Clinical Neurology and Neurosurgery 171 (2018) 79–84

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Low HDL-C levels are associated with cervicocerebral atherosclerotic stenosis in Southern Chinese patients with large artery atherosclerotic ischemic stroke

Weihua Mai[a,*], Hanwei Liu[a], Xingwei Liu[b], Ling Chen[c], Wenying Zhou[d]

[a] Department of Neurology, The Fifth Affiliated Hospital of Sun Yat-sen University, China
[b] Department of General Surgery, The Fifth Affiliated Hospital of Sun Yat-sen University, China
[c] Department of Medical Quality Control, The Fifth Affiliated Hospital of Sun Yat-sen University, China
[d] Department of Laboratory Science, The Fifth Affiliated Hospital of Sun Yat-sen University, China

ARTICLE INFO

Keywords:
High density lipoprotein-cholesterol
Large artery atherosclerosis
Cervico-cerebral atherosclerotic stenosis
Ischemic stroke

ABSTRACT

Objectives: The aim of this study is to investigate the association of HDL-C with CCAS, as well as its intracranial or extracranial location in the Southern Chinese population.

Patients and methods: 123 Southern Chinese patients with large-artery atherosclerotic(LAA) ischemic stroke were enrolled for the final analysis. Based on the stenosis severity defined by digital subtraction angiography, the patients were categorized into CCAS and non-CCAS groups. The degree of artery stenosis among patients of CCAS was classified into three grades. CCAS were further categorized into intracranial AS (ICAS), Extracranial AS (ECAS) and combined intra-/extra-cranial AS (IECAS).

Results: It was showed that patients with CCAS had a lower HDL-C level compared to NCCAS, and HDL-C levels were correlated to the degree of artery stenosis among CCAS. After adjusting for multiple potential confounders, low HDL-C level remained independently associated with CCAS(adjusted OR = 2.860). Patients with the lowest HDL-C quartile had a significantly increased risk for CCAS(adjusted OR: 5.771), referred to the highest quartile. But HDL-C levels in patients with ICAS, ECAS and IECAS were not significantly different, and there was no significant correlation between HDL-C levels and ICAS.

Conclusion: Our data indicate that low HDL-C level is associated with CCAS in Southern Chinese patients with LAA ischemic stroke. But the effects of HDL-C on the distribution of CCAS is required to be further explored.

1. Introduction

Large artery atherosclerosis (LAA), including atherosclerosis of aortic arch and intra-/extracranial large arteries, is one of the common etiologies for ischemic stroke in Asia [1]. Population-based studies estimated that about 15～40% of ischemic stroke were caused by LAA [2–5]. The distribution of cervico-cerebral atherosclerotic stenosis (CCAS) due to LAA varies among different races. Extracranial AS (ECAS) is more prevalent in Western population, whereas intracranial AS (ICAS) is more common in Asians [1]. It was reported that ICAS accounted for one fifth of all stroke events in South Asians [6]. Multiple traditional risk factors including age, gender, hypertension, diabetes mellitus(DM), dyslipidemia, smoking et al. were involved in the development of ICAS and ECAS [5,7,8]. But concerning the specific risk factors for ICAS or ECAS, conflicting data were obtained. Some studies suggested that female and metabolic syndrome were more associated with ICAS, while smoking and dyslipidemia were more correlated to ECAS [9]. Others showed that patients with smoking, DM and a higher apoB/apoAI ratio were more likely to suffer from ICAS than ECAS [10–12]. Another study indicated that vascular risk factors might not be major determinants of location for atherosclerosis in the EC or IC arteries [13]. So, what are the specific risk factors for CCAS and its distribution remain to be elucidated.

