

Correspondence to Daniel H. O'Leary, MD, Department of Radiology, New England Medical Center, 750 Washington St, Boston, MA 02111.

Abstract

```
Thickening of the Carotid Wall : A Marker for Atherosclerosis in the Elderly? -- O'Leary et al. 27 (2): 224 -- Stroke
```

Background and Purpose We investigated the relationships between prevalent coronary heart disease (CHD), clinically manifest atherosclerotic disease (ASD), and major established risk factors for atherosclerosis and intima-media thickness (IMT) in the common carotid arteries (CCA) and internal carotid arteries (ICA) separately and in combination in older adults. We wished to determine whether a noninvasive measurement can serve as an indicator of clinically manifest atherosclerotic disease and to determine which of the two variables, CCA IMT or ICA IMT, is a better correlate.



Methods IMT of the CCA and ICA was measured with duplex ultrasound in 5117 of 5201 individuals enrolled in the Cardiovascular Health Study, a study of the risk factors and the natural history of cardiovascular disease in adults aged 65 years or more. Histories of CHD, peripheral arterial disease, and cerebrovascular disease were obtained during baseline examination. Risk factors included cholesterol levels, cigarette smoking, elevated blood pressure, diabetes, age, and sex. Relationships between risk factors and IMT were studied by multiple regression analysis and canonical variate analysis. Prediction of prevalent CHD and ASD by IMT measurements in CCAs and ICAs were made by logistic regression, adjusting for age and sex.

Results IMT measurements of the CCAs and ICAs were greater in persons with CHD and ASD than those without, even after controlling for sex (P<.001). IMT measurements in the ICA were greater than those in the CCA. Risk factors for ASD accounted for 17% and 18% of the variability in IMT in the CCA and ICA, respectively. These same risk factors accounted for 25% of the variability of a composite measurement consisting of the sum of the ICA IMT and CCA IMT. The ability to predict CHD and ASD was greater for ICA IMT (odds ratio [confidence interval]: 1.36 [1.31 to 1.41] and 1.35 [1.25 to 1.44], respectively) than for CCA IMT (1.09 [1.05 to 1.13] and 1.17 [1.09 to 1.25]).

Conclusions Whereas CCA IMT is associated with major risk factors for atherosclerosis and existing CHD and ASD in older adults, this association is not as strong as that for ICA IMT. The combination of these measures relates more strongly to existing CHD and ASD and cerebrovascular disease risk factors than either taken alone.

Key Words: carotid arteries • diagnostic imaging • elderly • atherosclerosis

Introduction

Stroke

Lesions in the extracranial carotid arteries can be measured noninvasively by ultrasonography and appear to reflect the extent and severity of atherosclerosis in population groups. $1 \ 2 \ 3 \ 4 \ 5 \ 6$ The changes seen in the extracranial carotid arteries have been shown to correlate with atherosclerotic lesions in other arterial beds. $7 \ 8 \ 9 \ 10 \ 11 \ 12 \ 13$ Lesions found on coronary arteriography correlate with the presence of lesions in the carotid arteries. $14 \ 15$ The carotid arteries are of particular interest to investigators because they are easily accessible to noninvasive examination by B-mode ultrasound. Quantitative measurements of IMT performed in the distal segment of the CCA just proximal to the carotid bulb have come to be

equated with atherosclerosis, mostly because this variable is associated with clinically manifest cardiovascular disease.⁴ 16 <u>17 18 19 20 21 22 23</u> Increased IMT in this segment of the CCA has been accepted as indicating ASD despite the fact that this zone of wall thickening is distinct from the plaques that typically form in the proximal ICA.²⁴ Emphasis is given to the measurements made on this segment of the carotid system for at least two reasons: (1) CCA wall-thickness measurements can be obtained with a high degree of reproducibility, whereas measurements made in the ICA have three times greater variability¹⁸; and (2) some studies have reported a significant amount of missing data in relation to ICA IMT measurements.²⁵ In other words, more disease can be found in the ICA, but it is harder to visualize and quantitate these lesions than for the CCA.



🔺 Тор

Methods

— Results

— Discussion

— References

Abstract

Introduction

Subjects and

There is, however, no direct evidence that increases in CCA wall thickness parallel the development of focal atherosclerotic lesions in the ICA. Focal atherosclerotic lesions, or plaques, in the ICA grow through a process linked to lipid accumulation but also experience superimposed episodes of intraplaque hemorrhage. ²⁶ 27 28 29 These episodes are thought to be one source for the atherosclerotic process is typically one of a large proportion of clinically observed strokes. This is not the case for the CCA, where the manifestation of the atherosclerotic process is typically one of a diffuse thickening of the wall due to progressive smooth muscle proliferation and ground substance accumulation. ³⁰ 31 32 33 34 Therefore, the two need not be interchangeable when used as measures of atherosclerosis. In a recent editorial, Crouse¹⁵ commented that "some of the features that contribute to the strength of the B-mode method pose new questions related to the definition of atherosclerosis, the quantification of the outcome variable, the differences in associations based on various levels of the [carotid] artery, the potential for differences in various clinical samples, the precise relation between wall thickness and lumen diameter, and the use of the carotid artery wall as a `surrogate' for coronary disease."

Our objectives were to (1) determine which of two derived measurements, CCA IMT or ICA IMT, is more strongly related to the presence of clinically manifest CHD and ASD; (2) compare their relation to the presence and severity of recognized major risk factors for CHD and ASD; and (3) establish whether both these measurements are needed or whether one (eg, CCA IMT) might serve as a measurement of the extent of atherosclerotic changes linked to cardiovascular risk factors.

Subjects and Methods

Subject Population

troke

The CHS is a prospective cohort study of risk factors for the development and progression of heart disease and stroke among the elderly. Begun in June 1988, the CHS enrolled 5201 men and women aged 65 years and older between April 1989 and May 1990. The CHS cohort was recruited from a random sampling of the Health Care Financing Administration Medicare eligibility lists in four communities: Forsyth County, North Carolina; Sacramento County, California; Washington County, Maryland; and Pittsburgh, Pa. Persons aged 65 years and above who were living in the sampled household and were able to give informed consent were eligible to participate in the study. Individuals who were wheelchair-bound in the home or receiving treatment for cancer were excluded. Individuals with prevalent cardiovascular

disease were included in the sample. Details of the study design and examination procedures have been previously published.³⁵ ³⁶ This article is based on baseline examination data collected from June 1989 through May 1990.

