Concordance Rate Differences of 3 Noninvasive Imaging Techniques to Measure Carotid Stenosis in Clinical Routine Practice

Results of the CARMEDAS Multicenter Study

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Background and Purpose—To replace digital subtraction angiography (DSA) in carotid stenosis evaluation, noninvasive imaging techniques have to reach a high concordance rate. Our purpose is to compare the concordance rates of contrast-enhanced MR angiography (CEMRA) and CT angiography (CTA) with Doppler ultrasound (DUS) in clinical routine practice.

Methods—We evaluated prospectively with DUS, CEMRA, and CTA 150 patients suspected of carotid stenosis. The overall concordance rates of the 3 techniques were calculated for symptomatic stenosis ≥50% and ≥70%, for asymptomatic stenosis ≥60%, and for occlusion. For the carotid arteries treated by surgery (n=97), the results of each method and combined techniques were recorded, and misclassification rates were evaluated from surgical reports.

Results—The overall concordance rates of DUS-CEMRA, DUS-CTA, and CEMRA-CTA were not statistically different. However, the concordance rate of DUS-CEMRA (92.53%) was significantly higher than that for DUS-CTA (79.10%) in the surgical asymptomatic stenosis group (P=0.0258). CTA considered alone would misclassify the stenosis in a significant number of cases (11 of 64) in the surgical asymptomatic group compared with CEMRA (3 of 67) and DUS (1 of 66) (P=0.0186 versus MRA, P=0.0020 versus DUS).

Conclusions—With the techniques as utilized in our study, the overall concordance rates of combined noninvasive methods are similar for measuring carotid stenosis in clinical routine practice, but in asymptomatic carotid stenosis, the decision making for surgery is significantly altered if DUS and CTA are considered in place of DUS and CEMRA. (Stroke. 2004;35:682-686.)

Key Words: carotid endarterectomy ■ carotid stenosis ■ computed tomography ■ magnetic resonance angiography ■ ultrasonography, Doppler

Three randomized trials defined the indications for endarterectomy in patients with atherosclerotic stenosis of extracranial carotid arteries. The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) reported a high benefit of surgery for symptomatic patients with a stenosis of ≥70% (NASCET criteria). The benefit of surgery for symptomatic patients with stenosis ranging from 50% to 70% is moderate. In asymptomatic patients, the Asymptomatic Carotid Atherosclerosis Study (ACAS) showed some benefit of endarterectomy for stenosis ≥60%, but this benefit is extremely small in terms of absolute risk reduction.

Digital subtraction angiography (DSA) remains the reference method to determine the degree of stenosis, but DSA is invasive and cannot be used to study plaque tissue components that may identify patients with higher risk of ischemic events.

Alternatively, noninvasive methods (Doppler ultrasound [DUS], MR angiography [MRA], and CT angiography [CTA]) have been developed. The combination of DUS and...
Materials and Methods

Protocol Management

One hundred fifty patients (121 men, 29 women; mean age, 70.5 years; range, 46 to 94 years) were examined in 5 centers over a period of 20 months for suspected carotid stenosis. The DUS inclusion criteria were either a stenosis ≥50% in diameter defined by measurement of the narrowest segment of the arterial lumen compared with the normalized lumen distally or a peak systolic velocity (PSV) ≥120 cm/s. We excluded patients who had contraindications to MRA (metal implants not suitable for MRI, claustrophobia) and patients who had contraindica- tions to administration of iodine contrast media (severe renal insuffi- ciency, history of severe adverse events caused by iodine contrast media, noncompensated cardiac insufficiency, dehydration). All patients underwent CEMRA and CTA with a maximum of 15 days between each examination. The decision to perform surgery was made by a vascular surgeon according to the appropriate indications defined in NASCET and ACAS. Operative endarterectomy was performed on 96 carotid arteries (29 symptomatic arteries, 67 asymptomatic arteries), and 1 carotid artery underwent an endovascular treatment (endoprothesis).

Clinical data and results of imaging were centralized on a website (Theralys, Lyon). The study was approved by the consultative Committee for Patients’ Protection in Biomedical Research. All patients gave written informed consent.

Neurological Expertise

All patients were examined at the inclusion time by a senior neurologist to assess the neurological status of each carotid artery, either symptomatic or asymptomatic.

