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.

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 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 plaque only in the RICA but accentuated LICA plaque formation.

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.
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.

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**Response**

We appreciate Dr Njemane’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 in primary hypertensive patients.

To evaluate the possibility of side-related influences on the relationship between overweight or obesity and carotid intima-media thickness, we performed a separate analysis for the right and left common carotid artery in our cohort of free-living middle-aged women. No side-related differences were detected in the mean values of common carotid intima-media thickness (right common carotid artery, 0.98±0.01; left common carotid artery, 0.97±0.01 [mean±SE]). The results of further multivariate regression analyses are reported in the Table. The multivariate analyses evaluating intima-media thickness in relation to estimates of adiposity and taking into account the influence of age, blood pressure, and traditional risk factors (cigarette smoking, serum cholesterol) demonstrated almost the same results for both sides. There are reasons for the different outcome of our study as evaluated comparatively with that of Dr Njemane. One reason is the different number and sex distribution of the individuals who underwent ultrasound examination (310 women in our study, 60 men and 30 women in Dr Njemane’s series). A second reason was the different clinical condition: healthy women in our population-based 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 Njemane 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.

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**Table 1: Relationship Between Estimates of Adiposity and Right and Left Common Carotid Intima-Media Thickness as Determined by Multiple Regression Analyses**

<table>
<thead>
<tr>
<th>Model</th>
<th>RCXA-IMT</th>
<th>LCA-IMT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>0.008 (0.001)</td>
<td>0.0001 (0.001)</td>
</tr>
<tr>
<td>Systolic BP, mm Hg</td>
<td>0.001 (0.001)</td>
<td>0.017 (0.0001)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>0.007 (0.002)</td>
<td>0.003 (0.002)</td>
</tr>
<tr>
<td>WHR</td>
<td>0.46 (0.16)</td>
<td>0.005 (0.16)</td>
</tr>
</tbody>
</table>

The following variables did not enter the regression models: LDL cholesterol, triglycerides, diastolic blood pressure, cigarette smoking, and insulin. β (SE) indicates regression coefficient (standard error), R², the coefficient of determination, represents the percentage of the variation in the dependent variable explained by the independent variables in the model.
Differential Effects of Body Adiposity and Serum Lipids on Right and Left Carotid Artery Lesions
Philip Njemanze

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