Diagonal Ear-Lobe Crease is Correlated With Atherosclerotic Changes in Carotid Arteries

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Background: The diagonal ear-lobe crease (ELC) is reported to be a marker of cardiovascular disease. Very few reports have assessed the relationship of ELC with atherosclerosis. This relationship is investigated here using a Japanese population.

Methods and Results: A prospective cross-sectional study included 212 consecutive patients. Bilateral ear lobes were checked for the ELC and this was followed by carotid ultrasonography to measure the far wall common carotid artery intima-media thickness (CCA-IMT), plaque score (PS) and plaque number (PN). Patients with ELC had significantly higher carotid IMT than controls (0.90±0.24 vs 0.77±0.15, respectively, P<0.001). ELC presence correlated significantly with carotid IMT, PS, and PN (r=0.306, P<0.001; r=0.198, P<0.008 and r=0.221, P<0.0001, respectively), and also with age, male sex and hypertension. ELC presence and absence in mild or no PS and moderate or severe PS subgroups was significant, with a chi-squared value of 7.59 (P<0.006). In multivariate regression analysis, ELC presence correlated with CCA-IMT independently. The odds ratio for the presence of ELC in patients with CCA-IMT of <0.8 mm vs patients with CCA-IMT of ≥0.8 mm (the median value) was 0.41 (95% confidence interval, 0.22–0.76).

Conclusions: The present study showed an association between ELC and increased CCA-IMT, PS, and PN. (Circ J 2009; 73: 1945–1949)

Key Words: Atherosclerosis; Carotid intima-media thickness; Diagonal ear-lobe crease; Plaque score

Ear-lobe crease (ELC) is the fold or crease in the skin of the ear-lobe, first described by Frank in 1973.1 Since then, there have been many other reports about ELC as a risk factor for coronary artery disease (CAD). While many studies have been reported regarding the relationship of ELC with CAD, very few have been reported regarding the correlation with atherosclerosis of the carotid artery.2,3 The carotid artery intima-media thickness (IMT) is not only taken as one of the risk factors for cerebrovascular disease (CVD), but it is also considered as a reliable marker of systemic atherosclerosis.4,6 This study has been designed in this regard, to study the prevalence of the ELC in relation to the carotid atherosclerosis, and to find out whether it can be used as a marker of carotid atherosclerosis and thus an indicator of future stroke. In this study, we also investigated the association of ELC with other established risk factors for atherosclerosis (ie, hypertension, hyperglycemia, dyslipidemia and smoking habits).

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Methods

A continuous prospective cross-sectional study was conducted. Patients were recruited from consecutive cases undergoing clinically indicated ultrasonographic examination of the extracranial carotid artery systems, and included a wide age-group range and underlying diseases or diagnoses, including patients with CVD history, CAD history, patients with other neurological and systemic problems and also the patients undergoing carotid ultrasonography for pre-operative screening purposes, in the department of Neurology, Hiroshima University Hospital. Exclusion criteria included the inability to obtain a good carotid sonograph, and the inability to obtain informed consent from the patient. Informed consent was obtained from all the participants before they enrolled in the study.

The bilateral ear lobes were assessed manually for the presence of typical diagonal ELC, with the patients in sitting position using an evaluation sheet (Figure 1). The structure of the ear lobe, presence or absence of the ELC and if present, the length and depth of the crease were recorded on the sheet. An illustration of an ear lobe was also included on each sheet where the ELC was drawn exactly as present and later on tallied with a photograph of a typical ELC. The typical ELC was recorded as being present if a subject had a deep diagonal crease extending obliquely from the tragus towards the outer border of the ear lobe, covering at least two-thirds of the ear lobe length. Whenever there was more than 1 crease, at least 1 should have met the above criteria. A typical ELC in one of the patients is shown in Figure 1.
as an example, along with the recording of the crease in the evaluation sheet illustration (Figure 1). To minimize the risk of examiner's bias, the ear lobes were evaluated prior to the ultrasonographic examination. The examiner conducting the ultrasonography was blinded to the patient ELC findings.

