Additive impacts of diabetes and renal failure on carotid atherosclerosis

Dear Sir,

Patients with diabetes mellitus (DM) have a higher risk of cardiovascular disease than the general population [1]. The cardiovascular mortality is much higher when DM patients are complicated with nephropathy [2], which may be accounted for by advanced atherosclerosis in diabetic nephropathy. Atherosclerosis is advanced in type 2 DM [3,4] and also in end-stage renal disease (ESRD) [5,6]. So far, no study is available in the literature that reports the possible change in carotid artery intima-media thickness (CA-IMT) in DM patients with ESRD as compared to CA-IMT of those having DM or ESRD alone. In the present study, we made such comparisons.

This study included healthy control subjects (Control group, N = 300), type 2 DM patients without renal complication (DM group, N = 309), ESRD patients without (ESRD group, N = 222) and with DM (DM + ESRD group, N = 66). These subjects were randomly selected from our database after categorization by age range and gender, so that the four groups were comparable for age and gender. Carotid artery intima-media thickness (CA-IMT) was measured by B-mode ultrasound, as previously reported [3–5,7]. Plasma total cholesterol and triglycerides were measured by enzymatic methods [8]. Other parameters were obtained by routine laboratory methods. Table 1 gives characteristics of the subjects.

As compared with the control value, CA-IMT was significantly greater in the DM and the ESRD patients, but no significant difference was found between the two groups (Fig. 1). The DM + ESRD patients had the greatest CA-IMT among the four groups and the difference was significant. Analysis of variance indicated that the effects of DM (P < 0.0001) and ESRD (P < 0.0001) on CA-IMT were both significant and there was no significant interaction (P = 0.474) between DM and ESRD. Since the subjects were different in some of the background data, including blood pressure and plasma lipids, multiple regression analysis was performed to examine whether the impacts of DM and ESRD are independent of these confounding variables. The results indicated that the effects of DM (β = 0.163, P < 0.0001) and ESRD (β = 0.295, P < 0.0001) were both significant and independent of age (β = 0.320, P < 0.0001), gender (male, β = 0.077, P = 0.028), smoking (β = 0.089, P = 0.009), systolic blood pressure (β = 0.078, P = 0.020), HDL-cholesterol (β = 0.022, P = 0.522) and non HDL-cholesterol (β = 0.152, P < 0.0001).

These data clearly demonstrate that DM and ESRD have adverse and additive impacts on CA-IMT. Since significant changes were found in blood pressure and plasma lipid levels in the DM, ESRD and DM + ESRD groups, we first speculated that the atherogenic effects of DM and ESRD would have been mediated by the changes in blood pressure and lipoproteins. Interestingly, our results suggested that the influence of DM and ESRD were independent of these changes. Possible explanations for such observations might include modifications of lipoproteins and accumulation of intermediate-density lipoprotein and other remnant lipoproteins in DM and ESRD, that are difficult to detect in routine lipid measurements [8]. Also, elevated Lp(a) levels [9,10] and altered blood coagulation–fibrinolysis system may play important roles in atherosclerosis in these conditions.

In conclusion, we demonstrated that patients with DM + ESRD had significantly greater CA-IMT than those with either DM or ESRD and the impacts of DM and ESRD were additive. These results would explain the elevated risk for cardiovascular mortality in diabetic nephropathy.
were all significant (betes and ESRD (DM and ESRD). Diabetes Care 1999;22:1851–7.


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Fig. 1. Effects of diabetes, renal failure and both on carotid atherosclerosis. Carotid artery intima-media thickness (CA-IMT) was measured as an index of atherosclerosis in healthy control subjects (N = 300), patients with type 2 diabetes (DM, N = 309), patients with end-stage renal disease (ESRD, N = 222) and those with both diabetes and ESRD (DM + ESRD, N = 66). Differences among groups were all significant (P < 0.05 by Scheffe’s F-test) except between the DM and the ESRD groups. The effects of DM and ESRD on CA-IMT were both significant (P < 0.0001) by analysis of variance.

References


Table 1
Characteristics of the subjects

<table>
<thead>
<tr>
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<th>Healthy</th>
<th>DM</th>
<th>ESRD</th>
<th>DM + ESRD</th>
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<tbody>
<tr>
<td>Number of subjects</td>
<td>300</td>
<td>309</td>
<td>222</td>
<td>66</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>43</td>
<td>52</td>
<td>51</td>
<td>53</td>
</tr>
<tr>
<td>Age (year)</td>
<td>55 ± 11</td>
<td>56 ± 13</td>
<td>54 ± 13</td>
<td>56 ± 11</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>22.6 ± 2.8</td>
<td>23.0 ± 4.0</td>
<td>21.3 ± 2.7b,c</td>
<td>21.2 ± 3.1b,c</td>
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<td>Smoker (%)</td>
<td>38</td>
<td>49</td>
<td>39</td>
<td>54</td>
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<td>SBP (mmHg)</td>
<td>125 ± 19</td>
<td>133 ± 24b</td>
<td>145 ± 22b,c</td>
<td>161 ± 21b,c,d</td>
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<td>DBP (mmHg)</td>
<td>76 ± 11</td>
<td>74 ± 12</td>
<td>78 ± 11c</td>
<td>79 ± 10b,c</td>
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<td>Plasma TC (mg/dl)</td>
<td>198 ± 37</td>
<td>205 ± 49</td>
<td>163 ± 37b,c</td>
<td>176 ± 55b,c</td>
</tr>
<tr>
<td>HDL-C (mg/dl)</td>
<td>57 ± 18</td>
<td>48 ± 16b</td>
<td>39 ± 12b,c</td>
<td>38 ± 12b,c</td>
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<tr>
<td>Non-HDL-C (mg/dl)</td>
<td>140 ± 35</td>
<td>156 ± 47b</td>
<td>123 ± 37b,c</td>
<td>138 ± 54b,c</td>
</tr>
</tbody>
</table>

* Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; non-HDL-C, non-high density lipoprotein cholesterol; NS, not significant. P-values by analysis of variance.
  b P < 0.05 versus healthy control by Scheffe’s F-test.
  c P < 0.05 versus DM by Scheffe’s F-test.
  d P < 0.05 versus ESRD by Scheffe’s F-test.
  * By χ²-test.