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Trends in mortality and heart failure after acute myocardial infarction in Italy from 2001 to 2011☆

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ABSTRACT

Background: Uncertainties on long-term outcomes after acute myocardial infarction (AMI) still exist, despite the ongoing progresses in the management of patients with AMI.
Aim of the study: Our aim was to appraise both the early prognosis and prognosis at 1-year after discharge of patients hospitalized due to AMI.
Methods: This is a retrospective nationwide cohort study based on data from an administrative database on patients admitted with AMI from 2001 to 2011 in all Italian hospitals sites. Mortality and readmission rates within 30 days, 60 days and 1 year were calculated, as well as re-hospitalizations for all causes and for HF.
Results: A total of 1,110,822 patients were included. Index admission mortality rate (I-MR) and total in-hospital mortality rate (T-MR) at up to 1 year both decreased respectively from 11.34% to 8.99% and from 16.46% to 14.68% in the years 2001 to 2011 (both $p < 0.0001$), while fatal readmission rate (F-RR) at 1 year increased from 4.75% to 5.28% ($p = 0.0019$). Patients that developed HF during the index admission had significantly higher I-MR and F-RR. I-MR, F-RR, and T-MR, however, remained low at any time point considered (30 days, 60 days and 1 year) in a subgroup of low-risk optimally-treated patients.
Conclusions: The risk of fatal readmission at 1 year increased slightly over time, in spite of the remarkable improvements currently achieved in overall prognosis after AMI. The identification of patients at high risk (mainly due to HF complicating AMI), and of patients at low risk is crucial to define and support management strategies.

1. Introduction

Many reports published during the last decade have shown a steady reduction of in-hospital mortality due to acute myocardial infarction (AMI) [1–5]. This decrease has generally been considered as a consequence of the progresses reached in the in-hospital management of cardiovascular diseases in developed countries. These progresses are mainly due to the introduction and adoption in clinical practice of either fibrinolytic or mechanical reperfusion, and to the diffusion of pharmacological therapies including beta-blockers, angiotensin-converting enzyme inhibitors, antiplatelet agents and statins. The proportion of patients with ST segment elevation myocardial infarction (STEMI) has concurrently decreased in several countries as compared to the proportion of patients with non-ST segment elevation myocardial infarction (NSTEMI). Continuous efforts in the primary prevention of MI may have led to a variation in the frequency of different types of AMI, with smaller infarcts becoming more common than larger ones, in spite of a less favorable overall profile of index patients who became older and having a higher number of comorbidities [6]. However, it is still unclear if the increase in survival during index hospitalization actually continues after discharge. Apparently, while in-hospital mortality seems to decrease, some authors reported a paradoxical increase in short and long-term post-discharge deaths [2,7–10]. The increasing prevalence of heart failure (HF), mainly among the elderly with AMI, has been considered as one of the possible explanations for these unfavorable trends, along with all the potential implications on the organization of post-acute care services [7,11–14]. Most of the evidence supporting these hypotheses, however, is based on data from registries, which may be limited by selective and non-consecutive enrolment causing lower external validity [15].

We aimed at analyzing short- and long-term mortality trends among patients with AMI based on a large, comprehensive and universal administrative database including more than one million of patients over 11 years, with a special focus on the outcomes of patients surviving the index admission date and discharged with a diagnosis of heart failure.

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2. Material and methods

2.1. Study design

This was a retrospective cohort study based on data from an administrative database including all Italian hospital admissions and discharges. Given the retrospective nature of the study and the use of anonymized patient data, ethical approval was not required.

2.2. Study population

The Italian National Registry of Hospital Discharge Records (HDR), including all records from January 1, 2001 and December 31, 2012 was used as the main source of data. All hospital discharge records of patients aged 18 to 100 years, resident in Italy, and reporting a primary diagnosis of AMI (International Classification of Disease, 9th Revision, Clinical Modification [ICD 9 CM] 410) or a secondary diagnosis of AMI with any concomitant AMI complication within the primary diagnosis (ICD-9-CM codes 411, 413, 414, 426, 427, 428, 423.0, 429.5, 429.6, 429.71, 429.79, 429.81, 518.4, 518.81, 780.01, 780.2, 785.51, 799.1, 997.02 and 998.2) were selected (*Outcomes evaluation National program [PNE] Ed. 2013; available at* http://95.110.213.190/PNEed13/). All patients alive at discharge (within 48 h from admission) and all patients with a previous AMI admission (within 30 days from the index admission) were excluded to minimize the inclusion of false AMIs and multiple admissions due to the same event [16,17]. For the purpose of this study AMI was classified as complicated by HF if a patient was discharged with a diagnosis of AMI and an additional diagnosis of HF (ICD-9-CM codes 428 [heart failure], 518.4 [acute pulmonary edema], and 785.51 [cardiogenic shock]). HF was chosen among all the other possible AMI complications, as the most suitable diagnosis to assess the prognosis of patients with AMI, their quality of life, and the impact on the national health system (in particular the need of re-hospitalizations) [18–20].

