Color Doppler ultrasonography and multislice computer tomography angiography in carotid plaque detection and characterization

Primena kolor dopler ultrasonografije i višeslojne kompjuterizovane tomografske angiografije u otkrivanju i karakterizaciji karotidnog plaka

Viktorija Vučaj-Ćirilović*, Milos Lučić†, Kosta Petrović*, Olivera Nikolić*, Mira Govorčin*, Sanja Stojanović*

*Clinical Center of Vojvodina, Radiology Department, Novi Sad, Serbia; †Vojvodina Institute of Oncology, Center for Imaging Diagnostics, Sremska Kamenica, Serbia

Abstract

Background/Aim. Cerebrovascular diseases are the third leading cause of mortality in the world, following malignant and cardiovascular diseases. Therefore, their timely and precise diagnostics is of great importance. The aim of this study was to compare duplex scan Color Doppler ultrasonography (CDU) with multislice computed tomography angiography (MSCTA) in detection of morphological and functional disorders at extracranial level of carotid arteries.

Methods. The study included 75 patients with 150 carotid arteries examined in the period from January 2008 to April 2009. The patients were firstly examined by CDU, then MSCTA, followed by the surgery of extracranial segment of carotid arteries. In 10 patients, the obtained material was referred for histopathological (HP) examination. We used both CDU and MSCT in the analysis of: plaque surface, plaque structure, degree of stenosis, and the presence of intraplaque hemorrhage. Results. The results obtained by CDU and MSCTA were first compared between themselves, and then to intraoperative findings. Retrospective analysis showed that MSCTA is more sensitive than CDU in assessment of plaque surface (for smooth plaques CDU 89% : MSCTA 97%; for plaques with irregular surface CDU 75% : MSCTA 87%; for ulcerations CDU 54% : MSCTA 87%). Regarding determination of plaque structure (mixed plaque CDU 66% : MSCTA 70%; correlation with HP findings CDU 94% : MSCTA 96%) and localization (CDU 63% : MSCTA 65%), and in terms of sensitivity and specificity, both methods showed almost the same results. Also, there is no statistical difference between these two methods for the degree of stenosis (CDU 96% : MSCTA 98%). Conclusion. Atherosclerotic disease of extracranial part of carotid arteries primarily affects population of middle-aged and elderly, showing more associated risk factors. Sensitivity and specificity of CDU and MSCTA regarding plaque composition, the degree of stenosis and plaque localization are almost the same. These results and the fact that there are no adverse effects (high radiation dose) compared to MSCTA indicate that CDU should be the initial method in diagnostic algorithm for carotid arteries.

Key words: ultrasonography, doppler, color; cerebral angiography; carotid artery diseases; carotid stenosis; tomography, x ray computed.

Apstrakt

Introduction

Carotid atherosclerotic disease is the cause of cerebrovascular insult in 20% of cases and is often associated with atherosclerotic changes in coronary and peripheral vessels. Carotid disease is determined by the level of arterial stenosis, morphology of plaque and present ulceration. Ulceration of plaque is defined as “intimal defect greater than 1000 µm in depth covered with necrotic atherosclerotic plaque”.

The presence of ulceration in plaque is an important risk factor for the occurrence of neurological symptoms, while high-grade stenosis associated with ulceration carries high risk of developing cerebrovascular insult (CVI). The incidence of ulceration in the carotid artery varies from 14% to 68%, and is more often in symptomatic patients.

Conventional or digital subtractional angiography (DSA) is still considered to be the gold standard for assessing the level of stenosis, but is somewhat insufficient in determination of plaque morphology (sensitivity 46%, specificity 74%) \(^2\).

In spite of constant improvement of angiographic technique, it is sometimes followed by some complications. There are local, general \(^3\) and neurological complications \(^4\).

These complications are the main reason for common use of non-invasive techniques, such as color Doppler ultrasonography (CDU), \(^5\) magnetic resonance angiography (MRA) and multislice computed tomographic angiography (MSCTA) in the diagnostics and assessment of carotid disease, as well as in determination of plaque morphology.

Stenosis of carotid arteries is one of the main factors in defining further treatment of a patient \(^6\). Treatment modalities in a preventive programme of cerebrovascular insult are: carotid endarterectomy (CEA), stenting of the carotid artery (CAS) and medicamentous therapy.

The aim of this study was to determine reliability of CDU and MSCTA in diagnostics of carotid artery stenosis and morphologic features of plaque, in comparison to the intraoperative findings.

