Long pentraxin PTX3 as a prognostic marker of cardiovascular mortality in patients with chronic kidney disease

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Pentraxin 3 (PTX3) is a soluble component of the family of pentraxins, which is promptly released by endothelial cells and fibroblasts during acute immunoinflammatory responses and actively participates in immune resistance to pathogens, like aspergillosis. PTX3 might be produced at sites of inflammation and injury where it plays a critical role in controlling the homeostasis of the damaged tissue by influencing extracellular matrix deposition and local inflammation and tissue repair. PTX3 deficiency has been associated with augmented macrophage infiltration in the vascular wall, atherosclerosis, and increased vascular thrombosis.

The clinical translation of these findings led to the discovery of PTX3 as a rapid and sensitive marker of acute manifestation of vascular damage like stable angina and heart failure as well as a good predictor of 3-month mortality following myocardial infarction. Further analysis showed that increased plasma PTX3 levels predicted the incidence of CKD in subjects over 75 years of age and positively correlated with renal function, end-stage renal disease, and protein-energy wasting. The key role of PTX3 in cardiovascular diseases and the evidence that PTX3 levels are associated with CKD progression raise the question about the potential implication of PTX3 as a biomarker of cardiovascular deterioration and death in CKD patients. Data available so far have documented that PTX3 is a robust marker of cardiovascular outcome in CKD, as it correlates with markers of preclinical atherosclerosis (carotid intima-media thickness) and endothelial dysfunction (flow-mediated dilation) in CKD patients not on dialysis and predicts increased incidence of cardiovascular events in patients with CKD stages 3 and 4.

Plasma PTX3 levels correlate not only with peripheral artery disease but also with all-cause mortality in dialysis patients. The work by Krzanowski et al. published in this issue of the Pol Arch Intern Med confirms and extends these findings by evaluating the prognostic value of PTX3 for all-cause and cardiovascular mortality in a cohort of predialysis and dialysis patients. Although at baseline PTX3 was significantly correlated to other markers including C-reactive protein, osteoprotegerin, and osteopontin, the prognostic value of PTX3 was independent of these markers as well as others including transforming growth factor β, hepatocyte growth factor, stromal cell-derived factor α, tumor necrosis factor receptor II, thrombomodulin, intact parathyroid hormone, interleukin 6, fibroblast growth factor 23, and osteocalcin.

More importantly, after 5 years of follow-up, increased plasma PTX3 levels were the strongest predictor of all-cause and cardiovascular mortality independently of biological age, dialysis vintage, and all the tested biomarkers; this observation was not confirmed for C-reactive protein levels. Whether this observation is the consequence of the limited number of patients enrolled in the study could not be excluded. In summary, data provided by Krzanowski et al. together with those from other studies, demonstrate that plasma PTX3 levels are an independent predictor of all-cause and cardiovascular mortality (Figure 1) in patients with mild to moderate CKD stages, and they were triplicated in patients on dialysis.

The above data suggest that PTX3 might reflect the inflammatory milieu and the elevated cardiovascular risk in uremic patients. It remains to be addressed whether PTX3 is only a bystander of the vascular immunoinflammatory process or a player in cardiorenal disease. Available preclinical data strongly support an atheroprotective role. Further studies are needed to elucidate whether this is the case also in humans and
PTX3 as a prognostic marker of cardiovascular mortality in CKD

**REFERENCES**


**FIGURE 1** Prognostic value of increased plasma pentraxin 3 (PTX3) levels for cardiovascular mortality in patients with renal disease. The forest plot shows hazard ratio (HR) with 95% confidence intervals (CIs) for all-cause and cardiovascular mortalities predicted by 1-SD change in plasma PTX3 levels. The x axis is in log10 scale. Right-side table: a P value of less than 0.05 considered significant; renal disease stage (chronic kidney disease [CKD]) of the studied cohort is provided in brackets.

<table>
<thead>
<tr>
<th>Study</th>
<th>HR (95% CI) for mortality</th>
<th>P value</th>
</tr>
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<tbody>
<tr>
<td>Janda et al 15 (dialysis)</td>
<td>3.16 (1.03–9.64)</td>
<td>0.020</td>
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<tr>
<td>Tong et al 10 (CKD stage 5)</td>
<td>1.92 (1.24–2.97)</td>
<td>0.003</td>
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<tr>
<td>Krzanowski et al 14 (CKD stage 5)</td>
<td>1.83 (1.05–3.21)</td>
<td>0.030</td>
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<td></td>
<td>1.28 (1.05–1.55)</td>
<td>0.012</td>
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<tr>
<td></td>
<td>1.28 (1.04–1.57)</td>
<td>0.017</td>
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