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Original article

Treatment and outcomes of patients with recurrent myocardial infarction: A prospective observational cohort study☆

Dragana Radovanovic (MD)[a,*], Lea Maurer (BMed)[a], Osmund Bertel (MD)[b], Fabienne Witassek (MSc)[a], Philip Urban (MD)[c], Jean-Christophe Stauffer (MD)[d], Giovanni Pedrazzini (MD)[e], Paul Erne (MD)[f]

[a] AMIS Plus Data Center, Epidemiology, Biostatistics and Prevention Institute, University of Zurich, Zurich, Switzerland
[b] Cardiology Center, Klinik im Park, Zurich, Switzerland
[c] Cardiovascular Department, La Tour Hospital, Geneva, Switzerland
[d] Service de Cardiologie, Hôpital Cantonal, Fribourg, Switzerland
[e] Division of Cardiology, Cardiocentro Ticino, Lugano, Switzerland
[f] AMIS Plus, Zurich, Switzerland

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ABSTRACT

Background: Little is known about differences in therapies and outcomes of patients with first myocardial infarction (MI) or recurrent MI (reMI). This study aimed to evaluate the impact of prior MI on therapies and outcomes in patients who presented with ST-elevation MI (STEMI).
Methods: All STEMI patients enrolled from 2002 to 2014 in the AMIS Plus registry were included. Outcome was analyzed using logistic multivariate regression.
Results: From 19,665 STEMI patients, 2845 (14%) had reMI. These patients were older (69.5y vs. 64.2y; $p < 0.001$), more frequently male, with more risk factors (hypertension, dyslipidemia), and more comorbidities. Patients with reMI presented 25 min earlier than those with first MI, were more frequently in Killip class 3/4 (12% vs. 7%; $p < 0.001$), and were less likely to receive guideline-recommended drug therapy: aspirin (93% vs. 97%; $p < 0.001$), $P2Y_{12}$ inhibitors (76% vs. 83%; $p < 0.001$), or statins (73% vs. 77%; $p < 0.001$), or undergo primary percutaneous coronary intervention (77% vs. 87%; $p < 0.001$). These patients developed more frequently cardiogenic shock (7% vs. 5%; $p < 0.001$) and reinfarction (2% vs. 1%; $p < 0.001$) during hospitalization, and had higher crude mortality (10% vs. 5%; $p < 0.001$) than patients without prior MI. Prior MI was an independent predictor of in-hospital mortality in STEMI patients (OR 1.27; 95% CI 1.05–1.53; $p < 0.001$).

A subgroup ($n = 4486$) was followed 1 year after discharge (3893 with first MI and 593 with reMI at initial hospitalization). Crude mortality was 2.9% for patients with first MI vs. 6.7% for those with reMI (OR 1.68, 95% CI 1.14–2.47; $p = 0.008$).
Conclusions: Although patients with reMI are high-risk patients, they were less likely to receive evidence-based treatment and had worse in-hospital and 1-year outcomes compared to patients with first MI. Short- and long-term management of patients with recurring MI should be improved.

Introduction

Survivors of acute myocardial infarction (AMI) have a substantial risk of recurrent infarction after discharge. In the HORIZONS AMI Trial, a prospective study of patients with ST-elevation myocardial infarction (STEMI) who were all treated with primary percutaneous coronary intervention (PCI), the 3 year incidence of recurrent myocardial infarction (MI) was 6.9% [1]. Many studies that investigated various factors which could be associated with a reduced risk of recurrent MI such as drugs, risk factors, or comorbidities, emphasize the importance of secondary prevention after the first coronary event [2–7].

However, little is known about pretreatment, presentation patterns, in-hospital treatment, and outcome of patients with reinfarction who are not enrolled in studies of highly selected subgroups of STEMI patients.

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* Corresponding author at: AMIS Plus Data Center, Epidemiology, Biostatistics and Prevention Institute (EBPI), University of Zurich, Hirschengraben 84, 8001 Zurich, Switzerland. Tel.: +41 44 634 48 34; fax: +41 44 634 49 86.
E-mail address: dragana.radovanovic@uzh.ch (D. Radovanovic).

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We need to find out what the patients or doctors in charge of the patients have learnt from their experiences of a first MI.

We therefore present data from a nationwide infarction registry on patients who were admitted with STEMI with or without history of prior MI comparing their presentations, in-hospital treatments, outcomes, and 1-year follow-up.

Methods

The AMIS Plus project is an ongoing nationwide prospective cohort of patients admitted with acute coronary syndromes (ACS) to hospitals in Switzerland. It was founded by the Swiss Societies of Cardiology, Internal Medicine, and Intensive Care Medicine in 1997 with the goal to understand the transfer, use, and practicability of knowledge gained from randomized trials in the real world of daily clinical practice. Details have been previously published [8–16].

