Thus, the three major goals of future biomarker studies, as discussed in our review, should be the following: (1) to differentiate types of AKI at the time of diagnosis (acute tubular necrosis vs. prerenal vs. other); (2) to predict or diagnose AKI earlier than the ‘delayed’ clinical diagnosis via creatinine; (3) to predict hard outcomes (need for dialysis, length of stay, death) at the time of injury. In the absence of associations between biomarkers and these hard end points, the availability of another biomarker that ‘mimics’ creatinine will not be beneficial in advancing the field of AKI. We would encourage Ferrannini et al. to perform the analyses we have mentioned in order to determine how cystatin C performs for predicting these types of end points.


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Dialysis hypotension: don’t blame the targets

To the Editor: The article by Davenport et al.1 suggests that improved blood pressure control increases intradialytic hypotension. It is unlikely that the reported higher incidence of hypotension is caused by trying to achieve the Renal Association targets alone.

In a study of 991 dialysis treatments in 111 patients over a 3-week period, we documented predialysis blood pressures of 136.9 ± 23.4/67.8 ± 14.0 mm Hg and postdialysis blood pressures of 133.0 ± 24.0/65.8 ± 12.5 mm Hg. The Renal Association targets were achieved by 56.8% of patients predialysis, 44.1% postdialysis, and 37.8% achieved both targets. Intradialytic hypotension occurred in 2.4% of all treatments. No significant differences were demonstrated in the blood pressure, interdialytic weight gains or prescribed medication of those who experienced hypotension and those who did not.

Two critical factors implemented in our unit may contribute to these findings. We recognize that short dialysis times make ultrafiltration more difficult to tolerate and increase the potential for hypotension. Longer treatment times are utilized whenever possible with the modal dialysis time being 4.5 h. Our center utilizes postdilution hemodiafiltration as standard. There is increasing evidence that the use of hemodiafiltration is associated with improvements in blood pressure control, incidence of intradialytic hypotension and a reduction in mortality.2-4

Preadialysis hypertension does not obviate hypotension episodes2 and not having targets for blood pressure control will not necessarily reduce the frequency of hypotension episodes. When improved control of blood pressure is desired, modifications to the dialysis treatment itself should be considered as part of the management strategy.

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Response to ‘Dialysis hypotension: don’t blame the targets’

High blood pressure is a major health issue in all regions of the world,1 and myocardial infarction and stroke are the commonest causes of death and disability worldwide.2 However, although there is a strong relationship between blood pressure and the risk of cardio- and cerebrovascular disease in the general population,1,2 this relationship is less clear for hemodialysis patients, despite the increased incidence of hypertension in this patient group. Assuming a normal distribution, then the 95% confidence limits for pre-dialysis blood pressure recordings were 183/95–91/39 mm Hg, and 181/91–85/41 mm Hg post-dialysis recordings for the patients dialysing in Kilmarnock, and as such only just over one-third of patients achieved the current KDOQI blood pressure targets. Thus even in a single unit,
using hemodialfiltration rather than standard hemodialysis and dialysing patients for a modal dialysis session time of 4.5 h, only a minority of patients were able to achieve the KDOQI and previous UK Renal Association blood pressure targets,3 in keeping with our multicenter study.4 The UK Renal Association, recently revised its guidelines and withdrew specific targets for pre- and post-dialysis blood pressure, on the basis of a lack of evidence-based data.5

However this does not necessarily imply that blood pressure control is not important for hemodialysis patients. It may be that, compared to the general population, the etiology of hypertension may be more complex, although sodium and volume overload play an important role in determining blood pressure control.6 In addition, although pre- and post-hemodialysis blood pressure recordings are relatively simple to perform in clinical practice, they may not accurately reflect interdialytic blood pressure control.

Intradialytic hypotension remains a major side effect of standard outpatient hemodialysis,7 and is, in part, related to interdialytic weight gain and increased ultrafiltration requirement.8 One potential side effect of strict pre- and post-blood pressure targets could be an increased incidence of symptomatic intradialytic hypotension. Intradialytic hypotension has been shown to be associated with both myocardial and cerebral ischemia,9 and in particular repetitive myocardial stunning could exacerbate myocardial fibrosis and so potentially predispose to cardiac arrhythmias. Thus, although blood pressure control is a vital part in the management of the hemodialysis patient, more study is required to determine which blood pressure measurements should be used for setting any future clinical target.


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Dietary alkalinization and darusentan for prevention of decline in glomerular filtration rate in rats fed a casein diet


To the Editor: To the best of our knowledge, human studies and meta-analyses on low-protein diets as a measure for the prevention of progression of renal disease have never differentiated between sources of protein.1,2 We therefore read with great interest the report by Phisitkul et al.,3 in which it is shown that a diet in which protein is derived from casein is associated with a more rapid decline in glomerular filtration rate in remnant kidneys in rats than a diet in which protein is derived from soy. Large variation in effect of low-protein diets on progression of renal disease between different human studies may therefore be the consequence of variation in the prescription of the preferred source of protein in a low-protein diet rather than the consequence of publication bias favoring low-protein diets.1 In our opinion, the study by Phisitkul et al. challenges the currently held view that the benefit of a low-protein diet in slowing down progression in human renal disease is negligible.4 New studies and meta-analyses should be performed in which sources of protein and potentially individual amino acids are taken into account before it is decided whether the effect is negligible for all low-protein diets.

Phisitkul et al. performed additional experiments and analyses from which they conclude that the casein-induced renal injury is mediated by metabolic acidosis through endothelin A receptors. Their conclusion that metabolic acidosis is important is substantiated by experiments in which they show that rats on casein diet have metabolic acidosis and that decline in glomerular filtration rate can be prevented by alkalinization with either sodium bicarbonate (if concomitant blood pressure elevation by the associated acidosis and that decline in glomerular filtration rate occurring in rats on casein diet. As far as we can oversee, however, the authors did not perform experiments reported in the paper that substantiate their overall conclusion that casein-induced renal injury is mediated by metabolic acidosis through endothelin A receptors. In the experiments they performed, neither daily net acid excretion, $\text{NH}_4^+$ excretion, nor total acid excretion in urine was affected by darusentan treatment. Systemic metabolic acidosis in rats on casein diet was also not affected by treatment with darusentan. Thus, treatment with darusentan seems to block the deleterious effect of casein diet on renal injury independent of its effect on metabolic acidosis rather than dependent on it. It is important that this issue is clarified, because acknowledgment of independent pathways holds the prospect of identification of intriguing

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