Comparison of Carotid Arterial Resistive Indices With Intima-Media Thickness as Sonographic Markers of Atherosclerosis

Beat Frauchiger, MD; Hans Peter Schmid, MD; Christian Roedel, MD; Peter Moosmann, MD, PhD; Daniel Staub, MD

Background and Purpose—The intima-media thickness (IMT) of the carotid artery is a (morphological) sonographic parameter that depends on the degree of atherosclerosis. In the renal arteries, the value of the (hemodynamic) resistive index (RI) is correlated with the severity of atherosclerosis. In contrast to the well-known IMT, no study has yet applied the carotid RI to estimate generalized atherosclerosis.

Methods—The SMART atherosclerosis risk score was determined in 157 patients (94 men and 63 women; mean age 63 [range 19 to 80] years) with at least 1 vascular risk factor or a known vascular disease. Duplex sonography of the common carotid (CCA) and internal carotid artery (ICA) was then performed, with determination of IMT and RI.

Results—The mean risk score of all patients was 8.8±3.5 (range 1 to 17), the mean IMT value in the CCA was 0.727±0.161 mm, the mean RI in CCA was 0.79±0.066, and the mean RI in ICA was 0.661±0.082. Highly significant correlations were found between the score and IMT CCA and the score and RI ICA (r=0.62, P<0.0001 and r=0.55, P<0.0001). The score–RI CCA correlation was much less marked (r=0.354, P<0.0001). The intraobserver and interobserver agreement was less for IMT than for RI CCA and ICA. The areas under the curve of the receiver operating curves to distinguish between low-risk and high-risk patients resulted in values of 0.86, 0.81, and 0.69 for IMT, RI ICA, and RI CCA, respectively.

Conclusions—Although RI reflects the atherosclerotic process in an indirect manner, the correlation between the RI ICA and the SMART atherosclerosis score as well as the ability to distinguish between low- and high-risk patients are comparable to those of the well-known IMT. (Stroke. 2001;32:836-841.)

Key Words: atherosclerosis □ carotid arteries □ ultrasonography

The intima-media thickness (IMT) is at present the best-studied sonographic marker for early atherosclerotic vascular wall lesions.1-3 A thickening of the intima-media complex not only reflects local alterations, mostly of the common carotid artery (CCA), but also corresponds to generalized atherosclerosis. The same applies to CCA distensibility, which diminishes with increasing severity of atherosclerosis.4,5 A correlation between IMT, distensibility, and atherosclerosis has recently been shown.3 Measurement of IMT enabled a better discrimination of high- and low-risk patients compared with distensibility. In addition, the total arterial wall thickness can be determined sonographically and put into relation to atherosclerosis.6

Assessment of arterial distensibility requires a relatively arduous procedure and is subject to interobserver and intraobserver variability of up to 19%.7,8 The IMT up to 12%. The validity of total wall thickness has not yet been established in this context. Furthermore, the measurement of morphological wall parameters requires the use of high-resolution ultrasound probes.

In contrast, the resistive index (RI) according to Pourcelot is a hemodynamic parameter that is easily determined by Doppler sonography and basically reflects vascular resistance.9,10 In the renal arteries, the RI has been studied thoroughly as a surrogate marker of atherosclerotic alterations. Age, vascular risk factors, and clinically demonstrated vascular diseases are associated with an increase in RI.11-13 However, no study has yet addressed the possible correlation between carotid RI and the degree of atherosclerosis, even though the CCA and internal carotid artery (ICA) are more accessible to sonographic examination than are the renal arteries. Ishimura et al12 previously demonstrated a (moderate) correlation between the IMT of the CCA and the RI in the renal parenchyma. This relationship could indicate that the RI ICA could be used to assess atherosclerosis.
Accordingly, it was the purpose of this study to investigate the relationship between atherosclerosis and the RI in CCA and ICA in a group of patients with vascular risk factors or documented manifestations of atherosclerosis and to compare this parameter with the established IMT.

**Subjects and Methods**

**Patients**

The study involved 157 patients treated on an inpatient or outpatient basis in our clinic from December 1, 1999, through February 28, 2000. The inclusion criteria were either a vascular risk factor or a clinical manifestation of atherosclerosis. The exclusion criteria were malignant diseases with an estimated life expectancy of <2 years and age <16 or >80 years. The study was approved by the local ethics committee, and all patients gave their written consent.

