Prevalence and severity of coronary disease in patients with familial hypercholesterolemia hospitalized for an acute myocardial infarction : data from the RICO survey

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► BACKGROUND

Individuals with heterozygous familial hypercholesterolemia (FH) are at high risk of early myocardial infarction (MI). However, the severity of coronary artery disease (CAD) has been poorly described in patients with FH hospitalized for an acute MI. Moreover, no data are available on the prevalence and characteristics of French patients with FH and hospitalized for MI.

► METHODS

Consecutive patients hospitalized for an acute MI in a multicenter registry of all the coronary care units of the region of Côte d’Or in France (RICO survey) were considered from 2001-2017.

Blood sample was taken at admission for lipid profile and baseline characteristics including demographic data, risk factors, treatments for hypercholesterolemia, family history of CAD, cardiovascular history and chronic treatments were collected. All patients were assessed for the presence of FH based on the Dutch Lipid Clinic Network (DLCN) criteria. Missing informations (presence of tendon xanthomas or corneal arcus, family history of hypercholesterolemia or vascular disease) were counted as zero. A probable/definite FH diagnosis was considered when the DLCN score was ≥ 6 , a possible diagnosis when the score was 3-5 and unlikely when the score was < 3 points. The group of patients with probable/definite FH was compared with the group unlikely FH, called “no” FH.

In addition to the full cohort, a matched subset was built, with one FH patient matched with 3 patients without FH, based on age, sex and diabetes mellitus

Table 2: Coronary lesions for patients with and without FH: Full cohort and matched subset data

	Full cohort			Matched subset		
n (%) or median (IQR)	no FH (n=8970)	Probable/ definite FH (n=249)	p value	no FH (n=699)	Probable/ definite FH (n=233)	p value
Coronary angiography	8465 (94%)	244 (98%)	.014	682 (98%)	229 (98%)	.524
GRACE risk score	151 (128-177)	112 (96-134)	<.001	118 (102-140)	111 (97-134)	.015
SYNTAX score	10 (5-18)	11 (5-19)	.622	7 (1-13)	11 (4-19)	<.001
Multivessel disease	4504/8465 (54%)	134/244 (55%)	.691	273/682 (40%)	125/229 (55%)	<.001

► RESULTS

Among 11624 patients hospitalized for acute MI, 249 (2.1%) had a probable/definite FH (score ≥ 6), 2405 (20.7%) a possible FH (score 3-5) and 8970 (77.2%) no FH (score < 3). The baseline characteristics of patients with (probable/definite) FH and without (no) FH are reported on *Table 1* for the whole population (called “Full cohort”) and for the 2 matched cohorts built after adjustment with age, sex and diabetes (called “Matched subset”).

The "probable/definite" FH groups was ≈ 20 years younger ($p < .001$), had a higher BMI ($p = .016$), a greater prevalence of smoking ($p < .001$), premature CAD ($p < .001$), family history of CAD ($p < .001$), but a lower prevalence of diabetes ($p = .007$), hypertension ($p < .001$) and stroke ($p = .016$). However after adjustment with age, sex and diabetes, the prevalence of hypertension was higher for patients with probable/definite FH ($p = .002$), and the history of stroke does not differ between the two groups, whereas patients with probable/definite FH have more history of peripheral artery disease ($p = .018$).

As expected, median LDL-C was about twice higher (207 vs 112 mg/dL) for patients with probable/definite FH and more patients with probable/definite FH were receiving lipid-lowering medications. However chronic statin treatment was only used in 48% of probable/definite FH patients and only 8% were receiving ezetimibe.

Table 2 shows data on coronary lesions at coronary angiography. After adjustment (post-matching data), the use of coronary angiography was similar for patients with and without FH.

The GRACE risk score was lower for patients with probable/definite FH in both full cohort and matched subset cohort.

However, after adjustment for age, sex and diabetes, patients with probable/definite FH were characterized by increased extent of CAD (SYNTAX score 11 vs 7, $p < .001$) (*Figure 1*) and multivessel disease (55% vs 40%, $p < .001$) (*Figure 2*) (*Table 2*).

After adjustment, no significant differences appear on in-hospital outcomes.

► OBJECTIVES

To investigate the prevalence of FH, the risk factor burden and the severity of CAD at the time of admission in a coronary care unit (CCU) from a large database of a regional French registry (RICO registry) of patients with acute MI.