High density lipoprotein-cholesterol(HDL-C) is known to be protective against cardiovascular diseases [14–16], and it is inversely associated with coronary artery stenosis [17,18]. Recent studies have provide evidence that lower HDL-C level is associated with increased risk of ischemic stroke, particularly for atherosclerotic stroke [19,20]. However, so far, the associations of HDL-C with CCAS and its distribution in ischemic stroke have not been well defined, especially in the Southern Chinese population. Therefore, in this study, we sought to investigate the association of HDL-C level with CCAS, as well as EC or

* Corresponding author at: Department of Neurology, The Fifth Affiliated Hospital of Sun Yat-sen University, NO. 52 East Meihua Road, Zhuhai, Guangdong Province, 519000, China.
E-mail address: weihuamai2004@163.com (W. Mai).

https://doi.org/10.1016/j.clineuro.2018.05.021
Received 28 August 2017; Received in revised form 8 February 2018; Accepted 28 May 2018
Available online 29 May 2018
0303-8467/

IC location defined by digital subtraction angiography(DSA) in the unique Southern Chinese population. We supposed that low HDL-C level might be associated with CCAS, and related to its distribution in Southern Chinese patients with LAA ischemic stroke.

2. Patients and methods

2.1. Study design and patients

This was a prospective, cross-sectional study performed in the Southern Chinese population. Consecutive patients admitted to Department of Neurology in the Fifth Affiliated Hospital of Sun Yat-sen University between March 2009 and December 2016 were recruited according to the following criteria: 1)18 to 80 years old, diagnosed as acute ischemic stroke within two weeks of onset, based on clinical manifestation and CT or/and MRI evidence. 2) categorized as LAA ischemic stoke according to Chinese ischemic stroke subclassification (CISS) system [21]. Based on CISS system, ischemic strokes with stenosis (> 50%) or unstable plaque in corresponding arteries, or penetrating artery territory infarction with atherosclerotic plaque on HR-MRI or any degree of stenosis were defined as LAA ischemic strokes [1]. Cases with cardioembolic stroke, CCAS caused by other etiologies such as Takayasu arteritis, dissecting aneurysm et al, previous vascular stenting or angioplasty in intra/extracranial arteries, unstable medical conditions, use of statin or other concomitant lipid lowering drugs prior to the study were excluded. After exclusion as above, a total of 123 patients were enrolled for the final analysis.This study was approved by the Local Ethical Committee in the Fifth Affiliated Hospital of Sun Yat-sen University, and the procedures were carried out with the consent of all patients.

2.2. Definition of clinical index

Clinical information including age, gender, hypertension, DM, a history of ischemic stroke, physical activity, smoking and drinking habits were collected from each patient. Hypertension was defined as a high baseline blood pressure (systolic blood pressure ≥ 140mmHg and/or diastolic blood pressure ≥ 90mmHg), a prior history of identified hypertension, or current use of antihypertensive medication. DM was defined as a fasting plasma-glucose ≥ 7.0 mmol/L, OGTT 2hPG ≥ 11.1 mmol/L, a prior history of DM, or current use of antidiabetic medication. History of ischemic stroke was defined as previous neurological symptoms caused by cerebral infarction confirmed by CT/MRI. Physical activity was classified into physical active and physical inactive using a questionaire, which records the frequency and duration of 14 different recreational activities during 2-week period before admission [22]. Smoker and drinkers were described as current smokers/drinkers or ex-smokers/ex-drinkers with a history of smoking/drinking habits.

2.3. Digital subtraction angiography (DSA)

All patients underwent DSA for three-vessels study within 3 days following admission, including left and right internal carotid arteries and basilar artery (PHILIPS INTEGRIS CV 12. System). The severity of stenosis was analyzed by AVA software. According to the severity of stenosis defined by NASCET criteria [23], the patients were categorized into two groups: CCAS (with 50–100% stenosis in cervico-cerebral arteries) and non-CCAS (NCCAS, with 0–49% stenosis in cervico-cerebral arteries). The degree of artery stenosis among patients of CCAS was further classified into three grades: Grade 1 (with 50–75% stenosis), Grade 2 (with 75–90% stenosis) and Grade 3 (with 90–100% stenosis). In addition, acoording to the location of atherosclerotic stenosis, CCAS was furthered categorized into three subgroups: ICAS, ECAS and combined intra- and extra-cranial atherosclerotic stenosis (IECAS). Intracranial arteries include the proximal portion of middle cerebral artery (MCA: M1), anterior cerebral artery (ACA: A1), posterior cerebral artery (PCA: P1); intracranial portion of internal carotid artery (ICA) or vertebral artery (VA), and basilar artery (BA). Extracranial arteries include extracranial portion of ICA or VA, common carotid artery (CCA), and the proximal portion of subclavian artery (SCA).