Imaging Techniques

DUS Examinations

DUS examinations were performed according to the good-quality criteria recently described by the Society of Radiologists in Ultrasound, including gray-scale, color Doppler, and spectral DUS and using an angle of insonation ≤60°. All studies included measurements of PSV, end-diastolic velocity, the ratio of the internal to common carotid artery velocities, and a planimetric estimation of the stenosis.

MRA Examinations

CEMRA of extracranial carotid arteries was performed with either 1.0-T equipment (1 center) or 1.5-Tesla equipment (remaining centers). All centers used a 3-dimensional gradient echo acquisition. Because the study was conducted in real-life conditions using different equipment, optimized CEMRA parameters were necessarily different among centers. The parameter ranges were as follows: repetition time, 4 to 5.7 ms; echo time, 1.4 to 2.2 ms; and acquisition time, 23 to 44 seconds. The minimal voxel size was 0.45×0.45×1.2 mm, and the maximal voxel size was 1.53×1.09×1.2 mm. A nonmagnetic power injector was always used for intravenous administration of gadolinium. Acquisition delay was calculated by a bolus test or automatic detection. The volume of gadolinium was 15 to 30 mL, and the flow rate was 2 to 3 mL/s. Maximum-intensity projections were used to show extracranial vessels with multiple angles of view.

CTA Examinations

Patients with a creatinine clearance (Cockroft method) <30 mL/ min were excluded. Iodine contrast media (80 to 100 mL) was injected at a flow rate of 3 to 4 mL/s. In 4 centers, CTA was performed with a multislice acquisition of 4×1-mm slices per rotation and reconstruction of 1- to 1.25-mm slice thickness with an interval of 0.5 to 0.8 mm (129 patients). In 1 center, CTA was performed with a single-slice spiral acquisition using 3-mm-thick slices with a reconstruction increment of 1 mm (21 patients).

Stenosis Measurement and Image Analysis

The degree of carotid stenosis for CEMRA and CTA was measured with the NASCET criteria. Readers were asked to estimate the stenosis with methods routinely used in each center. Thus, CEMRA analysis was based on maximum-intensity projections and source images: CTA was based on analysis of axial slices, multiplanar reconstructions, maximum-intensity projections, and sometimes 3-dimensional volume-rendering reconstruction. To compare DUS with CEMRA and CTA, we chose PSV, which is considered the best single velocity parameter for detecting surgical carotid stenosis. The cutoff values used to define stenosis in symptomatic arteries were defined according to the Society of Radiologists in Ultrasound consensus (slightly modified). No significant stenosis was diagnosed when PSV was <125 cm/s. Moderate (50% to 69%) stenosis was diagnosed when PSV ranged from 125 to 230 cm/s. Severe (70% to 99%) stenosis was diagnosed when PSV was ≥230 cm/s. Occlusion was suspected when no flow was detectable in DUS. The point near occlusion was not considered.

For asymptomatic carotid artery stenosis, DUS results were assessed as nonsignificant for surgery (PSV <160 cm/s; <60%), significant for surgery (PSV ≥160 cm/s; ≥60%), and occlusion (The threshold value of 160 cm/s was defined by a panel of experts involved in the trial).

Surgical Expertise

The vascular surgeon made his decision on the basis of all clinical information and imaging data. In the cases of imaging discordance, the decision was based on his own opinion and confidence in the results of imaging techniques. In addition, the surgeon was asked to evaluate peroperatively the stenosis for the 97 surgical carotid arteries and to give feedback as to whether the stenoses were accurately estimated in the preoperative imaging assessment. This surgical estimation was made on cut-open specimens.

Statistical Analysis

According to the NASCET and ACAS criteria for surgery, the data for degree of stenosis were classified into 4 categories for CEMRA and CTA in symptomatic carotid arteries (<50%, 50% to 69%, 70% to 99%, occlusion) and into 3 categories for asymptomatic carotid arteries (<60%, >60%, occlusion). For comparison purposes, the results of DUS were classified in a grade scale according to the systolic velocities defined above (for symptomatic arteries: none, moderate, severe, occlusion; for asymptomatic arteries: nonsignificant, significant, occlusion). For carotid stenosis treated by surgery or by stent, the results of each method and of combined techniques were recorded and classified into 3 groups (discordance, all tech- niques agree, partial concordance, 2 techniques agree, perfect concordance, all techniques agree). For concordance rates, 95% confidence intervals (CIs) were calculated, and χ² test was used to calculate the probability values (GraphPad Instat, GraphPad Software, Inc).