Methods

This randomized retrospective study included 75 patients with 150 arteries examined, in one-year period (May 2008 – May 2009). There were 24 female and 51 male patients, average age of 63.7 years (ranging from 37 to 86). All the patients were referred to examination by the vascular surgeon, with prior MRA findings.

The following symptoms were analyzed: headache, dizziness, vertigo, tingling in extremities, sight problems. The following risk factors were analyzed: smoking, diabetes, hypertension, chronic renal insufficiency, hyperlipoproteinemia, and associated pathology: cerebrovascular insult, coronary infarction and peripheral arterial occlusive disease.

Prior vascular interventions, such as classical surgical intervention (TEA), coronary stenting, peripheral stenting (aortoiliac or femoropopliteal segment) or contralateral carotid stenting were also taken into account. Neurological status included history of prior CVI.

The patients were firstly subjected to CDU, and then to MSCTA of carotid arteries in the same day, and afterwards (with the maximum of two-days delay) operation of the extracranial segment of carotid arteries was performed. After thrombendarterectomy, plaque sample was referred to pathohistological analysis.

CDU was performed by the experienced radiologist on the GE LOGIC 7 sonographic unit, with a transducer of 12MHz. MSCTA was performed by the same radiologist at multislice spiral CT scanner Somatom Sensation 64 Siemens, using the bolus-triggering technique. After a short explanation of examination technique, all the patients signed the standard informed consent. No patients presented with contraindications to application of iv contrast agent (all the patients had normal values of urea and creatinine, and no history of allergic reactions to iodine).

Intravenous non-iodine contrast agent (iopromid – Ultravist 370, Bayer Shering) was applied via cubital vein in the dose of 100–120 mL, flow 4 mL, programme Carotid vascular. The contrast agent was applied using an automatic injector, followed by the bolus of 40 mL of physiologic solution (NaCl) via the same system.

The technical parameters were as follows: matrix 512 × 512; FOV 14–19 cm; tube voltage mA 180–200 K V 120; slice thickness 1.6 mm. The center of the window was placed at the level of 200 HU, and attenuation range of 750 HU.

Scanning was performed from the level of aortic arch with visualization of the circle of Willis.

The total examination time (with a patient preparing) was 10–20 min. After the examination protocol, data processing was done using software packages: MIP, MPR and VRT. Time necessary for postprocessing as well as for the interpretation of the obtained information depends on the

diologist’s experience and software package and ranges from 20 to 30 min.

Ultrasound cross-sectioning of the extracranial segment of carotid arteries in B mode using CDU transversal and longitudinal scans, was performed in order to assess: plaque localization, plaque structure, plaque surface, intraplaque hemorrhage, the degree of stenosis of carotid arteries. The same parameters were analyzed using MSCTA.

**Plaque localization**

Plaques were divided in several groups according to localization: localized exclusively in the bulb, localized in the bulb and proximal part of ACI, in the bulb, proximal parts of ACI and ACE, localized in ACC, the bulb and proximal parts of ACI and ACE.

**Plaque structure**

According to the O’Donnel’s 10 postulates, in B-mode (black-white scale) modified by Bluth 11, there are 5 different types of plaques depending on echogenicity: type 1 – anechoic plaque with echogenic fibrous cap; type 2 – predominantly anechoic plaque but with echogenic fields that takes up to 25% of plaque volume; type 3 – predominantly hypeerechogenic plaque with hypeerechogenic areas that take up to 25% of plaque; type 4 – echogenic and homogenous plaque and type 5 – non-classified plaques that are covered with calcium and have acoustic shadow which masks plaque morphologic structure. Plaques were classified as homogeous or inhomogenous according to their echogenicity (uniform echogenicity makes it homogenous).

Following the Shroeder et al. 12 MSCTA classification, plaques were divided into 3 groups on axial images: group I – “fatty” plaque (attenuation < 50 HU); group II – mixed plaque (attenuation 50–119 HU) and group III – calcific plaques (attenuation > 120 HU). Attenuation was measured in Hounsfield units using circular cursor placed in the plaque.

**Plaque surface – intraplaque hemorrhage**

According to Kardoulus et al. 13 plaque surface is defined as: smooth, irregular, ulcerated and all three types with intraplaque hemorrhage.

Ulceration following this definition is continuous contour with focal lesion greater than 1 mm in both depth and width, with well-defined posterior wall at the plaque base, and with anechogenic surface in the plaque which is more than 1 mm deep and wide.

In B-mode and CDU intraplaque hemorrhage is presented as focal, echolucent zone in the irregular plaque with heterogeneous structure.

