Prevalence and Outcomes of Familial Hypercholesterolemia Patients in a Chinese Myocardial Infarction Cohort

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Patients and Methods

Study sample

e study samples were collected from subjects in the China PEACE-prospective AMI [12] as well as the pilot phase cohort. In brief, the China PEACE-prospective AMI study enrolled approximately 4,000 consecutive patients admitted for acute myocardial infarction. ese subjects are aged 18 years or older, within 24 h of symptom onset, and from more than 50 diverse hospitals across China from December 30, 2012 to June 1, 2014. e inclusion criteria for pilot phase AMI cohort are the same except that there was no strict record of the symptom onset time. Details of medical history, treatment, and in-hospital outcomes were abstracted from medical records. Comprehensive baseline interviews were conducted to characterize patient demographics, risk factors, presentation, and healthcare status. Post-discharge follow-up interviews were conducted

BMI 25	720 (21.4)	8 (29.6)	121 (29.7)	591 (20.2)	<0.000	44 (30.6)	347 (25.3)	329 (17.7)	<0.000
Comorbidities									
Pre-exiting CHD	1445 (42.9)	14 (51.9)	182 (44.6)	1249 (42.6)	0.266	67 (46.5)	572 (41.8)	806 (43.5)	0.758
Premature CHD[a]	1062 (31.5)	21 (77.8)	322 (78.9)	719 (24.5)	<0.001	116 (80.6)	737 (53.8)	209 (11.3)	<0.000
Heart failure	865 (25.7)	10 (37.0)	86 (21.1)	769 (26.2)	0.172	36 (25.0)	332 (24.3)	497 (26.8)	0.14
Family history									
Premature CHD[a]	368 (10.9)	8 (29.6)	136 (33.3)	224 (7.6)	<0.000	52 (36.1)	149 (10.9)	167 (9.0)	<0.000
Lab test at admission									
TC (mmol/L)	4.7 (3.9, 5.5)	8.1 (6.6, 8.7)	5.9 (4.9, 6.9)	4.5 (3.8, 5.3)	<0.000	6.5 (5.8, 7.8)	5.4 (4.8, 6.0)	4.1 (3.5, 4.7)	<0.000
LDL-C[b] (mmol/L)	3.0 (2.4, 3.6)	6.6 (5.6, 7.5)	4.2 (3.2, 4.9)	2.9 (2.4, 3.5)	<0.000	5.1 (4.0, 6.2)	3.7 (3.2, 4.1)	2.6 (2.1, 3.0)	<0.000
HDL-C (mmol/L)	0.9 (0.7, 1.0)	0. 9 (0.8, 1.1)	0.9 (0.7, 1.1)	0.9 (0.7, 1.0)	<0.000	0.9 (0.8, 1.1)	0.9 (0.8, 1.1)	0.8 (0.7, 1.0)	<0.000
Triglycerides (mmol/L)	1.4 (1.0, 2.0)	1.9 (1.2, 2.9)	1.8 (1.3, 2.4)	1.3 (0.9, 1.9)	<0.000	2.0 (1.4, 2.8)	1.6 (1.1, 2.2)	1.2 (0.8, 1.7)	<0.000
Statins use at admission	246 (7.3)	13 (48.1)	50 (12.3)	183 (6.2)	<0.000	36 (25.0)	105 (7.7)	105 (5.7)	<0.000

e statistical analysis was performed by SAS version 9.4 so ware (SAS Institute Inc, Cary, NC, USA).

Results

Prevalence of FH by DLCN and MDLCN

FH patients were diagnosed by DLCN and MDLCN according to published criteria summarized in Supplementary Table 1 [10]. By DLCN criteria, we identif ed 27 potential FH, the prevalence was 0.80% (95% CI, 0.50%-1.10%) in all 3367 AMI patients. It di erentiated in 2572 men 0.78% (95% CI, 0.44%-1.12%) and 795 women 0.88% (95% CI, 0.23%-1.53%). Using the MDLCN criteria, we identif ed 144 potential FH, the prevalence increased to 4.28% (95% CI, 3.59%-4.96%). It was signif cantlmlower in men 4.00% (95% CI, 3.25%-4.76%) than in women 5.16 (95% CI, 3.62%-6.69%) (Figure 1). Compared to the whole AMI cohort, the 1062 patients with premature MI have more than 2 times higher FH prevalence at 1.98% (95% CI, 1.14%-2.81%) by DLCN and it dramatically increased to 10.92% (95% CI, 9.05%-12.80%) by MDLCN (Figure 1).
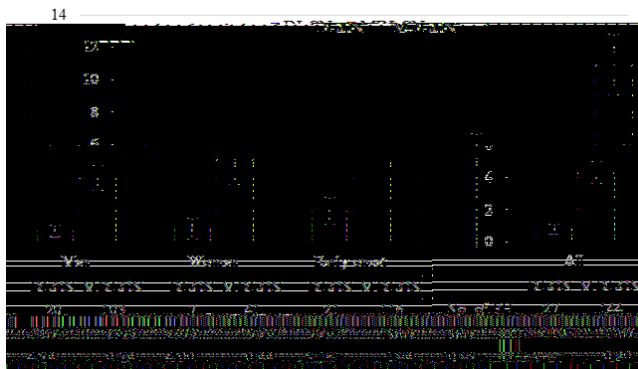
Prevalence of potential FH in the AMI cohort

