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CT-angiography and doppler ultrasonography in atherosclerotic carotid artery disease. A comparative study.

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Abstract

Background: Different diagnostic modalities to investigate atherosclerotic carotid artery disease (ACAD) are nowadays available. The aim of this study was to test the concordance of the findings of the two most widely used diagnostic modalities namely computed tomography angiography (CTA) and doppler ultrasonography (DUS).

Material and methods: 29 patients with acute ischemic stroke were subjected to CTA and DUS and included in this analysis; 17 patients were males (59 %). The mean age was 70.5 ± 8 years (Mean ± SD). The correlation and the degree of concordance between the findings of CTA and DUS were tested. The associations between the occurrence of ACAD and the degree of severity of stenosis with the age, the gender and the side of stenosis were also tested. The statistical significance was set to < 0.05.

Results: This study showed almost perfect agreement between CTA and DUS in detection of stenosis with kappa value of 0.92 (95 % CI 0.82–1.02). Intraclass correlation coefficient for the agreement between CTA and DUS in the estimation of the degree of stenosis was almost perfect and estimated to 0.96 (95 % CI 0.93–0.97). The differences of the measurements of the degree of carotid artery stenosis by the two methods was not statistically significant (p=0.04) with random error of 9.9 %. Spearman´s correlation and linear regression showed strong correlation between the measurements of stenosis by CTA and DUS with $P< 0.001$, correlation coefficient of 0.933, and R^2 linear of 0.92, respectively. The stenosis was more severe in males.

Conclusion: CTA and DUS are non-invasive diagnostic modalities with good correlation with regard to the detection of ACAD and the estimation of the degree of stenosis and can be used separately or as complementary to each other in the work-up of ACAD.

Introduction

Atherosclerotic carotid artery disease (ACAD) is a degenerative disease of carotid arteries often associated with atherosclerosis of other arteries e.g. coronary arteries and arteries of the lower limb. Atherosclerosis affect internal carotid artery (ICA) at the level of bifurcation. The cause of atherosclerosis is unknown. However, risk factors for development of atherosclerosis are well known and include: genetic factors, smoking, hypertension, hyperlipidemia, obesity, estrogen therapy and contraceptive pills [1].

Other causes of ICA stenosis are carotid artery dissection, arteritis, fibromuscular dysplasia, kinks and radiation. Atherosclerosis causes formation of plaques consisting of necrotic cells, lipids, and cholesterol crystals. The symptoms resulted from ACAD are attributed to stenosis/occlusion, plaque ulceration, embolization, thrombosis, dolichoectasia and development of fusiform aneurysm. ACAD causes a wide spectrum of pathological conditions ranging from TIA to fulminant ischemic stroke. Hypoperfusion with development of watershed infarctions are also well known phenomenon in patients with ACAD. ACAD is responsible for about 50 % of ischemic stroke. The incidence of ACAD increases with age. Up to 10 % of patients aged >80 years have ICA stenosis exceeding 50 % [1].

According to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) carotid artery reconstructive surgery in form of carotid endarterectomy is indicated in symptomatic patients with stenosis > 70%. Only 9 % of patients operated developed cerebral infarction within 2 years compared with 26 % in patients received only medical management [2]. Asymptomatic patients with stenosis benefit less than symptomatic patients with stenosis. In the last few years carotid artery stenting has been increasingly recommended instead of endarterectomy especially in patients with high perioperative risk [3]. Investigation of ACAD was performed with conventional angiography until the advent of doppler ultrasonography (DUS), multidetector computed tomography (MDCT) with the possibility to perform CT-angiography (CTA), and magnetic resonance imaging with the possibility to perform contrast enhanced angiography (MRA). Nowadays the use of conventional angiography is restricted to the pre- and perioperative evaluation in conjunction with stenting the ICAs mainly because angiography is an invasive procedure including arterial puncture and means exposure to high radiation doses by the fluoroscopic exposure during the procedure. Although CTA also means radiation exposure, the radiation doses are much less than those of conventional angiography and with modern CTs tube current modulations [4–5] enables dose reduction and adjustment. MRA has the advantage of non exposure to ionizing radiation but has the disadvantages of being less available than CT, higher cost and longer examination time. DUS is more available than MRI and do not include exposure to ionizing radiation. One clear disadvantage of DUS is its dependence on the experience of radiologist or the biomedical analyst who perform the examination.

