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Long-term outcomes after myocardial infarction: A cohort study in the French national claims database

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Abstract

Background: Long-term survival and factors influencing long-term survival after myocardial infarction are rarely described in clinical trials**. Objectives:** The present study aimed to describe real-life outcomes in stable post-myocardial infarction (MI) patients. **Methods:** One-year event-free post-MI patients were identified in the French claims database representative 1/97 sample (2005-2010) and followed up for 3 further years. Outcomes were a composite of all-cause death or hospital admission for MI or stroke, the individual events, and major bleeding. Analysis used fully adjusted multiple Cox proportional hazards models. **Results:** There were 1585 post-MI patients totalling 3926 person-years (PY); 68% were male; mean age was 66 (SD 15) in post-MI. At inclusion, one year after the initial MI, 98.2% of all patients were still exposed to evidence-based secondary prevention drugs (EBD) including aspirin (88.5%), beta-blockers (86.1%), angiotensin converting enzyme inhibitors or angiotensin receptor blockers (82.0%), and statins (90.9 %). Outcomes per 100 PY [95%CI] were 6.3 [5.6-7.1] for the composite outcome, 5.1 [4.4-5.8] for all-cause death; 1.0 [0.7-1.3] for MI; 0.6 [0.4-0.9] for stroke; 1.3 [0.9-1.6] for major bleeding. Event rates were stable over the three study years. Factors present at inclusion associated with outcomes were: for death, age (HR [95%CI] 1.05 [1.03; 1.06] per year, diabetes (1.53 [1.13; 2.08]), previous ACS (1.40 [1.00; 1.97]), atrial fibrillation (1.49 [1.06; 2.10]), heart failure (1.56 [1.14; 2.14]), chronic renal disease (1.59 [1.05; 2.39]), COPD (1.58 [1.08; 2.31]), cancer (2.01 [1.43; 2.83]), and peripheral arterial disease (1.75 [1.18; 2.61]). Factors associated with repeat acute coronary syndrome were diabetes (1.65 [1.05; 2.59]) and COPD (2.33 [1.34; 4.07]). Because of small numbers of unexposed patients and low event rates, it was not possible to assess the effects of EBD. **Conclusions**: In a national representative claims database, one year post MI and three years thereafter, event rates were low in this extensively treated population. The main predictors of repeat ACS were diabetes and COPD, probably also proxies of overweight and smoking. Studies of EBM effectiveness or lack thereof will need to access much larger populations to generate meaningful information.

Conflict of Interest Statement

This study was supported by an unconditional grant from AstraZeneca, and supervised by an independent cardiologist expert. It was designed, conducted, and analysed independently by the Bordeaux PharmacoEpi Platform, CIC Bordeaux CIC1401 of the Bordeaux University. This study was registered with the European Medicine agency's EUPAS registry (www.encepp.eu), under study number 5816. The funder assisted as an observer to all the meetings of the study. The funder did not have any role in study protocol, data acquisition, management or analysis.

Background

- Long-term survival and factors influencing long-term survival after myocardial infarction (MI) are rarely described in clinical trials**.**

Objectives

- To describe real-life outcomes in stable post-MI patients.
- To assess risk factors for death (all-cause) and cardiac outcomes.

Methods

- **Design:** cohort study of patients identified with stable MI in a representative French health insurance and hospitalisation claims database (EGB) with up to 3 years of follow-up until 31/12/2012 (Figure 1).

