Associations between Carotid Artery Wall Thickness and Cardiovascular Risk Factors Using Multidetector CT

BACKGROUND AND PURPOSE: It has been demonstrated that the increase in CAWT is associated with an increased risk of stroke and its severity. The aim of this study was to determine whether CAWT evaluated by MDCTA is associated with the following cardiovascular risk factors: hypertension, diabetes mellitus, dyslipidemia, and smoking.

MATERIALS AND METHODS: This was a retrospective study. One hundred sixty-eight patients (120 men; mean age, 68.96 years ± 12.2 years SD) were analyzed by using a multidetector row CT scanner. Continuous data were described as the mean value ± SD and were compared by using the Student t test. We performed simple logistic regressions to evaluate the association between CAWT and the following: hypertension, diabetes mellitus, dyslipidemia, and smoking. A P value < .05 indicated statistical significance.

RESULTS: The distal common CAWT varied from 0.5 to 1.5 mm. We observed that hypertension and diabetes mellitus were associated with increased (>1 mm) CAWT (P = .0041 and P = .0172, respectively). There was no significant association between increased CAWT and dyslipidemia or smoking.

CONCLUSIONS: In our selected group, the results of this work show that an increased CAWT is associated with the cardiovascular risk determinants hypertension and diabetes. Further studies are necessary to evaluate whether it is possible to apply our observations to the general population.

ABBREVIATIONS: Az = area under each ROC curve; CAWT = carotid artery wall thickness; CCA-IMT = common carotid artery intima-media thickness; CI = confidence interval; CTA = CT angiography; IMT = intima-media thickness; +LR = XXX; −LR = XXX; MDCTA = multidetector row CTA; NC = not calculable; ROC = receiver operating characteristic analysis; Std. = standard; TIA = transient ischemic attack
plaque. We defined “symptomatic” as a patient who had a TIA or stroke. We considered “TIA” as a brief (<24 hours) episode of neurologic dysfunction, such as dysarthria, dysphasia, hemiparesis, hemiparesis, or monocular blindness. If the episode of neurologic dysfunction exceeded 24 hours, it was classified as a “stroke.” We defined “asymptomatic” as descriptive of a patient who had no history of symptoms, either remote or present, at the time of the examination.

In our department, we studied the carotid arteries of asymptomatic patients with diabetes older than 50 years of age and of patients who were undergoing cardiac interventions for coronary artery disease, aortic interventions, and lower leg artery surgery.

Exclusion criteria for the study consisted of contraindications to iodinated contrast media, such as a known allergy to iodinated contrast material, or elevated renal function test results.

This retrospective review evaluated existing clinical data and records. No additional procedures were performed. The review was conducted in accordance with the guidelines of the research committee of our institution. Part of our patient cohort had been included in previous studies.15,17-19

Vascular risk factors that are known before a stroke or TIA, coexisting comorbidities, and treatment before a stroke or TIA are systematically recorded at our institution. “Essential hypertension” was defined in those individuals who had systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg or who were being treated with blood pressure—lowering drugs. “Diabetes” was indicated by abnormal fasting plasma glucose levels (>7.9 mmol/L) or the current use of insulin or an oral hypoglycemic agent. The use of insulin or oral diabetes medication was also considered diagnostic for diabetes. “Dyslipidemia” was defined as abnormal fasting plasma cholesterol (low-attenuation lipoprotein cholesterol) levels (fasting cholesterol, >5.0 mmol/L) or the current use of lipid-lowering agents. Cigarette smoking status was categorized as never, former (24 months), or current.

**MDCTA Technique**

We use a standardized technique as previously described.15,17-19 All patients underwent MDCTA of the supra-aortic vessels by using a 4-multidetector-row CT system (MX8000, Philips Healthcare [formerly Picker International], Andover, Massachusetts). Written consent to perform MDCTA was obtained after discussion of the risks associated with contrast-enhanced MDCTA and the potential benefits derived from this examination. Patients were placed in the supine position, with the head tilted back to prevent dental artifacts on the images. Patients were also instructed not to breathe and not to swallow. One hundred ten milliliters of a contrast medium (iopromide, Ultravist 370; Schering, Berlin, Germany) was injected into an ante-cubital vein, by using a power injector at a flow rate of 5–6 ml/s and an 18-ga intravenous catheter. CT technical parameters were as follows: matrix, 512 × 512; FOV, 11–19 cm; mA, 180–220; kV, 120–140. Images were reconstructed with a section thickness of 0.6 mm. Angiographic acquisition included the circle of Willis; the lower landmark was the aortic arch. None of the patients included in the study had a medical history of cardiac output failure; any contraindications to iodinated contrast media, such as a known allergy; or elevated renal function test results.

