Noninvasive assessment of carotid stenosis caused by atherosclerosis: a correlation between color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography

A.M. Surur a,*, T.V. Buccolinia, H.F. Londero b, M.A. Marangonia and N.J. Allende c

a Imaging Diagnosis Department, Sanatorio Allende, Córdoba, Argentina
b Hemodynamic and Catheterization Intervention Department, Sanatorio Allende, Córdoba, Argentina
c Vascular Surgery Department, Sanatorio Allende, Córdoba, Argentina

Received: December 2012; Accepted: August 2013.

Abstract

Introduction: Carotid angiography is used to confirm carotid bifurcation (CB) stenosis. However, as this is an invasive method with some morbidity and mortality, there is growing interest in non-invasive methods such as gadolinium-enhanced magnetic resonance angiography (Gd-MRA) and color Doppler ultrasound (CDUS). The aim of this study is to determine the correlation between the color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography in the evaluation of the degree of stenosis.

Materials and methods: We analyzed 100 cases of carotid bifurcation studied by color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography performed between January 2009 and August 2011 at Sanatorio Allende. The level of agreement was determined using the Kappa coefficient, analyzing the percentage of carotid stenosis according to diameter narrowing and peak systolic velocity (PSV) by color Doppler ultrasound and estimating luminal narrowing by gadolinium-enhanced magnetic resonance angiography. The NASCET criteria were used for both methods. The plaque surface was also assessed.

Results: A very good correlation was obtained between color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography, with a Kappa coefficient of 0.90 and a confidence interval (CI) of 95% (0.786-0.99). However, US/MRA results were discordant when assessing the plaque surface. Gd-MRA demonstrated to be superior in detecting plaque irregularities or ulcerations.

Conclusion: Technological advances and the growing number of studies demonstrating diagnostic reliability and correlation of non-invasive methods lead us to assume that in the short term these methods will replace angiography for the diagnosis and assessment of carotid disease.

Keywords: stenosis; internal carotid artery; color Doppler ultrasound; gadolinium-enhanced magnetic resonance angiography.

Introduction

A large number of studies have clearly demonstrated the benefits of carotid endarterectomy in patients with severe (70-99%) or moderate (50-69%) carotid bifurcation stenosis (BS) 1-4. Carotid stenting has become an effective and less invasive method, with clear advantages for certain patient subsets 5,6.

Invasive and noninvasive methods are available for the evaluation of the neck arteries. Color Doppler ultrasound (CDUS) provides mainly hemodynamic data, while gadolinium-enhanced magnetic resonance angiography (Gd-MRA), multislice computed tomography angiography (MSCTA) and digital subtraction angiography (DSA) show the anatomy of the CB, the origin of carotid arteries and the intracranial segment of the internal carotid arteries.

Carotid angiography is used to confirm and assess internal carotid artery (ICA) stenosis, previously detected by noninvasive techniques. However, as this method is associated with some morbidity and mortality7-9, there is a growing interest...
in noninvasive methods for the detection and assessment of carotid stenosis. Thus, it is possible to identify candidates for confirmatory diagnostic angiography and potential candidates for endovascular stent therapy or carotid surgery.

At our institution, we use CDUS and Gd-MRA as standard practice for the diagnosis and assessment of ICA stenosis, limiting the use of DSA to the confirmation of severe stenosis or to cases of inconsistency or inaccuracy as regards the degree of carotid stenosis determined by noninvasive methods. The aim of this study is to correlate two noninvasive methods that provide complementary information for the study of carotid bifurcation and to determine their diagnostic correlation in carotid stenosis.

Materials and methods

We conducted a descriptive, retrospective and observational cross-sectional study of a number of cases where supra-aortic trunks (SATs) were evaluated by CDUS and Gd-MRA in all (non consecutive) patients referred to the Radiology Department of Sanatorio Allende from January 2009 to August 2011. The study was submitted to and accepted by the Institutional Review Board. There was a maximum interval of three months between the scans, and the analysis was focused on the carotid bulb and bifurcation because this is the site with the highest incidence of atheromatous plaques.

Inclusion criteria: all patients of any age and gender who underwent both diagnostic procedures at our institution during the time period established.

