Response to 'Is inflammation the missing link between low fat mass and low survival in hemodialysis patients?'

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Dr Tsilpanilis[1] has proposed an interesting hypothesis that a low fat mass may play a causative role in poor survival by inducing enhanced inflammatory responses. Although this possibility was not discussed in our recent paper,[2] describing the inverse association between fat mass and mortality risk in hemodialysis patients, it may be another explanation for the reverse epidemiology in the dialysis population.

It is important to note that most of studies reporting the reverse epidemiology were based on data of mortality, not occurrence of cardiovascular event, for example, as an end point. These studies are reporting that obese dialysis patients have a lower risk of death, but they are not saying that obese dialysis patients have a lower possibility to have cardiovascular events. According to the data from Japanese Society for Dialysis Therapy,[3] the risk of death from myocardial infarction or heart failure was inversely associated with body mass index in 39 725 non-diabetic hemodialysis patients. In contrast, the risk of occurrence of new myocardial infarction had no significant association with body mass index in the same report,[4] suggesting that a higher body mass index is protective against death after getting heart disease. Thus, it is clear that the risk of death consists of two components, namely the risk of event occurrence and the risk of death following the event (fatality).[5] As we previously discussed,[6] hemodialysis patients have several times higher risk of occurrence of cardiovascular events than the general population, and several times higher risk of fatality after getting a cardiovascular event. The product of these two components explains the 10–30 times higher risk of death due to cardiovascular disease in the hemodialysis population.[7]

The reverse epidemiology among hemodialysis patients gives us many hints to understand the real problems they have. We speculate that wasting associated with chronic inflammation in uremia plays an important role in the elevated risk of fatality. To improve their outcomes, further studies are needed to test individual hypotheses in observational and interventional settings.

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Urotensin in ESRD: Not so surprising

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To the Editor: We read with interest the nice review on urotensin (UTN) by Dr N Ashton.[1] While commenting on papers by our group, reporting (unexpected) inverse relationships of UTN with brain natriuretic peptide (BNP), sympathetic activity, and other biomarkers of cardiovascular risk and with incident cardiovascular events, Dr N Ashton[1] says that '… possible explanation for this apparent anomaly is … that the relationship between plasma UII and cardiovascular events is disease-specific'. We believe that this explanation is unlikely because, evidence is emerging that in coronary syndromes (i.e. a condition where high UTN has long been considered as a marker of high cardiovascular risk) low rather than high UTN predicts adverse outcomes.[2,3] Furthermore, still unpublished results by our group show that UTN is inversely related with left ventricular mass and mean wall thickness (the muscular component of the left ventricular) in the end-stage renal disease population. These findings are again apparently counterintuitive when compared with studies in the rat or in '*in vitro*' models, showing that UTN causes myocardial cell hypertrophy and myocardial fibrosis.[4] We feel that interpreting UTN as a 'bad guy' in human pathophysiology and extrapolating results of animal models to humans is a risky exercise at this stage of knowledge. We do fully agree with the concluding comments of the editorial '…whether… (urotensin)… role is protective or causal remains to be determined'. Studies in humans based on specific antagonists of this most intriguing peptide are needed to understand whether UTN is noxious or protective in man.

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