

Comparison between Carotid Artery Wall Thickness Measured by Multidetector Row Computed Tomography Angiography and Intimae-Media Thickness Measured by Sonography

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The increased thickness of the carotid wall >1 mm is a significant predictor of coronary and cerebrovascular diseases. The purpose of our study was to assess the agreement between multidetector row computed tomography angiography (MDCTA) in measuring carotid artery wall thickness (CAWT) and color Doppler ultrasound (CD-US) in measuring intimae-media thickness (IMT). Eighty-nine patients (aged 35–81) were prospectively analyzed using a 64-detector MDCTA and a CD-US scanner. Continuous data were described as the mean value \pm standard deviation, and were compared using the Mann–Whitney U test. A p value <0.05 was considered significant. Bland–Altman statistics were employed to measure the agreement between MDCTA and CD-US. CAWT ranged from 0.62 to 1.60 mm, with a mean value of 1.09 mm. IMT ranged from 0.60 to 1.55 mm, with a mean value of 1.06 mm. We observed an excellent agreement between CD-US and MDCTA in the evaluation of the common carotid artery thickness, with a bias between methods of 0.029 mm (which is a highly statistically important difference of absolute values [$t = 43.289$; $p < 0.01$] obtained by paired T test), and limits of agreement from 0.04 to 0.104. Pearson correlation coefficient was 0.9997 (95% CI 0.9996–0.9998; $p < 0.01$). We conclude that there is an excellent correlation between CAWT and IMT measurements obtained with the MDCTA and CD-US.

KEYWORDS: carotid artery, stroke, MDCTA, CAWT, IMT

INTRODUCTION

Cerebrovascular diseases[1,2,3] are the third highest causes of death, following coronary artery disease and malignant diseases. Although morphologic markers of atherosclerosis are frequently detected in the elderly, several authors have indicated that they already exist in 20% of the general population within the age range of 30 to 40 years[1]. Atherosclerosis is a primary disease of the artery intima; measurement of the intima-media thickness (IMT) of carotid arteries is used as an important predictor of coronary and cerebrovascular events[4,5,6,7,8,9]. Treatment for atherosclerosis may include lifestyle changes, medications, and surgical procedures[4,10].

Ultrasonography is usually the first-line examination for investigating carotid artery diseases, although the sonographic method provides only moderate accuracy in assessing plaque complications[11,12,13,14,15,16]. Ultrasonographic examination of the distal common carotid artery (CCA) beyond the carotid bifurcation is particularly challenging. This technique suffers from inter- and intraobserver variability, determined by several parameters (e.g., sonographer experience and type of sonographic scanner)[17,18,19,20].

The diagnostic potential of multidetector row computed tomography angiography (MDCTA) has widely improved due to its high spatial and temporal resolution, the use of fast contrast material injection rates, and postprocessing tools[21,22,23]. Besides the degree of stenosis, MDCTA clearly depicts carotid artery wall thickness (CAWT), showing also a great efficacy in the detection of plaque complications, such as ulcerations and fissuration of the fibrous cap[12]. This methodology cannot depict IMT, which is possible only with ultrasonography. The purpose of this study was to assess the agreement between color Doppler ultrasound (CD-US) and MDCTA in the study of the common carotid CAWT (CC-CAWT) and the common carotid IMT (CC-IMT).

MATERIALS AND METHODS

Patients

The present study included consecutive symptomatic and asymptomatic patients with stenoses of the internal carotid artery (ICA), but not stenoses of the CCA at the level up to 25 mm below bifurcation or 4–6 cm distally to the plaque. All patients underwent clinical assessment, MDCTA, and CD-US examination. Data were collected prospectively by the examiner blinded for clinical and CAWT/IMT data. The study was approved by the Ethics Committee of the Faculty of Medicine in Belgrade.