Results

Among the 150 included patients, 48 were symptomatic (hemispheric stroke, n=27; transient ischemic attack, n=15; retinal symptoms, 4; silent stroke with recent ischemic lesion on MRI,
TABLE 1. CEMRA and CTA Compared With DUS for Grading Stenosis in Symptomatic Carotid Arteries

<table>
<thead>
<tr>
<th></th>
<th>None (n=7)</th>
<th>Moderate (n=11)</th>
<th>Severe (n=28)</th>
<th>Occlusion (n=2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEMRA &lt;50%</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50%–69%</td>
<td>2</td>
<td>8</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>70%–99%</td>
<td>1</td>
<td>3</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Occlusion</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Excluded</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CTA &lt;50%</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>50%–69%</td>
<td>1</td>
<td>6</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>70%–99%</td>
<td>2</td>
<td>3</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>Occlusion</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Excluded</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

n=48. Data are number of carotid arteries.

n=2) and 100 were asymptomatic. The 2 other patients included presented a confusion that was not clearly related to carotid disease and were excluded from the analysis. The main risk factors of vascular diseases were hypertension in 65.4%, dyslipidemia in 57.4%, smoking in 43.8%, and diabetes in 24.9%. Carotid stenosis was judged nonassessable by CTA, DUS, and CEMRA in 10, 3, and 2 carotid arteries, respectively.

Surgical and Nonsurgical Carotid Arteries (n=296)

CEMRA and CTA results compared with DUS are shown in Table 1 for symptomatic arteries and Table 2 for asymptomatic arteries. CT results compared with CEMRA are reported in Table 3 for symptomatic and asymptomatic arteries. The concordance rates of DUS-CEMRA, DUS-CTA, CEMRA-CTA, and the 3 methods combined are summarized in Table 4 for symptomatic and asymptomatic arteries. For the same surgical threshold, no statistically significant difference was noted between the overall concordance rates of DUS-CEMRA, DUS-CTA, and CEMRA-CTA.

CEMRA identified 10 carotid occlusions. Among these 10 cases, CTA agreed with CEMRA in 9 cases (nonassessable in 1 case), and DUS was concordant with CEMRA in 8 cases.

Versus, DUS alone identified 3 carotid occlusions that were not confirmed by the other 2 techniques or by surgery. CTA identified an occlusion in 1 case in which both DUS and MRA diagnosed a preoccluded stenosis.

Surgical Carotid Arteries Only (n=97)

In the 30 carotid symptomatic arteries treated by surgery (n=29) or by stent (n=1), 2 or 3 techniques were always concordant (perfect or partial concordance), and combined methods were below the surgical threshold in 1 case (DUS-CTA) (Table 5). Three carotid arteries were classified <50% in DUS. In 1 case, DUS misclassified the carotid stenosis as an occlusion. In 2 cases, CTA underestimated the stenosis according to the surgeon’s feedback.

In the 67 asymptomatic surgical carotid arteries, perfect or partial concordance was always obtained between methods (Table 6). In this group, DUS-CEMRA (62 of 67) was more often concordant than DUS-CTA (53 of 67) (P=0.0258); DUS-CEMRA was also more often concordant than CEMRA-CTA (55 of 67) (P=0.0692, not quite significant). The concordance rates of DUS-CTA and CEMRA-CTA were statistically similar (P>0.05). In 3 cases, DUS-CTA or CEMRA-CTA was concordant and <60%. In these 3 cases, surgical decision was made on the results of CEMRA or DUS alone. Only 1 carotid artery was referred for surgery with a DUS result <60%.
CEMRA, 3 surgical carotid arteries had a result <60%. Eleven carotid arteries were operated on despite a stenosis <60% in CTA, and all were confirmed as CTA false negatives by the surgeon. Thus, when the results of CTA alone are considered, the surgical decision would have been altered in 11 cases among the 64 assessable asymptomatic arteries treated. This result is statistically significant compared with the rate of altered decisions based on the results of CEMRA or DUS alone (\( P < 0.0186 \) and \( P < 0.0020 \), respectively).

