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Lipid-lowering therapy and lipid goal attainment in patients with metabolic syndrome in China: Subgroup analysis of the Dyslipidemia International Study-China (DYSIS-China)

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ABSTRACT

Objective: To objectively evaluate lipid-lowering therapy and low-density lipoprotein cholesterol (LDL-C) and non-high-density lipoprotein cholesterol (non-HDL-C) goal attainment in metabolic syndrome (MetS) patients in China.

Methods: Data regarding patient demographics, lipid-lowering agents, lipid parameters, and cardiovascular risk profiles were analyzed for 25,317 patients of the Dyslipidemia International Study-China. MetS was defined according to criteria of the NCEP-ATP III and the 2007 Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults.

Results: The prevalence of MetS was 39.9% and 37.4% according to the NCEP-ATP III and 2007 Chinese Guidelines, respectively. LDL-C goal attainment occurred less frequently among MetS patients than in those without MetS (NCEP-ATP III: 46.9% *vs* 68.6%; 2007 Chinese Guidelines: 52.2% *vs* 67.1%; $p < 0.001$). Similar results were obtained for non-HDL-C goal attainment (2007 Chinese Guidelines: 51.0% *vs* 72.0%; $p < 0.001$). As the risk class increased, LDL-C and non-HDL-C goal attainment decreased. In multivariate logistic regression analysis, DM, CHD, ischemic cerebrovascular disease, and higher SBP were independently associated with failure to achieve LDL-C and non-HDL-C goal attainment. The type of lipid-lowering agent was not significantly correlated with LDL-C not at goal attainment but was correlated with non-HDL-C not at goal attainment.

Conclusion: Goal attainment for both LDL-C and non-HDL-C occurs less frequently in MetS patients than in those without MetS. The residual risk due to elevated non-HDL-C levels should be considered in MetS patients. Strategies for controlling multiple risk factors in order to decrease the residual risk related to dyslipidemia in MetS patients should be recommended in future guidelines.

1. Introduction

Metabolic syndrome (MetS) is associated with an increased risk for the development of cardiovascular disorders worldwide. Patients with MetS have a 2-fold greater relative risk for cardiovascular disease (CVD), a 5-fold greater risk for type 2 diabetes mellitus (DM), a 2.2-fold greater risk for stroke, and a 2.6-fold greater risk for chronic kidney disease [1–3]. A meta-analysis of 172,573 individuals demonstrated a significantly higher risk of cardiovascular events associated with MetS [4]. Lipid abnormalities in MetS contribute substantially to these high cardiovascular risks.

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Dyslipidemia in MetS is characterized by low high-density lipoprotein cholesterol (HDL-C) levels and high triglyceride (TG) levels, together with the presence of small, dense, atherogenic LDL particles, referred to as atherogenic dyslipidemia [5]. Recently, the concept of non-HDL-C [calculated as non-HDL-C = total C (TC) − HDL-C] was promoted by some guidelines [6]. Several studies have shown that non-HDL-C is more strongly related to the risk for CVD than LDL-C [7]. In particular, an increased non-HDL-C level is common in dyslipidemia among MetS patients.

Evidence from major statin trials supports the use of these agents in MetS patients with dyslipidemia [8]. According to the Treating to New Targets (TNT) trial, the presence of MetS indicates the need for more aggressive therapies [9]. However, recognizing the residual cardiovascular risk, beyond using statins for LDL-C reduction, combined therapy may be necessary to achieve target levels for HDL-C and/or TG. Thus, the updated National Cholesterol Education Program Adult Treatment Panel (NCEP-ATP III) recommends that therapeutic intervention targeting high TG levels be initiated in high-risk individuals with additional lipid abnormalities [10]. In addition, the 2011 European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS) guidelines for dyslipidemia recommend that in patients with combined hyperlipidemias, diabetes, or MetS, a secondary lipid goal for non-HDL-C should be considered [6]. Furthermore, the Global Recommendations for the Management of Dyslipidemia issued by the International Atherosclerosis Society (IAS) in 2013 recommend that the term atherogenic cholesterol be applied to either LDL-C or non-HDL-C, and that both LDL-C and non-HDL-C are major targets of therapy [11].

However, little is known regarding the use of lipid-lowering agents and the corresponding lipid goal attainment in MetS patients in China. Here, we present a subgroup analysis of MetS patients from the Dyslipidemia International Study of China (DYSIS-China). The aim of this analysis was to objectively assess therapy outcomes, specifically the achievement of LDL-C and non-HDL-C goal attainment, with respect to dyslipidemia in MetS patients in the "real world" and provide evidence for an appropriate therapeutic strategy for dyslipidemia in MetS.

