Response to Birth Factors and Retinal Vascular Caliber in a Twin Study

We thank Cheung1 for his interest in our article and, in particular, for highlighting the issues relating to the use of birth size as a sensitive marker of fetal growth restriction and its relationship with retinal vascular caliber. The prevalence of prematurity is relatively high in twins compared with singletons, and as such, we used birth weight for gestational score under the 10th percentile as a proxy for fetal growth restriction in our analysis. Although we could not adequately analyze birth weight relative to gestation in this study, because few twins had low birth weight for gestation and the majority of the twin pairs (67%) were concordant for birth weight by gestational scores, such analytic issues highlight the value of within-pair analyses. This method provides greater precision in controlling for gestation in a study of this size than other methods, such as adjusting for gestation in the regression analysis, because of collinearity between birth weight and gestation. In addition, we observed that the association between gestation and retinal arteriolar caliber did not persist after adjusting for birth weight. Consistent with this finding, another study reported recently that low birth anthropometry, not prematurity, was linked to elevated blood pressure.2 Clearly, additional support is required to confirm the associations identified in our relatively small study.

Finally, we thank Cheung1 for his suggestion to include more direct measures of ocular magnification (eg, axial length) in the analysis rather than optic disc area. The reason that we included optic disc area in our models is that it has been suggested to be a sensitive marker of fetal growth restriction and its relationship with retinal vascular caliber. The magnification effect is unlikely to influence the reported association because of collinearity between birth weight and gestation.

In a twin study, because few twins had low birth weight for gestation and the majority of the twin pairs (67%) were concordant for birth weight by gestational scores, such analytic issues highlight the value of within-pair analyses. This method provides greater precision in controlling for gestation in a study of this size than other methods, such as adjusting for gestation in the regression analysis, because of collinearity between birth weight and gestation. In addition, we observed that the association between gestation and retinal arteriolar caliber did not persist after adjusting for birth weight. Consistent with this finding, another study reported recently that low birth anthropometry, not prematurity, was linked to elevated blood pressure.2 Clearly, additional support is required to confirm the associations identified in our relatively small study.

Finally, we thank Cheung1 for his suggestion to include more direct measures of ocular magnification (eg, axial length) in the analysis rather than optic disc area. The reason that we included optic disc area in our models is that it has been suggested to be associated with both birth size and retinal vascular caliber,3,4 and the measurement of optic disc itself is affected by ocular magnification effect. Nevertheless, we repeated our analyses using the Bengtsson formula5 to obtain magnification-corrected arteriolar caliber, and the results remained unchanged, and thus, magnification effect is unlikely to influence the reported associations (Table).

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Disclosures

None.


Table. Associations Between Birth Length and Magnification-Corrected Arteriolar Caliber in Total Sample and by Zygosity

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MZ + DZ (n = 266)</th>
<th>P</th>
<th>MZ (n = 98, 49 Pairs)</th>
<th>P</th>
<th>DZ (n = 168, 84 Pairs)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \beta_x )</td>
<td>–5.00 (–8.78 to –1.22)*</td>
<td>0.009</td>
<td>–5.84 (–11.31 to –0.37)*</td>
<td>0.04</td>
<td>–4.43 (–9.52 to 0.66)*</td>
<td>0.09</td>
</tr>
<tr>
<td>( \beta_y )</td>
<td>–7.50 (–11.65 to –3.35)†</td>
<td>&lt;0.001</td>
<td>–7.60 (–13.26 to –1.93)†</td>
<td>0.009</td>
<td>–8.66 (–13.96 to –3.35)†</td>
<td>0.001</td>
</tr>
<tr>
<td>( \beta_z )</td>
<td>–6.34 (–10.49 to –2.18)*</td>
<td>0.003</td>
<td>–6.63 (–12.46 to –0.79)*</td>
<td>0.03</td>
<td>–5.70 (–11.38 to –0.01)*</td>
<td>0.05</td>
</tr>
<tr>
<td>( \beta_0 )</td>
<td>–9.50 (–14.29 to –4.72)†</td>
<td>&lt;0.001</td>
<td>–7.55 (–17.06 to 1.97)†</td>
<td>0.12</td>
<td>–10.50 (–16.65 to –4.35)†</td>
<td>0.001</td>
</tr>
<tr>
<td>Test for difference‡</td>
<td>0.12</td>
<td>…</td>
<td>0.58</td>
<td>…</td>
<td>0.25</td>
<td></td>
</tr>
</tbody>
</table>

Linear mixed-regression models were used. MZ indicates monozygotic; DZ, dizygotic; \( \beta_0 \), common regression coefficient.

*Data were adjusted for age, sex, alcohol consumption, maternal smoking, prematurity, and optic disc area.

†Data were further adjusted for body mass index and mean arterial blood pressure.

‡Likelihood ratio test of heterogeneity of between- and within-pair effects was used (\( \beta_0 \) and \( \beta_0 \)).

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