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BACKGROUND AND PURPOSE: Gradation of high-grade intracranial internal carotid artery (ICA) stenosis poses a challenge to noninvasive neurovascular imaging, which seems critical for angioplasty in the ICA segments C1 and C5. We investigated cutoff values of intracranial ICA stenosis for transcranial color-coded sonography (TCCS) and compared this method with the "gold standard," digital subtraction angiography (DSA).

MATERIALS AND METHODS: Forty patients (mean age, 58.9 ± 13.8 years) with intracranial ICA lesions were prospectively examined by using TCCS and DSA. Two standard TCCS coronal imaging planes were used to evaluate the intracranial ICA. In addition, a control group of 128 volunteers without cerebrovascular disease (mean age, 48.8 ± 15.9 years) was investigated to establish standard velocity values.

RESULTS: DSA confirmed 96 stenoses and 8 occlusions of the intracranial ICA in the study population. In 9% and 7% of cases, stenosis confined to the C1 or C5 segment was >50% and 70%, respectively. Receiver-operating curves demonstrated cutoff values for >70% stenosis in C1 when the peak systolic velocity (PSV) was >200 cm/s (specificity, 100%; sensitivity, 71%) or the C1/submandibular ICA index was >3 (specificity, 93%; sensitivity, 86%).

CONCLUSIONS: TCCS is a reliable adjunctive method to detect and quantify significant stenosis of the intracranial ICA. The assessment of the C1/ICA index and peak systolic velocities maximizes the diagnostic accuracy of C1 stenosis to >70% when extracranial ICA stenosis coexists. Further studies need to be performed to compare the diagnostic accuracies of MR angiography and TCCS with that of DSA.

D etection of atherosclerotic narrowing of intracranial cerebral arteries is important in stroke management and aids in the identification of patients with high risk for vascular events.[1-3] Ischemic stroke due to atherosclerosis of intracranial large arteries has been reported in approximately 8%–29% of adults in general, with a higher prevalence in African and Asian populations.[4-6] The intracranial internal carotid artery (ICA) is the most common location for intracranial stenosis of >50%; such cases compose up to 49% of all intracranial artery stenoses.[1,7] Patients with severe (≥70%) intracranial stenosis have a higher risk of stroke than patients with moderate (50%–69%) intracranial stenosis.[8] Treatment of significant stenosis relies on antiplatelet and antithrombotic agents as well as on aggressive lipid-lowering therapies.[9,10] Endovascular treatments involving angioplasty for 50%–99% ICA stenosis have also been applied but are considered experimental approaches in need of validation by controlled studies.[11-13]

Because the course of intracranial ICA is complicated due to its tortuosity and variability, classification of this portion of the vessel may differ between authors,[14-16] in turn complicat-

ing interpretation of the data. The "gold standard" used to assess the intracranial ICA remains digital subtraction angiography (DSA). DSA is usually performed only after noninvasive imaging procedures, such as MR angiography (MRA) and, to a lesser degree, conventional transcranial Doppler (TCD) sonography, have suggested intracranial stenosis. With TCD sonography, intracranial ICA stenosis is considered when flow velocities exceed normal values and/or exhibit abnormal flow patterns. Unlike cases of extracranial ICA disease, stenosis gradation of the intracranial ICA has not been calculated.[17,18] With MRA, intracranial ICA stenosis in the C5 as well as the C3 and C1 segments is frequently indicated by flow-void artifacts, especially when using time-of-flight sequences, because of the inherent signal-intensity loss of parallel imaging, which can only be compensated in part by the use of MR imaging contrast agents.[19] Due to these MRA artifacts, calculation of ICA stenosis gradation is difficult, and semiquantitative scales, rather than percentages of stenosis, are frequently used to describe the lesion.[20]

Although the criteria for detecting significant (>50%) stenosis of basal cerebral arteries has been defined for transcranial color-coded sonography (TCCS),[21-24] little data can be found on grading intracranial ICA stenosis. The aim of this study was to elaborate the TCCS criteria for detection and quantification of significant intracranial ICA stenosis and to correlate them with conventional DSA criteria as the standard of reference.