2. Patients and methods

2.1. Study design and patients

The subgroup of DYSIS-China patients with MetS was taken as the study population in the present study. The DYSIS is a global series of epidemiological multicenter cross-sectional studies. The DYSIS-China was performed from April 2012 to October 2012 and included 25,697 patients treated at 122 centers across China [12]. It was a purely observational study, as only available data were documented and treatment or assessment of patients was not changed by participation in the study. Patients were eligible if they were greater than 45 years old, were taking a stable, approved dose of any kind of lipid-lowering agent, and had a documented fasting lipid profile recorded during the previous 6 months after lipid-lowering therapy for at least 3 months with no dose adjustment for a minimum of 6 weeks. All patients provided written informed consent before entering the study, and the study protocol was approved by the ethics committee of each clinic.

A total of 25,697 patients were eligible for inclusion in this survey. Of these, the lipid parameters of 380 (1.48%) patients were inappropriate or missing, and thus, 25,317 patients were analyzed in the present study. The subgroup of patients with MetS included 10,121 patients according to NCEP-ATP III criteria and 9747 patients according to the criteria of the 2007 Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults.

2.2. Data collection and anthropometric measurements

Patient data were collected from clinical examinations and medical charts from a single outpatient visit over a 6-month recruitment period. Information regarding smoking status, medication use, and history of hypertension, DM, and CVD was obtained by self-reporting using a face-to-face counseling method. The documentation of chronic medication focused on statins and other lipid-lowering agents, including cholesterol absorption inhibitors, fibrates, nicotinic acid, and Xuezhikang, which is a traditional Chinese medicine extracted from red yeast rice. The name and daily dose of the lipid-lowering agents taken by the patient at the time of the visit as well as during the previous 6 months were noted. Furthermore, antihypertensive, antidiabetic, and antiplatelet drug use was recorded. The investigators included internists, cardiologists, endocrinologists, geriatricians, and neurologists who were trained by the research team.

Physical examination included anthropometry and blood pressure measurement. Height, weight, and waist circumferences were measured. Blood pressure was measured using calibrated desktop sphygmomanometers after the patients were seated for at least 5 min, consistent with current recommendations. Blood pressure was measured three times consecutively, with at least 1 min between measurements, and the reported blood pressure was the average of these three measurements.

Fasting lipid profiles were recorded. Of 25,317 eligible patients, the LDL-C levels of 2309 patients were calculated using the Friedewald equation, and those of the other 23,008 patients were measured directly in the biochemistry departments of 122 hospitals. Meanwhile, the levels of serum uric acid, serum creatinine, fasting plasma glucose, and 2-h postprandial plasma glucose were recorded. Non-HDL-C levels were calculated as non-HDL-C = total C (TC) − HDL-C [6].

2.3. Definition of variables

Cigarette smoking was assessed by asking each individual whether he or she was a current smoker. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared (kg/m^2).

DM was defined as previous diagnosis of DM or current treatment with antidiabetic or insulin therapy. Elevated fasting plasma glucose was defined as a serum glucose level between 6.1 and 7.0 mmol/L from the latest available laboratory test. MetS was recorded based on NCEP-ATP III criteria [13] and 2007 Chinese Guidelines criteria [14]. Hypertension was defined as treatment of previously diagnosed hypertension. History of CVD included definite coronary heart disease (CHD), ischemic cerebrovascular disease, and peripheral arterial disease (PAD).

2.4. Risk classification and treatment goals

Classification of patients' risk and definition of therapeutic goals for LDL-C and non-HDL-C were based on NCEP-ATP III criteria and 2007 Chinese Guidelines criteria.

Based on NCEP-ATP III criteria, the patients were categorized into low, moderate, moderate-high risk, high-risk, and very high-risk groups (see Supplemental Table 1). LDL-C treatment goals were as follows: <4.1 mmol/L (160 mg/dL), <3.4 mmol/L (130 mg/dL), <3.4 mmol/L (130 mg/dL), <2.6 mmol/L (100 mg/dL), and <1.8 mmol/L (70 mg/dL) for low-, moderate-, moderate-high-, high-, and very high-risk patients, respectively.

Based on the 2007 Chinese Guidelines criteria, patients were categorized into low (10-year risk score of ischemic CVD <5%), moderate (10-year risk score 5–10%), high-risk (having CHD or