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Blood pressure instability during hemodialysis

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Most patients with end-stage renal disease (ESRD) maintained on hemodialysis have chronic hypertension. However, hypotension is a frequent complication of hemodialysis, probably because of impaired baroreflex function. Less frequently, increases in pressure can be a complication of hemodialysis. Detailed studies of patients with these abnormalities in arterial pressure during hemodialysis may yield insights into the regulation of arterial pressure during ESRD.

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Blood pressure is frequently increased in end-stage renal disease (ESRD), and chronic hypertension contributes significantly to the high incidence of cardiovascular disease and the markedly reduced lifespan of hemodialysis patients.[1,2] Volume expansion in ESRD is an important contributor to this hypertension, and, as a consequence, adequate control of blood pressure can be difficult or impossible despite multidrug antihypertension regimens.[1–3] The endemic nature of persistently high blood pressure in ESRD has a paradoxical effect on epidemiological studies: normotension and hypotension become surrogate markers for comorbid conditions with arterial underfilling, such as congestive heart failure.[4] In this circumstance, lower blood pressure correlates with poor outcome, and the association of high blood pressure with its clinical complications can be obscured. Nonetheless, clinical studies in hypertensive patients with ESRD show that improvement of the hypertension leads to a diminution of morbidity and mortality and that hypertension in ESRD is deleterious to health and inimical to long life.

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However, if volume is a key element in the problem of chronic hypertension in ESRD, why is volume removal by hemodialysis not an effective solution? The answer, generally, lies in the high incidence of hypotension during hemodialysis that limits removal of extracellular fluid volume.[1,5,6] The 'dry weight' goal for a dialysis treatment is empirically derived and reflects the weight that just avoids precipitating symptomatic decreases in blood pressure.[5,6] The reflexes of the hemodialysis nurse faced with symptomatic hypotension are telltale: the transmembrane potential is decreased, and intravenous saline is administered. The 'dry weight' goal is thus raised, but at a cost of increased volume and hypertension between treatments.

Many potential etiologies are often listed for intradialytic hypotension, and this usually signals a hopeless morass.[7] However, one set of mechanisms occurs in a majority of patients with significant frequency and therefore merits critical attention. The abrupt removal of fluid by hemodialysis acutely decreases intravascular volume and can compromise ventricular preload. Depending on the rate of refilling and any impairment of ventricular compliance, cardiac output can decline, and the maintenance of blood pressure now hinges on a reflex increase in systemic vascular resistance. However, for many patients this fluid removal frequently fails to elicit the systemic vasoconstriction expected for acute decreases of blood volume, and occasionally, frank vasodilation is observed.[8,9]

Deranged regulation of vascular tone during hemodialysis is not generally related to a defect in the renin–angiotensin II or catecholamine response. Plasma renin activity rises during hemodialysis with significant fluid removal, and plasma catecholamine levels frequently increase. However, we recently implicated a role for vasopressin in the failure of systemic vascular resistance to increase with fluid removal during hemodialysis (S van der Zee *et al.*, *J Am Soc Nephrol* 2003; **14**: 41A, abstr.). We confirmed the observation that plasma vasopressin does not rise during hemodialysis with significant ultrafiltration and discovered that vasopressin administration stabilizes blood pressure. Vasopressin as a treatment for intradialytic hypotension could, paradoxically, provide a treatment for hypertension between treatments: Improved control of extracellular volume overload may normalize blood pressure and improve the response to antihypertensive agents. The benefits from improved control of extracellular fluid volume are suggested by the experience with extended-duration hemodialysis. Extended duration permits a decreased rate of fluid removal and improves hemodynamic stability on hemodialysis, thus resulting in better extracellular fluid control and diminished chronic hypertension.

A less common and much more obscure derangement of blood pressure control during hemodialysis in ESRD patients are increases in pressure; that is, intradialytic hypertension.[10] This syndrome is the subject of investigation by Chou *et al.* in this issue.[11] Fifteen control patients and 15 hypertension-prone patients were studied. The baseline blood pressure in the hypertension group was significantly higher than that of the control and increased throughout the treatment. The blood volume declined significantly in the control group but not the hypertensive group. Given comparable ultrafiltration volumes for the groups, this was consistent with faster refilling of

the intravascular volume in the hypertension-prone group. These findings suggested the possibility that hypertension was driven by increased cardiac output. However, this was considered unlikely, because indirect determination of the cardiac output suggested that it decreased comparably in both groups and that systemic vascular resistance increased in the hypertension-prone group.

Activation of the renin–angiotensin II system and activation of the sympathetic nervous system have been suggested as underlying defects for this syndrome, and renin, norepinephrine, and epinephrine were measured before and at the conclusion of dialysis. The control group showed the expected pattern with hemodialysis and removal of more than 2 liters of fluid: renin, norepinephrine, and epinephrine all rose significantly.[11] Interestingly, these hormones did not increase in the hypertension-prone patients. Further, an analysis of heart rate variability showed in controls, but not hypertension-prone patients, a significant elevation of the power index during the course of treatment that is indicative of increased sympathetic-to-parasympathetic activity. Neither increased hematocrit nor hypokalemia could explain the increase in resistance, and the authors suggest endothelial dysfunction with a nitric oxide–endothelin imbalance as a focus for future investigation. Vasopressin would also be a reasonable target for investigation, but, for now, the pathophysiology underlying increased resistance during hemodialysis with hypertension-prone patients remains a mystery.

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Detection of pattern of myocardial fibrosis by contrast-enhanced MRI: Is redefinition of uremic cardiomyopathy necessary for management of patients?

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Cardiac magnetic resonance imaging (CMR) can detect cardiac tissue components for several kinds of cardiac myopathies. Mark *et al.* found two patterns of late gadolinium enhancement (LGE) in patients with uremic cardiomyopathy: focal LGE and diffuse LGE. The impact of these contrast-enhanced CMR findings on clinical outcomes warrants assessment in future studies.

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Cardiovascular disease is the main cause of death in patients with end-stage renal failure and accounts for almost 40% of the deaths in this population.[1] However, uremic cardiomyopathy has not been investigated in detail, and its etiology and pathophysiology are unclear. One study showed that the pathologic characteristics of uremic cardiomyopathy are severe myocyte hypertrophy, occasionally with disarray, and a high percentage area of fibrosis, and the extent of left ventricular fibrosis was a strong predictor of cardiac death.[2] The causes of these pathologic changes may be associated with volume overload, pressure overload, malnutrition, anemia, uremic toxins, high catecholamine levels, and hyperparathyroidism. Hypertrophy due to pressure and volume overload is associated with a distinct myocyte phenotype and differential induction of peptide growth factors, which may stimulate both the loss and the hypertrophic growth of myocytes. Collagen fibers and other interstitial matrix molecules increase during hypertrophy, followed by the loss of myocytes due to myocardial injury.

From a clinical point of view, it is important to assess the cardiac function

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