Materials and Methods

All data were obtained from the neurology departments at the University of Regensburg, Germany, and the University of Vilnius,

Table 1: Age-dependent hemodynamic parameters of the carotid siphon segments C1 (upper) and C5 (lower)

Factor	<39 Years Mean	(95% CI)	SD	40–59 Years Mean	(95% CI)	SD	>60 Years Mean	(95% CI)	SD	P Value
C1 PSV	69.9	65.1–74.8	23.7	69.2	64.9–73.6	19.7	71.3	66.1–76.4	23.39	.96
C1 EDV	29.0	27.0–31.1	10.0	29.8	27.6–32.1	10.2	27.8	25.5–30.1	10.4	.28
C1 MFV	42.7	39.8–45.6	14.2	43.0	40.1–45.8	13.0	42.4	39.2–45.5	14.38	.72
C1 PI	0.86	0.82–0.91	0.22	0.86	0.81–0.90	0.19	0.96	0.91–1.01	0.21	.003
C1 RI	0.52	0.50–0.54	0.10	0.54	0.52–0.55	0.08	0.58	0.56–0.61	0.10	<.001
C1/ICA	1.24	1.15–1.34	0.45	1.31	1.20–1.42	0.49	1.53	1.41–1.64	0.52	<.001
C1/CCA	0.83	0.72–0.94	0.30	1.06	0.95–1.16	0.38	1.30	1.18–1.42	0.46	<.001
C5 PSV	50.9	47.9–53.9	14.4	49.4	45.9–53.0	15.9	51.6	47.8–55.4	17.0	.81
C5 EDV	19.3	18.0–20.6	6.04	20.7	18.9–22.4	7.8	19.6	17.7–21.6	8.7	.31
C5 MFV	29.8	28.1–31.6	8.4	30.3	28.0–32.5	10.1	30.3	27.8–32.7	10.9	.81
C5 PI	0.95	0.89–1.00	0.27	0.88	0.83–0.94	0.25	0.99	0.94–1.04	0.22	.02
C5 RI	0.55	0.52–0.58	0.12	0.54	0.51–0.56	0.11	0.59	0.57–0.61	0.10	.01
C5/ICA	0.73	0.68–0.78	0.26	0.80	0.73–0.86	0.29	0.89	0.82–0.96	0.31	<.001
C5/CCA	0.70	0.59–0.80	0.28	0.78	0.69–0.88	0.33	0.96	0.88–1.03	0.30	<.001

Note:—All velocities are given in centimeters per second. C1/ICA, C1/CCA, C5/M1, and C5/CCA indicate divisions of mean velocities; C5, the ganglionic segment of the carotid siphon; C1, the distal segment of the carotid siphon; ICA, the distal (submandibular) portion of the extracranial ICA; CI, confidence interval; CCA, common carotid artery; PSV, peak systolic velocity; EDV, end diastolic velocity, MFV, mean blood flow velocity; PI, pulsatility index; RI, resistance index.

Lithuania. Interinvestigational variability was minimized because all sonography investigations were performed by 1 experienced investigator (J.V.) on the basis of a preliminary study of standardized transcranial coronal imaging planes.[25] We analyzed data from 40 patients seen at our neurovascular laboratory in Regensburg (14 women and 26 men; mean age, 58.9 ± 13.8 years; range, 19–85 years) who were scheduled for intra-arterial DSA between 2002 and 2003 at the Institute for Neuroradiology in Regensburg. Diagnostic DSA was scheduled after MR images were suggestive of intracranial artery stenosis. Intracranial sonography findings had no influence on the selection of patients for DSA. Intracranial artery stenosis was suggested in patients with stroke or at high risk for stroke on the basis of pathologic findings on MRA and standard extra- and intracranial Doppler and duplex sonography. The clinical baseline characteristics in the study population are presented in Table 1. Only patients who had ischemic infarcts within the M2 branches of the middle cerebral artery (MCA) and modified Rankin Scale scores <3 were included to minimize the influence of large cerebral infarcts on cerebral hemodynamics.

For comparisons, we also analyzed data obtained in 128 control volunteers with no known cerebrovascular disease of white descent (54 women and 74 men; mean age, 48.8 ± 15.9 years; range, 19–78 years) at both clinics, Vilnius and Regensburg. The volunteers could provide age-matched reference values for carotid siphon segments C1 through C5. This control population consisted of relatives, colleagues, friends, and patients in the neurology departments with multiple sclerosis or polyneuropathy. In addition to clinical and neurologic examinations performed to exclude occult stroke syndromes and assessments of cerebral imaging if available (as in patients with multiple sclerosis), patients in whom extracranial duplex sonography revealed incidental findings of atherosclerosis were excluded. Only patients and volunteers with adequate acoustic bone windows were included in the study; no sonographic contrast agent was used.[21,26] This study was approved by the local ethics committee in accordance with the Declaration of Helsinki.