MDCTA Examination

MDCTA was performed for all patients in whom previous carotid CD-US examination evidenced ICA stenosis >50% (according to the North American Symptomatic Carotid Endarterectomy Trial [NASCET] criteria) and/or a plaque alteration (irregular plaque surface, ulcerated plaque). MDCTA was also performed in cases when CD-US provided insufficient information about stenosis degree and plaque morphology, i.e., in those patients with difficult neck anatomy (obese subjects, edema), large calcified plaques with acoustic shadowing, or high carotid bifurcation[3,24]. MDCTA examination was obtained within 1 month of CD-US (mean time interval 15 days). Exclusion criteria for the study consisted of contraindications to iodinated contrast media, such as a known allergy to iodinated contrast materials, elevated renal function tests. All patients underwent MDCTA of the supra-aortic vessels using a GE LightSpeed VCT 64 (e.g., see Fig. 1). All subjects were placed in the supine position, with the head tilted back to prevent dental artifacts on the images, and were asked not to breathe or swallow. The contrast medium (Optiray 350; Healthcare UK Ltd.) in a dose of 1.2–1.5 ml/kg body mass, was injected into a cubital vein using a power injector at a flow rate of 4–6 ml/sec and an 18-gauge intravenous catheter. We



FIGURE 1. MDCTA axial image of a 64-year-old male, CAWT.

used a delay time variable from 12 to 18 sec. CT technical parameters included matrix 512×512 , field of view 11–19 cm; rotation time 0.35, mA 700; kV120; collimation 0.625 mm and pitch 0.85. Angiographic acquisition included carotid siphon and circle of Willis.

MDCTA quantification of carotid stenosis was performed according to the NASCET criteria, where the ratio between the residual luminal surface (inner-to-inner lumen) at the stenosis and the surface of the distal normal lumen (inner-to-inner lumen) with no stenosis was calculated. Stenosis degree was calculated by selecting a reformat plane perpendicular to the lumen centerline. We measured the diameter of the normal CCA wall beyond the bulb where walls are parallel at 4–6 cm distally to the plaque.

The CC-CAWT was measured at its thickest point on the distal (far) wall of the CCA, where there was no evidence of plaque[27], 2.5 cm proximally to the bulb. Three measurements for each carotid artery were performed at the 6-, 9-, and 12-o'clock positions. We measured CAWT between the leading edge of the opacified lumen vessel and the external visible limit of the artery wall, where it was surrounded by adjacent adipose tissue. Three measurements were performed for each carotid artery and overall mean value was calculated.

Ultrasonographic Examination

The CD-US technique was performed by an experienced angiologist on a Siemens Acuson Antares US system with linear multifrequency probe of 5–10 MHz. Two transversal measurements and one longitudinal measurement of IMT were completed on the right and left CCAs (e.g., see Fig. 2), and then the overall mean values were calculated. In the longitudinal scan, only the far wall of the artery was used for calculations, while in the transversal scan, measurements for each carotid artery were performed at the 6- and 12-o'clock positions. All measurements using calipers were made by the angiologist at the time of examination (online), with accuracy of the electronic calipers set to the nearest 0.1 mm.

The IMT was defined as the distance between the interfaces of the leading edges of the lumen-intimae echo to the leading edge of the media-adventitia echo[26]. The IMT was measured 25 mm proximally to the bulb. Plaques were never included in the measurements; we considered plaques >2 mm in diameter and >100% increase compared with the thickness of adjacent wall segments[28]. According to this