Common carotid arteries were evaluated with high resolution B-mode duplex ultrasonography with a 7.5 MHz linear type probe (Aplio, Toshiba Medicals, Tokyo, Japan). Bilateral optimal visualization of the carotid arteries was performed with the patients lying comfortably in the supine position with their neck slightly hyper-extended. The mean value of the maximal IMT measured in the distal common carotid artery (CCA) far wall (10 mm section of the artery proximal to the starting point of the carotid bulb) on the both sides was taken. IMT is the distance between the lumen-intima interface and the media-adventitia interface. Based on multiple visualizations, the measurements were taken from the best longitudinal images possible to obtain for the segment of the artery. The plaques in the accessible segments of the CCA as well as internal carotid arteries (ICA) were recorded in terms of plaque number (PN) and plaque score (PS). Plaques are defined as an IMT of ≥1.1 mm, and the PN includes the total number of plaques recorded in the CCA-ICA segments bilaterally. The PS is the sum of the heights of all the number of plaques present, bilaterally.\textsuperscript{7,8}

Data regarding other established risk factors for atherosclerosis, namely hypertension, hyperglycemia, dyslipid-
emia, smoking habits and significant past medical illnesses such as transient ischemic attack (TIA)/stroke or ischemic heart disease (IHD)/CAD were drawn from hospital records. Risk factors were defined as follows: hypertension: SBP of ≥140 mmHg and/or DBP of ≥90 mmHg or using antihypertensive medication; hyperglycemia: fasting blood glucose of ≥7.0 mmol/L and/or glycosylated hemoglobin of ≥5.8% or using oral hypoglycemic agents or insulin; dyslipidemia: LDL-cholesterol of ≥3.6 mmol/L or using lipid lowering agents. Smoking was defined as “current smokers” or “non-smokers”.

Statistical Analysis
Data were expressed as mean±standard deviation or % unless stated otherwise. P values of <0.05 were considered statistically significant. Comparison of the variables between groups was carried out using a chi-squared test for categorical variables and a t-test for continuous variables. Spearman and Pearson correlation analysis were performed to assess the relationship between ELC and other parameters. Multivariate regression analysis was conducted to check the independent relationship between ELC and carotid IMT. Cross tabulation and an odds ratio calculation was conducted to check the ELC in the 2 IMT groups. All statistical analysis was conducted using SPSS (Statistical Package for Social Sciences, release 11.0) for Windows.

Results
The study subjects consisted of 212 patients, 61 with typical ELC and 151 without ELC (as control group). Of the total 212, 106 (50%) were male. The mean age of the subjects was 67±12 years. The clinical characteristics of the study subjects are shown in Table. Of the total patients, 93 had a history of stroke or TIA, 24 had a history of CAD/IHD and 8 had peripheral vascular disease.

IMT was significantly higher in the ELC group than in the control group (0.90±0.24 vs 0.77±0.15, respectively, P<0.001) (Figure 2). The presence of ELC showed a significant correlation with carotid IMT (r=0.31, P<0.0001). The presence of ELC was also significantly correlated with

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<th>Table. Characteristics of the Study Subjects</th>
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Data are presented as mean±standard deviations or as the number (%) of patients.

ELC, ear-lobe crease; H/o, history of; TIA, transient ischemic attack; NS, not significant; CAD, coronary artery disease; IHD, ischemic heart disease; PAD, peripheral arterial disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; CCA, common carotid artery; max, maximum; IMT, intima-media thickness.

Figure 2. Common carotid artery intima-media thickness (CCA-IMT) in patients with and without ear-lobe crease (ELC). Data are presented as mean±standard deviation. P<0.0001.

Figure 3. Common carotid artery intima-media thickness (CCA-IMT) in ear-lobe crease (ELC)-present and ELC-absent groups against quartiles of age.
age (r=0.24, P<0.001), male sex (r=0.24, P<0.0001) and presence of hypertension (r=0.15, P<0.05) but not with other risk factors, such as hyperglycemia, dyslipidemia and smoking habits.

The odds ratio for the presence of ELC in patients with CCA-IMT of <0.8 mm vs patients with CCA-IMT of ≥0.8 mm (the median value) was 0.41 (95% confidence interval, 0.22–0.76).

The subgroup analysis showed a graded and independent association of ELC and quartiles of age. The t-test analysis of the differences in the mean IMT in ELC-present and ELC-absent groups in different age quartiles showed significant differences between the 2 groups (0.72±0.02 vs 0.69±0.16 mm, P=0.036; 0.84±0.09 vs 0.78±0.13 mm, P=0.027; 0.96±0.34 vs 0.78±0.11 mm, P=0.008; respectively for the 1st, 2nd and 3rd quartiles but not for the 4th quartile (0.97±0.11 vs 0.91±0.15 mm, P=0.193, Figure 3)). ELC also showed an independent association with carotid IMT in the multivariate regression analysis (β=0.306, P≤0.0001) when adjusted for age, sex and hypertension.

Our results showed that the PS and PN were higher in ELC-present group compared to the control group. In the ELC-present group, almost 48% had moderate-to-severe atherosclerotic findings, whereas in the control group had only 27% moderate-to-severe atherosclerotic changes (Figure 4).

