Letters to the Editor

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The Relationship Between Leptin:Adiponectin Ratio and Carotid Intima-Media Thickness in Asymptomatic Females

To the Editor:

A leptin-to-adiponectin ratio (L:A) is a new index to assess atherogenesis in diabetic patients. More recently, Norata et al have reported that L:A shows a powerful correlation to intima-media thickness (IMT) of the common carotid artery (CCA) in healthy males. This expands the possibilities of the applications of L:A in clinical practice not only for diabetics but also healthy subjects. However, to establish the applications of L:A, further studies on various healthy populations are needed, as the Norata study was for males only and on a wide range of age (we found that a clinical significance of L:A could be modified with age). Thus, the present report adds to the results on an association of L:A with CCA-IMT in healthy females, with a restriction to older age.

We studied 129 asymptomatic Japanese postmenopausal females (mean age 73 ± 8 [SD]; range 55 to 89 years, mean body mass index 22 ± 3; range 16 to 29 kg/m²) not medicated, not currently smoking, and having no history of thyroid, liver, kidney, or cardiovascular diseases (relatively similar criteria to the Norata study). The following untreated subjects were included: mild hypertension (<160/90 mm Hg in systolic/diastolic blood pressure [SBP/DBP]), dyslipidemia (at serum levels, triglyceride [TG], 0.65 to 2.60 mmol/L in high-density cholesterol [HDL-C]), dysglycemia ((<7.0 mmol/L in plasma glucose). As metabolic parameters, SBP/DBP, TC, TG, HDL-C, glucose, immunoreactive insulin (IRI), homeostasis model assessment of insulin resistance (HOMA-IR: calculated by glucose and IRI), leptin, and adiponectin were respectively measured after a 12-hour fast. The measurements of each parameter including CCA-IMT has been described previously.

The mean levels (±SD) of each parameter were as follows: SBP 139 ± 13 mm Hg, DBP 78 ± 6 mm Hg, TC 5.1 ± 0.7 mmol/L, TG 1.0 ± 0.4 mmol/L, HDL-C 1.5 ± 0.4 mmol/L, glucose 5.4 ± 0.6 mmol/L, IRI 6.7 ± 4.6 μU/mL, HOMA-IR 1.6 ± 1.1, leptin 7.4 ± 8.0 ng/mL, adiponectin 7.7 ± 4.7 μg/mL, L:A 1.5 ± 1.9, CCA-IMT 0.95 ± 0.18 mm. In a simple correlation test (by Pearson rank correlation test), age, SBP, leptin, and L:A showed a significant and positive correlation to CCA-IMT, respectively (Table). In multiple regression analysis, only age and SBP persisted to show a significant and independent correlation to CCA-IMT. Other variables did not show any relative significance. Additionally, when leptin or adiponectin alone (not L:A) was entered in our multiple regression model, leptin (β=0.021, P=0.84) and adiponectin (β=−0.078, P=0.41) were nonsignificantly correlated to CCA-IMT.

Among asymptomatic older females, L:A was significantly correlated to CCA-IMT in the simple test, but the correlation attenuated to a nonsignificant level after multivariate adjustment. A significant, positive and independent association between CCA-IMT and both age and SBP observed in our study is consistent with prior reports. Our data were partly similar to the Norata study results that in the simple correlation test leptin was significantly correlated to CCA-IMT when the relationship of CCA-IMT with leptin or adiponectin alone was tested, and that in multiple regression analysis neither leptin or adiponectin showed a correlation to CCA-IMT. Thus, L:A may not always be a good predictor for carotid atherosclerosis in a population of healthy older females, even though L:A is such a marker in healthy males. There may be certain healthy or diseased populations that are especially applicable to L:A, and if so we should explore the populations.

Regarding the differences between our and the Norata study results, in addition to a different study method, the influences of sex and age in the subjects on the relationship between L:A and CCA-IMT may well-explain the results. Aging is generally associated with various hormonal/metabolic alterations and the fat distribution change, with sex differences, that can affect the secretion of leptin and adiponectin. For example, high circulating adiponectin levels with aging in healthy males, not females, have

Table. Correlations of Clinical Parameters to Carotid Intima-Media Thickness Among Asymptomatic Older Females

<table>
<thead>
<tr>
<th>Parameter</th>
<th>γ (P)</th>
<th>β (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>0.333 (&lt;0.0001*)</td>
<td>0.343 (&lt;0.0001*)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.123 (0.16)</td>
<td>0.101 (0.27)</td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>0.278 (0.001*)</td>
<td>0.204 (0.029*)</td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>0.031 (0.72)</td>
<td>−0.024 (0.80)</td>
</tr>
<tr>
<td>TC, mmol/L</td>
<td>0.105 (0.24)</td>
<td>0.108 (0.22)</td>
</tr>
<tr>
<td>TG, mmol/L</td>
<td>0.140 (0.11)</td>
<td>0.108 (0.22)</td>
</tr>
<tr>
<td>HDL-C, mmol/L</td>
<td>0.053 (0.55)</td>
<td>0.109 (0.23)</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>0.136 (0.13)</td>
<td>0.132 (0.13)</td>
</tr>
<tr>
<td>Insulin, μU/ml#</td>
<td>0.061 (0.50)</td>
<td>0.005 (0.95)</td>
</tr>
<tr>
<td>HOMA-IR#</td>
<td>0.078 (0.38)</td>
<td>...</td>
</tr>
<tr>
<td>Leptin, ng/ml#</td>
<td>0.211 (0.017*)</td>
<td>...</td>
</tr>
<tr>
<td>Adiponectin, μg/ml#</td>
<td>−0.137 (0.12)</td>
<td>...</td>
</tr>
<tr>
<td>L:A#</td>
<td>0.217 (0.014*)</td>
<td>0.077 (0.39)</td>
</tr>
</tbody>
</table>

HOMA-IR indicates homeostasis model assessment of insulin resistance (=fasting insulin/glucose/22.5). γ, Pearson rank correlation coefficient; β, standard regression coefficient by multiple regression analysis (adjusted for all measured parameters in considering collinearity between parameters).

*Analyzed after log-transformation because of the skewed distribution.

**Significance level: P<0.05.
also been reported.4 To establish the clinical applications of L:A, future studies on various populations and conditions are expected.

Disclosures
None.

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