Transcranial Sonography Investigation

Sonographic examinations were performed by using a standard color-duplex sonography system equipped with a linear-array transducer (5–8 MHz) for the extracranial examination and a low-frequency (2–3 MHz) phased-array transducer for transtemporal insonation (Elegra, 2.5PL20, 7.5L40; Siemens, Issaquah, Wash; or Logiq 500, 2.9/

2.0S222, 6.7/5.0L739; GE Healthcare, Tokyo, Japan). Standard extracranial color-coded duplex sonography (ECCS) was performed to evaluate atherosclerotic lesions in case the extracranial vessels were studied before transcranial insonation. Peak systolic (PSV), end diastolic (EDV), and mean blood flow (MFV) velocities of the distal extracranial ICA were registered. TCCS examinations were performed in a manner previously described.[25] Briefly, after optimization of the transmit frequency and power, focal zone, and pulse repetition frequency, the color gain was adjusted for the individual acoustic bone window so that random-color speckling outside the vessel borders could be avoided. The Doppler gate was 5 mm in all intracranial blood flow measurements. TCCS examination was started with axially oriented transtemporal insonation to identify the first segments of the basal cerebral arteries of the circle of Willis (M1 of the MCA, A1 of the anterior cerebral artery [ACA], and P1 of the posterior cerebral artery [PCA]). Rotation of the transducer 90° led to the coronal imaging planes. In the anterior scanning plane, the C1 segment of the ICA, colored red, and the A1 and M1 segments were depicted. Slightly frontal to the posterior coronal imaging plane, defined by the top of the basilar artery (BA) and both PCAs, the C5 segment was detected in blue as it ran vertically away from the transducer. The C5 segment can sometimes already be depicted in the anterior scanning plane (Fig 1).

Defined coronal planes were used to measure siphon segments, and the axial mesencephalic imaging plane was selected to measure the MCA. The M1 and the C1 through C5 segments were investigated bilaterally. Angle-corrected measurements were performed for the MCA in all cases. Due to the tortuous course of the C1 and C5 segments, which rarely allow angle correction, flow measurements were performed without angle correction. The maximum PSV, EDV, and MFV (based on the time-averaged maximum velocity); the pulsatility index (PI); and the resistance index (RI) were registered in each of these vessel segments. The Pourcelot RI was calculated automatically by using the following formula: $RI = (PSV - EDV) / PSV$; the PI was defined according to Gosling and King,[27] was calculated as $PI = (PSV - EDV)/MFV$. Additional MFV indices were calculated as follows: C1/ICA, C5/ICA, C1/common carotid artery (CCA), and C5/CCA. Significant stenosis within the C1 or C2 segment was diagnosed when focal flow velocity exceeded the standard mean PSV by 2 SDs. Indirect signs of stenotic lesions, such as high-intensity bidirectional low-frequency signals (HILFSs) or "musical murmurs," were taken
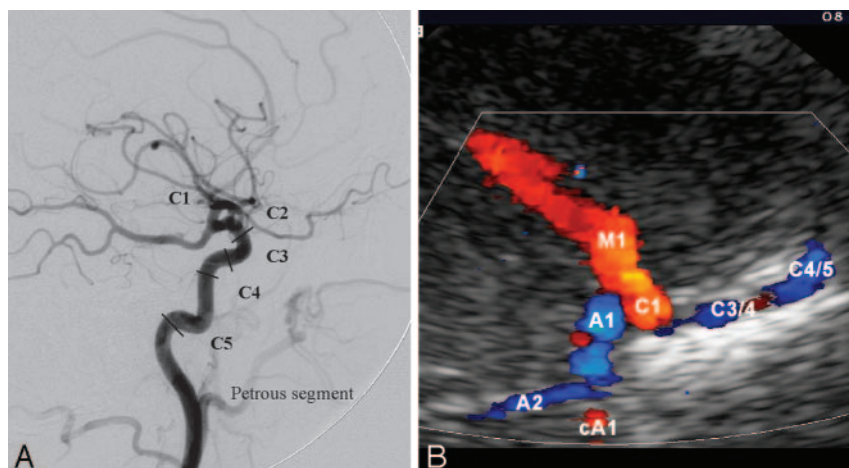
Fig 1. Normal anatomy of the carotid siphon, lateral view DSA (*A*) and anterior coronal imaging plane TCCS (*B*) *A,* C5 (precavernous/ganglionic segment), C4 (inferior carotid siphon), C3 (carotid knee), C2 (upper carotid siphon), and C1 (terminal ICA segment). *B,* Color coding showing flow toward (*red*) and away (*blue*) from the transducer. M1 indicates the first segment of the MCA; A1, the precommunicating segment of the ACA; A2, the postcommunicating segment of the ACA; cA1, the contralateral A1 segment, ICA segments C3/4 and C4/5.

