

Determinants of impaired renal and vascular function are associated with higher levels of procoagulant factors in the general population: Authors' response

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We thank Heng Fan and Jian-hua Zhu for their interest in our recently published article entitled “Determinants of impaired renal and vascular function are associated with higher levels of procoagulant factors in the general population” (1). They point out three relevant questions that relate to the findings of our study. First, Fan and Zhu note that although our study included a large sample size, we cannot rule out that other ‘potentially clinically relevant conditions’ could have affected our outcomes on renal and vascular function. We agree and acknowledge in our paper that when addressing confounding factors, one would like to be informed of any other clinically relevant conditions like recent illness or surgery as these even in non-acute situations may have prolonged impact on both vascular function and procoagulant factors like factor VIII. The Netherlands Epidemiology of Obesity (NEO) study is a population-based study, performed in an outpatients setting and representing the general population. Therefore,

we expect only minor influence of low prevalent conditions as for example recent surgery or an unknown cancer diagnosis.

With regard to the second question that the authors raise, measurements of ‘true glomerular filtration rate (GFR)’ via gold standard exogenous clearance measurements for renal function are seldom used in epidemiological studies and clinical practice because of invasiveness and high costs. For example ^{125}I -Iothalamate, which has been widely used for the measurement of ‘true GFR’ has been limited by the requirement of storage, administration, and disposal of radioactive ^{125}I -associated substances limiting the application of such measurements in large population-based studies and clinical practice (4). In contrast to the older MDRD equation, bias of GFR measurements based on the CKD-EPI formula is limited and has been estimated at 0.8% of measured GFR which corresponds to 1.9 ml/min/1.73 m² (95% CI, 0.2-4.0) for eGFR of 90-119 ml/min/1.73 m² (5). Since our population consists of a relatively healthy population with a mean eGFR of 86.0 (SD 12.4) ml/min/1.73 m², we expect that the influences of bias due to renal function measured by CKD-EPI is limited.

As final remark authors state that our study is limited to a single region in the Netherlands, and suggest conducting a nationwide prospective study to investigate the relationship between renal and vascular function and the development of venous thrombosis. Since replication is essential within evidence based medicine, we support the notion of conducting replication studies. However, many studies have already been conducted on renal function and increased levels of procoagulant factors (that all point toward an association), (2,3) but we are currently the only study that investigated vascular function measured as pulse-wave velocity using MRI and its association with procoagulant factors. In addition to such replication studies, also the application of novel methodologies such as Mendelian Randomization could provide causal inference on whether renal or vascular function plays a role in the etiology of venous thrombosis (6, 7, 8) as the precise relation of how impaired

renal/vascular function results in high levels of factor VIII and, potentially, venous thrombosis is still unclear (3).

We are thankful for the opportunity to further elaborate on our findings, that showed that in the middle-aged general population impaired renal and vascular function is associated with higher levels of coagulation factors, and we indeed hope that our findings will promote further research on the role of renal and vascular function in the development of venous thrombosis.

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