Medical History and Clinical Variables

Eligible subjects giving informed consent underwent a baseline clinical examination as well as medical history.³⁷ Smoking history was based on a selfreported estimate of pack-years of smoking. Blood pressure was measured in the right arm of seated subjects after a 5-minute rest with a random zero sphygmomanometer and was determined from the average of two measures. Duplicate measurements of supine blood pressure in both arms and both ankles were performed with a standard mercury sphygmomanometer and an 8-MHz Doppler probe to establish the ankle-arm index. Resting 12-lead ECG and echocardiography were also obtained. CHS echocardiographic methods and initial quality-control results have been published.³⁸ Venipuncture was performed during the clinic visit after subjects had fasted overnight. Plasma was prepared and frozen in a standardized fashion and shipped weekly to a central laboratory. Laboratory data included measurements of levels of total, LDL, and HDL cholesterol and of total triglycerides, creatinine, blood urea nitrogen, blood glucose, insulin, uric acid, fibrinogen, factor VII, and factor VIII. <u>39 40 41</u> All participants except diabetic subjects treated with insulin or oral hypoglycemic agents drank a 75-g oral glucose load, and repeat venipuncture was performed 2 hours later for measurement of postchallenge serum glucose and insulin levels.⁴² Diabetes was defined on the basis of participant-reported prior diagnosis of diabetes, use of insulin or oral hypoglycemic agents, fasting glucose \geq 140 mg/dL, or 2-hour postload glucose \geq 200 mg/dL. An abnormal ECG was defined as any major abnormality including evidence of myocardial infarction, T-wave abnormalities, arrhythmia, or left ventricular hypertrophy. 43 CHD was defined as self-reported and confirmed history of angina, myocardial infarction, congested heart failure, coronary revascularization, or old myocardial infarction documented on ECG.37 Stroke was defined as self-reported history of stroke confirmed by physical examination or medical records. Peripheral arterial disease was defined as an ankle-brachial pressure index of 0.8 or less or a confirmed medical history of intermittent claudication.⁴⁴ ASD was deemed present in individuals with any of the following: CHD, stroke, transient ischemic attacks, peripheral arterial disease, or a history of revascularization procedure.

Ultrasonography

Carotid artery ultrasound was performed during the baseline clinic visit with Toshiba SSA-270A imaging units (Toshiba America Medical Systems). Details of the scanning and reading protocols, as well as initial reproducibility results, have been published.¹⁹ All machines were identically equipped with a phased-array imaging probe with a characteristic -3-dB cutoff point of 6.7 MHz. The pulsed Doppler frequency was 4.0 MHz.

The imaging protocol involved obtaining a single longitudinal lateral view of the distal 10 mm of the right and left CCAs and three longitudinal views in different imaging planes of each ICA. The ICA was defined as including both the carotid bulb, identified by the loss of the parallel wall present in the CCA, and the 10-mm segment of the ICA distal to the tip of the flow divider that separates the external artery and the ICA.

All studies were recorded on optical disk and super VHS videotape and sent weekly to a central ultrasound reading center for standardized readings. The high-resolution images of the CCAs and ICAs were analyzed to calculate near- and far-wall IMT, lumen diameter, and vessel width at each arterial site. All measurements of lumen and wall thickness were calculated with a specially designed computer program. For the purposes of this article, the terms IMT and wall thickness are used interchangeably.

To quantify the degree of thickening of the carotid artery walls, the many measures of IMT were summarized into two variables: one for the CCA and one for the ICA. The maximum wall thickness of the CCA was defined as the mean of the maximum wall thicknesses for near and far wall on both the left and right sides: (mLNW+mLFW+mRNW+mRFW)/4. The maximum wall-thickness variable of the ICA was defined in the same way; the results from the three scans were averaged. The number of measurements available for averaging thus ranged from 1 to 4 for the CCA and 1 to 12 for the ICA.

troke

Analysis Plan and Statistical Methods

All analyses were conducted using SPSS/Windows software.⁴⁵ We chose to study CHD separately as well as within the definition of ASD. The twosample *t* test was used to compare carotid artery IMT measurements for variables with two categories, prevalent CHD and ASD. Only values of P<.01 were considered significant.

Correlation coefficients for the variables were computed as descriptive measures of the relationships between risk factors, and CCA IMT and ICA IMT measurements were calculated as the dependent variables.

Logistic regression analysis was used to study the independent contributions of the two wall-thickness measures to the prediction of a history of CHD and ASD after adjustment for age and sex. In the logistic regression analysis, only values of P<.01 were considered statistically significant. The tests and confidence intervals for the odds ratios were computed with the SPSS/Windows statistical software.

The independent variables selected for their possible relationship with IMT in the CCA and ICA included the following: age, sex, current systolic and diastolic blood pressures, current use of antihypertensive medication, smoking history, the amount of smoking in pack-years, the presence of diabetes, levels of HDL and LDL cholesterol, triglyceride levels, and abnormalities on ECG. A stepwise linear regression method was used, allowing entry of only those variables with a value of P<.01. Entry into stepwise regression equations was determined for variables for which the partial F test was significant at the P<.01 level. Exclusion from the regression was at the P>.05 level. The regression analyses included only participants with complete data on all variables.

One of the primary goals of our analyses was to determine the relative importance of CCA IMT for predicting prevalent CHD and ASD. To accomplish this, we wished to determine whether a linear combination of CCA and ICA IMT measurements correlated with a linear combination of recognized risk factors for the presence of ASD. Rather than arbitrarily defining the coefficients to be used in this correlation analysis, we opted to use a canonical correlation analysis to determine linear combinations of wall-thickness measurements that have the largest correlation with linear combinations of risk factors.⁴⁶ Because there are two wall-thickness measurements, canonical correlation analysis first finds a linear combination of these two variables that has the largest correlation to a linear combination of the risk factors for atherosclerosis. It then finds another set of linear combinations that are orthogonal to the first set of linear combinations and have a maximum correlation. Since there is no a priori selection rule that constrains the different coefficients in the linear combinations that are produced, these coefficients may lend themselves to a useful interpretation.

Results

Of the 5201 individuals enrolled in the CHS, 2946 (56.8%) were women and 2255 (43.2%) were men. A carotid ultrasound scan was done on 5176 (99.5%) of the participants. From these, maximum CCA wall-thickness measurements were available for 5164 (99.8%), and maximum ICA wall-thickness measurements were available for 5117 (98.9%). All of the analyses included over 4700 of the 5201 participants. The exact number in each analysis varied depending on the number of missing values for the variables used in the multivariate analyses.

Maximum ICA and CCA wall thicknesses were greater in men than women (Table 1...). Wall-thickness measurements of the ICA were consistently greater than those of the CCA. Both measurements were also greater in subjects with CHD when compared with those without. We examined CHD separately from ASD because we questioned whether different segments of the carotid artery had different relationships to coronary disease as opposed to more generalized atherosclerosis. The results for CHD and ASD were very similar, reflecting the fact that CHD is the largest component of the ASD variable; therefore, we chose not to present them in a separate table.



