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PERITONEAL DIALYSIS AND PRESERVATION OF RESIDUAL RENAL FUNCTION

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Residual renal function (RRF) is now generally recognized as an important factor in the prognosis of patients on dialysis. This review summarizes the differences between peritoneal dialysis (PD) and hemodialysis (HD) with regard to RRF. The literature supports PD as having a more beneficial effect on RRF.

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Preservation of renal function is important not only for pre-dialysis patients, but also for dialysis patients. Residual renal function (RRF) has been found to be an important predictor of outcome in both hemodialysis (HD) and peritoneal dialysis (PD) patients.

EVIDENCE FOR THE BENEFIT OF RRF IN DIALYSIS PATIENTS

Residual renal function not only provides small-solute clearance, but also plays an important role in maintaining fluid balance, phosphorus control, and removal of middle-molecular uremic toxins and shows strong inverse relationships with valvular calcification and cardiac hypertrophy in dialysis patients. The original CANUSA study, in which total (peritoneal and renal) small-solute clearance significantly predicted mortality, resulted in the assumption that peritoneal small-solute clearance must be important (1). However, a reanalysis of CANUSA by Bargman *et al.* (2), who compared renal small-solute clearance with volume of urine, found that peritoneal clearance lost statistical significance. Each increment of 5 L/1.73 m^2 per week in residual kidney glomerular filtration rate (GFR) was associated with a 12% reduction in the relative risk (RR) of death, but no similar association with peritoneal creatinine clearance was found. Every 250 mL of urine output daily showed a 36% reduction in mortality.

The ADEMEX study, a prospective randomized trial evaluating the effects of increased peritoneal small-solute clearances in 965 prevalent patients, showed no survival advantage for patients with an increase in peritoneal clearance, even when the data were adjusted for age, nutrition, and comorbidity. For each 10 L/1.73 m^2 weekly increment in RRF, an 11% decrease in the RR of death was observed; no similar association with peritoneal creatinine clearance was found (3).

The Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD)—a prospective, multicenter, observational cohort study of incident dialysis patients—analyzed 740 HD patients and showed that RRF and delivered Kt/V were both positively associated with better survival (4). Each weekly increase of 1 unit in renal Kt/V was associated with a RR for death of 0.44, and each increase in delivered Kt/V was associated with a RR for death of 0.76. However, the effect of delivered Kt/V on mortality was strongly dependent on the presence of RRF. The effect of RRF appeared to be stronger than the effect of delivered Kt/V.

POSSIBLE MECHANISMS OF BENEFIT OF RRF IN DIALYSIS

The importance of RRF is probably a result of the additional effects of native kidneys, such as better removal of middle and larger molecular weight toxins and organic acids than occurs during dialysis. Renal function includes not only glomerular filtration, but also tubular secretion and reabsorption, and various endocrine functions. Tubular secretion is especially important for the removal of organic acids such as hippuric acid, the plasma concentration of which, in patients treated with HD, is directly correlated with residual renal creatinine clearance and not with dialysis dose.

The presence of RRF is associated with lower β_2-microglobulin (β2m) and *p*-cresol levels. A study per-

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formed by Bammens and colleagues (5), which included 30 end-stage renal disease patients treated with PD, showed that the total and peritoneal clearances of β2m, *p*-cresol, and phosphate are significantly lower than the clearances of the uremic retention solutes urea nitrogen and creatinine. Their study demonstrated that the elimination of β2m and *p*-cresol depends largely on RRF.

In dialysis patients, residual renal function improves fluid control. It reduces the need for strict fluid restriction and plays an important role in the prevention of fluid overload in PD patients. This better volume control may help to optimize blood pressure control and to prevent or reduce the cardiac hypertrophy that is commonly seen in dialysis patients.

Cardiac hypertrophy is an important predictor of mortality in dialysis patients. Worsening volume control with loss of RRF may be one of the important contributing factors for the adverse cardiovascular outcomes observed in anuric patients. Menon *et al.* reported that blood pressure control worsened with time on PD as RRF declined—an effect that may partly be attributed to poor fluid control (6).

Anuric dialysis patients have a more adverse metabolic and cardiovascular profile, more severe anemia with greater erythropoietin resistance, more inflammation, higher Ca×P, worse nutrition, more hypertension, greater cardiac hypertrophy, and greater overall and cardiovascular mortality than patients with preserved RRF. By itself, RRF may have a beneficial effect on parameters of nutrition, and it is important to determine RRF over time, even in chronic HD patients (7).