Exclusion criteria: patients who had not undergone both diagnostic procedures at our institution or with a time interval longer than 3 months between the two studies. Patients with intracarotid stents or carotid endarterectomy or those with stenosis caused by non-atherosclerotic causes (including, but not limited to, vasculitis) were also excluded.

Doppler technique

CDUS of the neck vessels was performed using a Philips HD 11 ultrasound system with 3-12 MHz linear transducer. The patient was placed in supine position with neck hyperextension and rotation of the head in the direction opposite the probe. Images were obtained from both carotid axes with gray-scale, color Doppler and spectral Doppler ultrasound, examining the subclavian and vertebral arteries, the common, internal and external carotid arteries and the carotid bifurcation, recording the peak systolic velocity (PSV) at a Doppler angle of 60° (fig. 1a).

The presence of endothelial plaque was confirmed, with characterization of the plaque surface into three categories (regular, irregular or ulcerated), based on imaging features, according to the carotid artery stenosis consensus. Following Zweibel’s guidelines, ulceration was defined as any cavity within the plaque, having well-defined borders and intracavity flow.

For measuring the PSV in the internal carotid artery, the transducer was placed longitudinally to the vessel, examining the whole plaque and searching for the area with PSV. Based on hemodynamic findings, the degree of stenosis was classified as:

1) Normal: PSV < 125 cm/s. No endothelial plaques.
2) < 50% stenosis: PSV < 125 cm/s, considering the presence of endothelial plaque that narrows the arterial lumen diameter by < 50%.
3) 50-69% stenosis: PSV between 125 and 230 cm/s, considering the presence of endothelial plaque that narrows the arterial lumen diameter by > 50%.
4) 70-90% stenosis: PSV ≥ 230 cm/s, considering the presence of endothelial plaque that narrows the arterial lumen diameter by ≥ 50%.
5) > 90% stenosis ("near occlusion"): high, low or undetectable PSV, considering the presence of a visible plaque with almost total luminal occlusion and a thin flow on color Doppler.
6) 100% stenosis ("total occlusion"): undetectable flow, considering a visible occlusive plaque with undetectable arterial lumen.

According to its characteristics, the surface of the plaque visualized by CDUS and Gd-MRA was classified as:

- Regular surface
- Irregular surface
- Ulcerated surface

Plaque composition and texture (lipid, fibrous lipid, calcific or fibrous calcific plaques) are parameters that were evaluated only by CDUS and were not correlated with Gd-MRA, as no specific sequences for characterization of plaque structure were performed.

Gadolinium-enhanced magnetic resonance angiography technique

Magnetic resonance images were acquired on a 1.5 T Philips Intera™ scanner, using fast gradient-echo (GRE) sequences at the level of the SATs, with gadolinium bolus injection (Opa-cite™ 15 ml), in the coronal plane with acquisition times of 35 seconds. Technical parameters were: 5.1/2 (repetition time
Noninvasive assessment of carotid stenosis caused by atherosclerosis: a correlation between color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography

A.M. Surur et al.

In maximum intensity projection (MIP) reconstructions, the degree of stenosis of the internal carotid artery was measured by Gd-MRA according to NASCET criteria: comparison of the ICA diameter at the point of maximum stenosis with the distal lumen diameter at the point at which both arterial walls become parallel ([minimal residual lumen diameter/normal lumen diameter] × 100) (fig. 2).

Classification of the degree of carotid stenosis by Gd-MRA was performed using the same percentages as for CDUS: 1) normal, 2) <50%, 3) 50-69%, 4) 70-90%, 5) >90% and 6) 100%.

CDUS and Gd-MRA scans were reviewed in a non-simultaneous manner by two cardiologists blinded to the outcomes of the previously reviewed study.

Table 1: Assessment of Kappa coefficient

<table>
<thead>
<tr>
<th>Value of $k$</th>
<th>Strength of agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.20</td>
<td>Poor</td>
</tr>
<tr>
<td>0.21 - 0.40</td>
<td>Fair</td>
</tr>
<tr>
<td>0.41 - 0.60</td>
<td>Moderate</td>
</tr>
<tr>
<td>0.61 - 0.80</td>
<td>Good</td>
</tr>
<tr>
<td>0.41 - 1</td>
<td>Very good</td>
</tr>
</tbody>
</table>

Figure 1 (a) Color Doppler ultrasound shows the methodology to obtain the peak systolic velocity of the internal carotid artery. (b) Gadolinium-enhanced magnetic resonance angiography of supra-aortic trunks, in coronal plane. Scanning volume where the carotid arch, the proximal segment of the subclavian arteries and carotid and vertebral basilar territories are evaluated.