View this table:Table 1. Distribution of CCA and ICA IMT Values in Men and Women With and Without[in this window]CHD

Logistic regression (Tables 2 and 3) was used to assess independent relationships of wall-thickness measurements with prevalent CHD and ASD. A simple model for predicting the risk of prevalent CHD included the two measures of wall thickness and age and sex. It showed that, after adjustment for age and sex, maximum ICA IMT had a stronger relation to CHD than maximum CCA IMT. The likelihood of prevalent CHD was estimated to increase by 36% for a 1-SD (0.69-mm) increase in the maximum ICA IMT, after adjustment for CCA IMT. The relationship was weaker for the maximum CCA IMT, where a 1-SD (0.22-mm) increase corresponded to a 9% increase in risk, after adjustment for ICA IMT. A similar but less pronounced pattern emerged for ASD, where an increase of 1 SD in ICA wall thickness was related to a 35% increase in risk, whereas an increase of 1 SD in the CCA IMT represented a 17% increase in risk.

Two models predicting either the standardized (*z*) CCA or ICA IMT as outcome variables are shown in Table 4. Standardized is defined as (variablemean)/SD. The unadjusted and adjusted correlation coefficients for the independent variables, in this case the recognized risk factors for atherosclerosis, are given. The proportionate reduction in the total variability in the outcome variable accounted for by the variables in the model, adjusted for the number of variables in the model, is approximately 18% for CCA IMT and 17% for ICA IMT. Increasing age, male sex, history of hypertension, history of diabetes, and presence of any major ECG abnormality are associated with an increased IMT in the CCA and ICA. Two variables associated with smoking appear in the model. A history of smoking is associated with increased wall thickness in the CCA and ICA. The number of pack-years smoked by current smokers enters into the model predicting both ICA IMT and CCA wall thickness. In both models, high levels of HDL cholesterol are negatively associated with IMT, whereas high LDL cholesterol levels have a positive association. The role of blood pressure is clearly seen in both models: there is a positive correlation between IMT and a history of hypertension and systolic blood pressure, whereas there is a negative relationship with diastolic blood pressure. View this table:Table 4. Multiple Regression Analysis With Standardized CCA and ICA IMT as the Dependent[in this window]Variables

Canonical correlate analyses showed that the coefficients for the CCA (standardized) and ICA (standardized) were .591 and .613, respectively. This corresponds to an almost equal weighing of both measurements. For this first linear combination, 25% of the variability can be explained by a linear combination of the risk factors. For the second component, the coefficients were -.905 and .89, respectively. This corresponded roughly to the net difference between ICA and CCA (standardized) IMT measurements. The variability of this combined variable was only minimally explained by the atherosclerotic risk factors (R^2 =.008). We observed that the two canonical variates involving the two carotid wall-thickness measurements were almost equivalent to their sum and their difference. We therefore opted to replace the canonical variates by the sum and the difference of the ICA IMT and CCA IMT thicknesses and to carry out further analyses looking for the linear combinations of risk factors that could best predict these two variables.

The regression analyses in Table 5 examined the sum and the difference of the standardized CCA IMT and ICA IMT thicknesses as dependent variables. This is equivalent to the two canonical variates involving the two carotid measures. The regression gave the linear combination of risk factors that best predicted these two new variables. These results should be considered an approximation to the results found by the canonical correlation analysis. With the sum of the carotid measures as dependent variable, the magnitude of the standardized coefficients for each risk factor was similar to that observed when both carotid variables were treated separately. Again, 25% of the variability in this linear combination could be explained by these selected risk factors. The difference between standardized CCA IMT and ICA IMT measurements showed some positive relationship with a history of smoking and a mild negative relationship with systolic blood pressure.

View this table:Table 5. Multiple Regression Analysis With the Sum and Difference of the Standardized CCA and ICA IMT as the
Dependent Variables[in a new window]

Stroke

Discussion

The usefulness of different carotid artery sites as indexes of atherosclerosis for clinical trials and epidemiological studies has previously been studied by Howard et al⁴⁷ using data from the population-based ARIC study. Their approach was to look at the relations between IMT at different sites in the CCA, the bifurcation, and the ICA, presenting these as correlation coefficients and percentile regression techniques based on between 4034 and 9386 pairs of measurements. The variation in sample size depended on the paired sites, with far-wall CCA providing 9386 pairs and far-wall ICA, 4034 pairs. The

http://stroke.ahajournals.org/cgi/content/full/27/2/224 (7 of 28)7/10/2007 3:44:54 PM

correlation between right and left IMT at the same anatomic location in the carotid artery ranged from .34 to .49; the correlation at different anatomic locations on the same side ranged from .25 to .43. Their conclusion was that although increased carotid IMT at one site is positively associated with thickened walls at other carotid sites, the ability to accurately predict wall thickness at a site when given the wall thickness at other sites is modest. There are methodological differences between the two studies. ARIC deals with the carotid bulb and proximal ICA as separate segments, whereas CHS combines them into one segment. ARIC obtains one view of the bulb and one view of the proximal ICA; CHS obtains three views of the combined segments. ARIC looks at the far-wall IMT only; CHS averages the near- and far-wall IMT measurements. Our correlations are smaller than those reported from ARIC, ranging from .32 to .39 between right and left IMT at the same anatomic location in the carotid artery and from .17 to .25 at different anatomic locations on the same side. This is not



surprising, since CHS measured nearly everyone and ARIC did not make measurements in cases where interfaces were not clearly defined. The proportion of participants with visualized walls in ARIC was 79% for the CCA, 59% for the bifurcation, and 41% for the ICA. For CHS, the proportion of visualized walls was 99.8% for the CCA and 98.9% for the ICA, the latter segment defined to include the bifurcation and the initial 10 mm of the ICA distal to the tip of the flow divider. Also, CHS deals with an elderly population with much more focal disease, which undoubtedly reduces the correlations. Finally, CHS combines the bulb and ICA, which would also reduce the correlations. Nonetheless, results of the two studies are in general agreement.

Because our goal was to explore whether CCA IMT, ICA IMT, or the combination of both had a stronger association with atherosclerosis, we chose to explore this issue further by relating these three measures to clinically manifest CHD and ASD, as well as to recognized risk factors for atherosclerosis, in an elderly cohort. We observed that sonographic measurements of CCA IMT and ICA IMT are both related to CHD and ASD. Although both measurements can be used in models that predict prevalent CHD and ASD, an increase of the same relative magnitude in ICA IMT has more predictive value than a similar increase in the CCA IMT. In addition, although both variables are related to the traditional risk factors for ASD, they seem to relate more strongly to these factors when used in combination. One possible reason that the combined score using the average of the CCA IMT and ICA IMT is in large part the rationale for using the average of 12 measures of the ICA and four of the CCA.

