for the cohort between 2010 and 11 ($p < 0.001$). Among patients who developed in-hospital HF during the index admission, 31.1% developed LOHF within 2 years for the cohort 2004–05 and 35% for the cohort 2010–11 ($p < 0.001$) (Supplemental material, Fig. S1). The risk of LOHF decreased at 2 calendar year intervals across the study period in the Univariate analysis (Fig. 2).

3.4. Univariable predictors of LOHF

Increasing age, AHF, PAD, previous cancer diagnosis, diabetes mellitus, COPD, CKD, female gender, hypertension, prior MI, prior stroke and AF during the index admission increased the risk of LOHF whereas STEMI/LBBB and calendar year (2009–2013 vs 2004–2008) were associated with lower risk (Table 2).

3.5. Multivariable predictors of LOHF

After adjustment, age per five year increase, male gender and presence of ST-segment elevation on admission ECG were associated with an increased risk of LOHF and the composite event of LOHF/death. AHF increased risk of LOHF by 2–3 fold. Comorbidities such as COPD, CKD, PAD, DM, AF, prior stroke and previous history of cancer increased the risk of LOHF significantly. Calendar year (2009–2013 vs 2004–2008) was associated with a lower risk of LOHF and LOHF/death in the univariate analysis while it was associated with a marginally higher risk of LOHF and remained protective of the composite of LOHF/death in the multivariable analysis (Table 2).

The risk of LOHF in a given patient with AMI was considerably higher with increasing burden of co-morbidities. Compared to patients who had no identified risk factors, the risk of LOHF after AMI increased by 90% with one risk factor, by 226% with 2 risk factors, and by 450% with 3 or more risk factors (Supplemental material, Fig. S2). Comorbidities included in the model were, hypertension, diabetes mellitus, COPD, CKD, prior MI and prior stroke.

3.6. In-hospital HF by EF-category

Compared to patients with no clinical HF and normal ejection fraction (NEF), the risk of HF readmission was much higher for patients with in-hospital HF and normal ejection faction (HFNEF). In-hospital HF with reduced EF (HFREF) was associated with higher risk of HF

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