**Evaluation of Carotid Image Quality and Artifacts**

In this study, evaluation of image quality and artifacts was performed by 2 radiologists with 5 and 10 years of experience in MDCTA angiography of the carotid arteries. The readers were blinded to the patient’s symptoms. They were asked to evaluate the overall image quality on a 5-point scale. On this scale, 5 corresponded to excellent image quality; 4, to good image quality; 3, to adequate image quality; 2, to marginally acceptable image quality; and 1, to unacceptable image quality. Values 1 and 2 included those cases in which the carotid artery wall did not show a well-defined cleavage plane, with nearby structures such that it was not possible to clearly observe the hypoattenuated adipose tissue that allows the end of the carotid wall to be defined.

The readers were also asked to assess the impact of image artifacts on a 5-point scale. On this scale, 5 corresponded to the complete absence of imaging artifacts; 4, to mild artifacts not interfering with diagnostic decision making; 3, to moderate artifacts slightly interfering with diagnostic decision making; 2, to pronounced artifacts interfering with diagnostic decision making (though it was still possible to arrive at a diagnosis), and 1, to a situation in which artifacts completely hindered diagnostic decision making. Patients with image quality 1 and 2 and with image artifacts 1 and 2 were excluded from this study.

**Evaluation of CAWT**

For the MDCTA examination, both right and left carotid arteries were measured. CTA source axial images were considered. Two radiologists independently evaluated CAWT, blinded to each other’s results. Window level, window width, and magnification were freely modifiable. The CAWT was measured at the thickest point of the common carotid artery wall where there was no evidence of a plaque (Fig 1). This point was selected because if the wall is measured close to a stenosis, then it should be thicker. Three measurements for each carotid artery were performed, and the individual subject’s mean CAWT values were then obtained as an average of values for each carotid artery. We measured the CAWT between the leading edge of the opacified vessel lumen and the external visible limit of the arterial wall, where it was surrounded by adjacent adipose tissue. Measurements between the 2 observers were averaged; in fact, in a previous study15 we observed, by using this technique, a concordance correlation coefficient that was extremely high (r = 0.923).

For analysis of data in symptomatic patients, we considered only the measurements in the carotid artery concordant with the symptoms (though both right and left carotid arteries were measured), and in the asymptomatic patients, we considered the highest CAWT value of the right and left carotid arteries.

**Statistical Analysis**

The normality of each continuous variable group was tested by using the Kolmogorov-Smirnov Z-test. Comparison of mean CAWT values in patients with and without stroke was performed by using a Student t test because the normality of the variable was accepted in both groups. We performed logistic regression analysis to examine the relationship between CAWT and the independent variables hypertension, dyslipidemia, diabetes mellitus, and smoking. To consider CAWT a dichotomous variable, as required in logistic regression analysis, we considered increased CAWT values to be those >1 mm and normal CAWT values to be those ≤1 mm, because a risk of stroke was demonstrated by Saba et al15 for CAWT values >1 mm. ROC curve analysis was also performed and the Az was determined for hypertension, dyslipidemia, diabetes mellitus, and smoking, but in this case considering the CAWT as a continuous variable. A P value < .05 indicated statistical significance. R software (www.r-project.org) was used for statistical analyses.
Results

Patient Population

Among the 191 patients available, 8 were excluded because of an image quality rating ≤ 2 (we observed inadequate contrast opacification in 3 patients and an inadequate tube current that produced suboptimal images in 5). We excluded another 7 patients because of the presence of an image artifacts rating of ≤ 2 (we observed swallowing artifacts in 3 patients, respiration artifacts in 3, and artifacts deriving from large calcifications in 1). Moreover, patients who had intracranial masses (n = 2), cardiac thrombus (n = 3), stenosis from nonatherosclerotic causes such as radiation (n = 2), and fibromuscular dysplasia (n = 1) were also excluded.