The sonographic measurements reported in this study are compatible with CCA IMT measurements made in other studies.¹ ³ ⁵ ¹⁷ As previously observed, CCA IMT is larger in males than in females.⁴ ²⁵ It is also significantly greater in subjects with CHD than those without.⁴ ¹² We find that this pattern is maintained when a broader definition of ASD (one that includes CHD, cerebrovascular disease, and peripheral arterial disease) is used for stratifying subjects with and without disease. These relationships are also seen when measurements are made in the ICA. Our logistic regression analyses show that ICA IMT is more strongly related to the presence of prevalent CHD and existing ASD than is CCA IMT. The likelihood of prevalent CHD is estimated to increase by 36% for a 1-SD (0.69-mm) increase in the maximum ICA IMT, after adjustment for CCA IMT. For ASD, there is a 35% increased likelihood for existing disease for the same increase in wall thickness. These relationships are somewhat weaker for maximum CCA IMT, where after adjustment for ICA IMT a 1-SD (0.22-mm) increase is related to a 9% increase in risk for CHD and a 17% increase in risk for ASD.

Although CCA IMT measurements are more easily performed, ICA IMT measurements bear a stronger relation to prevalent disease, at least in the elderly. However, there are only slight differences in the associations seen between traditional risk factors for atherosclerosis and the two measurements of carotid wall thickness. Studies suggesting that it may be useful to use only CCA IMT measurements may have focused mainly on correlations with risk factors and may have been done without the benefit of sufficient wall-thickness measurements from the ICA.⁴⁸ ⁴⁹ The attraction of limiting wall-http://stroke.ahajournals.org/cgi/content/full/27/2/224 (8 of 28)7/10/2007 3:44:54 PM

thickness measurements to the distal CCA when using carotid IMT as a surrogate for atherosclerosis is clear. This segment of the artery has straight walls, is superficial, and usually lies parallel to the surface of the skin. It is easier to study, and the results are more reproducible than for the ICA. Studying and measuring the ICA is time consuming and requires more effort than studying the CCA. The ICA usually lies deeper in the neck, at its origin its walls are not parallel, and it does not lie parallel to the surface of the neck. Because focal plaques form in the proximal ICA, there is more anatomic variation in ICA IMT than CCA IMT. For all these reasons, measurement variability for the ICA is approximately three times greater than for the CCA.¹⁹

Our results indicate that maximum ICA IMT and maximum CCA IMT have very similar relations to established risk factors for ASD. In the univariate relations, increases in both wall-thickness variables are correlated to expected changes in risk factors. Thus, there are positive relationships with LDL cholesterol, blood pressure, smoking, and diabetes and negative relationships with HDL cholesterol and diastolic blood pressure. This last finding, the inverse relation of carotid IMT to diastolic blood pressure after adjustment for systolic blood pressure, has been previously reported by us.⁵⁰ We explained this finding as a reflection of decreased arterial compliance due to thickened walls, which resulted in increased pulse pressure. Diastolic blood pressure viewed alone has a positive relation to carotid IMT. If adjustment is made for systolic blood pressure, there is an inverse relation.

As much as 17% of the variability of IMT measurements in the CCA can be explained by changes in the risk factors. This also applies to ICA IMT measurements. The strength of these relationships is, however, tainted by a biological selection that might have eliminated those individuals who were severely afflicted by ASD. In our elderly population, these variables might have been indicators of morbidity, but the cross-sectional nature of our study does not permit us to verify this possibility. A longitudinal study may be more relevant, not only with respect to the predictive power of the carotid variables but also as to the impact of the risk factors. For example, a random sample of blood cholesterol might not have as specific a meaning for the development of atherosclerosis as prolonged exposure to cholesterol. The canonical correlate analysis suggests that both sonographic measurements combined together are more strongly related to established risk factors for ASD than either variable alone. This is confirmed by the regression analysis that we performed on the sum of the standardized CCA IMT and ICA IMT measurements. Changes in risk factors for ASD, instead of accounting for 17% of the variability as is the case for each separate wall-thickness measurement, account for 25% of the variability of the sum of both measurements, a relative increase of 50%.

The regression analyses in Table 5 examined the sum and the difference of the standardized CCA IMT and ICA IMT thicknesses as dependent variables. This is equivalent to the two canonical variates involving the two carotid measures. The regression gave the linear combination of risk factors that best predicted these two new variables. These results should be considered an approximation to the results found by the canonical correlation analysis. With the sum of the carotid measures as a dependent variable, the magnitude of the standardized coefficients for each risk factor was similar to that observed when both carotid variables were treated separately. Again, 25% of the variability in this linear combination could be explained by these selected risk factors. The difference between standardized CCA IMT and ICA IMT measurements showed some positive relation with a history of smoking and a mild negative relation with systolic blood pressure.

This latter finding raises an interesting possibility that was previously discussed in an article by Espeland et al,⁵¹ namely, that the difference in the two IMT measurements may be a measure of the variability of the IMT in a person, which in turn may be a measure of focal plaque. Although atherosclerosis is a generalized disease, focal plaques tend to be located at arterial bifurcations. Certain arteries, including the carotid, coronary, and iliofemoral arteries and the distal aorta, have a high incidence of plaque formation, while others, such as those in the upper extremities, are usually spared. Hemodynamic explanations for selective localization have included increased flow velocity and wall shear stress, reduced flow velocity and wall shear stress, flow

troke

separation, and oscillating shear stress. $30 \ 31 \ 32 \ 52 \ 53 \ 54$ Geometric configurations such as bifurcations, branch origins, and the inner curvature of bends seem particularly prone to local plaque formation. At the human carotid bifurcations, intimal thickening and plaque formation are most pronounced along the outer wall of the distal CCA in continuity with the proximal segment and sinus of the ICA. Plaques are usually thickest near the midpoint of the sinus opposite the flow divider. These focal lesions are more typically related to the risk of rupture as they increase in size. The diffuse thickening of the CCA may be a nonspecific aging response. As such, it is a confounder for focal lesions, since both will be more prevalent as aging takes place. A focal plaque in the proximal ICA is also likely to be the source of atheroembolic events, whereas the CCA wall is not likely to be the source of such events. The variable representing the difference between CCA IMT and ICA IMT does not appear to be related to age but is related to two well-recognized risk factors for clinical outcomes. The positive relationship with smoking is not unexpected if one considers smoking as a predictor for focal atherosclerotic lesions rather than as linked to a nonspecific response of the arterial wall. This reasoning does not appear to apply to the relationship with systolic blood pressure. This relationship is in the opposite direction than expected. It would suggest that CCA IMT relates more strongly to increases in blood pressures than do focal lesions in the ICA. Both these arguments are quantitatively supported by the relative β for both variables in Table 4. As noted, the effect of age and sex disappears.

In conclusion, we have found that in the elderly noninvasive sonographic measurements of carotid artery wall IMT can be used in models to predict the existence of clinically manifest CHD and ASD. In addition, it appears that a single measurement of wall thickness in the CCA has less predictive power for the presence of clinically manifest atherosclerosis than a measurement made in the ICA. Both variables, when used in combination, relate more strongly to established cardiovascular risk factors than either taken alone and seem to behave as a measure of ASD.