The aim of this study was to test the concordance of the findings of the two most widely used diagnostic modalities in the investigation of ACAD, namely CTA and DUS.

Patients and methods

Thirty one consecutive patients with ischemic stroke examined with both CTP and DUS of the carotid arteries. Two of these patients showed to have dissection of ICA and thus excluded from the analysis of this study. A total of 29 patients with ACAD were included in this analysis; 17 patients were males (59 %) and 12 patients were females. The mean age was 70.5 ± 8 years (Mean ± SD) and range of 49–86 years. Out of 29 patients, only 5 patients had acute hemispheric infarctions whereas the remaining 24 patients had repeated transient ischemic attacks (TIA). A total of 58 carotid arteries were subjected for analysis. Estimation of the degree of ICA stenosis on DUS was done according to the resistance profile recorded. The arteries were examined on transverse and longitudinal sections with and without colour doppler. Regions with increased flow velocity were examined with pulsed doppler. On CTA the estimation of the degree of stenosis was estimated on axial images according to NASCET-criteria (North American Symptomatic Carotid Endarterectomy Trial) by measurement of the diameter of ICA at the narrowest portion at the level of the stenosis and at the level of the normal ICA above the

stenosis [2]. Sagittal and coronal images were also used in the measurement of the degree of stenosis. The degree of ICA stenosis was expressed in percent. The severity of stenosis was classified into moderate stenosis (<70 %) and severe stenosis (≥ 70 %).
Morphological analysis of ICA, common carotid artery and the carotid bifurcation was done in both methods and the atherosclerotic plaque were classified on CT into calcified, cholesterol or mixed. CTA was performed on 16-slice CT scanner according to a standard protocol [6]. Beside axial images coronal and sagittal images, preferably with maximum intensity projection (MIP) were obtained with 3 mm thickness and 3 mm distance between images.
All statistical analysis was done in SPSS 15. The concordance between the two methods was tested by cross tabulation and calculation of kappa coefficient (K value). The intraclass correlation coefficient (ICC) was calculated to test the concordance of the two methods in the estimation of the degree of stenosis. The interpretation of the kappa coefficient and ICC was done according to the one proposed by Landis and Kock [7], Table 1.

K values	Degree of agreement
<0	Poor
0-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1.00	Almost perfect

Table 1: The interpretation of the kappa (K) value.

Spearman´s correlation test and linear regression were also performed to test the correlation between the measurements of the degree of ICA stenosis estimated by CTP and DUS. Chi square test and/or Fisher exact test were done to test the association between the gender and the side of stenosis with the occurrence of ICA stenosis as well as with severity of stenosis. The association between the age on one side and the occurrence and the severity of stenosis on the other side were tested with non parametric Mann-Whitney test. The statistical significance was set to < 0.05.