Among 106 hospitals treating ACS in Switzerland, 83 hospitals temporarily or continuously enrolled patients in AMIS Plus. Participating centers, ranging from community institutions to large tertiary facilities, provided blinded data for each patient through standardized internet- or paper-based questionnaires. All data were checked for completeness, plausibility, and consistency by the AMIS Plus Data Center in the Epidemiology, Biostatistics and Prevention Institute at the University of Zurich, and treating physicians or study nurses were queried when necessary. External monitoring has been carried out regularly since 2010 in randomly selected hospitals using randomly selected cases. The registry was approved by the Supra-Regional Ethics Committee for Clinical Studies, the Swiss Board for Data Security, and all Cantonal Ethics Commissions. Data collection is conducted in accordance with the EU Note for Guidance on Good Clinical Practice CPMP/ECH/135/95 and the Declaration of Helsinki.

The case report form comprised items addressing medical history, comorbidities, known cardiovascular risk factors, clinical presentation, out-of-hospital management, early in-hospital management, reperfusion therapy, hospital course, used or planned diagnostic tests, length of stay, drugs taken regularly before admission, discharge medication, and discharge destination. Patients were enrolled on the basis of their final discharge diagnosis.

Information on known risk factors was obtained from the patient's medical history. Patients were stated as having dyslipidemia, arterial hypertension, and diabetes if they had been previously treated for such a condition and/or diagnosed by a physician. Patients were defined as obese if the body mass index was $\geq$30 kg/m^2 and as smokers if they smoked at the time of the cardiovascular event. Patient comorbidities were assessed using the Charlson Index [17,18]. Immediate drug therapy was defined if administered within 24 hours after admission. Bleeding complications were recorded if deemed clinically relevant by the individual physician in charge of the patient, without the use of a classification system when data collection started. Reinfarction was defined as clinical signs or symptoms of ischemia with electrocardiographic changes indicative of new ischemia [new ST-changes or new left bundle branch block (LBBB)] and a re-rise of biomarkers following the initial infarction. A stroke was defined as any event due to ischemic, thrombotic, or hemorrhagic disturbances confirmed by a neurologist or imaging modality.

The primary outcome measure was in-hospital mortality. Secondary outcome measures were the rates of in-hospital major adverse cardiac or cerebrovascular events (MACCE) defined as a composite endpoint of mortality, reinfarction, and cerebrovascular events. An additional outcome measure in a subgroup of patients was 1-year mortality.

Patient selection

The present analysis included all STEMI patients enrolled in AMIS Plus between 2002 and 2014. STEMI was defined by characteristic symptoms, ST-segment elevation or new LBBB on the initial electrocardiogram and cardiac marker elevation (creatine kinase MB fraction at least twice the upper limit of normal, or troponin I, troponin T, or high-sensitive troponin above individual hospital cut-off levels for AMI).

In addition, patients were divided into two groups according to medical history of previous MI and compared in terms of presentations, treatments, and outcomes.

Subgroup analyses of 1-year mortality after discharge were performed using patients enrolled from 2006 to 2014, who had signed an informed consent form for follow-up participation.

Statistical analysis

The results are presented as percentages for categorical variables and analyzed using the non-parametric Pearson chi-square test or Fisher's exact test as appropriate. Continuous normally distributed variables are expressed as means $\pm$ 1 standard deviation (SD) and compared using the Student's two-tailed unpaired *t*-test. Continuous non-normally distributed variables are expressed as median and interquartile ranges and analyzed using the Mann–Whitney *U* test. The differences in clinical signs at presentation, risk factors, comorbidities, and therapies between the groups were additionally adjusted for age and gender.

A univariate analysis was carried out using all available variables and only calculated for patients with no missing variables. To determine which patient characteristics were independent predictors of in-hospital mortality a multivariate logistic regression model was first performed using the following variables: past history of MI, age, sex, Killip class >2, the risk factors dyslipidemia and hypertension, and the comorbidities diabetes, renal disease, cardiovascular disease, cancer, gastric, and chronic lung diseases. Comorbidities were also expressed as a Charlson comorbidity weighted index >1 [17,18]. To assess the impact of time, the time period of the event was also included in the regression model. To determine all independent predictors of in-hospital mortality, the guideline-recommended reperfusion and drug therapies [19] were additionally included in the regression model. The results of logistic regression analysis are reported as an odds ratio (OR) with a 95% confidence interval (95% CI). A probability value of p less than 0.05 was considered significant. The IBM SPSS Statistics Version 22 (Armonk, NY, USA: IBM Corp.) was used for statistical analyses.

Results

Between 2002 and 2014, a total of 20,551 patients with STEMI were enrolled in the AMIS Plus cohort and 19,665 (95.7%) had valid data on past history of MI and were included in this study (Fig. 1).

Of the patients, 2845 (5%) had prior MI. Table 1 shows the baseline characteristics of these patients compared to the 16,820 patients with first STEMI. Patients admitted with recurrent MI were 4 years older in mean age, more often male, presented frequently with less pain and more dyspnea, more atrial fibrillation, and were more often in Killip class 3 or 4 at admission. They more frequently had hypertension, dyslipidemia, and more comorbidities. Patients with recurrent MI suffered their prior MI, a median of 49 months (IQR 21–96 months) previously. The first medical contact median was 25 minutes earlier than patients with a first MI and their infarction was smaller, based on the peak CK blood levels (Table 1).

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