Selected Abbreviations and Acronyms

- ARIC = Atherosclerosis Risk in Communities
- ASD = atherosclerotic disease
- CCA = common carotid artery
- CHD = coronary heart disease
- CHS = Cardiovascular Health Study
- ECG = electrocardiography
- HDL = high-density lipoprotein
- ICA = internal carotid artery
- IMT = intima-media thickness
- LDL = low-density lipoprotein



View this table:Table 3. Stepwise Logistic Regression Models for Predicting the Presence of Atherosclerotic[in this window]Disease1

Acknowledgments

This study was supported in part by contracts NO1-HC85079 through NO1-HC85086 from the National Heart, Lung, and Blood Institute.

Footnotes

Reprint requests to Richard A. Kronmal, PhD, CHS Coordinating Center, Century Sq, 1501 4th Ave, Suite 2025, Seattle, WA 98101.

Received June 28, 1995; revision received October 11, 1995; accepted October 11, 1995.

References

- 1. Salonen R, Seppanen K, Rauramaa R, Salonen JT. Prevalence of carotid atherosclerosis and serum cholesterol levels in eastern Finland. *Arteriosclerosis*. 1988;8:788-792. [Abstract]
- 2. Gostomzyk JG, Heller WD, Gerhardt P, Lee PN, Keil U. B-scan ultrasound examination of the carotid arteries within a representative population (MONICA Project Ausburg). *Klin Wochenschr.* 1988;66(suppl 11):58-65.
- 3. Heiss G, Sharrett AR, Barnes R, Chambless LE, Szklo M, Alzola C, for the ARIC Investigators. Carotid atherosclerosis measured by B-mode ultrasound in populations: associations with cardiovascular risk factors in the

Str

ARIC study. Am J Epidemiol.. 1991;134:250-256. [Abstract/Free Full Text]

- 4. O'Leary DH, Polak JF, Kronmal RA, Kittner SJ, Bond MG, Wolfson SK, Bommer W, Price TR, Gardin JM, Savage PJ. Distribution and correlates of sonographically detected carotid artery disease in the Cardiovascular Health Study. *Stroke.*. 1992;23:1752-1760. [Abstract]
- Bots ML, Breslau PJ, Briet E, de Bruyn AM, van Vliet HHDM, van den Ouweland FA, de Jong PTVM, Hofman A, Grobbee DE. Cardiovascular determinants of carotid artery disease: the Rotterdam Elderly Study. *Hypertension*.. 1992;19:717-720. [Abstract]
- 6. Prati P, Vanuzzo D, Casaroli M, Di Chiara A, De Biasi F, Feruglio GA, Touboul P-J. Prevalence and determinants of carotid atherosclerosis in a general population. *Stroke.*. 1992;23:1705-1711. [Abstract]
- 7. Young W, Gofman JW, Tandy R, Malamud N, Waters ESG. The quantification of atherosclerosis, III: the extent of correlation of degrees of atherosclerosis within and between the coronary and cerebral vascular beds. *Am J Cardiol.*, 1960;6:300-308.
- 8. Mathur KS, Kashyap SK, Kumar V. Correlation of the extent and severity of atherosclerosis in the coronary and cerebral arteries. *Circulation*. 1963;27:929-934. [Medline] [Order article via Infotrieve]
- 9. Solberg LA, McGarry P, Moossy J, Strong JP, Tejada C, Loken AC. Severity of atherosclerosis in cerebral arteries, coronary arteries, and aortas. *Ann N Y Acad Sci.* 1968;149:956-973. [Medline] [Order article via Infotrieve]
- 10. Hertzer NR, Young JR, Beven EG, Graor RA, O'Hara PJ, Ruschhaupt WF, deWolfe VB, Maljovec LC. Coronary angiography in 506 patients with extracranial cerebrovascular disease. *Arch Intern Med.*. 1985;145:849-852. [Abstract]
- 11. Chimowitz MI, Lafranchise EF, Furlan AJ, Dorosti K, Paranandi L, Beck GJ. Evaluation of coexistent carotid and coronary disease in combined angiography. *J Stroke Cerebrovasc Dis.*. 1991;1:89-93.
- 12. Salonen JT, Salonen R. Ultrasonographically assessed carotid morphology and the risk of coronary heart disease. *Arterioscler Thromb.*. 1991;11:1245-1249. [Abstract]
- 13. Mautner GC, Mautner SL, Roberts WC. Amounts of coronary arterial narrowing by atherosclerotic plaque at necropsy in patients with lower extremity amputation. *Am J Cardiol.* 1992;70:1147-1151. [Medline] [Order article via Infotrieve]
- Craven TE, Ryu JE, Espeland MA, Kahl FR, McKinney WM, Toole JF, McMahan MR, Thompson CJ, Heiss G, Crouse JR. Evaluation of the associations between carotid artery atherosclerosis and coronary artery stenosis: a case-control study. *Circulation*. 1990;82:1230-1242. [Medline]
 [Order article via Infotrieve]
- 15. Crouse JR. B-mode ultrasound in clinical trials. Circulation. 1993;88:319-320. Editorial. [Medline] [Order article via Infotrieve]
- 16. Pignoli P, Tremoli E, Poli A, Oreste P, Paoletti R. Intimal plus medial thickness of the arterial wall: a direct measurement with ultrasound imaging. *Circulation*. 1986;74:1399-1406. [Medline] [Order article via Infotrieve]
- 17. Poli A, Tremoli E, Colombo A, Sirtori M, Pignoli P, Paoletti R. Ultrasonographic measurement of the common carotid arterial wall thickness in hypercholesterolemic patients. *Atherosclerosis.* 1988;70:253-261. [Medline] [Order article via Infotrieve]
- 18. Salonen JT, Salonen R. Association of serum low density lipoprotein cholesterol, smoking and hypertension with different manifestations of atherosclerosis. *Int J Epidemiol.* 1990;19:911-917. [Abstract/Free Full Text]
- 19. O'Leary DH, Polak JF, Wolfson SK, Bond MG, Bommer W, Sheth S, Psaty BM, Sharrett AR, Manolio TA. Use of sonography to evaluate carotid atherosclerosis in the elderly: the Cardiovascular Health Study. *Stroke.*. 1991;22:1155-1163. [Abstract]
- 20. Bonithon-Kopp C, Scarabin P-Y, Taquet A, Touboul P-J, Malmejac A, Guize L. Risk factors for early carotid atherosclerosis in middle-aged French women. *Arterioscler Thromb.*. 1991;11:966-972. [Abstract]
- 21. Mack WJ, Selzer RH, Hodis HN, Erikson JK, Liu CR, Liu CH, Crawford DW, Blankenhorn DH. One-year reduction and longitudinal analysis of carotid intima-media thickness associated with colestipol/niacin therapy. *Stroke*. 1993;24:1779-1783. [Abstract]



