single biomarker combining the two predictors of decline of renal function in various CKD stages showing increased protein permeability and decreased filtration function of the glomerulus.

Conflict of interest statement. None declared.

Editorial note: Dr McQuarrie et al. had no further comments on this letter.

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A simple four-grade score for aortic arch calcification by posteroanterior chest X-ray is associated with cardiovascular disease in haemodialysis patients

Sir,

We found the recent article by Noordzij et al. [1] extremely interesting read. The authors found that progression of aortic arch calcification (AoAC), which was associated with hyperparathyroidism, as assessed by lateral chest X-ray (CXR), was related to mortality from cardiovascular disease (CVD). While an annual lateral CXR may be recommended in other countries, such procedures are rarely implemented in daily dialysis practice in Japan. Instead, based on a manual published in the late 1990s, only posteroanterior CXR (PA-CXR) is routinely performed and interpreted by dialysis physicians to monitor cardiothoracic index for dry weight assessment [2]. As such, we feel that the medical community could benefit greatly from easily accomplished assessment of AoAC via routine PA-CXR.

We conducted a cross-sectional study involving maintenance haemodialysis patients [N = 51; mean age: 67 ± 12 years; median dialysis vintage: 4.5 years (interquartile range: 1.9–8.9)] at an outpatient dialysis centre. Using PA-CXR, AoAC was graded as follows: Grade 0, no visible calcification; Grade 1, small spots of calcification or thin calcification on the aortic knob; Grade 2, one or more areas of thick calcification and Grade 3, circular calcification on the aortic knob [3]. CVD was considered present if the patient had a past history of ischaemic heart disease (diagnosed by coronary angiogram), brain infarction with neurological symptoms (confirmed by brain imaging) or peripheral arterial disease (diagnosed by angiography or ankle–brachial index < 0.90).

![Fig. 1. Prevalence of CVD by AoAC grade in haemodialysis patients (N = 51). The proportion of patients with total number of CVD presence (sum of ischaemic heart disease, brain infarction and peripheral arterial disease numbers) is shown for each grade (range: 0–3).](https://academic.oup.com/ndt/article-abstract/26/5/1747/1894728)

Table 1. Factors associated with presence of CVD on binomial regression*

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>PD (95% CI)</td>
<td>P-value</td>
</tr>
<tr>
<td>Age (per 10 years)</td>
<td>0.15 (0.11–0.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender (female versus male)</td>
<td>–0.07 (–0.35 to 0.22)</td>
<td>0.648</td>
</tr>
<tr>
<td>Diabetes mellitus as a cause of dialysis (yes vs. no)</td>
<td>0.19 (0.09 to 0.47)</td>
<td>0.183</td>
</tr>
<tr>
<td>Dialysis vintage (above median versus below median)</td>
<td>0.02 (–0.25 to 0.29)</td>
<td>0.903</td>
</tr>
<tr>
<td>Hypertension (yes versus no)</td>
<td>0.12 (–0.22 to 0.46)</td>
<td>0.496</td>
</tr>
<tr>
<td>AoAC (versus Grade 0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 1</td>
<td>0.28 (–0.01 to 0.57)</td>
<td>0.058</td>
</tr>
<tr>
<td>Grade 2</td>
<td>0.50 (0.19–0.81)</td>
<td>0.002</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0.61 (0.14–1.1)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Binomial regression was performed by STATA version 11.0. The regression procedure in STATA fits generalized linear models estimating PD. Statistically significant values P < 0.05 in bold; all P < 0.20 in italics. Possible confounders with P < 0.20 in univariate analysis were entered into multivariate analysis. CI, confidence interval.
We examined the prevalence of CVD by AoAC grade and determined the association between AoAC and presence of CVD using binomial regression. CVD prevalence by AoAC grade was 14% (N = 14), 42% (N = 19), 64% (N = 14) and 75% (N = 4) for Grades 0–3, respectively (P for trend < 0.01; Figure 1). Univariate analysis revealed that CVD was associated with AoAC Grades 2 and 3 [versus Grade 0, prevalence difference (PD): 0.50 and 0.61, respectively; Table 1]. After adjustment for age and diabetes as a cause of dialysis, CVD was found to be associated with AoAC Grades 1, 2 and 3 (versus Grade 0, PD: 0.25, 0.43 and 0.62, respectively).

Despite the relatively small population and limited covariates available in our analyses, our results suggest that AoAC grade as assessed by using PA-CXR may be associated with CVD in haemodialysis patients, and CVD prevalence may increase with progression of AoAC. This simple four-grade system has been shown to predict CVD events in the general population [4] and appears applicable in haemodialysis facilities across Japan. A large longitudinal study is needed to clarify whether or not this grading system based on PA-CXR is able to predict CVD outcomes as well as lateral CXR in dialysis patients.

Conflict of interest statement. None declared.

Editorial Note: Dr Noordzij et al. had no further comments on this letter.

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Impact of renal impairment on the risk of severe hypoglycaemia associated with the use of insulin and glyburide

Sir,

With great interest, I read the article by Weir et al. [1], which addresses the impact of renal function on the risk of severe hypoglycaemia (SH) among users of insulin versus glyburide. In their large, retrospective nested case–control study, the authors demonstrated that renal function did not significantly modify glyburide’s risk for SH, whereas insulin’s hypoglycaemic risk was significantly attenuated in the setting of renal impairment. These results are unexpected contradicting the complex pharmacokinetics of glyburide, the experience of daily clinical practice and the results from recent studies.

The longacting sulfonylurea glyburide (half-life of 5–10 h) carries a high risk of SH due to its high binding affinity to the beta-cell sulfonylurea receptor with a low exchange rate. The two principal metabolites, which undergo 50% renal elimination, have significant hypoglycaemic activity, too. Thus, the half-life of glyburide as well as of its metabolites are indisputably prolonged by renal impairment. Furthermore, there are numerous potential metabolic drug–drug interactions with other commonly prescribed drugs. Additional medication metabolized through the genetically polymorphic cytochrome enzyme CYP2C9 (among others such as warfarin, torasemid, losartan) might reduce the metabolism of glyburide and potentiate its hypoglycaemic effects [2]. An additional analysis of concomitant medication metabolized as well through CYP2C9 would have been valuable for the present study. Concerning insulin therapy, neither the type of diabetes nor the type of insulin used was disclosed. Thus, also patients with type 1 diabetes had been included. Preliminary data indicate that insulin clearance and/or the metabolic activity of human and analogue insulin differ in the state of renal insufficiency [3].

Nowadays, SH associated with the use of longacting sulfonylureas can be regarded as a problem of uncritical prescription neglecting crucial contraindications—particularly renal insufficiency—and deficiencies of diabetes care in the mainly geriatric patients. Recent prospective population-based studies from Germany [4] and Italy [5] with a restrictive definition of SH—a symptomatic event requiring treatment with intravenous glucose that was confirmed by a blood glucose measurement of <50 mg/dL—demonstrated renal impairment in 73 and 50%, respectively, of patients with sulfonylurea-associated SH. Among other factors such as long duration of diabetes, multimorbidity and polypharmacy, a low HbA1c (6.6 and 5.9%, respectively) was the strongest predictor for the risk of SH indicating recurrent antecedent hypoglycaemic episodes. Unfortunately, the current study by Weir et al. [1] did not provide either the diabetes duration or HbA1c levels indicating the quality of antecedent metabolic control and allowing the evaluation