Differential Effects of Body Adiposity and Serum Lipids on Right and Left Carotid Artery Lesions

To the Editor:

I read with interest the article by De Michele et al in the December issue of Stroke. The authors acknowledged that the association between obesity and atherosclerotic disease is controversial. However, their study demonstrated a graded and independent association between general and abdominal obesity reflected by high body mass index (BMI) and waist-hip ratio (WHR) and carotid artery wall thickening in a population of middle-aged women.

A review of their results in the light of ongoing work in our laboratory revealed a rather complex interaction of carotid plaque, body adiposity, and serum lipoprotein levels. Ninety consecutive patients aged 56.2±14 years (60 male and 30 female) were studied. All were right-handed. Color-flow Doppler and B-mode ultrasound of the carotid were performed to determine the percentage stenosis in the internal carotid artery. BMI was calculated as weight divided by height squared (kg/m²); WHR was calculated as waist divided by hip.

Lipid profile was determined using the enzymatic method. Analysis of 3D surface plots of data obtained from results of piecewise linear regression (using ICA percentage stenosis as dependent variable, independent variables were in one analysis BMI and WHR, and in another LDL and HDL) with breakpoint set at 70% stenosis. All analysis was performed with statistical software package (Statistica for Macintosh, StatSoft, Tulsa, Okla).

Mild to moderate RICA (<70%) stenosis correlated positively with BMI (P=0.000001) and negatively with WHR (P=0.00006) (see Figure 1A), severe RICA (>70%) stenosis correlated positively with both BMI (P=0.0016) and WHR (P=0.0002); R=0.82, accounting for variance in 67% of all cases. Mild to moderate LICA (<70%) stenosis did not with BMI (P>0.05), but correlated positively with WHR (P=0.0009), (see Figure 1B), severe LICA (>70%) stenosis correlated positively with both BMI (P=0.000001) and WHR (P=0.01); R=0.79, and accounting for variance in 62% of cases.

Mild to moderate percentage RICA stenosis correlated positively with LDL levels (P=0.0001) and negatively with HDL levels (P<0.0001), severe LICA (>70%) stenosis correlated negatively with LDL (P<0.00001); R=0.81, and accounting for 65% of cases (Figure 1C). Conversely, mild to moderate LICA (<70%) stenosis correlated positively with both LDL levels (P<0.000001) and HDL levels (P<0.000001) (Figure 1D); severe LICA (>70%) stenosis correlated negatively with LDL (P=0.00045), but not with HDL (P>0.05); R=0.8, and accounting for variance in 65% of cases.

The results suggest that general body adiposity (high BMI) influences accumulation of plaque in the RICA at all levels of severity, but only accentuated an already severe plaque in the LICA associated with abdominal adiposity. Conversely, abdominal body adiposity (high WHR) facilitates accumulation of plaque in the LICA but accentuated an already severe plaque in the RICA due to general body adiposity. LDL levels facilitate the formation of carotid plaques in both RICA and LICA. Conversely, HDL reduces the formation of carotid artery plaque only in the RICA but accentuated LICA plaque formation.

The reason for these complex interactions is not known and could only be open to different interpretations at this time. One likely factor is that of anatomic asymmetry of both carotid systems. The left common carotid artery (CCA) takes its origin directly from the aortic arch, while the right CCA branches off from the brachiocephalic artery (BCA). There may be indications that LICA plaque formation is related to atheromatous process in the trunk and lower part of the body and the mechanisms of plaque formation differ from right. These mechanisms may involve active transport rather than the biochemical regulations implicated in right plaque formation. For example, the fact the HDL levels did not reduce LICA plaque but rather increased with plaque size may indicate that HDL cholesterol was actively incorporated in left plaque formation. This could only be possible if there was active transport to the site of lesion bypassing the regulatory mechanisms. What plausible mechanisms could be involved in plaque propagation from the lower part of the body into the left carotid system but not the right? The anatomic location of the left CCA at a critical point in the aortic arch curvature with a unique flow geometry involving helical flow pattern, bound-
ary conditions, secondary flow, and reflections from aorto-iliac bifurcation might serve as a clue. The plausible rise in blood column of low-specific-gravity fatty globules from areas of the abdominal aorta into the aortic arch outer curvature and propagation into left CCA due to secondary flow phenomenon are all clues that require further investigation. Another important issue raised by these findings is whether 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors, which lower lipid levels, will have a considerable impact on LICA plaque size as would be expected for RICA, considering a plausible difference in mechanisms of formation. Elucidation of these issues could have far-reaching pharmacological and clinical implications for stroke prevention.

Philip Njemanze, MD
Chadicon Medical Center
International Institutes of Advanced Research and Training
Owerri, Nigeria


Response

We appreciate Dr Njemanze’s comment on our article evaluating the relationship between intima-media thickness of the common carotid arteries, as assessed by high resolution B-mode ultrasound, and estimates of adiposity in middle-aged women. In that patient series, the author found side-related differences in the relationship between severity of carotid atherosclerosis, as evaluated by color-flow Doppler and B-mode imaging, and cardiovascular risk factors, including body mass index and waist-to-hip ratio (an estimate of abdominal adiposity). A previous report shows side-related differences in intima-media thickness of carotid arteries, as assessed by high-resolution B-mode ultrasound, and estimates of adiposity in middle-aged women. In that patient series, the author found side-related differences in the relationship between severity of carotid atherosclerosis, as evaluated by high-resolution B-mode ultrasound, and estimates of adiposity in middle-aged women. In that patient series, the author found side-related differences in the relationship between severity of carotid atherosclerosis, as evaluated by high-resolution B-mode ultrasound, and estimates of adiposity in middle-aged women.

In conclusion, the 2 surveys are quite different studies of different cohort, patients with overt cardiovascular disease in most cases (61%) in the other study. A third reason is the different methodology and site of examination. We measured intima-media thickness of the common carotid artery by quantitative B-mode imaging; Dr Njemanze used an estimate of percentage lumen stenosis of the internal carotid artery. We have demonstrated significant differences in the risk factors pattern between different, even contiguous, sites in the extracranial carotid arteries. A final reason was the difference in the statistical analyses that we applied on the whole cohort, whereas our colleagues from Nigeria focused on patient subgroups with different severity of carotid stenosis.

In conclusion, the 2 surveys are quite different studies of different statistical power, but both indicate a relevant role of increased adiposity in relation to the presence and severity of carotid atherosclerosis.

Paolo Rubba, MD
Mario De Michele, MD
Department of Clinical and Experimental Medicine
Federico II University
Naples, Italy

Differential Effects of Body Adiposity and Serum Lipids on Right and Left Carotid Artery Lesions
Philip Njemanze

Stroke. 2003;34:e185-e186; originally published online September 18, 2003;
doi: 10.1161/01.STR.0000094662.73951.3B
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 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/34/10/e185

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/