**Risk Score**

The enrolled patients completed a questionnaire with a risk score based on the SMART study (see Reference 3 for details). A score of 1 point was attributed for each of the following risk factors or vascular diseases: age >30 years, age >40 years, up to age >70 (1 point for each decade); male gender; smoker or ex-smoker; hyperlipemia or medication for hyperlipemia; diabetes mellitus or medication for diabetes; hypertension or medication for hypertension; body mass index >30 kg/m²; peripheral arterial occlusive disease (ankle-arm index 0.9 or plaques or stenoses detected by angiography or duplex sonography); previous interventions on the leg vessels; TIA or stroke; ICA stenosis ≥50% (detected by angiography or duplex sonography); and previous carotid thromboendarterectomy, angina pectoris, myocardial infarction, aortic or renal artery stenosis (detected by angiography or duplex sonography) or impaired kidney function. As in the SMART study, the questionnaire was valid when <3 items were unknown or not filled in. Missing items in valid questionnaires were scored as 0. The sum of scores was calculated for each patient. Five patients were excluded because of incomplete questionnaires. After definitive enrollment, all patients underwent duplex sonography of the carotid bed. For this imaging, the investigator had no knowledge of the atherosclerosis score.

**Duplex Sonography Measurements**

After patients rested for 5 minutes in a supine position, their pulse and BP measurements were recorded with a wrist cuff oscillometric blood pressure measurement device (OMRON R3) and duplex sonographic measurements were performed. The investigation was done with an Acuson Sequoia device with a 10-MHz linear-array probe for the IMT measurement (minimal axial and lateral resolution 0.1 mm) and a 5-MHz linear-array probe for the RI measurements. Plaques or other findings in the B-mode image were recorded. Pulsed-Doppler investigation was included at sites of color duplex sonographic findings, and any stenosis was graded according to the Washington criteria.

**Measurement of Resistive Index RI**

The wall filter setting was 50 Hz and the Doppler frequency 5 MHz. The pulsed-Doppler volume was carried out in the middle/distal CCA region with a maximum Doppler angle of 60° with a sampling volume of approximately three quarters of the vascular diameter. Using the cine-loop function, a scope length of perfect quality was recorded, and the maximum systolic and minimum diastolic flow rates were determined automatically in a cycle by means of inbuilt software. The measurement was then repeated twice and performed on the contralateral side in the same way. In the ICA region, the section immediately distal to the dilatation of the carotid bulb was chosen as the measurement site or, if the bulb was not detectable, 2 cm cranial to the start of the bifurcation. The same measurement method was applied to the CCA. The investigation was repeated on the left side, and the average of 6 measurements was again used for the further calculations. Figure 1A shows an RI ICA measurement.

When stenosis (≥16% Washington criteria) was found at the measurement site, or a stroke signal was seen or the ICA could not be imaged, the measurements for the ICA and for the CCA on the same side were not used. Measurements in patients with aortic stenosis were not used further for RI calculations on both sides. The RI was calculated according to Pourcelot as follows:

$$1 - \frac{\text{minimum diastolic velocity}}{\text{maximum systolic velocity}}.$$  

Only 7% of the pulse measurements were <50 or >90 bpm. Because the trial use of the Mostbeck correction formula for the RI values did not show any change in mean value or correlation, the formula was not further applied. The values from patients with atrial fibrillation (11%) were included.

Of the 157 patients, bilateral ICA and CCA measurements could be primarily included in 131 cases. One or both sides were excluded in 26 cases: 5 bilateral due to aortic stenosis, 13 due to unilateral ICA stenosis ≥16% (including 7 ≥50%), 4 due to unilateral stroke signals (suspected intracranial occlusion or ICA stenosis), and 4 due to inability to image the ICA on one side. Of the 21 cases in which measurements on one side could theoretically be used, 2 more were excluded from the ICA and CCA calculations because of massive ventricular extrasystoles with tachycardial phases, and another was excluded from the ICA calculation because of incomplete documentation. Consequently, 18 unilateral ICA measurements and 19 unilateral CCA measurements could be added to 131 bilateral ICA.
and CCA measurements. The curves and graphs of the RI calculations are thus based on unilateral or bilateral measurements of the CCA in 150 patients and of the ICA in 149 patients.

