Volume expansion is one of the most important factors that results in higher levels of blood pressure in patients with chronic kidney disease. This has been known for many years, and led to the original description of the concept of dry weight in 1967. This is especially important in patients with end-stage renal disease who require dialysis for volume control. Inadequate control of volume or inability to establish and maintain an appropriate dry weight for a dialysis patient may be an important factor in contributing to excess mortality. In this issue of Hypertension, Agarwal has importantly demonstrated the value of relative plasma volume slope monitoring in predicting overall mortality among >300 patients on long-term hemodialysis. A simple cross-sectional analysis of relative plasma volume slope during dialysis was predictive of mortality independent of conventional and unconventional cardiovascular risk factors, independent of ultrafiltration volume, ultrafiltration rate, ultrafiltration volume per kilogram, ultrafiltration rate index per postdialysis weight, and interdialytic ambulatory blood pressure. Why is the relative plasma volume slope such a powerful predictor for mortality? Is it simply that steeper slopes of relative plasma volume monitoring are associated with greater likelihood of the attainment of a more euvoletic state and, thus, may put less stretch and strain on the myocardium?

Probing for dry weight in clinical practice can be complicated. It is an inexact clinical science. The clinical examination is not always helpful to assess volume. Changes in body mass because of alterations in nutrition and dietary electrolyte and volume consumptions may complicate the process of dry weight assessment and achievement. Inadequate achievement of dry weight results in higher levels of blood pressure. Often, more antihypertensive medication is added as a consequence. Thus, a vicious cycle may ensue, whereby more volume-dependent hypertension is treated with vasodilators, which may make it more difficult to remove sufficient volume on hemodialysis to achieve dry weight. Thus, many hemodialysis patients end up on multiple medications for blood pressure control, at the expense of greater central blood volume and associated pressure-volume overload of the myocardium. The latter situation, if prolonged, may lead to remodeling and restructuring of the heart and my possibly induce heart failure and arrhythmias.

In some patients, efforts to achieve dry weight may result in uncomfortable symptoms. This may be more of an issue in patients with excessive interdialytic weight gain or those receiving too many antihypertensive medications. Although strategies such as reducing dialysate sodium concentration to reduce thirst and interdialytic weight gain may help some, symptomatology with weight reduction during dialysis remains a significant problem in many patients. Volume may be more effectively removed with linear sodium modeling or sequential ultrafiltration. The latter technique often requires more dialysis time, which may limit its applicability in some patients.

Thus, the development of a simple, safe, and reproducible technique to objectively assess the response to volume reduction may be important to achieve and maintain an appropriate dry weight. This may also be important in those dialysis patients who have reactive increases in blood pressure with volume removal. Relative plasma volume monitoring uses photo-optical technology to noninvasively measure absolute hematocrit through a transparent chamber attached to the arterial end of the dialyzer. The percentage of blood volume change during dialysis can be calculated. The slope of relative plasma volume change is a function of the removal of fluid and the plasma refill rate. Patients who are volume overloaded will have a high refill rate and a flat slope. Patients closer to dry weight will have a lower plasma refill rate and a steeper slope. Observational studies support the practice of probing dry weight that there is less antihypertensive drug use, lower left ventricular mass, better ventricular function, and fewer episodes of intradialytic hypotension.

Relative plasma volume monitoring has been used to guide dry-weight management in pediatric dialysis patients and has resulted in lower interdialytic ambulatory blood pressure and fewer hospitalizations. It is quite possible that similar observations would occur in adults. Agarwal et al have demonstrated previously that relative plasma monitoring can assist in probing dry weight and could predict subsequent reduction of interdialytic ambulatory blood pressure; those dialysis patients who initially had the flatter slopes had the greatest decline in blood pressure on probing dry weight. He has also demonstrated that interdialytic blood pressure is of importance in predicting mortality in dialysis patients.

The Figure is an example of relative plasma volume slope monitoring in a dialysis patient receiving 4 antihypertensive medications at baseline. Note that there is no change in relative plasma volume slope at baseline. With subsequent probing of dry weight over the next 8 weeks there was an

Powerful Indicators of Increased Mortality Among Hemodialysis Patients

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reduction in his volume by 2 kilograms. As a result, his relative plasma volume slope changed from flat to negative. His interdialytic blood pressure improved by >20/10 mm Hg despite no adjustments in his antihypertensive medication. It is likely that, with continued reduction in dry weight, he could be removed from some antihypertensive medication.

As Agarwal pointed out in his article, there are some important limitations to his observations. Perhaps the most important was that he used a single cross-sectional measurement of relative plasma volume monitoring. Longitudinal measurements of relative plasma volume slope monitoring would answer the question as to whether changes in relative plasma volume slopes are of prognostic importance. More likely than not, this would be the case. Yet, it is still surprising that a single measurement has such important predictive value.

In this study, he dichotomized the relative plasma volume slope changes. Albeit arbitrary, it was predictive of mortality outcome. An important question has to do with whether there is an optimal threshold or slope for determining mortality benefit? Also important would be the opportunity to evaluate the relationship between slope change of relative plasma volume monitoring with consequent change in 44-hour interdialytic systolic and diastolic blood pressures. This could tie together changes in relative plasma volume slope, dry weight, and blood pressure. Would steeper relative plasma slopes be associated with regression of left ventricular hypertrophy and improved diastolic and systolic functions of the heart? Might there be less risk of arrhythmia?

There is much debate about optimal blood pressure goals and cardiovascular events in dialysis patients. Some have suggested that there is a “reverse epidemiology” compared with the general population in that there is not a continuous relationship between blood pressure and cardiovascular events. The importance of the data from the Agarwal report should emphasize that the achievement of dry weight may be an important confounding factor when assessing the relationship of blood pressure and cardiovascular events.

Unfortunately, in clinical practice, more physicians use medication-directed approaches for blood pressure control in dialysis patients as opposed to probing dry weight. It is easier and often more acceptable to patients. This may result in flatter relative plasma volume slopes and may paradoxically increase the risk for mortality. Some studies have shown a direct correlation between the number of antihypertensive medications used in dialysis patients and levels of blood pressure. The importance of this study is that it indicates that a safe, simple technique may be useful from a cross-sectional standpoint to assess risk for mortality in hemodialysis patients. Future studies will be required to evaluate the benefits of monitoring relative plasma volume slopes longitudinally and to see whether close attention to volume control as opposed to just the blood pressure goals may influence cardiovascular mortality. Steeper relative plasma volume slopes in patients on nocturnal hemodialysis may explain the improved opportunity of achieving dry weight and reduction of blood pressure with the use of fewer antihypertensive medications. At last, we may have a strategy to objectively direct dry-weight management! The next hurdle is to individualize the approach for dry-weight maintenance in dialysis patients, especially if it proves to be important with regard to mortality.

Disclosures

None.

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