Table 1: Characteristics of patients at admission for acute MI with and without FH: Full cohort and matched subset data

	Full cohort			Matched subset		
n (%) or median (IQR)	no FH (n=8970)	Probable/ definite FH (n=249)	P value	no FH (n=699)	Probable/ definite FH (n=233)	P value
Patient characteristics						
Age (years)	71 (61-80)	51 (46-57)	<.001	51 (46-57)	51 (46-57)	.993
Female	2799 (31%)	78 (31%)	.967	216 (31%)	72 (31%)	1
BMI (kg/m ²)	26 (24-29)	27 (24-30)	.016	26 (23-30)	27 (24-30)	.092
Diabetes	2215 (25%)	43 (17%)	.007	117 (17%)	39 (17%)	1
Hypertension	5304 (59%)	117 (47%)	<.001	243 (35%)	107 (46%)	.002
Current smoking	2098 (23%)	140 (56%)	<.001	390 (56%)	128 (55%)	.819
Comorbidities						
Previous CAD*	1290/8909 (15%)	49/248 (20%)	.020	50/687 (7%)	37/232 (16%)	<.001
Premature CAD	1207/8304 (15%)	201/245 (82%)	<.001	535/687 (78%)	188/229 (82%)	.175
Family history of CAD	1619 (18%)	195 (78%)	<.001	33 (5%)	184 (79%)	<.001
Stroke	693/8910 (8%)	9/247 (4%)	.016	28/695 (4%)	7/231 (3%)	.491
PAD	479/8914 (8%)	20/247 (8%)	.864	23/696 (3%)	16/231 (7%)	.018
Lipid-lowering medications						
Statins	2078 (23%)	119 (48%)	<.001	91 (13%)	107 (46%)	<.001
Ezetimibe	156 (2%)	20 (8%)	<.001	5 (1%)	20 (9%)	<.001
Fibrates	490 (6%)	4 (2%)	.008	38 (5%)	4 (2%)	.018
Biological data						
TC (mg/dL)	184 (156-212)	284 (255-320)	<.001	190 (165-210)	284 (255-320)	<.001
LDL-C (mg/dL)	112 (88-136)	207 (175-241)	<.001	118 (96-136)	207 (176-238)	<.001
Corrected LDL-C ≥ 190 mg/dL	0	248 (99.6%)	<.001	0	232 (99.6%)	<.001
HDL-C (mg/dL)	44 (36-54)	43 (36-52)	.354	41 (33-51)	43 (36-52)	.021
TG (mg/dL)	114 (82-162)	152 (114-219)	<.001	131 (90-191)	150 (113-217)	<.001
Clinical data						
Blood pressure (BP), mmHg						
Systolic BP	139 (120-159)	140 (126-161)	.018	134 (119-153)	140 (126-161)	<.001
Diastolic BP	80 (69-90)	85 (76-99)	<.001	80 (70-94)	85 (77-99)	<.001
LVEF (%)	53 (43-60)	55 (45-61)	.039	55 (45-61)	55 (45-62)	.905
Heart failure	2291 (26%)	42 (17%)	.002	100 (14%)	37 (16%)	.557
STEMI	4841 (54%)	130 (52%)	.580	420 (60%)	123 (53%)	.050

* Previous CAD: previous MI, unstable angina, coronary artery bypass grafting or percutaneous coronary intervention
TC: total cholesterol; LDL-C: LDL cholesterol; HDL-C: HDL cholesterol; TG: triglycerides; STEMI: ST-segment elevation myocardial infarction; PAD: peripheral artery disease; BMI: body mass index; IQR: interquartile range; LVEF: left ventricular ejection fraction

Figure 1: Severity of CAD assessed by SYNTAX Score for patients with and without FH

Figure 2: Number of significant coronary lesions for patients with and without FH

►►► **CONCLUSIONS :** In a large cohort from a French region, we found a high prevalence of FH in real world patients hospitalized for an acute MI. Patients with FH were associated with a greater severity of CAD burden. Despite a greater use of lipid-lowering therapy compared with patients without FH, about half of patients with FH were not receiving statin therapy before the acute event. This study confirms that FH is underdiagnosed and undertreated and strategies to optimize the identification and the management of FH patients should be advocated.