The incidence and prevalence of ESRD in the United States continues to increase. Currently there are over 26,000 patients maintained on peritoneal dialysis. Mortality rates have fallen over the past several years, but long-term survival remains poor, with only 11% of peritoneal dialysis patients surviving past 10 years. Cardiovascular disease accounts for most deaths, and dialysis patients have many traditional and nontraditional cardiovascular risk factors. Lowering of these risk factors has not resulted in reduced cardiovascular morbidity and mortality in dialysis patients. Maneuvers to improve long-term peritoneal dialysis patient survival must therefore focus on modifiable risk factors including residual renal function, peritoneal membrane integrity, rate of infections, and peritoneal dialysis center size. This article reviews strategies for preserving residual renal function and peritoneal membrane integrity as well as strategies for reducing the rate of infections to enhance long-term survival in peritoneal dialysis patients.


Preservation of Residual Renal Function

Background

The Kidney Disease Outcomes Quality Initiative (KDOQI) gives specific guidelines for PD adequacy because higher total small solute clearance (peritoneal + residual renal) is associated with improved survival on PD. As demonstrated in the
Table 1. Risk factors in PD patients

<table>
<thead>
<tr>
<th>Nonmodifiable Risk Factors</th>
<th>Modifiable Risk Factors</th>
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<tbody>
<tr>
<td>Age</td>
<td>RRF</td>
</tr>
<tr>
<td>Gender</td>
<td>PM integrity</td>
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<tr>
<td>Race/ethnicity</td>
<td>Infection</td>
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<td>Diabetic status</td>
<td>Dialysis center size</td>
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<td>ESRD etiology</td>
<td>Patient education and training</td>
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<td>Patient genetics</td>
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Canada-USA (CANUSA) study, an increase of 0.1 unit of weekly Kt/V urea is associated with a 5% decrease in the relative risk of death (9). However, it is imperative to recognize that the decreased risk of death is clearly not due to enhanced peritoneal small solute clearance. In fact, both the ADEMEM study (10) and that of Lo et al. (11) performed in Hong Kong failed to demonstrate salutary effects on mortality by increasing peritoneal Kt/V above a minimal level of 1.5 to 1.7. Rather, the beneficial effects of increased solute clearance demonstrated in the CANUSA study are attributable only to residual renal function (RRF). A reanalysis of the CANUSA study demonstrated that for each 5-L/wk per 1.73 m² increase in residual GFR (rGFR), there was a 12% decrease in the relative risk of death [RR 0.88, 95% confidence interval (CI) 0.83 to 0.94]. Neither peritoneal creatinine clearance nor net peritoneal ultrafiltration (UF) was associated with patient survival. Similar results were found in The Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD-2), in which each 1-ml/min increase in rGFR was associated with a 12% reduction in mortality, and peritoneal clearance had no significant effect on patient survival (RR = 0.91, P = 0.47) (13). Greater urine volume is also associated with improved survival. For each 250-ml increment in urine volume, there is a 36% reduction in overall mortality (RR 0.64, 95% CI 0.51 to 0.80) (12). Furthermore, it appears that even more so than baseline RRF, the rate of decline in RRF predicts outcome. A recent study of 270 PD patients with urine output >100 ml at the start of PD followed for 4 years found that patients with the most rapid rate of decline in RRF had the worst survival and an increased risk of technique failure (14). Multivariate analysis confirmed that the rate of RRF decline was a more powerful prognostic factor than baseline RRF (HR 693, 95% CI 15.8 to 30475, P = 0.0007 and HR 0.78, 95% CI 0.63 to 0.96, P = 0.02, respectively).

In addition to better solute and volume removal, RRF is also associated with decreased levels of circulating inflammatory markers, reduced blood pressure (BP), reduced left ventricular hypertrophy, and higher hemoglobin levels (15,16). However, it should be noted that a direct causal relationship has not been demonstrated. There are also data that reduced RRF confers a higher risk of peritonitis. In a study of 204 PD patients, time to the first PD peritonitis episode was significantly longer in patients with higher rGFR (P < 0.001), and the risk of peritonitis decreased by 19% for every 1-ml/min/1.73 m² increase in rGFR (HR 0.81, 95% CI 0.74 to 0.88, P < 0.01) (17). Thus, preservation of RRF is of great importance for survival in PD patients.

