Letter and Reply

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Parasympathetic neuropathy and LVH

Sir,

We read with interest the article by Nishimura et al. [1], reporting an association between parasympathetic neuropathy and left ventricular hypertrophy (LVH) in diabetic patients on haemodialysis. We are pleased to see that the results of this study extend to the population of diabetic uraemic patients, observations that we made ~4 years ago and reported in this journal [2]. The study by Nishimura et al. makes even more compelling the need to establish whether the link between autonomic neuropathy and LVH found in our study and now confirmed in diabetic-uraemics is causal or non-causal. The authors speculate at length on the nature of this link, but miss the most likely mechanism explaining this intriguing association. In our study, which the authors may not have noticed (not quoted), we provided circumstantial evidence that nocturnal hypoxaemia may explain both dysautonomia and LVH, a pathogenetic possibility which appears even more likely in diabetics, a population at high risk for sleep apnoea as well as dysautonomia [3]. It would be of interest for Nishimura et al. to reanalyse their data taking into account heart geometry, because we found that parasympathetic hypertrophy is very frequent in patients with nocturnal hypoxaemia [4]. Considering sleep apnoea as a potential mechanism mediating dysautonomia and LVH is important because sleep apnoea is a modifiable, though systematically neglected, cardiovascular risk factor in end-stage renal disease patients.

Conflict of interest statement. None declared.

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Reply

Sir,

I thank Professor Zoccali for his interest in our paper, and for his meaningful suggestions to our study. As Zoccali et al. reported in their studies, nocturnal hypoxaemia is likely to be closely associated with autonomic dysfunction and concentric left ventricular hypertrophy (LVH) in patients with end-stage renal disease (ESRD) [1,2]. Zoccali et al. demonstrated that average nocturnal SaO2 was independently related to the deep breathing score, which was positively correlated with the SD of 24 h average heart rate, in dialysis patients. Furthermore, Zoccali et al. showed that nocturnal hypoxaemia as well as impaired parasympathetic activity was associated with the presence of concentric LVH in dialysis patients.

In the re-analysis of our data taking the heart geometry into consideration (Table 1), concentric LVH was associated inversely with SDANN in time–domain measures and positively with LF or LF/HF in frequency–domain measures in diabetic haemodialysis patients. In contrast, eccentric LVH was inversely associated with pNN50 in time–domain measures or HF in frequency–domain measures in diabetic patients. No relationship between the heart rate variability and heart geometry has been seen in non-diabetic haemodialysis patients. Therefore, impaired parasympathetic activity seems to be related to the eccentric type of LVH more strongly than the concentric type of LVH in diabetic haemodialysis patients. Sympatho-vagal imbalance in addition to impaired parasympathetic activity may be involved with concentric LVH in our diabetic haemodialysis patients.

Intermittent hypoxic apnea can elevate peripheral sympathetic activity possibly by altering chemoreceptor control of the peripheral sympathetic activity [3,4]. Zoccali et al. reported that neuropeptide Y, which is released during breathing score, which was positively correlated with the SD of 24 h average heart rate, in dialysis patients. Furthermore, Zoccali et al. showed that nocturnal hypoxaemia as well as impaired parasympathetic activity was associated with the presence of concentric LVH in dialysis patients.

In the re-analysis of our data taking the heart geometry into consideration (Table 1), concentric LVH was associated inversely with SDANN in time–domain measures and positively with LF or LF/HF in frequency–domain measures in diabetic haemodialysis patients. In contrast, eccentric LVH was inversely associated with pNN50 in time–domain measures or HF in frequency–domain measures in diabetic patients. No relationship between the heart rate variability and heart geometry has been seen in non-diabetic haemodialysis patients. Therefore, impaired parasympathetic activity seems to be related to the eccentric type of LVH more strongly than the concentric type of LVH in diabetic haemodialysis patients. Sympatho-vagal imbalance in addition to impaired parasympathetic activity may be involved with concentric LVH in our diabetic haemodialysis patients.

Table 1. Differences in the association of the heart rate variability with concentric or eccentric types of LVH in diabetic haemodialysis patients

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concentric LVH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SDANN</td>
<td>0.816</td>
<td>0.702–0.947</td>
<td>0.008</td>
</tr>
<tr>
<td>LF (×10² ms⁻²)</td>
<td>1.089</td>
<td>1.010–1.174</td>
<td>0.027</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>1.808</td>
<td>1.181–2.769</td>
<td>0.006</td>
</tr>
<tr>
<td>Eccentric LVH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pNN50 (%)</td>
<td>0.722</td>
<td>0.562–0.927</td>
<td>0.011</td>
</tr>
<tr>
<td>HF (×10² ms⁻²)</td>
<td>0.771</td>
<td>0.647–0.920</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Criteria for LVH are as follows: left ventricular mass index >134 g/m² body surface area in men, or >110 g/m² body surface area in women. Concentric LVH was defined when relative left ventricular wall thickness was ≥0.45, and eccentric LVH was defined when relative left ventricular wall thickness was <0.45, with left ventricular dilation (left ventricular end-diastolic dimension >56 mm).

SDANN = standard deviation of the average normal RR interval for all 5 min segments of a 24 h ECG recording; LF = power in the low-frequency range (0.04–0.15 Hz); HF = power in the high-frequency range (0.15–0.40 Hz); pNN50 = percentage differences between adjacent normal RR intervals exceeding 50 ms over the entire 24 h ECG recording.