

M. Zeitouni, JP. Collet¹, JS. Hulot, J. Silvain, M. Kerneis¹, B. Lattuca, O. Barthelemy, Y. Lavie-Badie, JB. Esteve, L. Payot, D. Brugier, S. Galier, A. Diallo, E. Vicaut, G. Montalescot
 Pitié-Salpêtrière Hospital, Sorbonne Université Paris 6 (UPMC), ACTION Study Group, INSERM UMRS_1166, Institut de Cardiologie, Paris, France *jean-philippe.collet@aphp.fr www.action-coeur.org

Abstract

Background: The long-term natural history of premature coronary artery disease (CAD), defined as ischemic heart disease before 45 year-old, is unknown.

Purpose: The primary objective was to describe the evolution of premature CAD over 20 years of follow-up and determine the risk of recurrent major adverse cardiovascular events (MACE) defined as death, MI, ischemic stroke and revascularization. The second objective was to assess the independent correlates of this primary endpoint.

Methods: The multicenter prospective AFJI (Appraisal of risk Factors in young Ischemic patients Justifying aggressive Intervention) registry was started in January 1996 enrolling all consecutive patients presenting with angiographically established CAD before the age 45. The last follow-up was obtained in January 2017.

Results: A total of 880 patients were enrolled and followed up on average for 9.6 years (IQR). Patients were mainly males (88%) active smokers (77%) aged 41 years(36-43) presenting with an acute MI (79%) due to single vessel CAD (60%). Family history of CAD (40%) and hypercholesterolemia (51%) were common while diabetes (11%) and systemic inflammatory disease (10%) were less frequent. The vast majority of patients (97%) underwent coronary revascularization predominantly with drug-eluting stents (51%). One out of three patients (n=263, 29.9%) presented a recurrent event (total number of MACE= 398). Myocardial infarction (n=209, 23.8%) and coronary revascularization (n=126, 14.3 %) were the most frequent events predominantly related to the occurrence of new coronary atherothrombotic lesions (15.4% vs 7.5%, p<0.001, HR=2.1, 95% CI [1.5- 2.6] for new versus initial lesion, respectively) (Figure). All-cause death (n=55, 6.3%) occurred within a median time of 8.4±years while ischemic stroke (n=9, 0.9%) was less frequent. Independent correlates of MACE were smoking continuation, the presence of a concomitant chronic inflammatory disease, a multi-vessel CAD status and diabetes.

Table 1 : Baseline characteristics

N=880 patients	
Age	39.8 +/- 4
Age ≤ 35	198 (22.5)
Women	117 (13.2)
BMI (kg/m ²)	26.1 +/- 4
Clinical presentation	
Acute Myocardial Infarction	693 (78.8)
Stable angina	187 (21.2)
LVEF ≤ 45 %	10 (1.1%)
Ethnic background	
Caucasian	638 (72.5)
Sub-Saharan Africa	46 (5.2)
Asian	30 (3.4)
Northern Africa & Middle East	166 (18.8)
Risk factors	
Familial history of CAD	359 (40.8)
Active smoking	679 (77.1)
Dyslipidemia	443 (50.3)
Arterial Hypertension	178 (20.2)
Diabetes	94 (10.7)
Chronic Inflammation	87 (9.8)

Coronary Anatomy and Revascularization

Single vessel	529 (60.1)
Two vessels	179 (20.3)
Three vessels	172 (19.5)
Coronary dissection	10 (1.1)
Sport-related plaque rupture	11(1.3)
Drug eluting stent	478 (54.4)
Bare metal stent	304 (34.7)
Thromboaspiration w/o stent	11 (1.3)
Coronary artery bypass graft	57 (6.5)
Optimal medical treatment	30 (3.4)

Table 2: major adverse cardiovascular events.

	1 st recurrence (n=264)	Time (y, median)	2nd recurrence (n=81)	Recurrences ≥ 3 (n=54)	Total
All-cause Death	39 (4.4)	8.4	11 (1.3)	5 (0.6)	55 (6.3)
MI	131 (14.9)	3.7	40 (4.5)	38 (4.3)	209 (23.8)
Revasc	88 (10.0)	5.1	28 (3.2)	11 (1.3)	127 (14.4)
Stroke	6(0.7)	5.4	2 (0.2)	0 (0)	8 (0.9)
Composite endpoint	264 (29.9)	4.2			399

Figure 1 : Primary endpoint according to new lesions versus initial culprit lesion. Time-to-Event Curves for Major Adverse Cardiovascular Events after inclusion in the AFJI cohort.

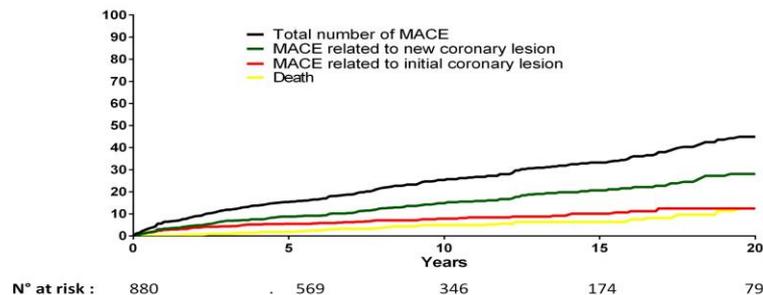
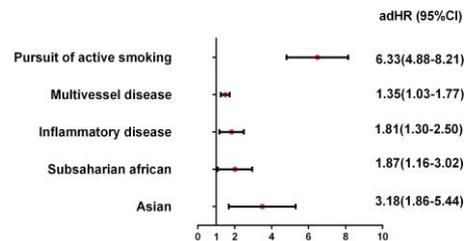


Figure 2 : HR plot for multivariate Cox Model using repeated measurements for multiple recurrences.



Conclusion: Premature coronary artery disease is an aggressive and chronic disease with a high rate of recurrences and a frequent evolution towards multivessel disease.