Results

(1) Concordance between CTA- and DUS-findings:
The diagnosis of “stenosis” versus “no stenosis” on DUS was concordant with that on CTP in 56 out of 58 arteries (97 %) included in the analysis. This resulted in an almost perfect agreement between CTA and DUS in detection of stenosis with Kappa value of 0.92 (95 % CI 0.82–1.02). Intraclass correlation coefficient for the agreement between CTA and DUS in the estimation of the degree of stenosis was almost perfect and estimated to be 0.96 (95 % CI 0.93–0.97). The paired sample t-test showed no statistically significant differences in the measurements of the degree of carotid artery stenosis by the two methods (p=0.04) with random error of 9.9 % and systematic error of 2.7 %. Spearman´s correlation and linear regression showed strong correlation between the measurements of stenosis by CTA and DUS with P< 0.001, correlation coefficient of 0.933, and R^2 linear of 0.92, respectively (Figure 1).
(2) ICA stenosis:
CTP and DUS were: (a) normal in 4 (14 %) out of 29 patients (all had TIA), (b) showed moderate stenosis (<70 %) in 11 patients (38 %), and (c) showed severe stenosis (≥ 70 %) in 14 patients (48 %). Out of 25 patients with ICA stenosis, 13 patients (52 %) had bilateral stenosis of various degrees. The total number of carotid arteries analyzed were 58; 18 arteries were normal on both CTP and DUS, 38 were abnormal on both CTP and DUS, two were classified as normal on one modality and abnormal on the other modality. Figure 2 shows example of CTA in a patient with severe ICA stenosis.

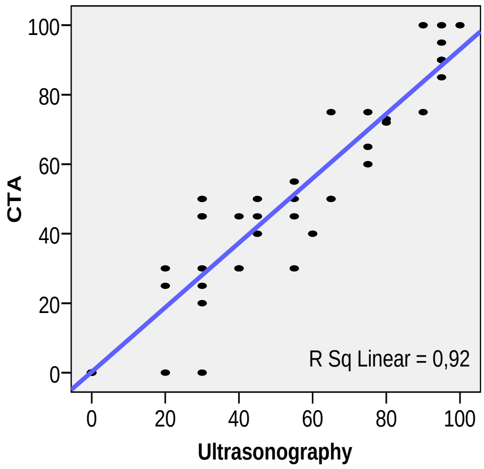

Figure (1): Linear regression scatter plot showing a very good correlation between the estimation of the degree of stenosis by CTA and DUS (R^2 of 0.92).

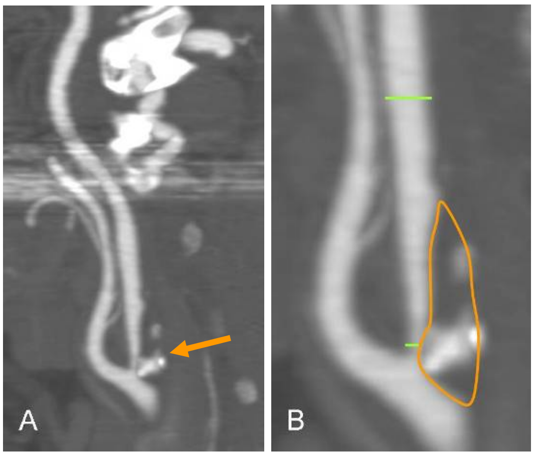

Figure 2 shows a 70 years old man with TIA. CTP showed severe left sided ICA-stenosis that amounts to 75 %. (A) sagittal image showing that stenosis is caused by cholesterol and calcified plaque (arrow). (B) Magnified image A at the level of carotid bulb. The elliptical orange drawing shows the whole plaque and the native limit of the carotid bulb. The little green line shows the remaining artery lumen which is only 25 % of the diameter of the ICA above stenosis (the larger green line).

Of 38 arteries with stenosis DUS overestimated the degree of stenosis in 23 patients, CTP in 9 patients and the estimation of the degree of the stenosis was similar in 6 patients. However, the mean value for the differences in the estimation of the degree of stenosis was less than 5 %. Chi square test showed significant association between the occurrence of stenosis and the side of stenosis (p=0.037) and between the severity of stenosis and the gender (p=0.004), Table 2.

Predictor		ICA stenosis		P-value
		No	Yes	
Gender	Male	1	16	
	Female	3	9	0.141
Side	Right	4	11	
	Left	0	14	0.037
		Stenosis ≥70 %		
		No	Yes	
Gender	Male	5	12	
	Female	10	2	0.004
Side	Right	8	7	
	Left	7	7	0.858

Table (2): The results of Chi-square test of association between ICA-stenosis and its severity with gender and the side of stenosis.