Stroke



- 22. Blankenhorn DH, Seltzer RH, Crawford DW, Barth JD, Liu CR, Liu CH, Mack WJ, Alaupovic P. Beneficial effects of colestipol-niacin therapy on carotid atherosclerosis: two- and four-year reduction of intima-media thickness measured by ultrasound. *Circulation*. 1993;88:20-28. [Medline] [Order article via Infotrieve]
- 23. Bots ML, Hofman A, Grobbee DE. Common carotid intima-media thickness and lower extremity arterial atherosclerosis. *Arterioscler Thromb.*. 1994;14:1885-1891. [Abstract]
- 24. Solberg LA, Eggen DA. Localization and sequence of development of atherosclerotic lesions in the carotid and vertebral arteries. *Circulation*. 1971;43:711-724. [Medline] [Order article via Infotrieve]
- 25. Howard G, Sharrett AR, Heiss G, Evans GW, Chambless LE, Riley WA, Burke GL, for the ARIC Investigators. Carotid artery intimal-medial thickness: distribution in general populations as evaluated by B-mode ultrasound. *Stroke.*. 1993;24:1297-1304. [Abstract]
- 26. Imparato AM, Riles TS, Gorstein F. The carotid bifurcation plaque: pathologic findings associated with cerebral ischemia. *Stroke.*. 1979;10:238-245. [Abstract]
- 27. Lusby RJ, Ferrell LD, Ehrenfeld WK, Stoney RJ, Wylie EJ. Carotid plaque hemorrhage: its role in production of cerebral ischemia. *Arch Surg.*. 1982;117:1479-1488. [Abstract]
- 28. O'Donnell TF Jr, Erdoes L, Mackey WC, McCullough J, Shepard A, Heggerick P, Isner J, Callow AD. Correlation of B-mode ultrasound imaging and arteriography with pathologic findings at carotid endarterectomy. *Arch Surg.*. 1985;120:443-449. [Abstract]
- 29. Bassiouny HS, Davis H, Massawa N, Gewertz BL, Glagov S, Zarins CK. Critical carotid stenoses: morphological and chemical similiarity between symptomatic and asymptomatic plaques. *J Vasc Surg.*. 1989;9:202-212. [Medline] [Order article via Infotrieve]
- 30. Zarins CK, Giddens DP, Bharadvaj BK, Sottiurai VS, Mabon RF, Glagov S. Carotid bifurcation atherosclerosis: quantitative correlation of plaque localization with flow velocity profiles and wall shear stress. *Circ Res.* 1983;53:502-514. [Abstract]
- 31. Friedman MH, Deters OJ, Bargeron CB, Hutchins GM, Mark FF. Shear-dependent thickening of the human arterial intima. *Atherosclerosis*.. 1986;60:161-171. [Medline] [Order article via Infotrieve]
- 32. Ross R. The pathogenesis of atherosclerosis: an update. N Engl J Med.. 1986;314:488-500. [Medline] [Order article via Infotrieve]
- 33. Glagov S, Zarins C, Giddens DP, Ku DN. Hemodynamics and atherosclerosis. *Arch Pathol Lab Med.*. 1988;112:1018-1031. [Medline] [Order article via Infotrieve]
- 34. Crouse JR, Goldbourt U, Evans G, Pinsky J, Sharrett AR, Sorlie P, Riley W, Heiss G, for the ARIC Investigators. Arterial enlargement in the Atherosclerosis Risk in Communities (ARIC) cohort: in vivo quantification of carotid arterial enlargement. *Stroke.* 1994;25:1354-1359. [Abstract]
- 35. Fried LP, Borhani NO, Enright P, Furberg CD, Gardin JM, Kronmal RA, Kuller LH, Manolio TA, Mittelmark MB, Newman A, O'Leary DH, Psaty B, Rautaharju P, Tracy RP, Weiler PG, for the CHS Collaborative Research Group. The Cardiovascular Health Study: design and rationale. *Ann Epidemiol.* 1991;1:263-276. [Medline] [Order article via Infotrieve]
- 36. Tell GS, Fried LP, Hermanson BH, Manolio TA, Newman AB, Borhani NO. Recruitment of adults 65 years and older as participants in the Cardiovascular Health Study. *Ann Epidemiol.* 1993;3:358-366. [Medline] [Order article via Infotrieve]
- Mittelmark MB, Psaty BM, Rautaharju PM, Fried LP, Borhani NO, Tracy R, Gardin JM, O'Leary DH, for the Cardiovascular Health Study Collaborative Group. Prevalence of cardiovascular disease among older adults: the Cardiovascular Health Study. *Am J Epidemiol.* 1993;137:311-317. [Abstract/Free Full Text]
- 38. Gardin JM, Wong ND, Bommer W, Kloptenstein HS, Smith VE, Tabatzbik B, Siscovick D, Lobodzinski S, Anton-Culver H, Manolio TA. Echocardiographic design of a multicenter investigation of free-living elderly subjects: the Cardiovascular Health Study. *Am Soc Echocardiogr.* 1952;5:63-72.
- 39. Herbert V, Lau KS, Gottlieb CW. Coated charcoal immunoassay of insulin. J Clin Endocrinol.. 1965;25:1375-1384. [Medline] [Order article via]

Stroke

Infotrieve]