On MSCTA intraplaque hemorrhage is seen as hyperdense zone in the plaque on precontrast images. After contrast injection, demarcation of the hemorrhage contour is more clear inside the plaque (so-called inhomogenous imbibition – MIP, MPR).

**The degree of stenosis**

As recommended in NASCET and ESCET studies 14, the degree of carotid artery stenosis was defined using CDU and MSCTA. Hemodynamic criteria used in CDU were maximum systolic velocity over 230 cm/s (average 50 to 100 cm/s) and systolic velocity in internal and common carotid artery ratio over 2.5. The degree of stenosis was defined according to residual volume on transversal scans. Following these criteria, stenosis of the carotid artery is divided into following groups: stenosis lower than 50%, 50–69%, 70–89%, 90–99%, occlusion.

The results obtained on CDU and MSCTA were compared between each other, and both with intraoperative finding, while in a certain number of patients 15, the material obtained from endarterectomy was referred to histologicpatho (HP) evaluation.

All the patients were subjected to a form of classical surgical method (eversion technique or thrombendarterectomy with patch or Dacron). Macropscopic evaluation of the plaque surface was performed by two experienced surgeons after extirpation from carotid artery (smooth, irregular, ulcerated). Ulceration is defined as macroscopic loss of intimal integrity wider and deeper than 1 mm.

HP analysis was performed at the School of Medicine, Novi Sad, Pathology Department, using haematoxylin and eosin, Van Gieson stain and Masson trixrom with anilin blue. As fixative 4% formaline was used. For Van Gie son staining paraffin cuts of 6 μm were made, so that elastic fibres turned to purpur red to dark brown color, nuclei were brownish and connective tissue yellow. Collagen fibres were deep red. Plaque structute and surface were defined using HP analysis.

The data were analyzed and showed in tables and figures with discussion, depending on the nature of the observed feature. Description of numeric variables was performed using classical methods of descriptive statistics (aritmetic mean, median) and measures of variability (standard deviation, variability coefficient and standard error, as well as minimum and maximum values). Relative numbers were used in all the tables. The Pearson's chi-square test was used (congruence test and contigency tables) for comparison of frequency difference in non-parametric variables. The unpaired Student's t-test for two independent data groups and variance were used. For comparing three or more groups of data, we used analysis of variance (ANOVA) for parametric data and non-parametric analysis of variance for non-parametric data.

**Results**

Average age of the patients included in this study was 63.7 years (min 47.0, max. 82.0, SD 8.5 years). Most frequently reported symptoms were associated in 47 (60%), vertigo in 29 (38.7) and tinnitus in 23 (30.7%) of the patients.

The leading risk factor was hyperlipoproteinemia (HLP) type Ilb, found in 50 (67%) of the patients, while 25 (33%) had normal values of blood lipids. The obtained difference was statistically highly significant ($\chi^2 = 11.067; df = 1; p < 0.01$) as a result of widespread HLP Ilb in the patients.
Cerebrovascular insult, together with myocardial infarction was the most frequent associated disease in patients with extracranial carotid disease, found in 46 (61%) of the patients. Peripheral arterial stenosis/occlusion was present in 4 (5.4%) of the patients. The difference between the two groups was statistically highly significant (F = 13.449; df = 3; p < 0.01).

Most patients, 55 (73%), included in the study had no prior history of vascular interventions, while in 12 (15%) patients coronary or peripheral/iliac stent had been placed (F = 17.679; df = 4; p < 0.01).

Considering plaque localization the results obtained by CDU and MSCTA were almost identical. By both methods, plaque was most often located in the bulb of ACC and proximal part of ACI (CDU 63% : F = 11.940; df = 5, p < 0.01; MSCTA 65% : F = 11.200; df = 6, p < 0.01) (Figures 1 and 2).

Analysis of plaque structure revealed that most plaques were of mixed type (fibrolipid and fibrous-calcificated) and the results of CDU and MSCTA were similar (CDU 55% : F = 20.279; df=4, p<0.01; MSCTA 54% : F = 22.147; df = 4, p < 0.01) (Tables 1 and 2).

