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ORIGINAL ARTICLE

Relationship between Atherosclerotic Risk Factors and Aortic Plaques in Patients with First-ever Ischaemic Stroke

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Objective Aortic plaque is considered a risk factor of ischaemic stroke, and both ulceration and plaque thickness are considered important. However, the relative importance of aortic plaque and carotid plaque remains unclear. The purpose of this study is to clarify the relation between aortic and carotid plaque lesions and atherosclerotic risk factors in patients with acute ischaemic stroke.

Methods We enrolled 76 patients with first-ever ischaemic stroke, undergoing transoesophageal echocardiography, whose aetiology of ischaemic stroke was unknown. We divided the patients into two groups according to aortic plaque thickness, based on previous reports, i.e., a high-risk group (over 4 mm) and a low-risk group (less than 4 mm). We also examined several atherosclerotic risk factors.

Results Mean age, gender and hypertension was not significantly different between the low-risk and high-risk group. HDL-cholesterol ($P < 0.01$), LDL/HDL ratio ($P < 0.05$), non-HDL-cholesterol ($P < 0.05$), HbA1c ($P < 0.05$) and eGFR ($P < 0.01$) were significantly different between the two groups. Max plaque thickness in the carotid artery was correlated with aortic plaque lesions.

Conclusion Multiple atherosclerotic risk factors are associated with greater aortic plaque lesions. Aortic plaque is important not only as an embolic source, but also as one of the atherosclerotic markers.

Keywords Aortogenic brain embolism • Artery-to-artery embolism • Transoesophageal echocardiography • Carotid plaque • Chronic kidney disease

Introduction

Presence of an aortic plaque is considered a risk factor of ischaemic stroke, and an embolism caused by an aortic plaque is known as an aortogenic brain embolism. Amarenco et al., [1] reported that an ulcerated plaque on the aortic arch could cause ischaemic stroke; both ulceration and plaque thickness were considered important. Fujimoto et al., [2] and Tullio et al., [3] reported that aortic plaques of over 4 mm were frequently observed in ischaemic stroke of unknown type and were related to increased recurrence and mortality regardless of treatments. Tanaka [4] reported that a maximum aortic plaque thickness of over 3.5 mm increased the likelihood of cardiovascular events and recurrence of cerebral infarction. The mobility of an aortic plaque and the presence of a branched plaque were suggested to be

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important factors [2,5]. On the other hand, Russo et al., [6] found that the presence of an aortic plaque was not an independent risk factor and suggested that comorbid risk factors might be of more importance, although vascular events occurred with high frequency in patients with aortic plaque thickness of over 4 mm. Increased carotid intima-media thickness (IMT), an important embolic source in patients with cerebral infarction, like an aortic plaque, is known to be a predictor of vascular events [7,8]. However, there are few reports comparing an aortic plaque with a carotid plaque as a risk factor for ischaemic stroke, and no significant benefit of warfarin or antiplatelet drugs has been found on the incidence of stroke and other embolic events in patients with severe thoracic aortic plaque [9]. The purpose of this study was to clarify the relationship between aortic and carotid plaques and various atherosclerotic risk factors in patients with acute ischaemic stroke.

Patients and Methods

The study included 76 patients with first-ever ischaemic stroke of unknown aetiology (National Institute of Neurological Disorders and Stroke-III), undergoing transoesophageal echocardiography (TEE), and admitted at Tokai University School of Medicine, Tokai University Hachioji Hospital between May 2009 and July 2013 (52 males and 24 females; mean ± standard deviation (SD), 66 ± 10 years of age). Patients with juvenile stroke (the upper age cut-off of 45 was inspired by the previous reports [10,11]) were excluded.

We checked aortic plaques from the ascending aorta to the aortic arch (from the end of the ascending aorta to the left subclavian artery, according to the guideline) [12]. We evaluated aortic plaques in the short axial view for maximal plaque thickness (MPT), mobility, ulcerative or calcified lesion, and presence of a branched plaque (extended plaque lesion from aortic arch to left subclavian artery). An ulcerative lesion was considered by the presence of surface defects showing a depth over 2.0 mm. We divided patients into two groups according to aortic plaque thickness based on previous reports, i.e., a high-risk (HR) group (at least 4 mm) and a low-risk (LR) group (less than 4 mm).