**IMT Measurement in the CCA**

The intima-media thickness was measured 1 cm proximal to the start of the carotid bulb dilatation on the CCA in the far wall. Using the cine-loop function, an optimal longitudinal freeze-frame image in the end-diastolic state was measured manually. On the basis of previous descriptions, the sonographic vascular lumen-intima transition was selected as the internal measurement site and the media-adventitia transition as the external limit.\(^1\) The measurement was repeated twice at the same site and then performed in the same way 3 times at the corresponding left site. The mean of 6 measurements was used for the further calculations (a total of 942 IMT measurements). There were no exclusions with regard to the IMT measurements. On the other hand, because of plaques, the planned measurement site had to be shifted proximally to a plaque-free site in the right CCA in 16 and in the left CCA in 18 cases. Figure 1B shows an example of an IMT measurement.

**Laboratory Tests**

Glucose, triglycerides, cholesterol, LDL, and creatinine were determined by enzymatic methods with the Hitachi Model 910 Automatic Analyzer. Microalbuminuria (>20 mg/L) was investigated with the Turbiquant (Behring Diagnostics GmbH).

**Statistical Evaluation**

The Statistical Package for the Social Sciences (SPSS Inc) was used for the statistics. The Q-Q plot analysis showed normal distribution for the scores and for the IMT, RI CCA, and RI ICA values. Correlation calculations were performed with the Pearson test. Differences between the right and left sides were analyzed with the unpaired \(t\) test. To test the discriminative power with regard to the atherosclerotic risk, the area under the curve (AUC) of the receiver operating curves were calculated. An AUC of 1.0 signifies perfect and 0.5 no discrimination. The null hypothesis was tested at a level of \(P<0.05\).

**Results**

**Patient Data**

The clinical data for all 157 patients are given in Table 1.

**Summary of Duplex Sonographic Parameters**

The summary of the results of IMT, RI CCA, and RI ICA measurements is shown in Table 2. In this, the left column shows the results for 157 patients. For comparison, the values for 13 much younger, healthy volunteers, used to calculate intraobserver and interobserver agreement, are shown on the right.

**Correlation Between Atherosclerosis Score and IMT or RI**

A highly significant correlation with the SMART score was found for all 3 parameters; that for RI CCA was least clear. Figure 2 illustrates the relationship for all 3 parameters.

**Correlation Between Morphological and Hemodynamic Parameters**

Both RI ICA and RI CCA were significantly correlated with the IMT. Again, the correlation between IMT and RI ICA was much greater than that between IMT and RI CCA (\(r=0.57\) and \(r=0.38\); \(P<0.0001\) and \(P<0.001\), respectively). The correlation between IMT and RI ICA is shown in Figure 3.
Discrimination of Low- and High-Risk Patients
The patients were divided into 4 roughly equal groups on the basis of their atherosclerosis scores. Group 1 comprised scores of 1 to 6, group 2 scores of 7 to 8, group 3 scores of 9 to 11, and group 4 scores of 12 to 17. Group 1 was considered the low-risk group for cardiovascular events and group 4 the high-risk group. The AUC in the high-risk group was 0.75 (CI 0.69 to 0.84) for IMT, 0.67 (CI 0.57 to 0.77) for RI CCA, and 0.72 (CI 0.64 to 0.81) for RI ICA. For the low-risk group discrimination, the AUC was 0.86 (CI 0.78 to 0.93) for IMT, 0.69 (0.59 to 0.78) for RI CCA, and 0.81 (CI 0.73 to 0.89) for RI ICA. Figure 4 shows the AUC values for the discrimination of low-risk patients relative to IMT, RI CCA, and RI ICA.

Precision of Measurements
To establish the precision of our measurements, interobserver and intraobserver agreement was determined by a modified method described by Bland and Altman17 and Montauban van Swijndregt 18 in 13 volunteers (mean age 38 years, range 28 to 56; 6 women and 7 men). Two blinded investigators performed the IMT and RI measurements in the CCA and ICA, respectively, at an interval of 7 days. The mean intraobserver differences for paired measurements were 11.4%/8.0% for IMT, 4.5%/4.2% for RI CCA, and 5.3%/7.8% for RI ICA. For interobserver differences, the values were 9.5%/8.3% for IMT, 3.3%/5.3% for RI CCA, and 6.4%/6.7% for RI ICA. The scatter for the differences between left and right was also examined. In the case of IMT, there were significantly greater left-right differences for means above the median than for values below the median (P<0.02). RI CCA showed the opposite: with higher mean values, the differences between the sides were slightly smaller (P<0.04); with RI ICA there were no significant differences.