Figure 2. Carotid stenosis measurement in relation to the normal diameter of the distal internal carotid artery (according to NASCET criterion).
Statistical analysis: for data correlation, the Kappa coefficient (k) was used (table 1) to determine if there was agreement or not between the measurements obtained by both methods.

Results

A total of 100 internal carotid arteries of 50 patients were analyzed by CDUS and Gd-MRA. They were classified, according to the degree of stenosis, as: 1) normal, 2) <50%, 3) 50-69%, 4) 70-90%, 5) >90% and 6) 100% (table 2). The percentage of stenosis detected by Gd-MRA was correlated with the PSV (cm/s) detected by CDUS and the agreement between the two methods, according to Kappa coefficient, was very good: k = 0.90 (95% confidence interval [CI]: 0.786-0.99); i.e. there was 90% agreement.

In group 1, of 57 arteries with stenosis below 50% by CDUS, only 2 were in the 50-69% range by Gd-MRA. Instead, in group 2 (50-69% stenosis) there was a very good agreement

Table 2: Number of internal carotid arteries, according to the degree of stenosis.

<table>
<thead>
<tr>
<th>Degree of stenosis</th>
<th>CDUS</th>
<th>Gd-MRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Normal or &lt; 50%</td>
<td>66</td>
<td>69</td>
</tr>
<tr>
<td>2) 50-69%</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>3) 70-90%</td>
<td>14</td>
<td>9</td>
</tr>
<tr>
<td>4) &gt;90%</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>5) 100%</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Gd-MRA: gadolinium-enhanced magnetic resonance; CDUS: color Doppler ultrasound

Table 3: Agreement between the degrees of stenosis, according to CDUS and Gd-MRA.

<table>
<thead>
<tr>
<th>CDUS: degrees of stenosis</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td>9</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>13</td>
<td>13</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gd-MRA: degree of stenosis 57 12 19 9 3

CDUS: color Doppler ultrasound; Gd-MRA: gadolinium-enhanced magnetic resonance angiography; 1: normal or < 50%; 2: 50-69%; 3: 70-90%; 4: >90%; 5: 100%

Figure 3 (a) and (b) Color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography of one of the cases in Group 2 (50-69% stenosis), where a disagreement was found about the degree of carotid stenosis. Stenosis was classified as 50-69% by color Doppler ultrasound, and as <50% by gadolinium-enhanced magnetic resonance image.
between the two methods, as of 12 arteries classified into this group by CDUS, only 3 were considered as < 50% stenosis by Gd-MRA (fig. 3). Within group 3 (70-90% stenosis) some disagreement was observed between CDUS and Gd-MRA, as of 19 arteries classified into this group by CDUS, 5 were considered as < 70% stenosis and 1 was considered as >90% stenosis by Gd-MRA. Finally, in groups 4 and 5 (>90% stenosis and 100% total occlusion) an excellent agreement was obtained as all near and total occlusions were detected both by CDUS and Gd-MRA (fig. 4; table 3). Carotid plaque surface was also assessed by both methods. It was classified as regular, irregular and ulcerated (table 4), and the Kappa coefficient was estimated at 0.45 (95% CI: 0.25-0.68). These figures show a disagreement between the two methods, as of 12 arteries classified into this group by CDUS, only 3 were considered as < 50% stenosis by Gd-MRA (fig. 3). Within group 3 (70-90% stenosis) some disagreement was observed between CDUS and Gd-MRA, as of 19 arteries classified into this group by CDUS, 5 were considered as < 70% stenosis and 1 was considered as >90% stenosis by Gd-MRA. Finally, in groups 4 and 5 (>90% stenosis and 100% total occlusion) an excellent agreement was obtained as all near and total occlusions were detected both by CDUS and Gd-MRA (fig. 4; table 3).

Table 4: Number of arteries, according to plaque surface.

