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Original article

Long-term use of first-line highly active antiretroviral therapy is not associated with carotid artery stiffness in human immunodeficiency virus-positive patients

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ABSTRACT

Objective: To evaluate whether or not highly active antiretroviral therapy is associated with carotid artery stiffness in human immunodeficiency virus-positive patients in Henan Province, China.

Method: Fifty human immunodeficiency virus-positive patients with at least a 5-year history of highly active antiretroviral therapy use and 50 human immunodeficiency virus-positive patients without a history of highly active antiretroviral therapy use were enrolled in this study. Carotid artery intima-media thickness and stiffness were determined by quantitative inter-media thickness and quantitative artery stiffness, respectively.

Results: No statistically significant difference in carotid artery intima-media thickness and stiffness was observed between groups. A significant association between human immunodeficiency virus infection time and carotid artery stiffness was observed, but no significant association between human immunodeficiency virus infection time and intima-media thickness was found. No significant association between intima-media thickness, stiffness, and $CD4^+$ and $CD8^+$ T-cell counts were observed.

Conclusion: The first-line highly active antiretroviral therapy currently used in China is not associated with carotid artery stiffness in human immunodeficiency virus-positive patients with good highly active antiretroviral therapy compliance. Human immunodeficiency virus may play a role in the development of atherosclerosis.

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Introduction

Highly active antiretroviral therapy (HAART) has benefited human immunodeficiency virus (HIV)-infected patients since 1996. Mounting evidence shows that HAART helps controlling HIV replication and lead to a remarkable reduction in mortality rates.[1] However, as HAART has become more widely used, reports of increased risks of cardiovascular diseases of those on HAART have emerged.[2–4] Some researchers have focused on subclinical atherosclerosis,[5–8] and endothelial functions, carotid intima-media thickness (IMT), artery distensibility coefficient, and pulse wave velocity (PWV) have been used to assess artery stiffness in HIV-infected patients.[9–12] However, whether HAART leads to artery stiffness remains unclear, and studies on the association between carotid artery stiffness and HAART, especially in China, are limited. The present research aims to study whether first-line HAART is associated with carotid artery stiffness in HIV-positive patients from Henan Province, China.

Subjects and methods

Study population

This was a cross-sectional study conducted from April 2013 to July 2013. All participants were recruited from the countryside of Henan Province, China and infected with HIV by blood transfusion. Participants were followed since first diagnosed with HIV infection and had over 10 years of HIV infection history.

All participants were approached by the interviewers during routine medical examination. Inclusion criteria were as follows: age between 18 and 60 years; normal body mass index (BMI); no family history of coronary artery disease, hypertension, or diabetes; and no history of cardiovascular disease, hyperlipidemia, or other disease, such as heart or kidney failure, and tumors. HIV patients received HARRT (D4T or AZT + 3TC or DDI + NVP or EFV) for over five years with treatment compliance above 80%. Compliance was evaluated by pharmacy supply of antiretroviral drugs every month. Operationally, treatment compliance was calculated as number of days without antiretrovirals in the period/number of days in the period. Individuals with active infection as well as those who received other medications that could affect artery stiffness for over three months during the past six months were excluded from the study. Smokers, alcoholics, and pregnant women were also excluded. All participants had normotension, ortholiposis, euglycemia, and normal BMI. Fasting blood glucose levels within 3.89–6.11 mmol/L, triglycerides less than 1.70 mmol/L, and total cholesterol less than 5.18 mmol/L was considered normal, according to Chinese adult dyslipidemia prevention guide (2007). BMI within 18.5–22.9 kg/m^2 was considered normal according to the diagnostic criteria of BMI by WHO for Asian-Pacific region. Normal blood pressure (BP) was defined as two measurements at different times wherein a systolic BP of no more than 140 mmHg and a diastolic BP of no more than 90 mmHg, according to the diagnostic criteria of hypertension detection in the seventh report of USA assessment and treatment of hypertension prevention detection of the Joint National Committee (JNC 7). Carotid artery IMT less than 1.0 mm and absence of atherosclerotic plaques were considered normal, according to the ultrasound examination and diagnostic criteria of Atherosclerotic stenosis in the ultrasound conference of Radiological Society of USA (October 2002).

Electrocardiogram showed a normal sinus rhythm without any remarkable abnormality, such as myocardial ischemia or myocardial infarction. Chest X-ray showed no serious findings, such as pulmonary hypertension, pneumonia, or tumor. Ultrasound examination showed no severe heart, liver, spleen, or kidney diseases, such as heart failure, myocardiopathy, severe valvular disease, or tumors. Carotid artery ultrasound showed no intima-media thickening, atherosclerotic plaque, or other arterial diseases (e.g., Takayasu arteritis and aneurysm). This study was conducted in accordance with the declaration of Helsinki and approved by the Ethics Committee of People's Hospital of Zhengzhou University. Written informed consent was obtained from all participants.

Data collection

Fifty HIV-infected patients who received first-line HARRT comprised the therapy group. Patients (males, 52%; females, 48%) received first-line HAART from 5 to 13 years (mean, 9.07 ± 2.16 years). Another 50 HIV-infected patients (males, 50%; females, 50%) who were not on HARRT comprised the non-therapy group. Gender and age were similar between the two groups.

In the morning after a 12-h fast, venous blood was sampled and tested for glucose, triglycerides, total cholesterol (via the enzymatic method; Olympus AU5400, Japan), and CD4$^+$ and CD8$^+$ T-cell counts (via cytometry; FacsCalibur (three colors), Becton Dickinson, USA). Patient height, weight, and BP were measured, and BMIs were calculated.

Carotid artery stiffness was determined by an Esaote MyLab90 ultrasound system (Esaote Company, Italy) with quantitative inter-media thickness (QIMT) and quantitative artery stiffness (QAS) software using a 5–13 MHz probe. Participants were asked to lie down in a horizontal position for 10 min, after which their BP was measured and entered into the computer system. The acoustic beam was placed vertically to the right carotid artery wall to obtain clear imaging of the three layers of the anterior and posterior artery walls. QIMT was used to determine the IMT of the right carotid artery. The ROI of QIMT was placed 1.0 mm below the carotid sinus, and the diameter and IMT of the carotid artery were automatically obtained for six continuous cardiac circles. The images were frozen and the data were recorded by the system (Fig. 1). QAS was used to obtain the stiffness parameters of the carotid artery, including compliance coefficient (CC), stiffness, and PWV with the similar method (Fig. 2). All carotid artery ultrasound examinations were performed by an experienced sonographer.

Statistically analysis

SPSS 15.0 was used to analyze the data. Continuous variables are described as mean ± SD, while categorical variables are described as percentages. IMT and stiffness parameters were compared between therapy and non-therapy groups.