Twelve out of 17 males (71 % of the males) had severe stenosis versus 2 out of 12 females (17 % of females). The mean value for the degree of ICA stenosis was 75 % in male compared with 42.5 % in females (Figure 3). Non-parametric Mann-Whitney test showed no association between the occurrence of stenosis and severity of stenosis on one hand and the patient's age on the other hand (p= 0.975 and 0.678 respectively). On CTA the cause of the stenosis was calcified plaque in 9 cases, pure cholesterol plaque in 3 cases and mixed type plaque in the remaining 13 cases.

Discussion

This study has shown that detection of ACAD on doppler ultrasonography were concordant with that on CT-angiography. The same applied to the evaluation of the severity of ICA stenosis. DUS showed to overestimate the degree of stenosis more often than CTA. For a long time conventional selective carotid angiography was considered gold standard to which all

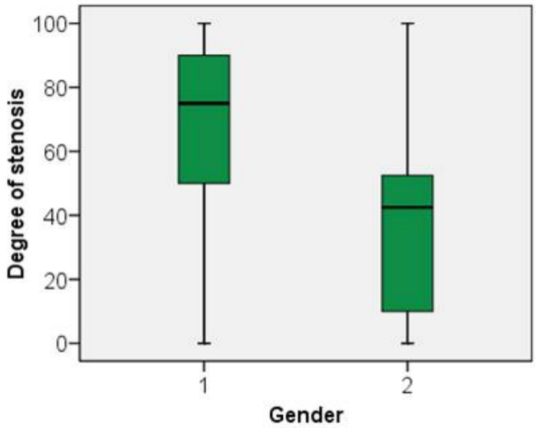

Figure 3: Box plot shows the distribution of the degree of ICA stenosis with the gender. 1=Male. 2= Female.

other methods of investigation of carotid arteries were compared. However, with the increasing use of CTA several studies were published reporting comparisons between CTA and MRA on one hand and the conventional selective carotid angiography on the other hand. Berg et al found that CTA underestimated the degree of stenosis compared with conventional selective carotid angiography. CTA showed to have a sensitivity of 0.95 and specificity of 0.93 [8]. A meta-analysis by Wardlaw et al including 41 studies (2541 patients), contrast-enhanced MR angiography showed a sensitivity of 0.94 and specificity of 0.93 for 70–99 % stenosis compared with sensitivities of (0.89 and 0.76) and specificities of (0.84 and 0.94), respectively for DUS and CTA [9]. They concluded that the accuracy of these modalities in the evaluation of stenosis <70 % should be subjected to further test [9]. Tiev et al showed that the ultrasonography and angiography findings were well correlated (r=0, 88; p<0.002) [10]. However, the assessments of the MRA were better correlated to the angiography than did the CTA [10]. In UK, analysis of the cost-effectiveness of different modalities showed that the use of DUS helped to shorten the time to surgery [11] and consequently reduces the total cost compared with using models that adopt selective angiography.

As these studies showed that all these modalities exhibit high sensitivity and specificity and as our study showed almost perfect agreement between the results of CTA and DUS, these methods should be regarded as equivalent. CTA, DUS or both can thus be used in the work-up of ACAD depending on their availability. However, there are four limiting factors for the use of the DUS: (a) the limited number of trained radiologists, clinical physiologists or biomedical analyst capable of performing and interpreting these examinations, (b) occurrence of interexaminer and intermachinary variability, (c) the fact that DUS only can quantify stenosis exceeding 40 %, and (d) inability to study the intracranial vessels and the collateral circulation as accurate as CTA.

Conclusion

Although studies have shown that MRA and selective angiography are better diagnostic modalities than computed tomography angiography and doppler ultrasonography, the latter two modalities has the advantage of being non-invasive and more available. CTA and DUS showed to correlate well with regard to the detection of ACAD and the estimation of the degree of stenosis and can be used separately or as complementary to each other in the workup of ACAD.

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