Table 1

<table>
<thead>
<tr>
<th>Plaque structure</th>
<th>CDU (n)</th>
<th>CDU (%)</th>
<th>MSCTA (n)</th>
<th>MSCTA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>6</td>
<td>8.0</td>
<td>10</td>
<td>13.3</td>
</tr>
<tr>
<td>Lipid</td>
<td>7</td>
<td>9.3</td>
<td>6</td>
<td>8.0</td>
</tr>
<tr>
<td>Fibrous</td>
<td>4</td>
<td>5.3</td>
<td>6</td>
<td>8.0</td>
</tr>
<tr>
<td>Calcified</td>
<td>3</td>
<td>4.0</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Mixed</td>
<td>55</td>
<td>66.4</td>
<td>53</td>
<td>70.7</td>
</tr>
<tr>
<td>Total</td>
<td>75</td>
<td>100.0</td>
<td>75</td>
<td>100.0</td>
</tr>
</tbody>
</table>

This study showed that sensitivity of CDU and MSCTA was almost the same regarding plaque surface, which was later confirmed intraoperatively and histopathologically. Most often, the surface was irregular. Sensitivity of MSCTA was 100% and of CDU 95.2% (Figures 3 and 4).

Table 2

<table>
<thead>
<tr>
<th>Degree of stenosis (%)</th>
<th>Number of patients (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>CDU</td>
</tr>
<tr>
<td>0–49</td>
<td>7</td>
</tr>
<tr>
<td>50–69</td>
<td>12</td>
</tr>
<tr>
<td>70–89</td>
<td>34</td>
</tr>
<tr>
<td>90–99</td>
<td>16</td>
</tr>
<tr>
<td>Occlusion</td>
<td>3</td>
</tr>
</tbody>
</table>

There was no statistically significant difference considering visualization of the ulceration by using CDU and MSCTA.
Furthermore, there was no statistically significant difference in determining the degree of stenosis between the two methods (Figures 5 and 6).

The study showed that most patients, 34 (45.3%), had stenosis of 70–89% confirmed by CDU and MSCTA (CDU: $F = 21.937; df = 5; p < 0.01$; MSCTA: $F = 23.322, df = 5, p < 0.01$). False negative findings in CDU were present in 4 (5.4%) of the patients in the group with low-grade stenosis (under 50%).

Sensitivity of CDU and MSCTA was proven to be the same (100%) in confirming occlusion of carotid arteries. Only in 1 (0.7%) patient there was a disagreement between CDU and MSCTA (false negative finding on CDU). Intraoperatively, occlusion of carotid artery was found (Figure 1).

**Discussion**

Carotid disease, which is a part of generalized atherosclerotic vessel disease, is one of the causes of CVI. This fact has been confirmed in the literature, particularly in the USA where CVI represents the third most frequent death cause, following cardiovascular and malignant diseases. In the USA there is one CVI occurring every three minutes, and the costs of treatment are about 51 billion dollars per year. Therefore, it is understandable that CVI has an extreme importance in socioepidemic and economy aspects. Consequently, adequate and timely diagnostics is important in treatment of carotid disease.

This study showed that plaque was most frequently localized in the bulb and proximal part of ACI: CDU – 41 (55.4%) patients, MSCTA – 48 (64%).

Analyzing the results obtained on CDU, we found 7 (10%) false negative results, compared to MSCTA and intraoperative findings. In those patients, plaque was not only seen in the bulb but could also be visualized in the proximal part of ACI. The explanation is, that in cases of highly positioned bulb or short neck, adequate visualization of the proximal part of ACI is not possible. In addition, visualization is problematic in circular proximal parietal calcifications both in the bulb and ACI.

Suboptimal visualization of plaque can occur on MSCTA examination due to artifacts caused by the surrounding bone structures (shoulder region, teeth) but it is less pronounced. Anyway, there is no statistically significant difference between the results on CDU and MSCTA.

Numerous authors confirmed that plaque is most often localized in the bulb and the proximal part of ACI, for the reason of the bulb anatomy, its size and hemodynamic characteristics. The bulb is almost double as wide as the internal carotid artery which results in specific hemodynamic features. We presented similar results.

Analyzing plaque surface in carotid arteries is one of the key questions in assessment of the risk of complications and for determining further treatment steps.

In this study, almost the same sensitivity was shown between two methods considering plaque surface, which was later confirmed intraoperatively and pathohistologically, and was in accordance with the literature. Sensitivity of CDU was 87.2%, while of MSCTA 91.4%.

In some studies on plaque surface in the carotid arteries, the advantages of MSCTA were reported. Kagava et al.
found the sensitivity of MSCTA to be 91.2% and specificity 91.4% on the sample of 68 carotid arteries, compared to intraoperative findings.

Niderkoorn et al. 17 reported that the sensitivity and specificity of MSCTA significantly correlate to the intraoperative and HP findings for plaque surface (MSCTA 92.5% compared to intraoperative findings and 89.7% compared to HP).

Link et al. 18 found the sensitivity of CDU to be low in detection of ulceration (37.6%) as compared to intraoperative findings. Low sensitivity of CDU is probably due to large calcificated areas that cover ulcerations, or misplacement of the transducer referring blood vessel and ulceration.