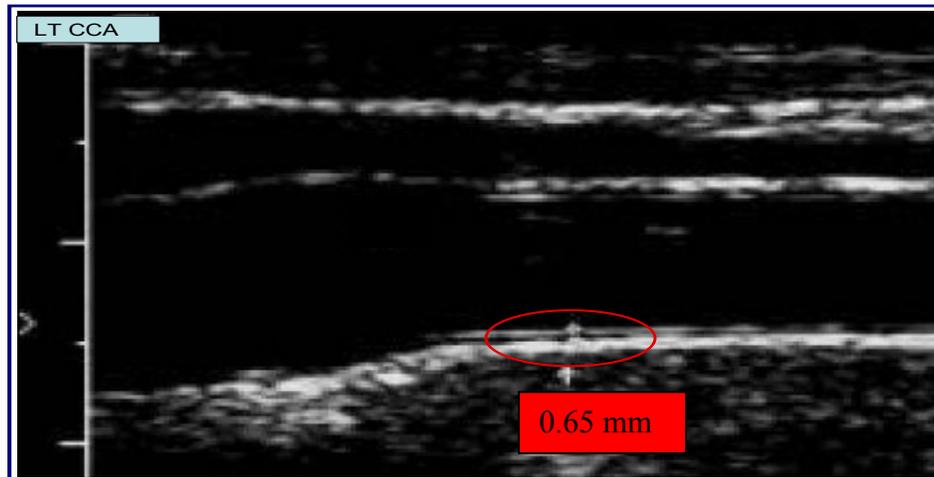


FIGURE 2. US image of the same patient as in Fig. 1. The white arrow indicates the IMT (0.65 mm)

protocol, the influence of the cardiac cycle was considered negligible[29]. Blood flow velocity >1.2 m/sec defined stenosis $>50\%$ lumen diameter reduction according to the NASCET criteria[25,26].

Statistical Analysis

A comparison of CAWT and IMT median values was performed using a Mann–Whitney U test (Monte Carlo method) because a normality of the variables was rejected in both groups and group sample size was unbalanced. We evaluated intermethod agreement using a Bland–Altman analysis, Pearson correlation, and Cronbach’s alpha. Testing of mean value differences of these two methods (CAWT and IMT) was performed with paired T test.

RESULTS

One hundred and seventy-eight CCAs and the same number of ICAs were analyzed in 89 patients (60 males, 29 females) aged 35–81 years (average age 64.7 ± 11.5). Sixty-two patients had surgically significant ICA stenosis, 17 (27.4%) asymptomatic and 45 (72.6%) symptomatic. In total, 68 surgical interventions were carried out. Vascular risk factor profile comprised coronary artery disease (stable angina pectoris in 25, myocardial infarction in 14), atrial fibrillation (5), diabetes (23), hyperlipidemia (24), obesity (30), hypertension (52), and smoking (38).

The average CC-CAWT value for all patients examined ranged from 0.62 to 1.60 mm, with a mean value of 1.09 ± 0.21 mm (95% confidence interval [CI] 1.05–1.14 mm) and a median value of 1.08 mm (Table 1).

The average CC-IMT value for all patients examined ranged from 0.60 to 1.55 mm, with a mean value of 1.06 ± 0.20 mm (95% CI 1.02–1.11 mm) and a median value of 1.05 mm (Table 1).

There were 85 (95.5%) carotid arteries with $>50\%$ stenosis and four (4.5%) with $<50\%$ stenosis.

In the four carotids with stenosis $<50\%$, CC-CAWT ranged from 0.62 to 0.88 mm, with a mean value of 0.77 ± 0.12 mm (95% CI 0.57–0.97 mm) and a median value of 0.79 mm (95% CI 1.06 \pm 0.20 mm). In these four carotids with stenosis $<50\%$, CC-IMT ranged from 0.60 to 0.85 mm, with a mean value of 0.75 ± 0.12 mm (95% CI 0.55–0.94 mm) and a median value of 0.77 mm.

TABLE 1
Summary Statistics in Patients Studied

Statistic	IMT	CAWT
Sample size	178	178
Lowest value	0.60	0.62
Highest value	1.55	1.60
Arithmetic mean	1.06	1.09
95% CI for the mean	1.02–1.11	1.05–1.14
Median	1.05	1.08
Standard deviation	0.20	0.21

In the 85 carotids with stenosis >50%, CC-CAWT ranged from 0.67 to 1.60 mm, with a mean value of 1.11 ± 0.19 mm (95% CI 1.07–1.15 mm) and a median value of 1.08 mm. In these 85 carotids with stenosis >50%, CC-IMT ranged from 0.65 to 1.55 mm, with a mean value of 1.08 ± 0.19 mm (95% CI 1.04–1.12 mm) and a median value of 1.05 mm.

