Long-term survival after myocardial infarction in a six-year follow-up cohort, EOLE

N. Moore[1,2], C. Droz-Perroteau[1], P. Blin[1], C. Dureau-Pournin[1], D. Thomas[3], N. Danchin[4], J. Tricoire[5], F. Paillard[6], S. Hercberg[7], M-A. Bernard[1], J. Benichou[8]

[1]Bordeaux PharmacoEpi, INSERM CIC1401, University of Bordeaux, Bordeaux, France – [2]INSERM U1219, Bordeaux, France – [3]Hopital Pitié-Salpêtrière, Paris, France – [4]Hôpital Européen Georges Pompidou, Paris, France
[5]Toulouse, France – [6]CHU de Pontchaillou, Rennes, France – [7]INSERM U557, Bobigny, France – [8]CHU de Rouen, Rouen, France

Background

- Studies of survival after myocardial infarction (MI) are often based on intent to treat analyses of short-term controlled trials.
- The EOLE study was performed at the request of the French regulatory authorities to assess the real-life impact of drugs for MI secondary prevention on overall mortality after 6 years of follow-up.

Objective

To describe and to quantify factors associated with 6-year mortality post-MI.

Method

- **National observational cohort with hospital and non-hospital cardiologists in France**
  - ✓ From April 2006 to June 2009;
  - ✓ 5,000 patients with recent MI (≤ 3 months) and followed for 6 years.
- **Data collection**
  - ✓ At inclusion: medical questionnaire (socio-demographic data, cardiovascular drugs, …), and patient self-administered questionnaire (drugs taken, tobacco use, …);
  - ✓ At 6 months, 2, 3, 4, 5, and 6 years: patient questionnaire (drugs taken, hospitalisation since MI, …), and vital status after 6 years of follow-up.
- **Compliant and non-compliant patients**
  - ✓ Compliants: patients with all possible questionnaires returned during the study or before death;
  - ✓ Non-compliants: patients with at least one possible questionnaire missing.
- **Exposure to secondary prevention drugs**
  - ✓ Beta-blockers, aspirin (or other antiplatelet agents), statins (or other hypolipemic agents), angiotensin converting enzyme inhibitors (or angiotensin II receptor blockers (ACEi or ARB)), Omega 3 supplementation;
  - ✓ Definition: at inclusion, any treatment prescribed by cardiologist or declared by patient, and during follow-up, any treatment declared by patient.
- **Statistical analysis**
  - ✓ Vital status at 6 years: from the national death registry, and failing that, through cardiologist, general practitioner or patient/relatives;
  - ✓ Estimation of the hazard ratio (HR) associated with all-cause death at 6 years using a Cox model with a time-dependent variable (expected patient questionnaires received), adjusted for age, gender, cardiovascular risk factors, exposure to each secondary prevention drug at inclusion and their propensity scores.

Results

- **Patient characteristics at inclusion**
  - ✓ 5,527 patients included : 2,717 (49.2%) compliants, and 2,810 (50.8%) non-compliants.
  - ✓ The main characteristics at inclusion for all population, for compliants and non-compliants are presented in Table 1: non-compliants were a little younger, more often active, more often still smokers, more often diabetic, with more often a history of previous MI.
  - ✓ Exposure to recommended drugs for secondary prevention was high and similar between compliants and non-compliants: from 82.4% for ACEI or ARB to 99.4% for aspirin or other antiplatelet agent.

Table 1. Main characteristics of patients at inclusion

	Non-compliants n = 2810	Compliants n = 2717	Total n = 5527
Men, n (%)	2150 (76.5)	2138 (78.7)	4288 (77.6)
Mean age, years	60.0	63.0	62.1
Retired, n (%)	1371 (48.8)	1600 (58.9)	2971 (53.8)
BMI ≥ 30 (kg/m^2), n (%)	552 (19.6)	500 (18.4)	1052 (19.0)
Current smoker, n (%)	372 (13.2)	159 (5.9)	531 (9.6)
Diabetes, n (%)	522 (18.6)	399 (14.7)	921 (16.7)
Previous MI, n (%)	405 (14.4)	329 (12.1)	734 (13.3)
Exposure to secondary prevention treatments, n (%)			
Beta-blockers	2493 (88.7)	2464 (90.7)	4957 (89.7)
Aspirin (or other antiplatelet agents)	2791 (99.3)	2705 (99.6)	5496 (99.4)
Statins (or other hypolipemic agents)	2682 (95.4)	2653 (97.6)	5335 (96.5)
ACEi (or ARB)	2297 (81.7)	2260 (83.2)	4557 (82.4)
Cardiovascular rehabilitation program, n (%)	1054 (37.5)	1186 (43.7)	2240 (40.5)

- **Vital status at 6 years of follow-up**
  - ✓ Among the 5,527 included patients, 721 died. Overall mortality at 6 years was 13.1% (95%CI [12.3%-14.0%]) with incidence rate of 2.34% person-years (PY);
  - ✓ Incidence rate of 6-year mortality: 2.98% PY in non-compliants and 1.69% PY in compliants.

