Factors associated with increasing vascular stiffness in PD

Sir,

We read with interest the article by Jung et al. [1] investigating factors associated with aortic stiffness in peritoneal dialysis (PD) patients. The authors report significant association between heart-to-femoral pulse wave velocity (hPWV), vascular calcification score and serum fetuin-A, but no significant association between fetuin-A concentration and change in hPWV >1 year.

This cohort of PD patients contains 35% diabetic subjects. Arterial stiffening occurs in diabetes at a faster rate and is proportional to glycated haemoglobin levels [2]. In addition, PD-related factors such as dialysis prescription, glucose absorption and advanced glycation end-products have the potential to contribute to the stiffening process.

The authors suggest that these results are discrepant to our published findings [3] because they relate to our use of singleton measurements of variables and not ‘time-averaged parameters’, thereby overestimating the effect of fetuin-A in our study. Merely on theoretical grounds, it is more likely that this would underestimate the effect of fetuin-A due to random error and biological noise. Furthermore, their own data does not support their assertion, as baseline and time-averaged values have very similar means and SDs. We believe the use of time-averaged values could potentially suppress important changes in these variables, where the directionality and magnitude of change may provide more relevant information.

The authors also discuss the apparent differences in fetuin-A concentrations reported in different studies and attribute this to variation in study populations and dialysis modality. While this undoubtedly contributes to the differences observed, a potentially far greater, yet relatively underappreciated problem, relates to the poor agreement between different fetuin-A assays [4].

We also note that the authors show a relationship between hPWV and triglycerides (TG) and hypothesize that this may be mediated via asymmetric dimethylarginine (ADMA). We thought it might be of interest to show the relevant results from our stage 3 & 4 chronic kidney disease (CKD) cohort. We found no significant correlation between change in aortic pulse wave velocity (aPWV) >1 year and serum free fatty acid (Half-Micro test; Roche Diagnostics, Burgess Hill, UK) \((r = 0.066, P = 0.576)\) or TG concentration \((r = 0.128, P = 0.282)\). However, we note that a link between vascular function and TG may only occur when patients have significant hypertriglyceridaemia. The authors cite the relationship between change in brachial artery flow (a measure of endothelial function rather than arterial stiffness) and TG in two cohorts (mean TG 2.85 and 4.03 mmol/L) [5, 6]. In the present study [1], the mean random TG level was only 1.52 mmol/L. A further study found that patients with lipoprotein lipase deficiency, who have severe hypertriglyceridaemia, have preserved endothelial function [7]. Finally, we also measured ADMA by tandem mass spectrometry and found no significant correlation between ADMA in the non-diabetic group for either baseline aPWV \((r = 0.10, P = 0.239)\) or change in aPWV >1 year \((r = 0.059, P = 0.617)\). Thus, while we agree that vascular calcification is accelerated in dialysis patients, we feel that it is difficult to draw firm conclusions from this study with respect to the role of either fetuin-A, TGs or ADMA.

Conflict of interest statement. SGH has previously been a member of Baxter and Amgen advisory boards, and has received honoraria for these services.

1Department of Clinical Pharmacology, Addenbrooke’s Hospital, Cambridge, UK
2Department of Renal Medicine, Monash University, Melbourne, Victoria, Australia
3School of Pharmacy and Biomolecular Science, University of Brighton, Moulescombe, Brighton, UK
4Department of Clinical Pharmacology, Addenbrooke’s Hospital, Cambridge, UK
5Department of Renal Medicine, Monash University, Melbourne, Victoria, Australia
6School of Pharmacy and Biomolecular Science, University of Brighton, Moulescombe, Brighton, UK
E-mail: edward.smith@bsuh.nhs.uk


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Reply

Dear Editor,

Drs. Smith et al. [1] raised several interesting issues regarding our recent publication which analyzed factors associated with aortic stiffness and its change over time in peritoneal dialysis (PD) patients. Their questions are based on their recent study [2] which was elegantly designed to prospectively observe the change of aortic stiffness over a 1-year period and analyzed factors associated with its change from patients with chronic kidney disease (CKD) stages 3 and 4. Their study shared several similarities with ours in the basic study design and follow-up period, although it was based on different CKD stages, ending up with somewhat different conclusion. While keeping in mind that our data was based on Asian PD patients at relatively younger age (mean age 50.4 years), we would like to share our thoughts on Drs. Smith’s points.

First, our study showed no association between baseline fetuin-A level and over-time change of aortic stiffness, while theirs did. We could ascribe such discrepancy to the differences in CKD stage, younger age group, and higher proportion of diabetic patients in our study. We also agree with Dr Smith et al. that the use of time-averaged values in our study could potentially suppress important changes in these variables. However, our data showed that time-averaged values were very similar to the baseline measurements. Nevertheless, the baseline triglycerides (TG) value had no correlation with over-time change of aortic stiffness, while time-averaged TG value had correlation with it (Refer to the supplementary Table 1). Therefore, it needs to be seen in the future whether control of adequate TG level may prevent progression of aortic stiffness.

Second, we employed the same fetuin-A assay kit as did Drs. Smith et al. Therefore, the differences in fetuin-A assay system might not have affected the discrepant results.

Third, another important thing to point out is that our study is based on PD patients, among whom 35% were diabetic. We agree with Drs. Smith et al. that analysis of non-diabetic and diabetic PD patients need to be separately performed. When we reanalyzed our data with non-diabetic patients only, no correlation was observed between baseline fetuin-A value and overtime change of aortic stiffness ($r = −0.113, P = 0.495$). However, our study cohort was relatively small, comprising 67 PD patients. Separate analysis for non-diabetics might have weakened the statistical power. Besides, whether diabetic or not, PD patients are constantly exposed to a tremendous amount of high glucose PD solutions and advanced glycation end products. Such PD-specific factors and dialysis-specific factors affected the change of aortic stiffness and could have overridden the influence of fetuin-A in our study.

In conclusion, we have shown that mean arterial pressure and time-averaged TG values were associated with over-time change of aortic stiffness, while baseline fetuin-A level was not. Nevertheless, we fully agree with Drs. Smith et al. that it is difficult to draw firm conclusions with respect to the role of fetuin-A or TG. Therefore, as we mentioned in the paper, a larger study over a longer period of time is warranted to investigate the roles of fetuin-A and other biological parameters in the change of aortic stiffness.

Supplementary data

Supplementary data is available online at http://ndt.oxfordjournals.org.

Conflict of interest statement. None declared.

1Department of Internal Medicine, Gachon University of Medicine and Science, Incheon, Korea
2Department of Internal Medicine, Seoul National University Hospital, Seoul, Korea

E-mail: khoh@snu.ac.kr


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Vancomycin catheter lock as a cause of gross overestimation of vancomycin pre-dialysis trough levels

Sir,

Vanholder et al. rightly recommended recently [1,2], in agreement with US guidelines [3], antibiotic lock solutions combined with systemic antibiotics for cases of catheter-related bloodstream infections (CRBSI) in which removal