A group of “low-risk AMI patients” was identified as “ideal benchmark” of optimally-treated patients with which to compare the high-risk group. This “low risk” group was defined according to previously published studies as patients having <70 years, with no heart failure at the time of the index admission, and treated with PTCA within 48 h from the admission [21].

2.3. Outcomes

Short- and mid-term mortality and readmission rates, and mortality and readmission within 30 days, 60 days and 1 year were considered as the main adverse outcomes. The Italian national HDR system cannot be systematically linked with comprehensive mortality registers, thus mortality rates refer only to events occurred during hospitalization. On this basis, three different in-hospital mortality estimates were computed for each time-point: index admission mortality rate (I-MR), total in-hospital mortality rate (T-MR) and fatal readmission rate (F-RR). Accordingly, I-MR refers to patients who died during the index admission for AMI (including transfers), T-MR refers to patients who died during the index admission for AMI or during any other subsequent admission within the considered time span, and F-RR refers to patients who were alive at discharged from the index admission but died during any other subsequent admission within the considered time span.

Readmission rates due to HF were also considered and calculated dividing the number of patients who had at least one re-hospitalization due to HF as primary diagnosis within the considered time span by the number of patients who were alive at discharge from the index admission. Trends in the proportion of re-hospitalizations from 2001 to 2011 were then analyzed.

2.4. Statistical analysis

A set of general linear models were designed to calculate annual variations in mortality and their corresponding 95% confidence intervals (CI). The goodness-of-fit of the linear regression models was assessed with the R^2 test and the probability value for the F test statistic. Trends of risk ratios between F-RR and I-MR were analyzed for each selected time point. Multivariate logistic regression analyses were performed, adjusting for age, sex, comorbidities, and invasive cardiac procedures, to provide adjusted outcome data. Re-hospitalizations due to HF within the considered time spans were analyzed separately for patients with AMI who did and did not develop HF during the index admission. All assumptions of statistical methods were explicitly checked. Statistical analyses were performed using SAS 9.2 (Cary, NC, USA).

3. Results

A total of 1,110,822 AMI events occurred from 2001 to 2011, were included. Results referring to the years 2001 to 2012 showed an increase in the proportion of NSTEMI from 23.2.% to 48.2% and a decrease in the proportion of STEMI decreased from 76.8% to 52.8%, while age remained substantially unchanged over time (mean age from 69.3 to 70.6 years) (p of trend = NS). I-MR decreased significantly from 11.34% to 8.99%, with a mean annual change of −0.23% (CI −0.27% to −0.20%). T-MR showed a significant decrease within each time span, specifically, T-MR within 30 days, 60 days and 1 year from index admission decreased respectively from 12.01% to 9.67%, from 13.12% to 10.93, and from 16.46% to 14.68%. Multivariate logistic regression analyses confirmed a significant decrease in in-hospital mortality rate (I-MR) per year after index admission (odds ratio [OR], 0.977; $p < 0.001$), and a significant decrease in total in-hospital mortality rate (T-MR) per year within 30 days (OR, 0.977; $p < 0.001$) and 60 days (OR, 0.988; $p < 0.0001$). The Cox regression model, adjusting for the above confounders, also showed a significant decrease in total in-hospital mortality rate within 1 year from index admission (hazard ratio [HR], 0.993; $p < 0.001$).

The percentage of patients who, between 2001 and 2011, were alive at discharge from the index hospitalization but were re-hospitalized and died during the stay, remained unchanged at 30 days (about 0.7%), and increased slightly at 60 days. However, this change of F-RR became larger and statistically significant at 1 year (mean annual change 0.04% [0.02% to 0.06%; $p = 0.0019$]) (Table 1).

Risk ratios between 1-year F-RR and 1-year I-MR showed a steady increase over the years (Fig. 1), while both the yearly admissions due to AMI and the number of AMI patients developing HF during the index admission showed no substantial variation over the years, with around 100,000 admissions due to AMI and 20,000 patients with AMI and HF from 2001 to 2011. Therefore, our findings show a prevalence of around 20% of HF complicating AMI that remains substantially, stable over time. Patients who had a diagnosis of HF during the index admission showed an almost 4-times higher mortality rate than those who did not have a diagnosis of HF, even if favorable mortality trends were confirmed in both groups (Fig. 2). In particular, patients with HF complicating AMI, showed a decrease in I-MR from 26.53% to 23.21%, and a decrease in T-MR at 30 days, 60 days and 1 year respectively from 27.70% to 24.40%, from 29.94% to 27.07%, and from 36.08% to 33.90%.

AMI patients with no diagnosis of HF at the index admission showed a decrease in I-MR from 6.97% to 4.83%, and a decrease in T-MR at 30 days, 60 days and 1 year respectively from 7.50% to 5.38%, from 8.29% to 6.22%, and from 10.82% to 9.07%. F-RR either remained stable or showed a slight increase over time, in spite of these favorable trends. F-RR, remained around 1% at 60 days in patients with no diagnosis of HF at the index admission, while raised from 2.63% to 2.95% in patients with HF complicating AMI. F-RR increased from 3.63% to 4.04% at 1 year in patients with no diagnosis of HF at the index admission and