Bordeaux PharmacoEpi platform,
Reseacrh platform on pharmacoepidemiology
INSERM CIC1401 - *http://www.pharmacoepi.eu*
Pr N. Moore (Head),
Dr P. Blin (Medical & scientific director)
C. Droz-Perroteau (Chief operating officer)
C. Dureau-Pournin (Project manager)

Scientific Committee
Pr L. Guizet†, D. Thomas (Presidents), Cardiologists
Pr N. Danchin, Dr F. Paillard, Dr J. Tricoire, Cardiologists
Pr S. Hercberg, Epidemiologist-Nutritionist
Pr J. Bénichou, Biostatistician

Events Validation Committee
Pr L. Guizet†, Pr D. Thomas, Dr J. Tricoire, Cardiologists
Dr F. Rouanet, Pr I. Sibon, Neurologists

Disclosure statement: This study was funded by *Pierre Fabre Médicaments*.
It was designed, conducted, and analysed independently by the Bordeaux PharmacoEpi platform, INSERM CIC1401 of the Bordeaux University. It was overseen by independent experts.

- **Factors associated with all-cause death (Cox model)** (Table 2)
  - ✓ Factors associated with higher mortality:
    - – Age: HR = 1.50 [1.01-2.22] for 50-59 years to 15.72 [10.67-23.15] for ≥80 years, vs. <50 years;
    - – Non-compliance to study protocol: 3.12 [2.63-3.57];
    - – Smoking at inclusion (1.76 [1.27-2.44]), previous MI (1.46 [1.22-1.75]), diabetes (1.39 [1.17-1.65]).
  - ✓ Factors associated with lower mortality:
    - – Statins or other hypolipemic agents (0.68 [0.51-0.90]), beta-blockers (0.79 [0.64-0.96]);
    - – Cardiovascular rehabilitation program (0.74 [0.62-0.89]).

Table 2. Hazard ratios associated with all-cause death after 6 years of follow-up post-MI

	HR$_{adjusted}$* [95% CI]	Alive at 6 years n = 4792	Died at 6 years n = 720	Total n = 5512**
Expected questionnaires no received, *vs. received* (time-depending variable with multiple changes)	**3.13 [2.63-3.57]**			
Man, *vs. Woman*	1.17 [0.97-1.41]	3760 (78.5)	517 (71.8)	4277 (77.6)
Age, *vs < 50 years*				
50-59 years	1.50 [1.01-2.22]	1359 (28.4)	72 (10.0)	1431 (26.0)
60-69 years	3.06 [2.10-4.46]	1100 (23.0)	114 (15.8)	1214 (22.0)
70-79 years	6.94 [4.77-10.12]	979 (20.4)	240 (33.3)	1219 (22.1)
≥ 80 years	15.72 [10.67-23.15]	334 (7.0)	254 (35.3)	588 (10.7)
Diabetes, *vs.no diabetes*	**1.39 [1.17-1.65]**	736 (15.4)	183 (25.4)	919 (16.7)
History of high blood pressure, *vs. no history*				
Moderate	1.20 [1.02-1.42]	1628 (34.0)	364 (50.6)	1992 (36.1)
Severe	1.15 [0.88-1.50]	337 (7.0)	75 (10.4)	412 (7.5)
History of hypercholesterolemia, *vs. no history*	0.94 [0.81-1.10]	2130 (44.4)	333 (46.3)	2463 (44.7)
Previous MI	**1.46 [1.22-1.75]**	576 (12.0)	157 (21.8)	733 (13.3)
Smoking, *vs. no smoking*				
Stop before MI	1.23 [1.02-1.48]	1329 (27.7)	247 (34.3)	1576 (28.6)
Stop after MI	**1.47 [1.13-1.92]**	1400 (29.2)	105 (14.6)	1505 (27.3)
Smoker at inclusion	**1.76 [1.27-2.44]**	476 (9.9)	53 (7.4)	529 (9.6)
Cardiovascular rehabilitation program	**0.74 [0.62-0.89]**	2071 (43.2)	166 (23.1)	2237 (40.6)
Exposed at inclusion, *vs. non-exposed*				
Beta-blockers	**0.79 [0.64-0.96]**	4347 (90.7)	597 (82.9)	4944 (89.7)
Aspirin (or other antiplatelet agents)	0.75 [0.42-1.33]	4774 (99.6)	707 (98.2)	5481 (99.4)
Statins (or other hypolipemic agents)	**0.68 [0.51-0.90]**	4666 (97.4)	655 (91.0)	5321 (96.5)
ACEi (or ARB)	0.95 [0.78-1.15]	3957 (82.6)	586 (81.4)	4543 (82.4)

**Adjusted for age, gender, cardiovascular risk factors, exposure to each secondary prevention drug at inclusion;* **Number of patients with data available

Conclusions

- This prospective long-term study of **post-MI all-cause mortality** found that beyond known predictors such as age, diabetes or previous MI, **poor patient compliance to study procedures** (non-returned questionnaires) was **strongly associated with excess deaths:** this is probably a proxy for general non-compliance with secondary prevention.
- Analyses of treatment effects were hindered by paucity of events and unexposed patients.

ACC 67th Annual Scientific Session & Expo, 10-12 March 2018, Orlando, USA