into account.[28] With sonography, stenoses of the MCA, ACA, PCA, and BA were assessed as previously described.[29] The sonography investigation was blinded to the results of the DSA but not to those of prior MRA studies, which led to further diagnostic work-ups.

DSA

For all 40 patients, intra-arterial DSA was performed by using a Polystar-TUP system (Siemens, Erlangen, Germany) within 2 weeks (5 ± 4 days, 0–14 days) after the sonographic examination. The FOV of the image was 230 or 330 mm, and the image matrix was 1024 × 1024. Standard lateral and anteroposterior views of the ICA were obtained, and in selected cases, other views were added. Stenosis assessment was based on the ratio of the narrowest diameter on any projection to the nearest portion of the artery judged to be normal according to the reference given by Samuels et al[30] for the Warfarin-Aspirin Symptomatic Intracranial Disease Study.[10,31] DSA was performed and the resulting images were analyzed by a single experienced neuroradiologist who was blinded to all sonographic data. Obstructive ICA lesions were classified as follows: 0%–29% (mild stenosis), 30%–49% (moderate stenosis), 50%–69% (higher grade stenosis), 70%–89% (severe stenosis), 90%–99% (subtotal stenosis), and 100% (occlusion).

Statistical Analysis

Data analysis was performed by using the Statistical Package for the Social Sciences (Version 12, SPSS, Chicago, Ill). Differences between means of studied hemodynamic parameters in patients with and without arterial obstructive lesions, as determined by using DSA, were compared by performing the nonparametric Mann-Whitney *U* test. Cutoffs of hemodynamic parameters were established by using receiver-operating curve (ROC) analysis to determine >70% stenosis. A statistically significant difference was considered if the *P* value was <.05. In the control population, hypotheses about homogeneity of mean values and dispersion of hemodynamic parameters (PSV, EDV, MFV, PI, and RI) in various sections (right/left hemispheres, C1 and C5 segments) were checked. The Wald-Wolfowitz test was applied to detect differences in both the locations and the shapes of the distributions of hemodynamic parameters of studied segments. To test the parametrical hypotheses, we performed the Student *t* test and analysis of variance. A statistically significant difference at a *P* value of <.05 was accepted.

Results

Reference Values

To establish reference parameters, we performed TCCS and ECCS examinations in 128 volunteers (control group): 54 women (42%) and 74 men (58%). The 3 groups were separated according to age: group 1 (<40 years; *n* = 46), group 2 (40–59 years; *n* = 42), and group 3 (>60 years; *n* = 40). No relevant asymmetry was found between distributions of hemodynamic parameters in the studied segments of both cerebral hemispheres. An analysis of location and shapes of distributions of the studied parameters confirmed that our results did not contradict the hypothesis about an equal distribution of hemodynamic parameters when the error probability was set at <.05. Because no statistically relevant asymmetry between the distributions of hemodynamic parameters of studied segments of right and left cerebral hemispheres was found, further analyses were performed by using the combined data of the studied segment velocities of both sides. Therefore, an additional combined analysis could be performed by using data from both hemispheres. The hemodynamic parameters of 256 hemispheres were analyzed, focusing on the evaluation of ICA segments C1 and C5 (Table 1). With TCCS, the identification rate for the C1 segment was 98.4% (252/256) and the rate for the C5 segment was 94.1% (241/256). No significant differences were found when we compared the PSV, EDV, and MFV of the C1 and C5 segments in all 3 age groups (all, *P* > .28), whereas the PI, RI, and all indices increased slightly with patient age, a finding statistically significant (all, *P* < .02).

Clinical Data of Patients

All patients scheduled for DSA due to suspected intracranial ICA stenoses were investigated by using ECCS and TCCS close to the time DSA was performed (5 ± 4 days, 0–14 days). The clinical characteristics of the patients are summarized in Table 2.

