Title: Association of physical signs with genotype, lipid-and inflammation-related markers, coronary stenosis or calcification, and outcomes in patients with heterozygous familial hypercholesterolemia

Ming-Ming Liu*, Jian-Jun Li*
Fu Wai Hospital, CAMS and PUMC, Beijing, China

Background

Although several previous studies indicated that the existence of physical signs [tendon xanthomas or corneal arcus (TX/CA)] was associated with the risk of coronary artery disease (CAD) in patients with heterozygous familial hypercholesterolemia (HeFH), its relations to genotypes and clinical characteristics have not been fully determined. The present study aims to examine the association of TX/CA with genetic mutation, lipid and inflammation-related markers, coronary calcification, coronary severity and cardiovascular events (CVE) in Chinese patients with HeFH.

Methods

A total of 489 HeFH patients diagnosed with Dutch Lipid Clinic Network (DLCN) criteria and/or genetic testing were consecutively recruited. To compare the patients with TX/CA versus those without, propensity score matching (1:4 matched) was performed to adjust for age and sex. Patients were finally divided into the TX/CA group (n=50) and non-TA/CA group (n=200). Data including genetic mutation [low-density lipoprotein receptor (LDLR), apolipoprotein B (APOB), and proprotein convertase subtilisin/kexin type 9 (PCSK9)] and laboratory analysis including lipoprotein (a), PCSK9, high-sensitivity C-reactive protein (hsCRP), computed tomography angiography, coronary angiography, and follow up CVEs were compared.

Results

Patients with physical signs presented significantly higher LDL cholesterol levels (8.65±2.53 vs. 7.70±2.18 mmol/L, p=0.025), more LDLR (+) mutations (OR 2.896, 95%CI 1.295-6.473, p=0.010), higher prevalence of high tertiles of Gensini, SYNTAX and Jeopardy score, and coronary artery calcium scores compared to those without. In addition, patients in the TX/CA group had a higher prevalence of high PCSK9 and hsCRP tertiles compared with those without signs. Over an average of 3.7 years of follow-up, patients with TX/CA were at a significantly greater risk of CVE (multivariate adjusted hazard ratio [HR] 2.81, 95% confidence interval [CI] 1.14–6.90, p=0.024).

Conclusions

The physical signs were associated with positive genetic mutation, higher PCSK9 or hsCRP concentration and worse outcomes in patients with HeFH, suggesting that these signs may help to risk stratification in patients with HeFH.

Figures