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Identification of familial hypercholesterolemia in patients with myocardial infarction: A Chinese cohort study

Sha Li, MD, Yan Zhang, PhD, Cheng-Gang Zhu, PhD, Yuan-Lin Guo, PhD, Na-Qiong Wu, PhD, Ying Gao, MD, Ping Qing, MD, Xiao-Lin Li, PhD, Jing Sun, MS, Geng Liu, MS, Qian Dong, MS, Rui-Xia Xu, PhD, Chuan-Jue Cui, MD, Jian-Jun Li, MD, PhD*

Division of Dyslipidemia, State Key Laboratory of Cardiovascular Disease, Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing, China

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BACKGROUND: Familial hypercholesterolemia (FH) is marked by an elevated plasma cholesterol and risk of premature cardiovascular disease. An increased burden of FH is being realized.

OBJECTIVE: To provide data on FH in Chinese patients with myocardial infarction (MI) and its potential contribution to early MI.

METHODS: A total of 1843 consecutive patients undergoing coronary angiography with their first MI were recruited. The clinical FH was diagnosed using the Dutch Lipid Clinic Network criteria. The prevalence and clinical features of FH and the relationship of FH to risk of early MI were investigated.

RESULTS: Of the 1843 patients, 48.2% were detected as premature MI (pMI, the onset age ≤55 years for men, ≤60 years for women). The prevalence of definite/probable FH reached 3.9% (7.1% in pMI and 0.9% in non-pMI). Furthermore, we found that the risk of pMI was significantly elevated in both definite/probable FH (vs. unlikely FH, odds ratio, 5.05 [1.10–23.23]) and possible FH (vs unlikely FH, odds ratio, 2.65 [1.22–5.77]), independently from classical risk factors and medications. Additionally, patients with definite/probable FH occurred 10 years younger than those with unlikely FH in the onset age of MI (48.63 ± 1.20 vs 58.35 ± 0.30 years, $P < .001$). When considered in subgroup of pMI or non-pMI, an early onset of MI was also observed in definite/probable FH (pMI, 45.83 ± 0.89 vs 47.87 ± 0.34 years; non-pMI, 60.75 ± 1.96 vs 65.07 ± 0.22 years; both $P < .05$).

CONCLUSION: The prevalence of FH among Chinese patients with MI appeared common, particularly among those with pMI. The phenotypic FH might significantly promote the early onset of MI.

Introduction

Familial hypercholesterolemia (FH) is a common autosomal dominant disorder of cholesterol metabolism to be increasingly recognized as a global call to arms.[1,2] The impaired cholesterol metabolism results in life-long accumulations in circulating low-density lipoprotein (LDL)

* Corresponding author. Division of Dyslipidemia, State Key Laboratory of Cardiovascular Disease, Fu Wai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing 100037, China.
E-mail address: lijianjun938@126.com
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cholesterol (LDL-C) and development of premature atherosclerotic cardiovascular disease (ASCVD), the most life-threaten issue known to mankind worldwide.[1]

Most cardiovascular risk factors are modifiable with the improvements of life style and medical treatment over the past decades.[3] As such, attention has focused on inherited causes of the ASCVD to explain these early events. The most worth concerning of which is FH. If left untreated, patients with heterozygous FH present a significant increase risk of premature coronary artery disease (CAD) than these unaffected individuals, the untreated homozygotes even develop clinically significant CAD in early childhood and generally fail to survive beyond 30 years.[4] However, FH remains widely underdiagnosed and undertreated so far,[5] thereby representing a major global public health challenge.

Particularly, myocardial infarction (MI) represents an critical clinical manifestation in patients with FH.[6,7] Although effects of risk factors on MI have been studied in several large population-based cohorts of different race or nationality, age-related pathophysiological differences are known little.[8] Therefore, the aim of the present study was to investigate the prevalence of clinical FH in a cohort of Chinese patients undergoing coronary angiography (CAG) with their first MI and evaluate its relative importance in developing MI early or late in life.

Materials and methods

Study population

Our study complied with the Declaration of Helsinki and was approved by the hospital's ethical review board (Fu Wai Hospital & National Center for Cardiovascular Diseases, Beijing, China). Informed written consent was obtained from all patients enrolled in this study.

We consecutively enrolled the subjects who referred to CAG for their first MI in our division from April 2011 to March 2016. The clinical characteristics were collected via the medical records or direct interview of the patients by trained nurses. Patients with significant hematologic disorders, infectious or systematic inflammatory disease, thyroid dysfunction, severe liver and/or renal insufficiency, and malignant disease were excluded. All patients underwent clinical examination and blood testing.[9] As a result, a total of 1843 patients were eligible for the analysis.

Diagnostic criteria for FH

The clinical FH was diagnosed using the Dutch Lipid Clinic Network (DLCN) criteria[5] including personal and family history of premature atherosclerosis, LDL-C levels, and xanthomas in the present study.

The cutaneous or tendous xanthomas from skin and joints were examined for patients by trained cardiologists, and the information from relatives was obtained by inquiring for the corresponding patients and/or their own medical records from clinics and hospitals. Individuals on lipid-lowering medications with their pretreatment LDL-C unavailable had their untreated LDL-C levels conservatively adjusted by a relative correction factor respectively that depended on the dose and potency of statins. The correction factors were developed from the analysis of 71 original articles that were collated before setting up these criteria.[10]

Specially, the following numerical score definition of FH according to the DLCN was used: (1) family history of a first-degree relative with known premature CAD or vascular disease (≤55 years for men; ≤60 years for women, 1 point) and/or a first-degree relative with known hypercholesterolemia (1 point) or xanthomas (2 points) or offspring(s) with known hypercholesterolemia (2 point); (2) personal history of premature CAD (ages as above, 2 points) or cerebral/peripheral vascular disease (ages as above, 1 point) or xanthomas (6 points); untreated LDL-C >8.5 mmol/L (8 points), 6.5–8.4 mmol/L (5 points), 5.0–6.4 mmol/L (3 points), or 4.0–4.9 mmol/L (1 point); (3) corneal arcus and molecular diagnosis (monogenic anomalies) were not available, and these missing information was counted as zero in this algorithm. Finally, a diagnosis of definite FH was considered if the total score was >8 points, probable if the score was 6–8 points, possible if the score was 3–5 points, and unlikely if the score was <3 points.

Diagnostic criteria for MI

Participants in the present study were included ST-segment elevation myocardial infarction (STEMI) and non ST-segment elevation myocardial infarction (NSTEMI) that were determined by at least two cardiologists. Of which, 889 (48.2%) patients were found as premature MI (pMI, the onset age of MI ≤ 55 for men, ≤60 for women), and 954 were non-pMI (the onset age of MI > 55 for men, >60 for women). The severity of CAD was assessed according to Gensini score system as described previously.[9]

Laboratory examination

Fasting blood samples were obtained for all patients from the cubital vein during the first 24 hours of hospital admission. The concentrations of lipid and lipoproteins were measured using an automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan). Triglyceride (TG), total cholesterol, and high-density lipoprotein cholesterol (HDL-C) levels were measured using an enzymatic assay. LDL-C was measured directly in the assay via standard methods. Apolipoprotein (apo) AI (apoAI) and apoB levels were measured using a turbidimetric immunoassay. Lipoprotein (a) [Lp(a)] levels were assayed by enzyme-linked immunosorbent assay using coated mouse monoclonal