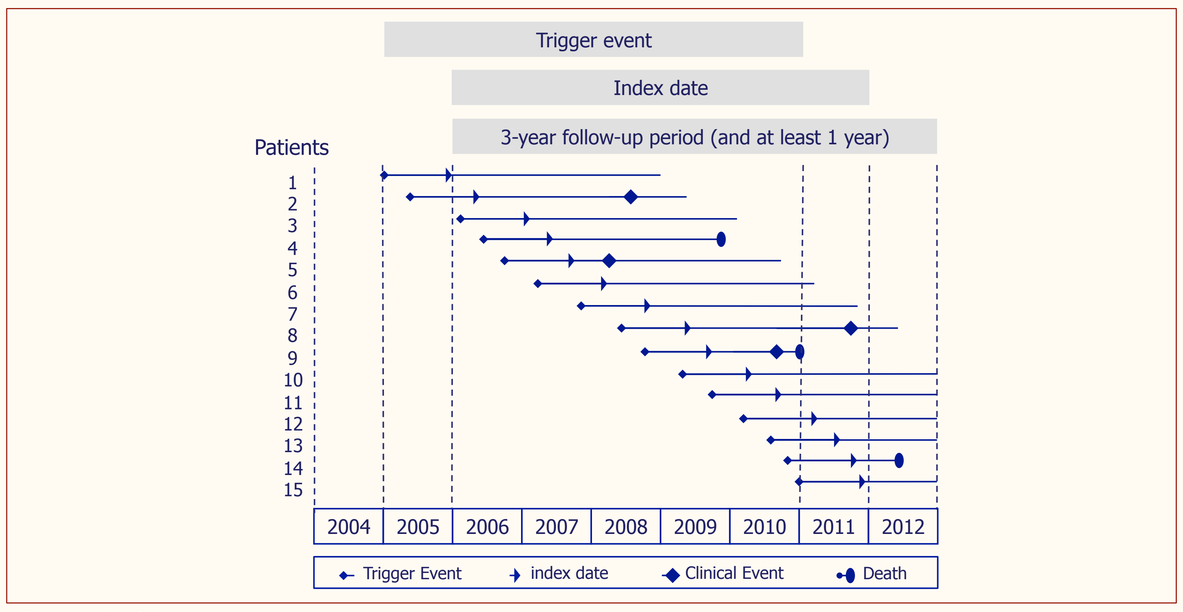

Figure 1. Study design

- **Data source:** EGB, *Echantillon Généraliste de Bénéficiaires*
  - Permanent 1/97 representative random sample of the national healthcare insurance database linked to the national hospital-discharge summary database, and the national death registry.
  - Includes approximately 780,000 persons.
  - Contains anonymised data on: demographic characteristics (gender, year of birth, month and year of death), long-term diseases (with full insurance coverage), reimbursed outpatient healthcare expenditures (visits, medical procedures, laboratory tests, dispensed drugs, medical devices), as well as, hospital procedures and discharge summaries.
- **Populations:**
  - **Source population:** all adults with main hospital discharge diagnosis of MI between 01/01/2005 and 31/12/2010 (trigger event), with database follow-up data until death or 31/12/2012.
  - **Stable post-MI population:** patients of the source population alive and free of MI 1 year after trigger event. Index date for inclusion in the cohort was the 1st anniversary of admission for initial MI.
- **Outcomes:**
  - A composite of death (all-cause), hospitalisation for MI or stroke.
  - Each event separately.
  - Hospitalisation for major bleeding.
- **Statistical analysis:**
  - Estimation of incidence rate of outcomes (per 100 person-years [PY]).
  - Estimation of hazard ratio (HR) of the risk factors using multiple Cox proportional hazards models, fully adjusted on risk factors and exposure to drugs at baseline (1 year after the trigger MI) and follow-up periods.

Results

- Among the 2226 adults with an MI hospitalisation during the period 2005-2010, **1585 patients** (71%) were included in the stable post-MI population, with 3926 PY of follow-up.
- **At index date**, 68% of patients were men, and mean age was 66 years.
- **During the 1-year period after the trigger event**:
  - 9% had myocardial revascularisation (percutaneous coronary intervention, coronary artery bypass graft).
  - 98% received at least one medication recommended for secondary prevention. Individual drugs are shown in Table 1.
- The **incidence rate** of the composite criterion of all-cause death, hospitalisation for MI or stroke was 6.3 per 100 PY (95% CI [5.6; 7.1]). Death was the most frequent individual event (5.1 per 100 PY). The incidence of hospitalisation for bleeding was 1.3 per 100 PY (Table 2).
- All-cause death was associated with age at inclusion (HR per year: 1.05, 95%CI [1.03; 1.06]), cancer (HR 2.01 [1.43; 2.83]), peripheral arterial disease (1.75 [1.18; 2.61]), renal disease (1.59 [1.05; 2.39]), COPD (1.58 [1.08; 2.31]), heart failure (1.56 [1.14; 2.14]), diabetes mellitus (1.53 [1.13; 2.08]), atrial fibrillation (1.49 [1.06; 2.10]), and coronary disease prior to trigger event (1.40 [1.00; 1.97]).
  Recurrence of MI was not significantly affected by the studied risk factors, probably because of the small number of events (n=40).
  ACS recurrence (n=98) was associated with COPD (2.33 [1.34; 4.07]) and diabetes (1.65 [1.05; 2.59]) (Table 3).