Effects of Angiotensin-Converting Enzyme Inhibitors and Angiotensin Receptor Blockers on RRF

Several studies in the nondialysis population have shown that angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) reduce the rate of renal function loss in diabetic nephropathy and chronic proteinuric nephropathy (18–20). It is reasonable to assume that interventions that slow the decline in renal function in CKD patients would also be effective in dialysis patients. An epidemiologic study of 1032 PD patients found that the use of an ACE inhibitor was independently associated with a decreased risk of RRF loss [adjusted odds ratio (OR) 0.69, P = 0.02] (21). This effect was independent of BP because there was no correlation between mean arterial pressure and loss of RRF [adjusted OR (per 10-mmHg increase in mean arterial pressure) 1.04, P = 0.41]. A small randomized open-label controlled trial of 60 continuous ambulatory peritoneal dialysis (CAPD) patients comparing ramipril (5 mg/d) to no treatment found that the decline in rGFR over 1 year was significantly lower in the ramipril group versus the control group (2.07 ml/min/1.73 m² versus 3.00 ml/min/1.73 m², P = 0.03) (22). Furthermore, patients receiving ramipril also had a lower risk of anuria than did the control group (adjusted HR 0.58, 95% CI 0.36 to 0.94). ARBs have also been shown to be effective in reducing the rate of kidney function loss in PD patients. In a small, prospective randomized trial of 38 CAPD patients, those using valsartan experienced a slower decrease in GFRF and urine volume at 24 months compared with the control group (P < 0.01) (23). Furthermore, ACE inhibitor/ARB therapy has been shown to reduce mortality in patients on PD (24). A retrospective study of 306 PD patients found that the use of an ACE inhibitor or an ARB reduced the risk of death by 62% (adjusted HR 0.38, 95% CI 0.23 to 0.63, P < 0.001) (24). This effect was independent of BP; if anything, the ACE inhibitor/ARB-treated patients had higher BP—at entry and during follow-up—than did the untreated group. Thus, the effects of ACE inhibitors/ARBs in PD patients likely extend beyond BP lowering.

Although large randomized trials of the use of ACE inhibitors and/or ARBs in dialysis patients have not been performed, KDOQI guidelines (25) recommend the use of these agents for the treatment of hypertension in patients who have RRF because these agents may help decrease the decline in GFR. This is now standard in our practice. KDOQI guidelines also suggest that these agents be considered for renal protection among normotensive PD patients because the effects of ACE inhibitors and ARBs may extend beyond BP lowering. In both studies of these agents in PD patients, the preservation of renal function was independent of changes in BP. However, it is unclear if normotensive patients were included in these studies. KDOQI opines that there currently is not enough evidence to recommend using these agents in normotensive patients unless they have other indications for their use (i.e., congestive heart failure) (25). We do routinely use ACE inhibitors and/or ARBs in our normotensive patients provided that systolic BP remains at or above 110 mmHg. Individual practitioners may wish to carefully consider the potential benefit of such therapy while monitoring the patient very carefully.
Dialysis Solutions and RRF

Most PD solutions that are currently used are bioincompatible (low pH, high glucose). This results in the production of reactive carbonyl compounds (RCOs) and advanced glycation end products (AGEs), thereby contributing to changes in peritoneal membrane (PM) function, which alter UF and solute transport. These glucose degradation products (GDPs) may also be absorbed from the peritoneum and promote apoptosis in renal tubular epithelial cells, thereby impairing RRF (26). The use of more biocompatible solutions (neutral pH, lactate-buffered, low glucose) has been suggested in some small studies to preserve PM integrity and RRF. Unfortunately, there have not been any well designed large randomized trials evaluating the effects of the different solutions on RRF. The Euro-Balance trial compared the use of a pH-neutral, lactate-buffered, low-GDP fluid (Balance) with standard PD fluid (acidic, lactate buffered) (27). Patients utilizing the low GDP solution had significantly decreased levels of circulating AGEs, inflammatory cytokines, and growth factors compared with patients using standard PD fluid, suggesting preserved PM integrity. Furthermore, patients utilizing Balance demonstrated an increase in RRF (P = 0.007). However, this study has several important limitations that need to be recognized. First, it was not adequately powered to detect changes in RRF. In addition, the short follow-up time (12-week crossover) and the small number of patients enrolled make it difficult to interpret the RRF results. Furthermore, the results may be confounded by the effect of changes in residual volume on urinary creatinine clearance because peritoneal UF decreased and urine volume increased in the patients using Balance. Thus, the Euro-Balance trial does not clearly demonstrate any real differences between the solutions.