**Discussion**

The appropriateness of carotid endarterectomy is based mainly on clinical criteria, comorbidity, and accurate imaging evaluation of stenosis grade. DUS, CEMRA, and CTA are presumed to be highly sensitive for the diagnosis of high-grade carotid stenosis and to distinguish preocclusion and occlusion, although, as described in our study, DUS alone was probably less accurate than CEMRA and CTA for detecting occlusion. Nederkoorn et al\(^9\) reported a sensitivity of 96.3% and a specificity of 80.2% when both DUS and TOF MRA are concordant. Johnston and Goldstein\(^10\) reported a low misclassification rate when both techniques are combined (7.9% versus 28% and 18%, respectively, for DUS and TOF MRA alone). However, these results were reported for DUS associated with TOF MRA and not with more recent CEMRA techniques, although similar accuracy has been recently reported for both methods.\(^11\) Single-slice spiral CTA was also found to be accurate for the detection of stenosis \( \geq 50\% \) but could not discriminate between moderate and severe stenosis.\(^12\) On the other hand, the misclassification rate of DUS combined with multislice CTA is not known. In our study, the overall concordance rate of 2 combined methods is high (up to 89.58%), whatever combination is used. However, when the surgical findings (Tables 5 and 6) are considered, concordant results of combined DUS-CEMRA are more frequent than for other combinations, and this result is statistically significant for the comparison with DUS-CTA. Moreover, DUS and CEMRA are never concordant below the surgical threshold in surgical carotid arteries (no false negatives). In the 4 surgical asymptomatic carotid arteries in which DUS and CEMRA are divergent, CTA is concor-

**TABLE 4. Overall Concordance Rates of Combined Methods in Symptomatic and Asymptomatic Carotid Arteries**

<table>
<thead>
<tr>
<th>Combined Methods*</th>
<th>Symptomatic Carotid Arteries, % (95% CI)</th>
<th>Asymptomatic Carotid Arteries, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Stenosis: ( \leq 50% )</td>
<td>Stenosis: ( \geq 70% )</td>
</tr>
<tr>
<td>DUS-CEMRA</td>
<td>89.58 (77.39–95.91)</td>
<td>81.25 (67.83–90.03)</td>
</tr>
<tr>
<td>DUS-CTA</td>
<td>83.33 (70.15–91.57)</td>
<td>75.00 (61.08–85.21)</td>
</tr>
<tr>
<td>CEMRA-CTA</td>
<td>89.58 (77.39–95.91)</td>
<td>85.41 (72.52–93.07)</td>
</tr>
<tr>
<td>DUS-CEMRA-CTA</td>
<td>81.25 (67.83–90.03)</td>
<td>68.75 (54.60–80.12)</td>
</tr>
</tbody>
</table>

*No significant difference \( (P>0.05) \) between DUS-CEMRA, DUS-CTA, and CEMRA-CTA for the same thresholds.

**TABLE 5. Results of DUS, CEMRA, CTA, and Combined Methods in Symptomatic Carotid Arteries Treated by Surgery or by Stent**

<table>
<thead>
<tr>
<th>Imaging Methods</th>
<th>Stenosis None Moderate Severe Occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS</td>
<td>3 4 22 1</td>
</tr>
<tr>
<td>CEMRA</td>
<td>0 6 24 0</td>
</tr>
<tr>
<td>CTA (1 excluded)</td>
<td>2 6 21 0</td>
</tr>
</tbody>
</table>

**TABLE 6. Results of DUS, CEMRA, CTA, and Combined Methods in Asymptomatic Carotid Arteries Treated by Surgery**

<table>
<thead>
<tr>
<th>Imaging Methods</th>
<th>Stenosis Nonsignificant Significant Occlusion Excluded</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS</td>
<td>1 65 0 1</td>
</tr>
<tr>
<td>CE-MRA</td>
<td>3 64 0 0</td>
</tr>
<tr>
<td>CTA</td>
<td>11 ( (P&lt;0.05) ) 53 0 3</td>
</tr>
</tbody>
</table>

**Combined methods**

<table>
<thead>
<tr>
<th>Partial agreement</th>
<th>DUS + MRA 0 10 0 ...</th>
</tr>
</thead>
<tbody>
<tr>
<td>DUS + CTA</td>
<td>1 0 0 ...</td>
</tr>
<tr>
<td>MRA + CTA</td>
<td>2 1 0 ...</td>
</tr>
</tbody>
</table>

**Perfect agreement**

| DUS + MRA + CTA | 0 52 0 1* |

\( n=67 \). Data are number of carotid arteries.