Table 1. Baseline characteristics of patients in the stable post-MI population

	Stable post-MI population n = 1585
Men at index date, n (%)	**1085 (68.5)**
Mean age at index date (in years) (± SD)	**66.1 (14.5)**
At least one of the following procedures during 1 year after trigger event, n (%)	**211 (13.3)**
Angiography	109 (6.9)
Percutaneous coronary intervention	104 (6.6)
Coronary artery bypass graft	31 (2.0)
Drug exposure during 1 year after trigger event, n (%)	
Coronary prevention treatment (ATC codes B01, C07, C09, C10)	1556 (98.2)
Statins	1440 (90.9)
Aspirin	1402 (88.5)
ß-blockers (ATC code C07)	1364 (86.1)
ACEi or ARB* (ATC code C09)	1300 (82.0)

* ACEi : Angiotensin-converting-enzyme inhibitors; ARB: Angiotensin II receptor antagonists

Table 2. Outcomes and incidence rates per 100 person-years during a 3-year follow-up after 1-year event-free survival post-MI in the stable post-MI population

	Stable post-MI population n = 3926 PY	
Composite criterion, n % [95% CI]	**249**	**6.3 [5.6; 7.1]**
Death (all-cause)	199	5.1 [4.4; 5.8]
Hospitalisation for MI	40	1.0 [0.7; 1.3]
Hospitalisation for stroke	24	0.6 [0.4; 0.9]
Hospitalisation for bleeding, n % [95% CI]	**49**	**1.3 [0.9; 1.6]**

Table 3. Cox proportional hazard ratios for death and cardiac outcomes in the stable post-MI population in a fully adjusted model (n=1585)

Outcomes	Death	MI*	ACS*
	n=199	n=40	n=98
Risk factors	HR [95%CI]	HR [95%CI]	HR [95%CI]
Age at index date (per year)	**1.05 [1.03; 1.06]**	1.02 [0.99; 1.04]	1.01 [0.99; 1.03]
Female	0.80 [0.58; 1.11]	0.83 [0.40; 1.71]	0.72 [0.44; 1.16]
Year of trigger event	1.04 [0.95; 1.14]	1.02 [0.84; 1.24]	1.07 [0.95; 1.21]
Diabetes	**1.53 [1.13; 2.08]**	1.69 [0.85; 3.39]	**1.65 [1.05; 2.59]**
ACS* prior to trigger event	**1.40 [1.00; 1.97]**	1.12 [0.52; 2.40]	1.33 [0.84; 2.12]
Stroke	0.94 [0.51; 1.72]	/	0.53 [0.13; 2.18]
Atrial fibrillation	**1.49 [1.06; 2.10]**	1.65 [0.69; 3.92]	0.86 [0.45; 1.64]
Heart failure	**1.56 [1.14; 2.14]**	1.09 [0.50; 2.33]	1.33 [0.82; 2.17]
Renal disease	**1.59 [1.05; 2.39]**	1.09 [0.30; 3.90]	0.86 [0.36; 2.09]
Hypertension	1.09 [0.78; 1.53]	0.74 [0.37; 1.50]	0.87 [0.56; 1.37]
Hospitalized bleeding	1.02 [0.65; 1.58]	0.52 [0.12; 2.30]	0.75 [0.34; 1.67]
COPD*	**1.58 [1.08; 2.31]**	1.93 [0.78; 4.74]	**2.33 [1.34; 4.07]**
Cancer	**2.01 [1.43; 2.83]**	0.14 [0.02; 1.06]	0.64 [0.32; 1.31]
PAD*	**1.75 [1.18; 2.61]**	2.13 [0.89; 5.11]	1.25 [0.66; 2.38]

* MI: myocardial infarction; ACS: acute coronary syndrome (MI or unstable angina); COPD: chronic obstructive pulmonary disease; PAD: peripheral arterial disease
In bold: HR whose lower 95% confidence interval does not overlap 1

Conclusions

- **For patients who survived 1 year after a MI, death represented the most frequent event.**
- **COPD and diabetes, probably proxies of smoking and overweight, were associated with an increased risk of recurrence of ACS.**

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