Angiographic Data

The angiographic data obtained in the 40 patients (80 extracranial and intracranial ICAs) were analyzed. Of the 400 C1 through C5 segments studied (40 patients × 2 sides × 5 ICA segments), 377 (94.3%) were suitable for a careful assessment. Of 80 extracranial ICA segments that were studied, 77 (96.3%)

Table 2: Clinical characteristics of 40 patients

Characteristics	No.
Mean age in years (range)	59 (19–85)
Male sex	26 (65%)
Arterial hypertension	30 (75%)
Hypercholesterolemia	24 (60%)
Diabetes mellitus	20 (50%)
Smoking	9 (23%)
Coronary artery disease	7 (18%)
Peripheral artery disease	5 (13%)
Obesity	13 (33%)
Hyperuricemia	8 (20%)
Hyperhomocysteinemia	3 (8%)
Cerebral ischemic infarct	17 (43%)
Transient ischemic attack	10 (25%)
Asymptomatic	6 (15%)
Other*	7 (18%)

* Other clinical indications for performing a vascular diagnostic work-up included syncope ($n = 2$), migraine headache ($n = 1$), suspected cerebral and temporal vasculitis ($n = 3$), and sleep apnea syndrome ($n = 1$).

Table 3: Angiographic data on ICA stenosis (DSA, $n = 40$ patients)

ICA Segment	Extracranial	C5	C4	C3	C2	C1	Total Intracranial ($n = 400$)
Normal	27	58	48	60	48	59	273
<50%	26	16	21	11	13	5	66
>50%	23	1	6	4	11	8	30
<30%	18	10	17	8	10	4	49
30%–49%	8	6	4	3	3	1	17
50%–69%	10	1	4	2	5	1	13
70%–89%	4	0	1	1	2	4	8
90%–99%	9	0	1	1	4	3	9
Occlusion	1	0	0	0	4	4	8
Not assessable	3	5	5	5	4	4	23
Total	80	80	80	80	80	80	400

were suitable; the remaining 3 could not be unequivocally assessed due to technical errors (inferior projection and image quality). Taken together, 454 of 480 (94.6%) ICA segments were analyzed. Due to insufficient projection of the ICA, 26 of 480 (5.4%) ICA segments were not sufficiently accessible to determine stenosis gradation by using DSA. The results of the DSA data analysis are presented in Table 3.

DSA showed 96 separate stenoses of the C1 through C5 segments (<50%, $n = 66$; ≥50%, $n = 30$; >70%, $n = 17$) and 8 occlusions in a total of 40 patients. Overall, 27 ICAs had no extracranial ICA disease, and 3 vessels were not analyzable due to technical difficulties and inferior projections. Tandem stenosis—coexisting extracranial ICA stenosis and carotid siphon disease—was detected in 36 of the remaining 50 ICAs of studied patients (72%); however, high-grade (≥50%) extracranial plus intracranial ICA stenosis was found in only 4 of all studied patients, in 4 of 77 ICAs (5%). No statistical analysis could be performed due to the low number of cases.

Intracranial ICA stenoses were located in the distal segment, C1, and C2, in 23% of patients (37/160) (Fig 2) and in the precavernous ICA segment, C4, and C5 in 27% (44/160). Additionally, 11 MCA lesions (3 < 30% stenotic, one 30%–49%, one 50%–69%, two 70%–89%, and two 90%–99% stenotic, as well as 2 cases of occlusion), 6 stenotic lesions of the ACA (2 < 30% stenotic, two 70%–89%, and one 90%–99% stenotic, as well as 1 case of occlusion), 5 PCA lesions (two 50%–69% stenotic and 3 cases of occlusion), 4 V4 lesions (1 < 30% stenotic, two 50%–69%, and three 70%–89% stenotic), and 4 BA lesions (1 < 30% stenotic, one 50%–69%, and two 70%–89% stenotic) were diagnosed by using DSA (data not shown).

TCCS Velocity Data
The data on ICA velocities derived from TCCS were grouped according to angiographic stenosis assessment. In addition, HILFSs and mirror-image parallel strings or bands of low-to-moderate frequency (musical murmurs, also referred to as "seagull cries") within the Doppler spectrum were observed in 85% of the DSA-confirmed cases of C1 stenosis (11/13).[28] Additionally, in 18 of 57 angiographically unaffected C1 segments (32%), HILFS were registered, whereas no musical murmurs were observed. The velocity data on intracranial ICAs are presented in Table 4.

