Response to ‘Vascular access calcification may be only an intermediate factor for mortality’


We thank Dr Lin for the letter to our article.

In our article,1 we gave the first systematic overview of vascular access calcification and described risk factors for the development of vascular access calcification such as male gender, diabetes mellitus, and dialysis vintage. Moreover, we found that the presence of vascular access calcification is related to an increased mortality risk, even after adjustment for these and other important confounders. Therefore, the detection of vascular access calcification represents a cost-effective and easy-to-perform method to identify patients at increased mortality risk.

As pointed out by Dr Lin, not only vascular access calcification, but also high-sensitive C-reactive protein, carotid intima media thickness, and iliacal/femoral calcification were related to increased mortality in our study (Table 4 of original article1), and therefore could be potential confounding factors on the predictive value of vascular access calcification on mortality. In addition, we performed a stepwise Cox regression analysis with the above-mentioned potential confounders plus age (Table 1). In this model we found that, even after adjustment of these confounders, the presence of vascular access calcification was associated with an approximately twofold mortality risk (ranging from 1.77 to 2.60).

Taken together, the presence of vascular access calcification is an important predictor of mortality in dialysis patients.

Table 1 | Effect of vascular access calcification on total mortality determined by stepwise Cox regression analysis

<table>
<thead>
<tr>
<th>Model</th>
<th>HR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1</td>
<td>Vascular access calcification</td>
<td>2.14</td>
<td>1.11–4.12</td>
</tr>
<tr>
<td>Step 2</td>
<td>Step 1 + gender</td>
<td>2.29</td>
<td>1.15–4.55</td>
</tr>
<tr>
<td>Step 3</td>
<td>Step 2 + diabetes mellitus</td>
<td>2.24</td>
<td>1.12–4.49</td>
</tr>
<tr>
<td>Step 4</td>
<td>Step 3 + dialysis vintage</td>
<td>2.60</td>
<td>1.25–5.40</td>
</tr>
<tr>
<td></td>
<td>Step 4 + iliacal/femoral calcification</td>
<td>2.39</td>
<td>1.14–4.99</td>
</tr>
<tr>
<td></td>
<td>Step 4 + CRP</td>
<td>2.27</td>
<td>1.08–4.80</td>
</tr>
<tr>
<td></td>
<td>Step 4 + IMT</td>
<td>1.99</td>
<td>0.87–4.53</td>
</tr>
<tr>
<td>Step 5</td>
<td>Step 4 + age</td>
<td>2.53</td>
<td>1.24–5.15</td>
</tr>
<tr>
<td>Step 6</td>
<td>Step 5 + iliacal/femoral calcification</td>
<td>2.38</td>
<td>1.16–4.90</td>
</tr>
<tr>
<td>Step 7</td>
<td>Step 6 + CRP</td>
<td>2.02</td>
<td>0.94–4.34</td>
</tr>
<tr>
<td></td>
<td>Step 7 + IMT</td>
<td>1.77</td>
<td>0.77–4.05</td>
</tr>
</tbody>
</table>

CRP, high sensitive C-reactive protein (mg/l); 95% CI, 95% confidence interval; HR, hazard ratio; IMT, carotid intima-media thickness (mm).

Angiotensin-converting enzyme 2 (ACE2) gene and protein expression in diabetic patients without nephropathy


To the Editor: Reich et al.1 investigated the angiotensin-converting enzyme 2 (ACE2) gene and protein expression in patients with diabetic nephropathy. The authors seem to interchangeably use kidneys in patients with diabetes and diabetic patients with kidney disease (i.e., diabetic nephropathy), which are two different diagnoses. For example, ‘The strengths of the current study are that we compared ACE2 and ACE expression in the kidney of subjects with type 2 DM with the kidneys of healthy control subjects’...1 seems to conflict with the study by Tikellis et al.,2 which reported ACE2 expression in rats with streptozocin-induced diabetes after 24 weeks. The different glomerular expression of ACE2 in these two studies may not be a conflicting report but a raising two questions: (1) Is there a difference in ACE2 gene and protein expression between patients with diabetes without nephropathy and diabetic patients with nephropathy? and (2) is there a specific pattern of expression that may predict future development of nephropathy in diabetic patients without nephropathy?

Also, Parving et al.3 reported the antiproteinuric effect of the renin inhibitor, aliskiren (in combination with Losartan) in patients with diabetic nephropathy. As ACE2 activity is dependent on production of angiotensin peptides from angiotensin I and II, and angiotensin I is produced by the action of renin on angiotensinogen, the use of renin inhibitors will decrease production of angiotensin I as well as angiotensin peptides 1–7 and 1–9. It would be interesting to know what the long-term effect of renin inhibitors will be. The use of renin inhibitors may reduce or eliminate the beneficial effect of the ACE2 pathway.


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Response to ‘Angiotensin-converting enzyme 2 (ACE2) gene and protein expression in diabetic patients without nephropathy’


We thank Dr Amao for the interest in our study of ACE2 expression in kidney biopsies of human subjects with diabetic nephropathy (DN), and other forms of glomerular disease. Indeed, we did not study ACE2 gene or protein expression in biopsies of diabetic subjects without DN and, as mentioned in our discussion, it is not known whether the same observation would occur in such individuals. The feasibility of this type of study is questionable, given that it would be difficult to justify kidney biopsy in human subjects without clinical evidence of renal disease. Similarly, it is not known whether ACE2 expression in diabetic patients could be used to predict the development of DN. We also agree that the reported differences in ACE2 expression in different animal models of DN and human studies could relate to disease stage. Appreciation of the complexity of the renin-angiotensin system and its intrinsic balances continues to grow. We agree with Dr Amao that the potential influence of direct renin inhibition on the protective effects of ACE2 merits further study.


High-volume peritoneal dialysis in acute kidney injury


To the Editor: In a study comparing high-volume peritoneal dialysis (HVPD) and daily hemodialysis (DHD), Gabriel et al. report their experience from a randomized controlled trial. The authors report a mortality of 58% for HVPD and 53% for DHD. Subsequently, the article mentions 24 survivors in HVPD and 29 survivors in DHD, each group comprising 60 patients. Taking the figures of survivors into account, the mortality for the HVPD group should have been reported as 60% and that for the DHD group as 51.66% (or as 52%, the nearest whole number).

The study also compares the efficacy of HVPD in metabolic control with that of DHD. However, they excluded patients with severe hypercatabolism according to Schrier’s criteria at the time of randomization, giving the impression that the authors accepted the limitations of HVPD beforehand. Chitalia et al. have earlier reported peritoneal dialysis to be reasonably effective in mild and moderate hypercatabolic acute renal failure. It would have been interesting to observe the efficacy of HVPD in severely hypercatabolic patients, especially when the authors have used very high volumes of 36–44 l/day of dialysis fluid for 7 days a week with a target $K_t/V$ of 0.65/day.


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Response to ‘Hormone therapy and loss of kidney function’


We appreciate the interest of Dr Palya and colleagues in our paper.2 We agree that further exploration of the relationship between progestin use, either with or without estrogen, and loss of kidney function would be of great interest. The importance of the type of progestin contained in hormonal preparations has been previously highlighted.3,4 Studies have suggested a link between adverse cardiac, vascular, and thrombotic events depending on the type of progestin exposure,3,4 and indicate that the type of progestin in a hormonal preparation may play a role in