Stroke

- 40. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972;18:499-501. [Abstract]
- 41. von Claus A. Gerinnungsphysiologische Schnellmethode zur Besttimmung des Fibrinogens. Acta Haematol.. 1957;17:237-246. [Medline] [Order article via Infotrieve]
- 42. National Diabetes Data Group. Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. *Diabetes*.. 1979;28:1039-1057. [Medline] [Order article via Infotrieve]
- 43. Furberg CD, Manolio TA, Psaty BM, Bild DE, Borhani NO, Newman A, Tabatznik B, Rautaharju PM, for the Cardiovascular Health Study Collaborative Group. Major electrocardiographic abnormalities in persons aged 65 years and older: the Cardiovascular Health Study. *Am J Cardiol.*. 1992;69:1329-1335. [Medline] [Order article via Infotrieve]
- 44. Newman AB, Sutton-Tyrrell K, Vogt MT, Kuller LH. Morbidity and mortality in hypertensive adults with a low ankle/arm blood pressure index. *JAMA*. 1993;270:487-489. [Abstract]
- 45. SAS Institute Inc. SAS User's Guide: Basics, Version 6 edition. Cary, NC: SAS Institute Inc; 1990.
- 46. Finn JO. A General Model for Multivariate Analysis. New York, NY: Holt Rinehart and Winston Inc; 1974.
- 47. Howard G, Burke GL, Evans GW, Crouse JR, Riley W, Arnett D, de Lacy R, Heiss G, for the ARIC Investigators. Relations of intimal-medial thickness among sites within the carotid artery as evaluated by B-mode ultrasound. *Stroke*. 1994;25:1581-1587. [Abstract]
- 48. Salonen R, Salonen JT. Determinants of carotid intima-media thickness: a population-based ultrasonography study in eastern Finnish men. J Intern Med.. 1991;229:225-231. [Medline] [Order article via Infotrieve]
- 49. Bonithon-Kopp C, Jouven X, Taquet A, Touboul P-J, Guize L, Scarabin P-Y. Early carotid atherosclerosis in healthy middle-aged women: a follow-up study. *Stroke*. 1993;24:1837-1843. [Abstract]
- 50. Psaty BM, Furberg CD, Kuller LH, Borhani NO, Rautaharju PM, O'Leary DH, Bild DE, Robbins J, Fried C. Assessing the use of medications in the elderly: methods and initial results in the Cardiovascular Health Study. *J Clin Epidemiol*. 1992;45:683-692. [Medline] [Order article via Infotrieve]
- 51. Espeland MA, Hoen H, Byington R, Howard G, Riley WA, Furberg CD. Spatial distribution of carotid intimal-medial thickness as measured by B-mode ultrasonography. *Stroke*. 1994;25:1812-1819. [Abstract]
- 52. Glagov S, Zarins C, Giddens DP, Ku DN. Hemodynamics and atherosclerosis. Arch Pathol Lab Med. 1988;112:1018-1031.
- 53. Ku DN, Giddens DP, Zarins CK, Glagov S. Pulsatile flow and atherosclerosis in the human carotid bifurcation. *Arteriosclerosis*. 1985;5:293-302. [Abstract]
- 54. LoGerfo FW, Nowak MD, Quist WC. Structural details of boundary layer separation in a model human carotid bifurcation under steady and pulsatile flow conditions. *J Vasc Surg.* 1985;2:263-269.[Medline] [Order article via Infotrieve]

This article has been cited by other articles: (Search Google Scholar for Other Citing Articles)



Rohan, A. R. Cappola, X. Xue, and B. M. Psaty Association of Total Insulin-Like Growth Factor-I, Insulin-Like Growth Factor Binding Protein-1 (IGFBP-1), and IGFBP-3 Levels with Incident Coronary Events and Ischemic Stroke J. Clin. Endocrinol. Metab., April 1, 2007; 92(4): 1319 - 1325. [Abstract] [Full Text] [PDF]



Circulation

HOME

C. Napoli, L. O. Lerman, F. de Nigris, M. Gossl, M. L. Balestrieri, and A. Lerman **Rethinking Primary Prevention of Atherosclerosis-Related Diseases** Circulation, December 5, 2006; 114(23): 2517 - 2527. [Full Text] [PDF]

diabetes diabetes

HOME



P. A. Cleary, T. J. Orchard, S. Genuth, N. D. Wong, R. Detrano, J.-Y. C. Backlund, B. Zinman, A. Jacobson, W. Sun, J. M. Lachin, D. M. Nathan, and for the DCCT/EDIC Research Group The Effect of Intensive Glycemic Treatment on Coronary Artery

Calcification in Type 1 Diabetic Participants of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) Study Diabetes, December 1, 2006; 55(12): 3556 - 3565.

[Abstract] [Full Text] [PDF]



Arterioscler. Thromb. Vasc. Biol., October 1, 2004; 24(10): 1951 - 1956. [Abstract] [Full Text] [PDF]

Stroke

	Stroke SH. H. Juo, HF. Lin, T. Rundek, E. A. Sabala, B. Boden-Albala, N. MY. Lan, and R. L. Sacco Genetic and Environmental Contributions to Carotid Intima-Me Thickness and Obesity Phenotypes in the Northern Manhattan Family Study Stroke, October 1, 2004; 35(10): 2243 - 2247. [Abstract] [Full Text] [PDF]	▶ HOME Park, ≥dia
oke	Neurology M. Diomedi, A. Pietroiusti, M. Silvestrini, B. Rizzato, L. M. Cupini, F. Ferrante, A. Magrini, A. Bergamaschi, A. Galante, and G. Bernardi CagA-positive Helicobacter pylori strains may influence the na history of atherosclerotic stroke Neurology, September 14, 2004; 63(5): 800 - 804. [Abstract] [Full Text] [PDF]	▶номе itural
Str	Image: Second state of the second s	▶ НОМЕ 1577.
IATION	Circulation G. B. J. Mancini, B. Dahlof, and J. Diez Surrogate Markers for Cardiovascular Disease: Structural Mark Circulation, June 29, 2004; 109(25_suppl_1): IV-22 - IV-30. [Full Text] [PDF]	HOME
AMERICAN HEART ASSOC	Arteriosclerosis, Thrombosis, and Vascular Biology M. Zureik, S. Kony, C. Neukirch, D. Courbon, B. Leynaert, D. Vervloe Ducimetiere, and F. Neukirch Bronchial Hyperresponsiveness to Methacholine Is Associated Increased Common Carotid Intima-Media Thickness in Men Arterioscler. Thromb. Vasc. Biol., June 1, 2004; 24(6): 1098 - 1103. [Abstract] [Full Text]	HOME t, P. With



http://stroke.ahajournals.org/cgi/content/full/27/2/224 (18 of 28)7/10/2007 3:44:54 PM



http://stroke.ahajournals.org/cgi/content/full/27/2/224 (19 of 28)7/10/2007 3:44:54 PM



[Abstract] [Full Text] [PDF]



Arteriosclerosis, Thrombosis, and Vascular Biology

Arteriosclerosis, Thrombosis, and Vascular Biology

T. J. Wang, B.-H. Nam, P. W.F. Wilson, P. A. Wolf, D. Levy, J. F. Polak, R. B. D'Agostino, and C. J. O'Donnell

HOME

HOME

Association of C-Reactive Protein With Carotid Atherosclerosis in Men and Women: The Framingham Heart Study

Arterioscler. Thromb. Vasc. Biol., October 1, 2002; 22(10): 1662 - 1667. [Abstract] [Full Text] [PDF]



A. B. Newman, B. L. Naydeck, K. Sutton-Tyrrell, D. Edmundowicz, D. O'Leary, R. Kronmal, G. L. Burke, and L. H. Kuller **Relationship Between Coronary Artery Calcification and Other Measures of Subclinical Cardiovascular Disease in Older Adults** Arterioscler. Thromb. Vasc. Biol., October 1, 2002; 22(10): 1674 - 1679. [Abstract] [Full Text] [PDF]

Stroke

http://stroke.ahajournals.org/cgi/content/full/27/2/224 (20 of 28)7/10/2007 3:44:54 PM





Stroke B. Lernfelt, M. Forsberg, C. Blomstrand, D. Mellstrom, and R. Volkmann Cerebral Atherosclerosis as Predictor of Stroke and Mortality in Representative Elderly Population Stroke, January 1, 2002; 33(1): 224 - 229. [Abstract] [Full Text] [PDF]



Stroke

Circulation

►HOME

HOME

P. H. Davis, J. D. Dawson, W. A. Riley, and R. M. Lauer Carotid Intimal-Medial Thickness Is Related to Cardiovascular Risk Factors Measured From Childhood Through Middle Age: The Muscatine Study Circulation, December 4, 2001; 104(23): 2815 - 2819. [Abstract] [Full Text] [PDF] **OBESITY RESEARCH**



 Stroke
 ►номе

 T.-C. Su, J.-S. Jeng, K.-L. Chien, F.-C. Sung, H.-C. Hsu, and Y.-T. Lee

 Hypertension Status Is the Major Determinant of Carotid

 Atherosclerosis: A Community-Based Study in Taiwan

 Stroke, October 1, 2001; 32(10): 2265 - 2271.