ROCs were calculated to determine the cutoff values to separate ≥70% from <70% stenosis of the C1 segment. A PSV of >200 cm/s had a specificity of 100% and a sensitivity of 71% (compared with a normal mean value of $69–71 \pm 20–24$ cm/s. A C1/ICA index of >3 had a specificity of 93% and a sensitivity of 86% (normal mean value, $1.24–1.53 \pm 0.45–0.52$). The last index, the C1/CCA, had a specificity of 97% and a sensitivity of 86% when >3.4 (normal mean value, $0.8–1.3 \pm 0.3–0.46$). No stenosis >70% was found in the C5 segment on angiography, and thus no ROC curves were calculated.

Discussion
Gradation of the distal ICA stenosis may be critical in the management and risk assessment of patients with stroke and in interventional therapies such as angioplasty. TCCS provides a flexible and accurate bedside tool for the investigation of intracranial ICA stenosis. In the current study, we demonstrated the following: First, we established age-related flow velocities for the precavernous (C5) and terminal (C1) ICA segments, which could serve as reference values for screening patients. Second, we demonstrated that by using standardized coronal imaging planes, we could achieve very high sensitivity and specificity for detection of high-grade intracranial ICA stenosis of >70% in the very distal C1 segment.

To date, reference velocity values for the intracranial ICA segments have been derived from TCD studies through the ophthalmic and temporal bone window. Ringelstein et al[32] and Russo et al[33] found mean velocities of 35–39 cm/s in the C1 segment; we found a mean velocity of 42 cm/s in this study. Because TCD sonography applies a significantly larger Doppler gate flow (normally 10–12 mm as opposed to 5 mm in TCCS), those values are comparable. We did not use transorbital TCCS, which must be performed at low-transmit-power levels (<17 mW/cm) to prevent damage to the patient's eye[34] and requires a high level of patient cooperation. Using transorbital color-flow Doppler imaging, Hu et al[35] could identify the C1 and C3 segments in most healthy volunteers. In contrast to findings of our study and previous TCD studies, those authors found significantly higher flow velocities (mean flow, 105 cm/s) with a very comparable RI. In our study, no significant differences in the 3 age groups were found when we compared the velocities in the C1 and C5 segments. Specifics of the anatomic course of the intracranial ICA might influence relative but not significantly higher velocities in the carotid
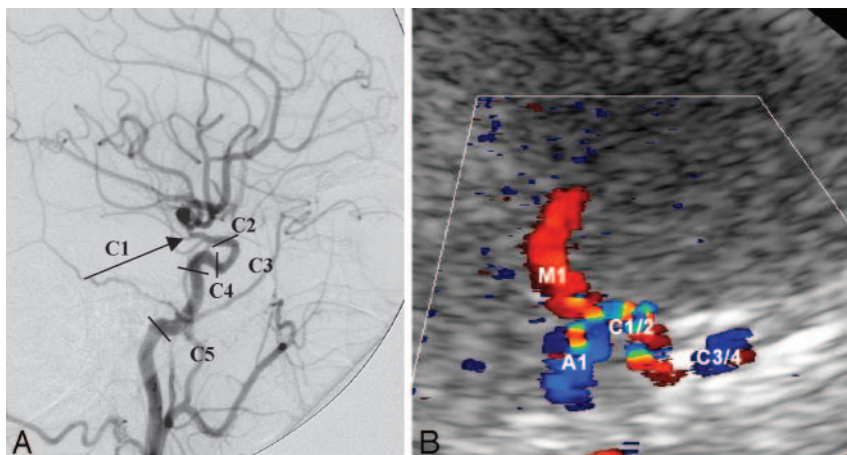
Fig 2. High-grade stenosis extending from the C1 segment into the C2 and C3 segments. *A,* DSA. Note the torturous and elongated course of the intracranial ICA. *B,* TCCS with a coronal imaging plane and aliasing phenomenon in the C1 and C2 segments.