The BALNET study (26) is another recent study of incident PD patients randomized to conventional PD solution or Balance solution that found that RRF trended toward being better preserved with the Balance solution (P = 0.057). The BALNET study had longer follow-up compared with the Euro-Balance trial, but baseline rGFR was significantly higher in the group randomized to Balance solution and the study lacked sufficient power to detect a statistically significant difference in RRF between the groups. A recent randomized trial by Fan et al. (28) of biocompatible solutions (Physioneal or Balance) versus conventional solutions found no difference in RRF between the groups. Unlike the previous two trials, this trial was powered to detect differences in RRF between the two groups; however, the short follow-up time in this study (9 months) is an important limitation. The differences in the findings of these three studies may in part be due to differences in the patient populations used. Thus, there are no convincing randomized trials to support the use of biocompatible solutions over standard solutions for the preservation of RRF. Large randomized trials are required to determine if these biocompatible solutions preserve RRF and affect long-term clinical outcomes.

Other Factors

Drugs and interventions that worsen kidney function in CKD patients may also worsen RRF in dialysis patients. Although some studies have found no change in RRF after radiocontrast dye (29,30), contrast should be avoided to the extent possible. If PD patients must undergo a radiocontrast study, they should be well hydrated (although, obviously not excessively so) and the lowest volume of an iso-osmotic or low-osmotic contrast agent should be used. The use of N-acetylcysteine to prevent contrast-induced nephropathy is controversial and there are very few studies evaluating its use in the dialysis population (31). Nonsteroidal anti-inflammatory drugs should be avoided in PD patients with preserved RRF. The use of diuretics in PD patients with RRF is unclear. RRF does not appear to be preserved with diuretics, but diuretics do allow for liberalization of fluid intake and a clinically significant improvement in fluid balance (32). Thus, diuretics should be considered in PD patients to prevent the need for high glucose exchanges for volume removal. Care must be taken to avoid volume contraction and/or hypotension, both of which may impair RRF.

Aminoglycoside antibiotics should be used with caution given the potential for nephrotoxicity. The data regarding aminoglycoside use and RRF are purely observational and contradictory. A retrospective examination of a cohort of 72 patients revealed a greater decrease in kidney function in patients using aminoglycosides compared with other antibiotics (33). However, in a larger, more recent study of 205 PD patients, there was no difference in the slope of kidney function decline in patients treated with or without aminoglycosides (34). The current recommendations by the International Society of Peritoneal Dialysis (ISPD) are that short-term aminoglycoside use (<3 days) is safe but repeated or prolonged courses of aminoglycoside therapy is not advisable (35).

It has been suggested that RRF may be better preserved on truly continuous modalities (CAPD) compared with more intermittent modalities [nightly intermittent peritoneal dialysis (NIPD) and continuous cyclic peritoneal dialysis (CCPD)]. Although many clinicians—including ourselves—consider CCPD a continuous modality, one must recognize that most fluid removal is accomplished only during the night and that the long day dwell results in a significantly smaller degree of solute clearance than occurs during the nighttime exchanges; thus, CCPD also appears to have some intermittent characteristics. In a prospective, randomized trial of 18 patients new to PD, loss of RRF was significantly less among patients treated with CAPD (+0.01 ml/min per month) than those treated with NIPD or CCPD (−0.29 and −0.34 ml/min per month, respectively, P < 0.05) (36). Similar results were found in a larger study of incident dialysis patients because monthly loss of RRF was significantly higher in the intermittent modality group (NIPD or CCPD) compared with the CAPD group (37). In both studies there was no difference in baseline rGFR, mean weekly Kt/V urea, PM integrity, or UF.

The factor(s) responsible for the potentially more rapid decline in RRF seen with the use of more intermittent PD modalities is unknown. Patients on intermittent therapies require larger amounts of hypertonic dialysate and have a less stable osmotic and fluid load. These variations in osmotic and fluid load may alter the hemodynamic status of the patient, resulting in ischemia, which will decrease rGFR.