The clinical characteristics of the remaining 168 patients are given in Table 1. We observed 66 patients with ischemic symptoms (24 strokes, 33 TIAs, 9 cases of amaurosis fugax) and 102 without ischemic symptoms.

Analysis of CAWT

The distal common CAWT ranged from 0.5 to 1.5 mm. In the patient group without cerebrovascular symptoms, the average CAWT was 0.85 ± 0.22 mm, and in the patient group with cerebrovascular symptoms, it was 1.074 ± 0.24 mm. The normality of the variability was accepted in both groups (in the patient group with symptoms, the P value of the Kolmogorov-Smirnov Z-test was .228; in the patient group without symptoms, the P value of the Kolmogorov-Smirnov Z-test was 0.22). The CAWT in patients without symptoms differed significantly (P < .001) from that in patients with symptoms.

Logistic Regression Analysis

The results of the logistic regression analysis are described in Table 2. In simple logistic regression, the dependent variable was the increased CAWT (≥ 1 mm), and a statistically significant positive association between increased CAWT and hypertension, diabetes, and cerebrovascular symptoms was observed with P values of .0041, .0172, and .001, respectively. Other variables did not demonstrate a significant statistical association with the presence of increased CAWT.

ROC Curve Analysis

The ROC curve analysis for hypertension, diabetes, smoking, and dyslipidemia versus CAWT is shown in Figs 2–5. The Az of hypertension was 0.627 ± 0.044; 95% CI, 0.549–0.700; P value = .0037. The Az of diabetes was 0.651 ± 0.056; 95% CI, 0.573–0.722; P value = .007. The Az of dyslipidemia was 0.504 ± 0.046; 95% CI, 0.426–0.582; P value = .9327. The Az of smoking was 0.508 ± 0.045; 95% CI, 0.43–0.586; P value = .8599. On the basis of the ROC analysis, we tabulated the sensitivity, specificity, +LR, and −LR values of each measure. A summary of these values is given in Tables 3–6 for hypertension, diabetes, dyslipidemia, and smoking, respectively.

Table 1: Clinical characteristics of the study population

| Characteristic    | Patients with Symptoms (%) | Patients without Symptoms (%) | P Value |
|------------------|----------------------------|-------------------------------|---------|
| Age (yr)         | 68.3 ± 10.7                | 69.4 ± 11.6                  | .521    |
| Male sex         | 52 (77)                    | 68 (66)                      | .101    |
| Tobacco use      | 32 (48)                    | 39 (38)                      | .201    |
| Hypertension     | 28 (42)                    | 45 (44)                      | .807    |
| Diabetes         | 14 (21)                    | 20 (19)                      | .814    |
| Dyslipidemia     | 41 (61)                    | 61 (59)                      | .797    |

Table 2: Logistic regression analysis

| Variable     | Coefficient | Std. Error | P Value | Odds Ratio 95% CI |
|--------------|-------------|------------|---------|------------------|
| Hypertension | 1.0983      | 0.3828     | .0041a  | 2.9991 1.4163–6.3504 |
| Diabetes     | 1.1061      | 0.4643     | .0172a  | 3.0225 1.2165–7.5096 |
| Dyslipidemia | −0.3055     | 0.376      | .4165   | 0.7368 0.3526–1.5394 |
| Tobacco use  | −0.5697     | 0.3865     | .1404   | 0.5657 0.2652–1.2065 |
| Symptoms     | 2.1296      | 0.3995     | <.001a  | 8.4115 3.8446–18.4031 |
| Age          | −0.0014     | 0.0162     | .9305   | 0.9986 0.967–1.0309 |
| Male sex     | −0.6163     | 0.4146     | .1372   | 0.5399 0.2386–1.2169 |

a P value < .05.
Discussion
The purpose of this article was to determine whether CAWT, evaluated by using MDCTA, is associated with the following cardiovascular risk factors: hypertension, diabetes mellitus, dyslipidemia, and smoking.