Table 4: Mean velocity data derived from TCCS and grouped according to stenosis assessed by angiography

Factor	≥70% Stenosis in C1 (n = 7)	<70% Stenosis in C1 (n = 59)	P Value	≥50% Stenosis in C1 (n = 8)	<50% Stenosis in C1 (n = 58)	P Value
C1 PSV	256.3 ± 84.5	82.9 ± 37.8	.0001	229.5 ± 109.0	83.7 ± 37.7	.001
C1 EDV	146.4 ± 72.5	29.1 ± 18.2	.0001	129.1 ± 83.0	29.4 ± 18.1	.001
C1 MFV	178.5 ± 69.3	47.0 ± 23.5	.0001	158.6 ± 85.4	47.5 ± 23.3	.001
C1 PI	0.62 ± 0.20	1.13 ± 0.4	.001	0.72 ± 0.34	1.13 ± 0.4	.005
C1 RI	0.42 ± 0.10	0.61 ± 0.13	.001	0.45 ± 0.13	0.61 ± 0.13	.004
C5 PSV	21.8 ± 5.5	48.2 ± 22.1	.0001	21.2 ± 5.3	48.8 ± 21.9	.0001
C5 EDV	12.2 ± 4.4	16.3 ± 8.0	.21	11.4 ± 4.5	16.4 ± 7.9	.07
C5 MFV	15.4 ± 4.6	26.9 ± 11.8	.005	14.7 ± 4.6	27.2 ± 11.7	.001
C5 PI	0.66 ± 0.22	1.16 ± 0.39	.001	0.70 ± 0.22	1.17 ± 0.40	.001
C5 RI	0.45 ± 0.11	0.63 ± 0.12	.001	0.46 ± 0.11	0.63 ± 0.12	.001
C1/M1	2.11 ± 1.9	0.82 ± 0.34	.008	1.89 ± 1.9	0.82 ± 0.34	.05
C1/ICA	7.06 ± 6.1	1.27 ± 1.2	.0001	6.28 ± 6.1	1.27 ± 1.2	.001
C1/CCA	5.48 ± 2.1	1.68 ± 0.9	.0001	4.87 ± 2.6	1.70 ± 0.9	.001
C5/M1	0.17 ± 0.10	0.48 ± 0.20	.0001	0.17 ± 0.09	0.49 ± 0.20	.0001
C5/ICA	0.60 ± 0.43	0.66 ± 0.47	.77	0.57 ± 0.40	0.67 ± 0.47	.66
C5/CCA	0.45 ± 0.11	0.94 ± 0.39	.0001	0.43 ± 0.11	0.94 ± 0.39	.0001

Note:—All velocities are given in centimeters per second. C1/M1, C1/ICA, C1/CCA, C5/M1, C5/ICA, and C5/CCA indicate divisions of mean velocities; C5, the ganglionic segment of the carotid siphon; C1, the distal segment of the carotid siphon; ICA, the distal (submandibular) portion of the extracranial ICA.

siphon area in the elderly group: The cavernous portion of the ICA is located in the rigid trabeculated cavernous sinus, which is confirmed at the points of its entry and exit.[36]

Our DSA data reveal that high-grade stenosis was most frequently seen in the C1 and C2 segments of the intracranial ICA. Stenosis of the C5 segment was a rare finding but was associated with a decrease in flow velocity, perhaps due to significant collateral flow from the posterior communicating artery and the ophthalmic collateral pathway. In our series, isolated C5 stenosis was not observed. In contrast, coexisting stenosis in the C2-C5 segments was a frequent finding in cases of C1 stenosis. Stenosis <50% was mostly seen in the C4 and C5 segments.

In our study, we demonstrated a high diagnostic accuracy of TCCS examinations in the diagnosis of intracranial ICA stenosis ≥50%. Using strictly defined coronal scanning planes for C1 and C5 measurements, we compared only these segments by using DSA data. The ROC analysis showed that a PSV of 200 cm/s with a C1/ICA index of 3 indicates ≥70% stenosis. A comparison between the TCCS and DSA data showed that it is not sufficient to evaluate the PSV and signals of disturbed flow to distinguish ≥50% C1 stenosis. Being the terminal ICA segment, C1 reflects obstructive changes in C2 through 5. It is known that increases in intrastenotic velocity

may extend a few centimeters beyond anatomic narrowing.[37] We found that if an increased PSV of the C1 existed, a normal C1/ICA index allowed us to exclude all false-positive cases (except 1 complicated case in which there was contralateral MCA occlusion with collateralization by the ACA and bilateral PCA occlusion with collateralization via the ipsilateral MCA branches and ACA). Diagnosing ≥50% stenosis in the C1 segment requires increases in the PSV and the C1/ICA index above an age-dependent mean value ± 2. Due to the lack of significant stenosis at C5, we cannot elaborate the criteria for detection of C5 stenosis ≥50%. However, flow velocities were significantly lower in >50% of cases compared with flow in normal arteries. This may be due to early collateralization via the ophthalmic artery and both communicating arteries. In cases of intracranial ICA dissection, we found increased values in these segments, probably because these lesions occur rapidly in contrast to atherosclerotic stenosis (unpublished observation).