IS THE RATE OF DECLINE OF RRF DIFFERENT IN HD AND IN PD?

Patients treated with PD have a lower risk of RRF loss than do patients treated with HD. This observation was first reported by Rottembourg *et al.* (8), who carried out a study to compare, over an 18-month period, residual GFR (rGFR) measured by creatinine clearance in two matched groups of 25 patients with end-stage renal disease. One group was treated with continuous ambulatory PD; the other, with maintenance hemodialysis. From the beginning of dialysis treatment to the 18th month, a significant and progressive decrease in GFR was observed in the group of patients treated with HD. In the PD group, GFR and peritoneal clearances remained stable. Later, the decline rates of rGFR in 522 incident HD and PD patients were evaluated prospectively in structured follow-up assessments (NECOSAD). A faster decline of rGFR in HD patients than in PD patients was found (9).

It has been reported that PD might delay the progression of advanced renal failure, preserving or improving RRF. Recovery of renal function sufficient to come off dialysis has been described in several reports of patients with interstitial nephritis and malignant hypertension. In a small series, Berlanga *et al.* (10) showed that PD might slow the natural progression of renal disease. If PD indeed slows the progression of chronic kidney disease, that effect would be a major advantage of early-start, incremental PD. However, the issue is not clear, because no controlled studies have addressed the influence of incremental PD on RRF, and no homogeneous definition of incremental PD exists. Several authors have reported on the stability of RRF in a number of patients started on incremental PD.

Several mechanisms may account for better preservation of RRF in PD. Fewer abrupt fluctuations in volume and osmotic load are seen in PD patients, leading to a more stable hemodynamic status. This hemodynamic stability is probably associated with more stable glomerular capillary pressure and more constant glomerular filtration. Episodes of renal ischemia because of rapid changes in osmolality and contraction of circulating volume are more common during HD. Mild overhydration of some patients on PD may contribute to better RRF preservation. The peritoneal membrane is more biocompatible than the membranes used in hemodialyzers, where RRF may be damaged by repeated exposure to inflammatory mediators such as interleukin 1 generated by the extracorporeal circulation (11).

DO BIOCOMPATIBLE PD SOLUTIONS OR BIOCOMPATIBLE DIALYZER MEMBRANES HAVE ANY ADVANTAGE IN RELATION TO RRF?

New solutions in multi-compartment solution bags with a higher PH and reduced glucose degradation products are accepted as more biocompatible. Biocompatible dialysis solutions are thought to improve the function and viability of peritoneal mesothelial cells and to preserve RRF. In the Euro-Balance study, 86 patients were randomized either to group I, which started with standard PD fluids for 12 weeks (phase I), and then switched to Balance solution (Fresenius Medical Care, Bad Homburg, Germany) for 12 weeks (phase II), or to group II, which was treated in reverse order. A total of 71 patients completed the study. Renal urea and creatinine clearances were higher in both treatment arms after patients were exposed to Balance solution (12). However, some studies showed no difference in RRF with these solutions.

Szeto *et al.* (13) randomized 50 new PD patients to a conventional lactate-buffered fluid (control) and a pH-neutral, lactate-buffered solution low in glucose

degradation products (Balance). They reported observing no difference in urine output or RRF at 1 year.

Fan *et al.* (14) conducted a randomized controlled study comparing the use of biocompatible solution with standard solutions in 93 incident PD patients during a 1-year period. Changes in the normalized mean urea and creatinine clearances were the same for both groups, with no significant differences in secondary endpoints.

The inflammation generated by the use of bioincompatible cellulose HD membranes is generally thought to be associated with a more rapid decline in RRF. Some studies have reported that the use of biocompatible membranes such as polysulphone is associated with a slower rate of decline of RRF than that seen with traditional bioincompatible cellulose membranes (15,16). However, some studies failed to demonstrate a significant difference in the rate of decline of RRF between synthetic and cellulose dialyzer membranes (17).

SUMMARY

One potential strategy to preserve RRF may be to preferentially use PD over HD in all incident patients with RRF. In PD patients, preservation of RRF is as important as preservation of the long-term viability of the peritoneal membrane. Additional studies are needed to determine if advantages are seen with longer-term use of the new glucose-sparing, more biocompatible PD regimes.

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