The results of the logistic regression analysis indicate that there is a statistically significant positive association between increased CAWT and cerebrovascular symptoms with a \( P \) value < .001. The data confirm a previous study by Saba et al., in which similar results were found. Moreover, a statistically significant positive association between increased CAWT and hypertension and diabetes was observed with a \( P \) value of .0041 and .0172, respectively. Johnsen and Mathiesen recently observed that the CCA-IMT, measured by using B-mode sonography, is strongly related to hypertension and ischemic stroke. Other authors have used a multiple logistic regression analysis to show an independent association of hypertension and diabetes with complex plaques, which also had a greater IMT, demonstrating a link between hypertension, diabetes, and a greater IMT that may reflect the instability of the atherosclerotic process.

It was recently demonstrated that CAWT and IMT show consistent results (with the Bland-Altman statistic, the discrepancy was 0.023 mm), supporting the observation by Gamble et al. that sonographic IMT measurements best correspond with histologically ascertained total artery wall thickness (i.e., including the tunica adventitia), rather than with
The association we observed between increased CAWT and hypertension (P = .0041) may be due to a variety of factors, not necessarily related to atherosclerosis. In fact, higher blood pressure and consequent changes in shear stress may cause the transportation of potentially atherogenic particles, which also involves thickening of the arterial wall. 

In our study, smoking and dyslipidemia were not significantly associated with an increased CAWT. These results were unexpected because they differ from previous publications that have demonstrated an association between active smoking and increased IMT and between dyslipidemia and increased IMT. It has been demonstrated that exposure to cigarette smoke is associated with progression of atherosclerosis, and that smoking is a powerful risk factor for stroke. However, the relationship between IMT and smoking is still debated; in fact, some authors have found no association between IMT increase and tobacco smoking.

Table 3: ROC curve analysis for CAWT and hypertension

| Criterion (mm) | Sensitivity (95% CI) | Specificity (95% CI) | +LR | −LR |
|---------------|----------------------|----------------------|-----|-----|
| 0.5           | 100.00 (95.0–100.0)   | 0.00 (0–0.3)         | 1.00| NC  |
| 0.6           | 91.76 (83.0–94.6)     | 12.66 (6.7–21.0)     | 1.05| 0.65|
| 0.7           | 80.62 (69.9–89.1)     | 28.42 (19.6–38.6)    | 1.13| 0.67|
| 0.8           | 69.66 (59.8–79.6)     | 43.16 (33.0–53.7)    | 1.23| 0.70|
| 0.9           | 57.53 (45.4–69.0)     | 58.95 (48.4–68.9)    | 1.40| 0.72|
| 1.0           | 52.05 (40.0–63.9)     | 71.58 (61.4–80.4)    | 1.83| 0.67|
| 1.1           | 36.99 (26.0–48.1)     | 83.16 (74.1–90.1)    | 2.20| 0.76|
| 1.2           | 28.77 (18.9–40.6)     | 89.47 (81.5–94.8)    | 2.73| 0.80|
| 1.3           | 12.33 (5.8–22.1)      | 97.89 (92.6–99.7)    | 5.86| 0.90|
| 1.4           | 9.59 (4.0–18.8)       | 98.95 (94.3–99.8)    | 9.11| 0.91|
| 1.5           | 0.00 (0.0–5.0)        | 100.00 (96.2–100.0)  | NC  | 1.00|

Table 4: ROC curve analysis for CAWT and diabetes

| Criterion (mm) | Sensitivity (95% CI) | Specificity (95% CI) | +LR | −LR |
|---------------|----------------------|----------------------|-----|-----|
| 0.5           | 100.00 (95.0–100.0)   | 0.00 (0.0–2.7)       | 1.00| NC  |
| 0.6           | 94.12 (80.3–99.1)     | 17.16 (11.2–24.6)    | 1.14| 0.34|
| 0.7           | 88.24 (72.5–96.6)     | 27.61 (20.2–36.0)    | 1.22| 0.43|
| 0.8           | 79.41 (62.1–91.3)     | 41.79 (33.5–50.6)    | 1.36| 0.49|
| 0.9           | 67.65 (49.5–82.6)     | 56.72 (47.9–65.2)    | 1.56| 0.57|
| 1.0           | 58.92 (40.7–75.3)     | 66.42 (57.8–74.3)    | 1.75| 0.62|
| 1.1           | 38.22 (22.2–56.4)     | 77.61 (69.4–84.4)    | 2.73| 0.80|
| 1.2           | 12.33 (5.8–22.1)      | 97.89 (92.6–99.7)    | 5.86| 0.90|
| 1.4           | 9.59 (4.0–18.8)       | 98.95 (94.3–99.8)    | 9.11| 0.91|
| 1.5           | 0.00 (0.0–5.0)        | 100.00 (96.2–100.0)  | NC  | 1.00|