 [Abstract] [Full Text] [PDF]

►HOME

HOME

A. Mavri, M. Stegnar, J. T. Sentocnik, and V. Videcnik
 Impact of Weight Reduction on Early Carotid Atherosclerosis in
 Obese Premenopausal Women
 Obesity, September 1, 2001; 9(9): 511 - 516.
 [Abstract] [Full Text] [PDF]



Stroke

Y. Nagai, K. Kitagawa, M. Sakaguchi, Y. Shimizu, H. Hashimoto, H. Yamagami, M. Narita, T. Ohtsuki, M. Hori, and M. Matsumoto **Significance of Earlier Carotid Atherosclerosis for Stroke Subtypes** Stroke, August 1, 2001; 32(8): 1780 - 1785. [Abstract] [Full Text] [PDF]



Stroke A. I. del Sol, K. G.M. Moons, M. Hollander, A. Hofman, P. J. Koudstaal, D. E. Grobbee, M. M.B. Breteler, J. C.M. Witteman, and M. L. Bots Is Carotid Intima-Media Thickness Useful in Cardiovascular Disease Risk Assessment? : The Rotterdam Study Stroke, July 1, 2001; 32(7): 1532 - 1538. [Abstract] [Full Text] [PDF]

troke



•

Berr, and C. Magne **Common Carotid Intima-Media Thickness Predicts Occurrence of Carotid Atherosclerotic Plaques : Longitudinal Results From the** Aging Vascular Study (EVA) Study Arterioscler. Thromb. Vasc. Biol., June 1, 2000; 20(6): 1622 - 1629. [Abstract] [Full Text] [PDF]



Circulation, August 24, 1999; 100(8): 838 - 842. [Abstract] [Full Text] [PDF]

http://stroke.ahajournals.org/cgi/content/full/27/2/224 (24 of 28)7/10/2007 3:44:54 PM



Arteriosclerosis, Thrombosis, and Vascular Biology

C. Thalhammer, B. Balzuweit, A. Busjahn, C. Walter, F. C. Luft, and H.

Endothelial Cell Dysfunction and Arterial Wall Hypertrophy Are Associated With Disturbed Carbohydrate Metabolism in Patients at Risk for Cardiovascular Disease

Arterioscler. Thromb. Vasc. Biol., May 1, 1999; 19(5): 1173 - 1179. [Abstract] [Full Text] [PDF]



S. Ebrahim, O. Papacosta, P. Whincup, G. Wannamethee, M. Walker, A. N. Nicolaides, S. Dhanjil, M. Griffin, G. Belcaro, A. Rumley, and G. D.O. Lowe Carotid Plaque, Intima Media Thickness, Cardiovascular Risk Factors, and Prevalent Cardiovascular Disease in Men and Women : The British Regional Heart Study Stroke, April 1, 1999; 30(4): 841 - 850. [Abstract] [Full Text] [PDF]



Stroke

►HOME

HOME

R. A. Bhadelia, M. Anderson, J. F. Polak, T. A. Manolio, N. Beauchamp, L. Knepper, and D. H. O'Leary **Prevalence and Associations of MRI-Demonstrated Brain Infarcts in Elderly Subjects With a History of Transient Ischemic Attack : The Cardiovascular Health Study**

Stroke, February 1, 1999; 30(2): 383 - 388. [Abstract] [Full Text] [PDF]



9

The NEW ENGLAND JOURNAL of MEDICINE

HOME

D. H. O'Leary, J. F. Polak, R. A. Kronmal, T. A. Manolio, G. L. Burke, S. K. Wolfson, and The Cardiovascular Health Study Collaborative Rese **Carotid-Artery Intima and Media Thickness as a Risk Factor for Myocardial Infarction and Stroke in Older Adults** N. Engl. J. Med., January 7, 1999; 340(1): 14 - 22. [Abstract] [Full Text] [PDF]





Strok

Stroke **HOME** R. L. Sacco, J. K. Roberts, B. Boden-Albala, Q. Gu, I-F. Lin, D. E. Kargman, L. Berglund, W. A. Hauser, S. Shea, and M. C. Paik Race-Ethnicity and Determinants of Carotid Atherosclerosis in a Multiethnic Population : The Northern Manhattan Stroke Study Stroke, May 1, 1997; 28(5): 929 - 935. [Abstract] [Full Text]

http://stroke.ahajournals.org/cgi/content/full/27/2/224 (26 of 28)7/10/2007 3:44:54 PM





HOME



J. F. Polak, R. A. Kronmal, G. S. Tell, D. H. O'Leary, P. J. Savage, J. M. Gardin, G. H. Rutan, and N. O. Borhani Compensatory Increase in Common Carotid Artery Diameter: Relation to Blood Pressure and Artery Intima-Media Thickness in Older Adults

Stroke, November 1, 1996; 27(11): 2012 - 2015. [Abstract] [Full Text]



R. B. D'Agostino, G. Burke, D. O'Leary, M. Rewers, J. Selby, P. J. Savage, M. F. Saad, R. N. Bergman, G. Howard, L. Wagenknecht, and S. M. Haffner Ethnic Differences in Carotid Wall Thickness: The Insulin Resistance Atherosclerosis Study Stroke, October 1, 1996; 27(10): 1744 - 1749. [Abstract] [Full Text]

This Article

Abstract FREE

- Alert me when this article is cited
- Alert me if a correction is posted
- Citation Map

Services

- Email this article to a friend
- Similar articles in this journal
- Similar articles in PubMed
- Alert me to new issues of the journal
- Download to citation manager

Stroke

Request Permissions

Google Scholar

- Articles by O'Leary, D. H.
- Articles by Furberg, C. D.
- Articles citing this Article
- Search for Related Content

PubMed

- PubMed Citation
- Articles by O'Leary, D. H.
- Articles by Furberg, C. D.

STROKE

Stroke