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EDITORIAL

Nontraditional and traditional factors in renal atherosclerosis

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In this issue of the Netherlands Journal of Medicine, the reader will find two interesting views on traditional and nontraditional risk factors for the progression of renal disease and cardiovascular disease on the one hand, and a new view of a traditional renin-angiotensin system (RAAS) with respect to peritoneal dialysis treatment on the other.

The review by Nanayakkara touches on the toughest problem we currently face in nephrology: patients with renal failure die of cardiovascular disease and we do not understand the mechanism. This is illustrated on the one hand by the 'inverse epidemiology', a horrible term indicating that we do not find the same relationships between traditional risk factors and cardiovascular disease in patients with end-stage renal disease as in people without renal disease. Another factor must have taken control; the authors indicate that the pathophysiological process in end-stage renal disease is probably dominated by an increase in oxidative stress driving inflammation, endothelial dysfunction and anaemia.[1] On top of all this is a disturbance in calcium/phosphate metabolism and a defect in the vascular repair by endothelial progenitor cells.[1] On the other hand, the 'nontraditional' risk factors are unable to explain the increased morbidity and mortality. There is a lack of tools to accurately measure these factors, in particular oxidative stress, in humans, as well as a lack to strongly inhibit these factors. Finally, as is the case for cholesterol and for haemoglobin, these factors fail to fulfil Koch's postulates; this stresses so much the necessity to perform careful clinical testing of hypothetical constructs. All in all, a definitive proof that these factors are of eminent importance is lacking. Hidden in this review are some extremely challenging issues. One is the clear separation of initiating factors for cardiovascular disease (i.e. risk factors), factors that form a reflection of the actual disease process, biomarkers, and factors that are involved in maintenance and repair (such as endothelial progenitor cells). There is currently confusing nomenclature, and the reason that nontraditional risk factors may not assist strongly in predicting cardiovascular disease may well be related to the notion that these factors are indicators of the disease process initiated by the traditional risk factors (e.g. CRP). Second is that, although the model that is presented by the authors is attractive and strongly supported by experimental data, it illustrates the strong need to better understand the clinical pathophysiology of atherosclerosis in renal disease. It clearly is not the traditional cardiovascular disease we have been associating with increased lipids levels and diabetes, but another disease. Finally, the review illustrates the necessity for *in vivo* assessment of the mechanisms and the need for more potent tools to manipulate the mechanisms that favour progression of cardiovascular disease in humans with renal disease.

The second view by Kolesnyk[2] discusses a very traditional risk factor for renal and cardiovascular disease, the RAAS. It sums up the evidence that inhibition of the RAAS is beneficial for the progression renal disease and CVD. Somehow intriguing is that the RAAS is not considered a traditional risk factor, while altogether complying very nicely with Koch's postulates. The authors extend their views beyond the conventional patterns: they consider whether ACEi or ARB administration is beneficial for the membrane function of the peritoneal membrane in peritoneal dialysis patients. The evidence is not extremely strong, but supports a role for angiotensin II in the fibrosis of the peritoneal membrane. These authors take a stand for a traditional factor in the process that limits the application of peritoneal dialysis, fibrosis of the peritoneal membrane. Implications of local RAAS activity have substantially accumulated in the last decade and a role of the RAAS in the pathophysiology of peritoneal membrane pathology is likely. They also emphasise that the involvement of the RAAS in the progression of renal disease in transplant patients is unresolved; this in the face of all the strong evidence supporting a role for the RAAS in chronic kidney disease. It so much emphasises that the RAAS will never be really traditional.

It is very nice to have these two views in one issue of the Journal, the one emphasising a new mechanism, the other emphasising a new role for an old mechanism. The authors are to be complimented for their summaries and views of where things stand in these two areas. We are now at the stage where these issues will need to be translated from theory to practice; one more call for translational studies with joint efforts of basic researchers and clinicians. One of the tools we have at hand is applying the knowledge about the RAAS as much as we can, and we should. The other is to perform genuine translational research, using patient materials, bringing this to the lab and then back again to the clinic. It would not be a surprise if these studies would again place angiotensin II very central in the pathogenesis of renal disease.

REFERENCES

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