There was significant correlation between ELC and PS, as well as PN (r=0.198, P<0.008 and r=0.221, P<0.0001, respectively). Grading of atherosclerotic changes is conducted based on the PS, where a PS of <5 is considered as mild, 5–10 as moderate and >10 as severe.8 PSs in the subjects were further divided into mild or no PS and moderate to severe PS sub groups, and compared between ELC-present and -absent groups. The chi-squared value for this analysis was 7.59 (P<0.006).

Discussion

The main finding of this study is that ELC is significantly associated with carotid artery IMT and also with the PS and PN, the markers of atherosclerotic changes in the arteries. Since the first reporting of ELC by Frank in 1973, many other studies about ELC as a risk factor for CAD have been reported.1–9 While many studies have been reported regarding the relationship of ELC with CAD, very few have been reported on the correlation with atherosclerosis of the carotid artery.2,3 Few have studied the correlation of ELC with carotid atherosclerosis, but they also have studied only the relationship with carotid IMT, not other indices of carotid artery ultrasonography such as PS and PN. Celik et al have reported a significant association between ELC and the carotid IMT in a population sample of middle-aged adults without known atherosclerotic disease.3 In this regard, the present study also supports the association between ELC and carotid IMT. To the best of our knowledge, this is the first published report regarding the association between carotid IMT, carotid PS and ELC in an oriental population.

Studies in the past have examined the clinical and pathological correlations and found degeneration of elastin in the ELCs, tear in elastic fibers and pre-arteriolar wall thickening.20,21 In contrast, atherosclerotic changes in the arterial wall could include smooth muscle cell proliferation, deposition of lipid and accumulation of collagen, elastin and proteoglycans, without the compensatory development of scar collagen. Changes in the ratio of collagen to elastin have been known to structurally affect the elastic behavior of the arterial wall.22–24 This pathological mechanism might be the possible explanation for the correlation we found for the first time between the ELC and the atherosclerotic changes, especially the plaques in the carotid artery. Thus, in addition to the primary role of ageing and hypertension, some other atherogenic stimuli might be involved in the development of the ELC and also the atherosclerotic changes in the arteries.

Most studies in past agree that, although the prevalence of the ELC increases with advancing age, the correlation of the ELC with CAD is independent of this phenomenon,10 however, some reports have tried to attribute the relationship between ELC and CAD as being solely dependent on age. On par with most of the past studies, we also found an increasing trend of ELC prevalence with increasing age, but the relationship of ELC with IMT was independent of age and sex. Tranchesi Jr et al have also reported a significant association between ELC and CAD in quite a large sample of patients (1,424 patients), irrespective of patient’s chronological age and sex, however, they did find the growing prevalence of ELC with advancing age.15 Many other investigators have also reported similar findings.11,13,14,19,20,25 Studies have shown that ELC has a reasonably high predictive value for cardiac events.15,26 Kirkhim et al and Elliot and Karrison have reported the association of ELC with an increased risk of cardiovascular cause of death.16,17 Higuchi et al, in a recent study, demonstrated an association between...
ELC and atherosclerotic cardiovascular disease in metabolic syndrome patients. Various studies have found varying degrees of association between ELC and CAD, and various mechanisms of association are suggested. Systemic arterial atherosclerosis is a progressive condition and involves various arteries leading to some of the most devastating outcomes. Hoshino et al report that metabolic syndrome and intracranial large artery atherosclerosis might be potential predictors for identifying patients with cerebral infarction who are at the highest risk of asymptomatic CAD.

Li et al have demonstrated the importance of the detection of the vulnerable plaques. These and many other studies highlight the importance of the simple and reliable predictors of atherosclerosis like ELC for the detection of the atherosclerotic changes as early as possible. Identification of the persons at risk of such major outcomes in the earlier stages would lower the burden of morbidities and mortalities associated with these disorders.

Agreeing with the previous studies, we also suggest that ELC should be promoted as a marker of possible atherosclerotic changes, and it might serve as a reminder to those patients who might not otherwise be screened for modifiable risk factors for atherosclerosis and also provide caution for possible future diagnosis of CAD or CVD. As ELC is a very easily detectable sign, it can be promoted as a simple index of carotid atherosclerosis, and therefore a simple predictor of a possible devastating consequence. It can easily be applied in any setting, even by primary level healthcare professionals for the screening of the patients in terms of a future risk of stroke.

The present study had some limitations; small sample size, and having a cross-sectional study design. In conclusion, this study suggests that the presence of ELC might be considered as a possible sign of underlying atherosclerotic disease, although further studies are still required to establish it as a reliable (diagnostic) sign in clinical practice.

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Disclosure
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References