We investigated the following characteristics: age, gender, Body Mass Index (BMI; body weight [kg]/height [m^2]), smoking history (Brinkman index [BI]: number of cigarettes per day × number of years of smoking), hypertension (systolic blood pressure over 140 mmHg and diastolic blood pressure over 90 mmHg or use of antihypertensive medication), diabetes mellitus (HbA1c [NGSP; National Glycohemoglobin Standardization Program] >6.5%), dyslipidaemia (triglyceride [TG] >160 mg/dL, high-density lipoprotein cholesterol [HDL-C] <40 mg/dL, low-density lipoprotein cholesterol [LDL-C] >140 mg/dL), history of coronary artery disease (CAD), concomitant medications (antiplatelet agent, anticoagulant, antihypertensive drug [angiotensin converting enzyme inhibitor or angiotensin II receptor blocker], antidiabetic drug [thiazolidinediones], or antilipidaemic agent [HMG-CoA reductase inhibitor]), distribution of lesions and disease types (diagnostic criteria: cardiogenic cerebral infarction that was caused by cardiac factors [atrial fibrillation, valvular disease, congestive heart failure, cardiopathy, smoke-like echo, or endocardial thrombus], paradoxical cerebral infarction that was caused by RL shunt [patent foramen ovale or pulmonary arteriovenous fistula] and deep vein thrombosis without other cerebrovascular risk factors, aortogenic cerebral infarction that was caused by aortic plaques [MPT ≥4 mm] without other cerebral risk factors, indeterminate type that was caused by aortic plaques [MPT ≥4 mm] with other cerebral risk factors)), serum lipid levels (TG, total cholesterol [TC], HDL-C, LDL-C, non-HDL-C [TC – HDL-C], LDL-C/HDL-C ratio), glucose tolerance (HbA1c [NGSP]), renal function ([eGFR (= $194 \times Cr^{-1.094} \times Age^{-0.287}$ (female, × 0.739) (mL/min/1.73 m^2), except for dialysis patients), and carotid lesion evaluated by ultrasound sonography (the presence of carotid artery stenosis >50% [using the NASCET method [13]]), maximum intima-media thickness [max IMT], and MPT [based on the guideline] [14]).

Statistical Analysis

For comparison of the two groups, we used the *t* test for normally distributed variables, the Mann-Whitney U test for non-normally distributed variables, and the chi-square test for gender, co-morbidities [CAD, hypertension, diabetes mellitus, dyslipidaemia and carotid stenosis], characteristics of aortic atheroma and concomitant medications. Additionally, we used multivariable logistic regression to assess the contribution of worsening aortic plaque thickness and characteristics. To investigate the correlation of risk factors with aortic plaque thickness, we used the Pearson correlation coefficient for normally distributed variables and Spearman rank correlation coefficient for non-normally distributed variables. Statistical analyses were performed using SPSS (Ver. 19) software package (IBM, Armonk, NY), and we defined a P-value of <0.05 as significant. For normally distributed variables, the mean ± standard deviation is shown, while for non-normally distributed variables, only the average is given, unless otherwise noted.

Results

Among the 76 patients, 29 and 47 were in the HR (38.2%) and LR groups (61.8%), respectively.

The characteristics of the subjects in the two groups are summarised in Table 1. There was no significant difference between the two groups, except in the characteristics of aortic atheroma. The distributions of stroke subtypes and vascular territory in the LR and HR groups are illustrated in Fig. 1 and Fig. 2, respectively. There was no significant difference in the distribution of lesions between the two groups. Indeterminate type in the HR group was seen in seven patients: there was one patient with Af, three patients with smoke-like echo, and three patients with PFO as comorbidity. In the HR group,