Table 5: ROC curve analysis for CAWT and dyslipidemia

| Criterion (mm) | Sensitivity (95% CI) | Specificity (95% CI) | +LR | −LR |
|---------------|----------------------|----------------------|-----|-----|
| 0.5           | 100.00 (94.9–100.0)   | 0.00 (0.0–3.8)       | 1.00| NC  |
| 0.6           | 91.55 (82.5–96.8)     | 12.37 (6.6–20.6)     | 1.04| 0.68|
| 0.7           | 77.46 (66.0–88.5)     | 25.77 (17.4–35.7)    | 1.04| 0.87|
| 0.8           | 61.97 (49.7–73.2)     | 37.11 (27.5–47.5)    | 0.99| 1.02|
| 0.9           | 45.07 (33.2–57.3)     | 49.48 (39.2–59.8)    | 0.98| 1.04|
| 1.0           | 28.77 (18.9–40.6)     | 89.47 (81.5–94.8)    | 2.73| 0.80|
| 1.1           | 12.33 (5.8–22.1)      | 97.89 (92.6–99.7)    | 5.86| 0.90|
| 1.4           | 9.59 (4.0–18.8)       | 98.95 (94.3–99.8)    | 9.11| 0.91|
| 1.5           | 0.00 (0.0–5.0)        | 100.00 (96.2–100.0)  | NC  | 1.00|

Table 6: ROC curve analysis for CAWT and smoking

| Criterion (mm) | Sensitivity (95% CI) | Specificity (95% CI) | +LR | −LR |
|---------------|----------------------|----------------------|-----|-----|
| 0.5           | 100.00 (94.9–100.0)   | 0.00 (0.0–3.8)       | 1.00| NC  |
| 0.6           | 91.55 (82.5–96.8)     | 12.37 (6.6–20.6)     | 1.04| 0.68|
| 0.7           | 77.46 (66.0–88.5)     | 25.77 (17.4–35.7)    | 1.04| 0.87|
| 0.8           | 61.97 (49.7–73.2)     | 37.11 (27.5–47.5)    | 0.99| 1.02|
| 0.9           | 45.07 (33.2–57.3)     | 49.48 (39.2–59.8)    | 0.98| 1.04|
| 1.0           | 28.77 (18.9–40.6)     | 89.47 (81.5–94.8)    | 2.73| 0.80|
| 1.1           | 12.33 (5.8–22.1)      | 97.89 (92.6–99.7)    | 5.86| 0.90|
| 1.4           | 9.59 (4.0–18.8)       | 98.95 (94.3–99.8)    | 9.11| 0.91|
| 1.5           | 0.00 (0.0–5.0)        | 100.00 (96.2–100.0)  | NC  | 1.00|

the intima plus media complex per se. On the basis of these data, the authors considered the 2 methods to be interchangeable.

Although it seems clear that IMT is strongly associated with atherosclerosis, not all thickening of the artery wall is due to atherosclerosis. In general, wall thickening may take place in the intimal layer or in the medial (muscular) layer, whereas the media is not necessarily related to atherosclerosis. In fact, the intima becomes thinner and the media becomes thicker. Several authors have demonstrated that with advancing age and the development of atherosclerosis, the intimal and the medial layers change in different directions; in fact, the intima becomes thicker and the media becomes thinner.

The association we observed between increased CAWT and hypertension (P = .0041) may be due to a variety of factors, not necessarily related to atherosclerosis. In fact, higher blood pressure and consequent changes in shear stress may cause the transportation of potentially atherogenic particles, which also involves thickening of the arterial wall.
In our selected group, the results of this work showed that an increased CAWT is associated with the cardiovascular risk determinants hypertension and diabetes. These data should be considered in risk stratification and the follow-up of these patients. Further studies are necessary to evaluate whether it is possible to apply our observations to the general population.

Conclusions

In our selected group, the results of this work showed that an increased CAWT is associated with the cardiovascular risk determinants hypertension and diabetes. These data should be considered in risk stratification and the follow-up of these patients. Further studies are necessary to evaluate whether it is possible to apply our observations to the general population.

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