<table>
<thead>
<tr>
<th>Plaque surface</th>
<th>CDUS</th>
<th>Gd-MRA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>84</td>
<td>65</td>
</tr>
<tr>
<td>Irregular</td>
<td>13</td>
<td>23</td>
</tr>
<tr>
<td>Ulcerated</td>
<td>3</td>
<td>12</td>
</tr>
</tbody>
</table>

Gd-MRA: gadolinium-enhanced magnetic resonance angiography
CDUS: color Doppler ultrasound

Table 5: Agreement on surface plaque characterization by color Doppler ultrasound and by gadolinium-enhanced magnetic resonance angiography.

<table>
<thead>
<tr>
<th>CDUS: Plaque Surface</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>U</td>
</tr>
<tr>
<td>R 64 1</td>
</tr>
<tr>
<td>I 15 8</td>
</tr>
<tr>
<td>U 5 4 3</td>
</tr>
</tbody>
</table>

Gd-MRA: gadolinium-enhanced magnetic resonance angiography; I: irregular; R: regular; U: ulcerated

**Figure 4 (a) and (b)** Color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography agree in the classification of significant carotid stenosis > 90%, near occlusion.
methods, as of 84 arteries with regular surface on CDUS, 15 were irregular and 4 ulcerated on Gd-MRA. In turn, of 13 arteries with irregular surface on CDUS, 4 were ulcerated and 1 was regular on Gd-MRA. All 3 ulcerations detected by CDUS were also detected by Gd-MRA, therefore, it is assumed that Gd-MRA characterizes ulcerated surface better than CDUS (fig. 5; table 5).

Discussion

This study evaluated the correlation of the degree of stenosis in atherosclerotic lesions of the CB between two noninvasive methods that are widely used in standard practice. The objective was to correlate two noninvasive methods that provide complementary data for the evaluation of SATs: on the one hand, CDUS provides hemodynamic and directional data on carotid flow, but it is an operator dependent method; on the other hand, Gd-MRA provides detailed anatomical and/or morphological data. Furthermore, Gd-MRA provides images of the aortic arch and origin of the neck vessels (adding important data for carotid angioplasty indication and planning), and allows assessment of the brain parenchyma and intracranial arteries. This is highly useful to determine the brain status and coexisting malformations or intracranial arterial occlusions (this information is required before any invasive surgical or non-surgical therapy).

The combination of Gd-MRA and CDUS might be preferable over DSA for preoperative evaluation in most patients, as it reduces the risk of perioperative morbidity. Even if DSA has been regarded as the reference method in the diagnosis and assessment of carotid stenosis, CDUS and Gd-MRA or MDCTA currently tend to replace DSA as screening or first imaging method, mainly in patients with mild or moderate stenosis of the CB. In our study, we used CDUS and Gd-MRA for the diagnosis and assessment of carotid stenosis, on the basis of the sensitivity and specificity of each method, taken individually or jointly, according to literature reports 9,10,13. Previous studies have demonstrated that Gd-MRA, when performed under ideal technical conditions, achieves 92% sensitivity and 83% specificity, with 85% accuracy10, 13 in the assessment of carotid stenosis. Even if these figures are not

![Figure 5](a) and (b) Color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography show disagreement about plaque surface. Color Doppler ultrasound failed to show the ulcer observed on the gadolinium-enhanced magnetic resonance angiography.
and gadolinium-enhanced magnetic resonance angiography

Noninvasive assessment of carotid stenosis caused by atherosclerosis: a correlation between color Doppler ultrasound and CDUS achieve 100% sensitivity and 91% specificity, with 94% accuracy.9

In the analysis by Borisch et al.12, Gd-MRA had a sensitivity and specificity of 94.9% and 79.1%, respectively, for the identification of ICA stenoses of ≥ 70%. Sensitivity and specificity of CDUS were 92.9% and 81.9%, respectively. Thus, the author concludes that combining data from Gd-MRA and CDUS increases diagnostic sensitivity to 100%. In their study, angiography was performed in almost 80% of carotid arteries evaluated.

In addition, Sabeti et al.14 studied 1006 internal carotid arteries in 503 patients and analyzed the degree of carotid stenosis, comparing PSV by CDUS with DSA (after obtaining the patient’s informed consent). They concluded that CDUS is an excellent method to screen for high-grade stenosis (above 70%), but it has a moderate performance for the diagnosis of stenoses lower than 50%, as CDUS alone tends to overestimate the degree of angiographic stenosis (which is further elucidated by computed tomography or magnetic resonance angiography). The correlation between CDUS and the degree of angiographic stenosis according to the NASCET criterion was $r^2 = 0.66$; $p < 0.001$.