Figure 1: e prevalence of potential FH diagnosed by DLCN criteria and MDLCN criteria in China PEACE-Prospective AMI cohort. Potential FH was def ned as combining def nite and

Early onset of CHD is an important indicator of potential FH. ﾔｅ prevalence of FH among premature CHD patients was reported 1.5-20%, which is about 3 times higher than that in the general CHD population [6,7,11,21]. Our study also showed more than 2 times higher incidence of FH in premature AMI patients. Screening such patients may be an eﬀective way to identify the index case followed by cascade screening in family members to facilitate early identifcation and treatment of FH. ﾔis strategy should be promoted especially in areas or countries where universal screening is impracticable.

Clinical characteristics

Our fndings on the FH clinical characteristics are mostly comparable to that in Western populations. ﾔe age of onset in potential FH is 50 by DLCN and MDLCN which is comparable to the results from SPUM_ACS (50 years) in the Switzerland cohort [6] but is considerably lower than that in EUROASPIRE IV study (58 years) [7].

ﾔe AMI patients with FH in our cohort were more than 10 years younger than non-FH patients. ﾔe frequency of personal or familial history of premature CHD and level of triglycerides were signifcantlm higher in the potential FH than in the unlikely group, especially when diagnosed by MDLCN. In addition, by both DLCN and MDLCN, the FH prevalence in women was higher than in men, which is consistant with other studies [7].

In the present study only 7.3% patients reported statin treatment. Even in FH patients, only 48.1% (by DLCN) and 25.0% (by MDLCN) patients were on statin treatment, which is lower than that in the Western cohorts [5,7]. It refects the current status of the early screening and management of AMI patients in China, especially when concomitant with FH.

Clinical outcomes

Our study also for the frst time reported an almost 2-fold signifcantlm increased risk of recurrent cardiovascular events in potential FH patients diagnosed by MDLCN in China. Nanchen et al. reported that patients with FH (by DLCN) had a 1.88 increased risk of recurrent cardiovascular event in an acute coronary syndrome (ACS) cohort aﬔer adjusted for age and sex. ﾔe ratio increased to 2.31 aﬔer adjusted for age, sex and traditional risk factors [24]. Our fndings on the harzard ratio (1.97) were similar to Nanchen's report only when using MDLCN. It indicated that early identifcation and treatment of AMI patients with FH by MDLCN could more eﬀectivelmprevent the recurrence of cardiovascular events aﬔer myocardial infarction.

FH diagnostic criteria in chinese population

ﾔe clincial characteristics analysis showed discontinuous trend of some characteristics (e.g. personal and family history of premature CHD and current smoker) in three subgroups of FH patients by DLCN. ﾔe risk of recurrent cardiovascular events was not signifcantlmdiﬀerentiated by DLCN either. ﾔe reason could be that some Chinese FH patients were diagnosed "possible" by DLCN criteria with higher LDL-C threshold. Indeed, the mean LDL-C level of 3367 Chinese myocardial infarction patient was 3.10 mmol/L. It is lower than mean value of 3.45 mmol/L derived from a 4778 European cohort with acute coronary syndrome [6]. Nevertheless, the current LDL-C diﬀerence between general ethnics populations awaits large scale epidemiology studies. ﾔe MDLCN criteria defne LDL-C threshold according to actual LDL-C distribution in Chinese population. However, the LDL-C data for the MDLCN were from a 2002 report [9].

With the economic growth and Western-like diet being adopted over the past decade, the population LDL-C level in China is speculated to have increased. An ongoing epidemiology study (led by NCCD) investigating nationwide Chinese resident LDL-C levels will give more accurate estimation and guidance for the ft-for-7hinese diagnostic criteria.

Limitations

ﾔe current study have several limitations. Information of physical examination such as tendon xanthomas and corneal arcus were unavailable. But it should have minimum impact because the majority of heterozygote FH patients as this study normally do not have such physical signs. Family LDL-C level was not available in this group of patients. ﾔis could potentially lead to a slightly underestimated FH prevalence. In addition, the correction factor 1.43 used to estimate untreated LDL-C levels in patients using statins has not been validated in Chinese population. However, only a few patients (7.3%) on statin were corrected LDL-C level in the cohort. Finally, we used self-reported information on family history of premature CHD which may have recall bias and lead to an overestimation of FH prevalence.

Conclusion

FH is highly prevalent among patients who had CHD/AMI, especially among patients with premature CHD. ﾔe 1 year follow-up study demonstrated that AMI patients with FH compared to non-FH had an almost 2-fold adjusted risk of recurrence cardiovascular events.

ﾔe cascade screening starting from a proband identifed in CHD/AMI patients could be a good strategy for early treatment and prevention.

References

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