2.4. Assessment of lipid profiles

Blood samples were collected after 12-hour fasting following enrollment. Plamsa lipid profiles including total cholesterol(TC), triglyceride(TG), HDL-C, low density lipoprotein-cholesterol(LDL-C) were analyzed by automatic biochemical analyzer (Hitachi 7600, Hitachi, Tokyo, Japan). All assessments were conducted in the hospital clinic laboratory. Lipid values were defined based on Adult Treatment Panel III guidelines of the National Cholesterol Education Program(NCEP) [24]: high TG level (≥ 1.7 mmol/L), high TC level (≥ 5.18 mmol/L), high LDL-C level (≥ 2.59 mmol/L) and low HDL-C level (< 1.03 mmol/L for men, < 1.30 mmol/L for women).

2.5. Statistical analysis

Comparisons among groups were performed using Chi-square test, one way analysis of variance (ANOVA) and Mann-Whitney U test as appropriate. A stepwise multivariate logistic regression analysis was performed to determine whether plasma HDL-C level was independently associated with CCAS and ICAS after adjusting for potential confounding factors. Only variables with $P < 0.05$ by univariate analysis were selected for entry into binary logistic regression analysis. Results were given by odds ratios(ORs) and 95% confidence intervals (95% CI). Plasma HDL-C concentrations were further stratified into four quartiles. ORs for atherosclerotic stenosis in different HDL-C quartiles were evaluated by binary logistic regression analysis, using the highest quartile as a reference. There were no missing data in all patients enrolled. All statistical analyses were conducted using SPSS version 16.0. P values less than 0.05 were considered statistically significant.

3. Results

3.1. Characteristics of patients

Among 123 enrolled patients, 94 (76.4%) were classified as CCAS, and 29 (23.6%) as NCCAS. Among CCAS group, 48(51.1%) were subclassified as ICAS, 22(23.4%) as ECAS, and 24(25.5%) as IECAS. Spatial distribution of cerebral infarction on CT or/and MRI in patients with all enrolled patients were as below: cerebral cortical infarct lesions (85), cerebellar infarct lesions (33), brain stem infarct lesions (16) and subcortical infarct lesions (24). Demographics and clinical characteristics for CCAS and NCCAS, as well as ICAS, ECAS and IECAS groups were summarized in Tables 1 and 4. Compared to NCCAS group, patients with CCAS showed higher frequencies of old age, male, hypertension, DM and history of stoke, and plasma HDL-C levels in CCAS patients were lower. Similarly, compared to ECAS and IECAS groups, patients with ICAS had higher frequency of DM. But HDL-C levels in patients with ICAS, ECAS and IECAS were not significantly different.

3.2. Relationship between HDL-C levels and the degree of artery stenosis

Relationship between HDL-C levels and the degree of artery stenosis among patients of CCAS was eveluated. It was shown that HDL-C levels in Grade 2(n = 33) and Grade 3(n = 21) were significantly lower than that in Grade 1(n = 40) (1.00 ± 0.161 *vs* 1.18 ± 0.225 mmol/L, $P = 0.037$; 0.92 ± 0.140 *vs* 1.18 ± 0.225 mmol/L, $P = 0.015$). But HDL-C levels between Grade 2 and Grade 3 were not significantly different (1.00 ± 0.161 *vs* 0.92 ± 0.140, $P = 0.494$).