There was a significant difference in CC-CAWT between patients with <50% carotid stenosis and those with >50% carotid stenosis (Mann–Whitney U test, $p < 0.01$), and a significant difference in CC-IMT between patients with <50% carotid stenosis and those with >50% carotid stenosis (Mann–Whitney U test, $p < 0.05$).

Agreement and correlation between MDCTA and CD-US by analyzing the Bland–Altman plot can be seen in Fig. 3. We observed an excellent agreement between CD-US and MDCTA in the evaluation of the CCA thickness, with a bias between methods of 0.029 mm and limits of agreement from 0.01 to 0.04. Pearson correlation coefficient was 0.9997 (95% CI 0.9996–0.9998; $p < 0.01$; Fig. 4). We also used Cronbach’s alpha to measure the agreement of these two methods: a value of 0.958 indicated that these two methods highly agree. There is a highly significant statistical difference of 0.029 ($t = 43.289$; $p < 0.01$).

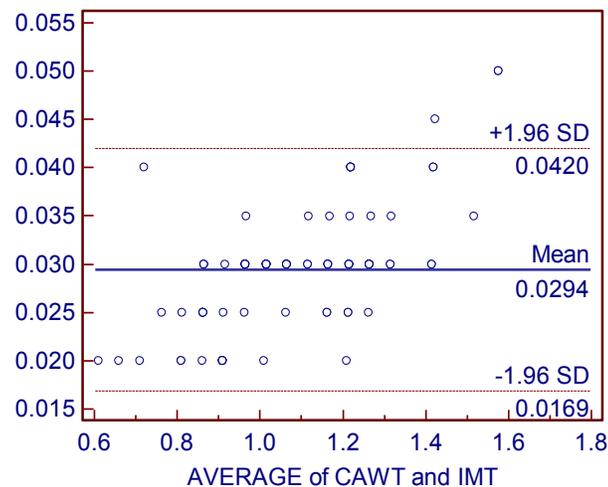


FIGURE 3. Agreement between CAWT measured using MDCTA and IMT measured using CD-US by using Bland–Altman plot. The mean difference and the limits of agreement are also indicated.

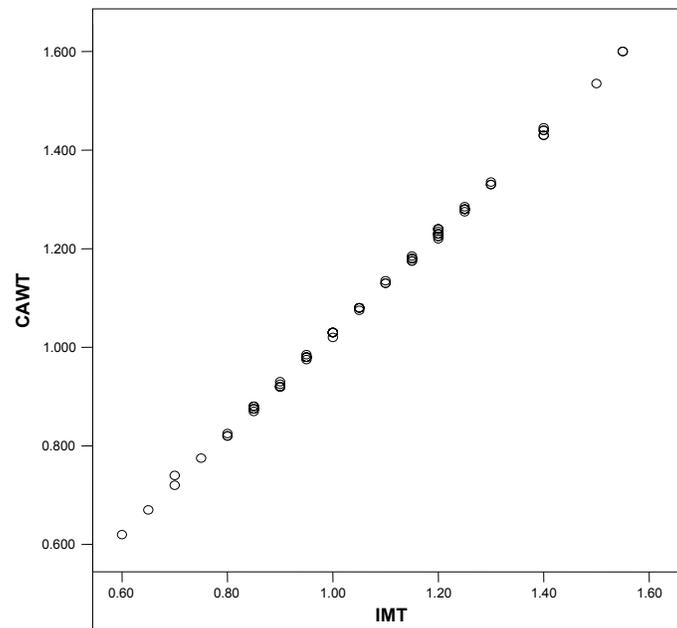


FIGURE 4. Relationship between CAWT and IMT. X axis: IMT values measured by US; Y axis: CT-CAWT values for the same patient.