Our study, however, did not show a statistically significant difference in depicting the ulceration between CDU and MSCTA.

Data presented in this paper are in accordance with results found in the literature on MSCTA, but there is a certain disagreement regarding CDU examinations (95.2% : 37.4%) 18. This disagreement could be explained by the fact that in this study examinations were performed by the same experienced radiologist in all the patients, on the same US unit, using the same hemodynamic and morphologic criteria for the degree of stenosis, plaque morphology and structure. A relatively small number of patients and a low number of calcified plaques might also contribute to this difference to a certain degree.

The disadvantages of B-mode and CDU in plaque surface defining are that it is a subjective method depending on the radiologist’s experience and sonography unit quality. Nevertheless, all the studies showed that MSCTA has high sensitivity and specificity in detection of plaques with irregular surface and ulcers as compared to CDU findings 8, 17, 18.

Analysis of plaque structure in this study showed that most plaques were mixed, fibrolipid and fibrous-calcific in 55 (66.4%) of the patients, and the results reported by CDU and MSCTA were similar (66% – CDU and 70% – MSCTA). Both methods highly correlated to intraoperative and HP findings (CDU 94% and MSCTA 96%).

The results showed that CDU is less reliable in patients with short neck, highly positioned bulb and rough calcifications, which as well degrade the quality of MSCTA examination.

Geroulakos et al. 19 indicate that fibrous plaque does not have thromboembolic potential, which is present in ulcerated mixed plaques and those with intraplaque hemorrhage.

Walker et al. 20 reported that ulcerations are more frequent in lipid plaques than in calcificated. Relationship between plaque structure and clinical manifestation of the disease is still not clearly defined, but it is shown that cerebrovascular insults more frequently occur in patients with lipid plaques.

Fisher et al. 21 reported that the number of “silent brain infarctions” is greater in patients with ulcerated and lipid plaques compared to calcific, and implied that the presence of calcium is important for plaque stability.

A group of authors 17, 19-22 showed that plaque calcification negatively affects visualization and precise definition of plaque morphology on CDU and MSCTA. Ulcerations smaller than 5 mm are hardly visualized with MSCTA, even more if there are artifacts from surrounding bone structures and movements of the patients during examinations. Shaalan et al. 22 analyzed 48 plaque samples after CEA, and reported that in patients without calcifications in plaque, cerebrovascular symptomatology occurred more frequently.

The degree of stenosis in carotid disease directly correlates to size and structure of plaque. It is possible to evaluate stenosis as a hemodynamic feature in real time using CDU, while MSCTA enables only depiction of its morphologic aspect. The degree of stenosis and disrupted hemodynamic are the crucial parameters in extracranial carotid disease.

There are some limitations in determination of flow velocity in the carotid arteries using CDU, but most authors rely on the NASCET and ECST criteria 14. Some authors recommend the following exclusively hemodynamic criteria (maximum systolic and diastolic velocities, systolic velocities ratio in ACI and ACC). Priorly, systolic velocity over 130 m/s was considered as criterion for stenosis over 70% while Niderkoorn et al. 17 and Kagawa et al. 8 imply that those velocities can go up to 300 m/s.

Meta-analyses 8, 14, 17 have shown that MSCTA is a diagnostic method of high sensitivity (97%) and specificity (99%) in cases where the degree of stenosis in carotid arteries is lower than 70%. On the contrary, when stenosis is higher than 70%, sensitivity and specificity decrease (sensitivity 85%, specificity 93%) 23. It is pronounced in patients with calcified circular plaques in carotid arteries, because they are susceptible to artifacts which disable adequate evaluation, as confirmed in several studies 13, 18, 20. The disadvantage of MSCTA is also a high radiation dose during the examination 24.

Conclusion

Atherosclerotic carotid arteries disease affects mostly middle-aged and elderly patients, and is often associated with various risk factors. Sensitivity and specificity of CDU and MSCTA in determination of plaque composition, the level of stenosis and plaque localization in carotid arteries are almost the same. The results obtained in the study and the fact that there is no significant adverse effect (radiation dose level) compared to MSCTA, favour CDU as the initial method in diagnostics algorithm in carotid artery disease.

REFERENCES


3. Till V. Contribution to the diagnosis of nontraumatic subarachnoid hemorrhage by the method of spiral computed tomography [thesis]. Novi Sad: School of Medicine; 1999. (Serbian)


Accepted on March 4, 2010.
Revised on July 21, 2010.
Accepted on August 31, 2010.