Authors reply: Urine albumin excretion and the risk of incident atrial fibrillation

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Urine albumin excretion and the risk of incident atrial fibrillation—predictive or aetiological relevance: Authors' reply

We appreciate the continuing interest of Abbasi[1] in the PREVEND cohort. Our article showed that in a community-based cohort increased albumin excretion, and not estimated glomerular filtration rate, was associated with incident AF, even after adjustments for established cardiovascular risk factors.[2] We agree that we cannot rule out unmeasured confounding or reverse causality. Theoretically, a randomized controlled trial or Mendelian randomization may be approaches to provide more causal evidence.[3] However, the Mendelian randomization as brought forward based on GWAS variants are also not immune against unmeasured confounding or reverse causality, simply because the instrumental variable assumptions are not satisfied here (e.g. supported by strong biological understanding). To our knowledge, there is no therapy available that solely targets microalbuminuria that can be investigated to reduce incident AF. In addition, even when such therapies become available a large sample size will be required to perform a randomized trial in the primary prevention setting.

The magnitude of associations can indicate the predictive value of a biomarker, in our case albumin excretion. Indeed potential improvements in prediction need to be formally quantified in terms of calibration, discrimination and net reclassification improvement, before increased albumin excretion can be implemented into the risk prediction of incident AF. As a result of such analysis risk prediction schemes, which need external validation, can be build or modified to better identify those at lowest and highest AF risk. This was however not the aim of our analysis. We sought to investigate in our analysis different measures of renal function such as serum creatinine or cystatin C, estimated glomerular filtration rates, and albumin excretion, in relation to development of AF, and whether the magnitude of effect of renal measures and cardiovascular outcome may be influenced by AF.[2]

Finally, Abbasi brought up an interesting point that there may be a subset of individuals with increased urine albumin that may be considered as high risk for incident AF. Indeed targeting high risk groups specifically may help to reduce their risk of AF. However, more research is needed to study the characteristics of such high risk groups, and which specific therapies are needed. Unfortunately, our number of incident AF cases was rather modest to perform stratified analyses according to different severities of albumin excretion. We hope that our analysis further increases the interest in albumin excretion and its link with AF, and motivate others to help to investigate this further. Such research is warranted to determine whether personalized precision medicine approaches can improve treatment outcomes and minimize adverse events.[4]

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