Discussion
The present study clearly shows a correlation between the resistive indices in the carotid bed and the degree of generalized atherosclerosis. This has not been previously demonstrated for the carotid arteries, in contrast to the renal arteries, where the dependency of RI on age, risk factors, and vascular disease is well known.11–13 Furthermore, the RI measured in the ICA achieved nearly the power of the established IMT in identifying low- and high-risk patients.

The suitability of the ICA for such examinations might be due to Doppler sonographic properties similar to those of the renal arteries: like the latter, the ICA shows the properties of a low-resistance bed with a highly constant resistive index. This could be explained by the self-regulating intracranial flow.19 The extensibility of elastic vessels (such as the CCA and ICA), and thus the windkessel function, decreases with age, as does the diastolic flow fraction, and the vascular resistance increases.20–22 The correlation we find between RI and IMT of the ICA is much greater than that reported by Ishimura et al12 for IMT of the CCA and the RI of the renal arteries in diabetics, which clearly indicates that structural vascular wall alterations directly influence the RI.

The RI CCA provides a poorer cutoff than does the RI ICA. This may be due to the fact that the CCA precedes 2 different resistive beds, namely, the intracranial and the extracranial. The resistance in the ECA bed can thus undergo greater variations.23

IMT is thus far the best-studied sonographic parameter.1,3,24 It is defined as the section between the blood-intima and media-adventitia interfaces seen in the B-mode image procedure. An increase in IMT in relation to vascular risk factors or manifest atherosclerosis has been demonstrated many times.3,25,26 A direct correlation between IMT and the risk of myocardial infarction and stroke in a population of patients without a prior history of vascular diseases has recently been shown.27 The correlation between IMT and the atherosclerosis score in our study (r=0.62) is comparable to that of Geroulakos et al25 (r=0.55), whereby the latter used the score of the British Regional Heart Study. Drawbacks of the IMT determination are the need for high-resolution ultrasound probes, greater intraobserver and interobserver variability (compared with RI), and the marked side differences that increase with higher values.8,24 Although some authors27–29 have found an even better correlation with the degree of atherosclerosis when using IMT values for the ICA or a combination of ICA and CCA values, we have restricted ourselves to the determination of IMT in the CCA. IMT measurements in the ICA have a massive scatter.20 IMT CCA measurements are easier to obtain, are more reliable, and have been proved in many studies.3,31,32
When RI and IMT measurements are compared, the essential advantages of the former are the easier data acquisition by the use of simple duplex apparatuses, the tendency to have less interobserver and intraobserver variability, and the smaller side difference. The basic dependency on heart rate and rhythm and the effects of stenosis before and after the measurement site are disadvantages. Because we analyzed the possible validity of RI measurements in large populations, e.g., in epidemiological studies, we did not take heart rate and frequency into account and deliberately did not exclude patients with atrial fibrillation but did exclude those with detectable stenosis. Unilateral or bilateral RI measurements could nevertheless be used in 95% of all patients.

In summary, we conclude that the RI of the ICA can be assessed as a surrogate marker of generalized atherosclerosis, complementary to IMT. Although the RI as a hemodynamic value reflects the atherosclerotic process in an indirect manner, the correlation in our patient population is comparable to that of the former established IMT. Further studies will be needed to investigate the value of the resistive index as a direct predictor of cardiovascular morbidity and mortality. Compared with other
indirect measurements of atherosclerosis, eg, distensibility, the ease with which RI data are obtained is striking.

Acknowledgment
We would like to offer our sincere thanks for the secretarial work of Esther Brandner.

References
Comparison of Carotid Arterial Resistive Indices With Intima-Media Thickness as Sonographic Markers of Atherosclerosis
Beat Frauchiger, Hans Peter Schmid, Christian Roedel, Peter Moosmann and Daniel Staub

_Stroke_. 2001;32:836-841
doi: 10.1161/01.STR.32.4.836

_Stroke_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2001 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/32/4/836

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/