In this study, we correlated the percentage of carotid stenosis, anatomically assessed by Gd-MRA with the percentage of stenosis hemodynamically detected by CDUS according to PSV. When groups were analyzed as a whole, a very good agreement was found: $k = 0.90$; 95% CI: 0.786-0.99. Hathout et al. 15 performed a linear regression analysis correlating the percentage of stenosis by DSA and Gd-MRA, and found a strong correlation between the two methods ($r = 0.967$). They also correlated PSV with DSA, obtaining a moderate correlation ($r = 0.8601$) and DSA with Gd-MRA/PSV, finding a high correlation ($r = 0.965$).

The Gd-MRA technique described further above enables a comprehensive examination of SATs (from the aortic arch to the circle of Willis) with very good spatial resolution. This technique permits better assessment of the stenosis surface in a shorter examination time (30 to 40 s), at the same time that intravenous gadolinium avoids flow-related artifacts, such as signal loss due to turbulent flow or flow jet from critical stenosis.

One of the limitations of this study was the impossibility of taking into account the DSA (as the aforementioned authors did) and correlating only CDUS with Gd-MRA. Nevertheless, the strong correlation between Gd-MRA and DSA in carotid stenosis reported in the literature served as support for the development of our study. Additionally, in our setting DSA is difficult to perform in patients with non-significant stenosis, because of its invasive and non-complication-free nature. Agreement between the two methods was excellent for <70% (mild to moderate) stenosis: variations were found only in 3 arteries in which stenosis were classified as 50-69% by CDUS and then were found to be <50% by Gd-MRA. There was also a very good correlation in >70% stenosis; some variability was found only in the subset of 70-90% stenosis by CDUS: of the 14 arteries found to be within this range on ultrasound, 2 were classified as 50-69% stenosis and 3 as >90% stenoses by Gd-MRA.

The possible diagnostic difficulties of CDUS may be probably due to artifacts caused by calcific plaques, short necks in obese patients, the deep location of vessels within the neck, or by inter-observer variability. In addition, the end-diastolic velocity (a secondary parameter in the 2003 consensus) was not used for grading 70-90% stenosis. This might account for the fact that agreement between the two methods was not excellent. In >90% and 100% stenosis, an excellent agreement was obtained, as all near and total occlusions were detected both by CDUS and Gd-MRA.

According to Zwiebel, the performance of ultrasound in the assessment of plaque surface has been somewhat disappointing. Large series have shown that ultrasound has a sensitivity of 33 to 67% and a specificity of 31 to 84% for detecting ulcers 11-16. The problem with ultrasound might lie in the inability of this method to differentiate small ulcer craters from other plaque irregularities. From Zwiebel’s viewpoint, sources of error in ulcer diagnosis are manifold: they may be due to the longitudinal image plane not including the ulcer, to adjacent plaques simulating ulceration, to the presence of calcific plaques producing posterior shadowing and impeding visualization of the ulcer, or to technical limitations of the tests.

In this study, a disagreement was shown between the two methods for the evaluation of plaque surface. Kappa coefficient was 0.45 (95% CI: 0.25-0.68), as of the 84 arteries with regular plaque surface on CDUS, 15 were classified as irregular and 5 as ulcerated by Gd-MRA. This inconsistency may be probably due to the limitations mentioned above. An adequate characterization of plaque surface is important to predict stenosis severity and risks of complications.

**Conclusion**

A very good correlation was found between color Doppler ultrasound and gadolinium-enhanced magnetic resonance angiography in screening for and grading carotid stenosis in a noninvasive manner. As the two methods provide complementary data, they should be used in combination as a diagnostic tool. However, for surface plaque assessment, Gd-MRA is superior to CDUS.

Ongoing technological advances and the growing number
of studies demonstrating diagnostic reliability and diagnostic correlation of these two non-invasive methods lead us to assume that in the short term they will gradually replace DSA for the diagnosis and assessment of carotid disease. Anyway, both methods should be validated at each institution.

Conflicts of interest

The authors declare no conflicts of interest.

References