DISCUSSION

Numerous studies have shown that an increased IMT is an early marker of generalized atherosclerosis[30,31], and an important predictor of coronary and cerebrovascular complications[2,24,32]. Saba and colleagues[33] demonstrated that the thicker common carotid wall is associated with the development of cerebral ischemic events[37]. Clinically evident cardiovascular disease frequently arises as a late manifestation of widespread atherosclerosis, typically after a long subclinical phase beginning at an early age, and manifests as endothelial damage jointly with a gradual thickening of the IMT[24]. Results of this study confirm that CC-CAWT is conceptually equivalent to IMT with the difference that IMT analyzes two carotid layers (intimae and media), whereas CAWT comprises all three carotid layers (intimae, media, and adventitia)[30], so it is important to compare these two parameters as atherosclerosis markers. By analyzing the Bland–Altman plot, we observed an excellent agreement between CD-US and MDCTA in the evaluation of the CCA thickness. By performing reliability analysis using Cronbach’s alpha, we concluded that there was an excellent positive correlation between CAWT and IMT, which provided conceptually similar data.

On the basis of these data, both methods can be considered interchangeable. This excellent agreement between MDCTA and CD-US in the evaluation of CC-CAWT and CC-IMT was an unexpected result because a suboptimal concordance was early hypothesized due to the well-documented[9] “reproducibility problem” of CD-US in measuring CC-IMT[18,19,20,21,29,30]. One potential cause for this result can be ascribed to the technique employed. It is important that with the development of advanced CD-US hardware and automated computer software, the CC-IMT inter- and intraobserver agreement is excellent[34]. In cases with ICA stenosis <50% as well as in those with ICA stenosis >50%, analysis showed that the CC-CAWT and CC-IMT had an excellent agreement. The CAWT concept was recently introduced[33] and until now there have been no studies that evaluated CAWT reproducibility, whereas several studies have evaluated the reproducibility of IMT measurements. In IMT reproducibility analysis, absolute values ranged from 0.36 mm[35] to 0.007 mm[36].

Our results showed that MDCTA can also provide additional information with the CC-CAWT measurements. In most medical centers, CD-US is the first and frequently a sufficient method for evaluation of stenosis degree, type of plaque, and presence of ulceration; it gives enough data to diminish the risk for patients[37]. MDCTA is not recommended as a routine method[3], but in cases where clinically indicated (according to the guidelines accepted in each institution), CAWT should be always quantified by MDCTA[24,38]. Saba et al.[33] showed that the presence of CAWT >1 mm is significantly associated with cerebral symptoms.

CD-US provides a reliable and low-cost methodology compared to the MDCTA examination[39]. Both CD-US and MDCTA provide reliable and complementary data, which is confirmed in our study as well. There is an evident trend of increasing use of US diagnostic methods with the latest technological achievements in regard to plaque morphology, but there are also advantages of MDCTA and magnetic resonance angiography (MRA) use[40,41,42]. Recommendations, as well as conclusions, vary in different diagnostic centers[43,44,45,46,47,48]. There are numerous authors with whom our group also agree who advocate complementary use of the CD-US and MDCTA or MRA in order to exclude the tandem lesions or anatomical variants that would affect recanalization procedures.

There are some limitations in our study. First, statistical bias can be ascribed because the number of carotid arteries examined was 178 and the number of stenoses <50% was only four. A larger patient cohort may be useful to reduce statistical bias. Second, there was no control group comprised of patients without plaques and significant ICA stenosis. This study included patients with already-verified high-degree stenosis in the ICA, so that their IMT mean value and therefore their CAWT value in CCA exceeded the average obtained values (median population values of IMT range from 0.4 to 1 mm, accordingly, values above 1.0 mm are commonly regarded as abnormal)[49].

CONCLUSION

Results of our study demonstrate significant agreement between MDCTA and CD-US in the measurement of CAWT and IMT, where the difference in absolute values obtained by these two methods is due to the fact that three layers are measured by CAWT and only two by IMT. This study suggests that values obtained both by CAWT and IMT measuring can be considered reliable. We suggest that patients who are candidates for ICA revascularization should be evaluated both with CD-US and MDCTA or MRA in order to exclude tandem lesions or anatomical variants important for surgery.

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