As expected, the comparison of TCCS velocities and indices with DSA in the case of low-grade stenosis in the C1 segment revealed no differences ($P > .05$), because a lumen reduction <50% has no influence on flow velocities. Pathologic flow phenomena such as musical murmurs in most DSA examinations confirmed C1 stenosis (11 of 13 cases); however,

HILFSs were also registered in 18 of 57 angiographically unaffected C1 segments (32%). These signs of pathologic flow in cerebral vessels are believed to indicate the presence of early arterial lesions even before conventional angiography can detect the early morphologic appearances of such lesions. Other comparable TCD and conventional angiography studies have shown that abnormalities in the frequency spectrum of arterial signals have much greater diagnostic impact for detection of carotid siphon and MCA stenoses than velocity values.[38] In our study, the flow abnormalities were rather nonspecific but sensitive in cases of high-grade C1 stenosis. Due to the high signal intensity, these signals may be easily detected even in patients with an inferior transtemporal bone window. Recently, Lin et al[39] demonstrated the clinical significance of musical murmurs, which are indicative of high-grade intra- and extracranial artery stenoses. The presence of musical murmurs in the current study, in which we used TCCS, should prompt further diagnostic work-up and, potentially, treatment, if this approach is used for screening patients for intracranial artery disease.

The findings of the present study demonstrate that half of the angiographically confirmed high-grade intracranial obstructive lesions were located in the C1 through C5 segments. Similar data were obtained in other angiography studies, which showed high-grade intracranial lesions in 35%–49% of cases.[1,7,13] In our study, we did investigate 2 ICA segments in detail, especially those in which the MR imaging artifact problem frequently occurs and in which angioplasty may not be complicated by an extremely tortuous arterial course.[19]

Tandem stenosis of the ICA is of special interest in patients undergoing surgical ICA revascularization or stent placement. In our study, 72% of the studies of ICAs with extracranial ICA stenosis had coexisting carotid siphon disease. Overall, the combination of ≥50% obstruction in the extracranial and intracranial ICA was found in 4 of 77 (5%) patients. These data are in line with those from a study by Roederer et al,[40] who found 84% intracranial ICA disease with >50% stenosis in 5%–9% of patients scheduled for carotid endarterectomy.[41,42] Tandem stenosis is also critical because by using Doppler sonography, stenosis detection and grading are based on flow acceleration and changes in pulsatility and resistance. Therefore, we calculated ICA indices by dividing the MFVs in the intracranial ICA segment by those of the extracranial poststenotic ICA or CCA.

Generally, insufficient transcranial acoustic bone windows may limit direct assessment of ICA stenosis; these have been reported in up to 20% of cases, limiting the value of this approach.[43,44] Nevertheless, the use of sonographic contrast agents has been shown to increase significantly the number of valid sonographic investigations and should be kept in mind as an additional option in these patients.[45] Sonographic contrast agents improve detection of maximum flow velocities, which has to be kept in mind when applying our established data.[22] In a recent study, Lee et al[46] used extracranial ICA flow data for detection of >50% stenosis of the intracranial ICA, including the MCA, which can also be used for screening patients.[37,38]

Despite recent advantages in critical care, neurosurgery, and endovascular therapy, treatment of cerebrovascular disorders remains problematic. Such endovascular techniques as angioplasty and stent placement of symptomatic intracranial stenosis may allow the treatment of previously "untreatable" disorders. Marks et al[13] treated only intracranial artery stenosis >50% (124 cases of stenosis in 120 patients) with 118 of 124 lesions >70% stenotic. However, next to clinical follow-up, repeated angiography was performed in only 58%. The GESICA study also included patients with >50% stenosis for angioplasty; follow-up included only neurologic follow-up, no cerebrovascular imaging.[3]

In summary, by using defined coronal scanning plans, TCCS allows highly successful imaging of the C1 and C5 segments of the intracranial portion of the ICA. Assessment of the C1/ICA index, in addition to the PSV, maximizes the diagnostic accuracy of high-grade C1 stenosis. Apart from validation of the inter-rater reliability of this special TCCS technique, further studies need to be performed to address whether a battery of MRA or CT angiography and TCCS can achieve a diagnostic accuracy similar to that of DSA in the detection and follow-up of high-grade ICA stenosis.

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