*One case of DUS: 60% and MRA: 60% with CTA nonassessable; in all other cases, 2 or 3 techniques are concordant.
tant with either DUS or CEMRA but grades the stenosis below the surgical threshold in 3 cases. In these 3 cases, the decision for surgery was based on CEMRA or DUS alone, and the surgeon’s feedback was good. Thus, CTA, even with multislice acquisition, seems unable to replace CEMRA in association with DUS for measuring carotid stenosis in asymptomatic carotid arteries. Moreover, this lower confidence seems pertinent, considering the significant misclassification rate of CTA alone and the higher number of nonassessable CTA in contrast to DUS and CEMRA. Is DSA still necessary if DUS and CEMRA are divergent? For several reasons, the answer is probably not. First, a high degree of carotid stenosis is an accepted risk factor for stroke, but other criteria are emerging, especially the characteristics of atherosclerotic plaque, which are not assessable by DSA.3 Second, DSA is responsible for neurological complications in up to 1.8% of cases.13 Finally, the benefit of surgery in asymptomatic patients is marginal. Therefore, the utility and safety of DSA in asymptomatic carotid arteries are questionable.

Our study has some limitations. It is not a randomized trial but a descriptive study in routine conditions. However, this study has the advantage of reporting the real conditions of decision making. Our population is predominantly asymptomatic, but this can also be considered as an advantage because the consequences of misclassifications in asymptomatic stenosis are of tremendous importance in clinical practice. The number of inclusions is relatively small, so the 95% CIs are wide, especially for the description of symptomatic carotid arteries pool. Comparison of the 3 techniques is difficult because NASCET criteria used for CEMRA and CTA cannot easily be applied to DUS. However, recommendations for comparison of DUS velocities and stenosis degrees have recently been published and can be applied.3 The lack of a usual gold standard may be considered a major drawback, but we think that DSA will not remain a reference method in the near future. Finally, using surgical findings as a reference is debatable because the stenosis is estimated under operative conditions that alter the local hemodynamic parameters and probably alter the accuracy of stenosis measurement.

In conclusion, we did not find a significant difference in the overall concordance rates between combined DUS-CEMRA and other combinations. However, in the subgroup of surgical carotid arteries, the concordant results of DUS and CEMRA are significantly more frequent than combinations including CTA. This finding means that decisions can be made more confidently with DUS and CEMRA but also that CTA is more discordant than the 2 others. In our study, 81.8% (9 of 11) of the CTA misclassifications in surgical asymptomatic arteries came from one center, although this center provided only 55.8% of the concerned subgroup. These misclassifications are reported despite CTA being performed with multislice acquisition. This “center effect” is probably related to a lack of standardization of postprocessing and measurement methods. The measurement methods are more standardized for CEMRA, whatever equipment is used, giving a possible explanation for a lower misclassification rate, even with lower field strength and lower spatial resolution. Finally, if a noninvasive strategy is used to assess carotid stenosis, including CTA when DUS and CEMRA are discordant, caution is mandatory, and all methods have to be carefully compared in a multidisciplinary approach before decisions are made.

Appendix

Participants in the CARMEDAS Study Group were as follows: Anne Pasco-Papon, Jean-Michel Debray, Jacques-Olivier Fortrat, Xavier Papon (University Hospital, Angers); Jérôme Berge, Xavier Barreau, François Rouanet (University Hospital, Bordeaux); Michel Nonent, Ali Badra, Luc Bressollette, Bruno Guais, Pierre Gouy, Julien Linard, François Rouhart (University Hospital, Brest); Jean-Yves Gauvrit, Xavier Leclerc, Corinne Gauthier, Hilde Henon (University Hospital, Lille); Philippe Douek, Jean-Michel Serfaty, Pierre Chiros, Laurent Derex, Camille Diab, Olivier Jegaden, Norbert Nighoghossian, Carmen Rotaru, Jacques Villard, Jean-Michel Chevalier (University Hospital, Lyon); Yann Le Bras, Eric Thomas, Xavier Coll, Isabelle Besson (Hospital Center, Niort); Jean-François Heautot, Bernard Langella, Jean-François Pinel, Jean-Philippe Verhoye (University Hospital, Rennes); Charles Veyret, Pierre Garnier, Jean-Pierre Favre (University Hospital, Saint Etienne); Rémy Beaujeux, Agnès Doll (University Hospital, Strasbourg); Jean-Philippe Cottier, François Tranquart (University Hospital, Tours); Chahin Pachai, Emmanuel Olart, Fabrice Vincent (Theralys, Lyon); Valérie Buthion, Isabelle Jurs, Michel Lamure (Laboratory of Health Systems Analysis, Lyon).

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References

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