Recently published analyses of two large databases [Austra-
lia and New Zealand Dialysis and Transplant Registry (ANZDATA) and U.S. Renal Data Service (USRDS) have demonstrated comparable survival in patients performing automated PD compared with those performing CAPD (38,39). However, it should be noted that in neither of these studies was the relationship between PD modality and RRF examined. Thus, one can draw no firm conclusions from these studies regarding the possible clinically relevant effects of differences in RRF—if they existed—in determining survival. Larger randomized prospective trials and further basic science investigations are needed to determine whether, and if so, why CAPD may preserve RRF to a greater extent than does APD. The available data do not allow one to recommend one PD modality over the other. The choice of PD modality should continue to be driven by membrane physiology and patient preference.

**PM Integrity**

**Background**

The PM is a biologic dialysis membrane lined by a monolayer of mesothelial cells. The interstitium underlying the mesothelium is comprised of a gel-like matrix containing collagenous fibers and peritoneal capillaries. Water and solute transport across the PM has been postulated to be mediated by three different sizes of pores. Large pores allow for the transport of macromolecules such as proteins through the PM by convection. Fortunately, these comprise only a small percentage of the total pore area. Small solutes (e.g., urea, creatinine, and potassium), along with approximately half of the water removed, are transported through small pores, which likely represent intercellular gaps between endothelial cells. Small pores determine the intrinsic permeability of the PM because an increase in the number of perfused capillaries results in an increase of small pores and enhanced small solute transport. The remainder of the ultrafiltrate is transported through ultrasmall pores or aquaporins that are permeable only to water.

The existence of aquaporins in the PM is well established; however, the nature of the large and small pores postulated in the three-pore theory remains uncertain. Evidence has accumulated suggesting that rather than being two distinct structures, the large and small pores may instead represent different functional states of a single entity. This variability is postulated to be due to the density of the pore matrix, a glyocalyx barrier within the pore that determines solute permeability of the pore (40). This glyocalyx barrier is responsive to cytokines and other vascular mediators and may help explain why inflammatory states are associated with higher dialysate-to-plasma creatinine and why long-term PD therapy may result in progressive degradation of the PM. Loss of the PM function is a major factor leading to treatment failure in PD.

The pathophysiological changes that develop in the PM over time are due to several factors, including chronic uremia, exposure to PD solutions, and the response to the presence of the peritoneal catheter itself. Peritoneal dialysate contains many RCOs that result from heat sterilization. Chronic uremia in combination with RCOs results in the formation of AGEs within the PM (41). AGEs promote the secretion of inflammatory cytokines and growth factors that stimulate angiogenesis. Angiogenesis increases vascular permeability, which enhances small solute transport, resulting in faster reabsorption of glucose, early loss of the osmotic gradient, and ultimately UF failure (42,43). Furthermore, the secreted growth factors and uremia itself are associated with the development of peritoneal fibrosis. This fibrotic layer separates the dialyzing solution from the microvessels involved with exchange, eventually leading to decreased effective peritoneal surface area and decreased UF (44). This process may on occasion culminate in the development of encapsulating peritoneal sclerosis. Finally, the presence of the PD catheter itself may result in increased production of inflammatory cytokines, leading to structural and functional changes in the PM (45). It is speculated that the PD catheter itself is a platform for the activation of mesothelial cells that are shed from their basement membrane and for their transition from an epithelial to a fibroblastic phenotype with increased cytokine production within the peritoneal cavity (45).

Patients who develop a high transport state have a worse prognosis. In a large study of 3702 incident PD patients, a high transporter status was an independent predictor of technique failure and mortality (adjusted HR 1.23, 95% CI 1.02 to 1.49, \( P = 0.03 \) and adjusted HR 1.34, 95% CI 1.05 to 1.79, \( P = 0.02 \), respectively) (46). This observation has been confirmed by several other studies (47–49). Not all patients who have UF failure develop a high transport state. However, these patients still have an increased risk of mortality. In the European APD Outcomes (EAPOS) study, patients who did not achieve the target UF of 750 ml/d had an increased risk of mortality (\( P = 0.0047 \)) (50). Therefore, preservation of the PM is essential for improving long-term patient survival.

A period of peritoneal “resting” has been shown to restore peritoneal UF capacity and reduce the use of hypertonic dialysis solutions in PD patients with a high transport state. CAPD patients with a high transport state who underwent peritoneal resting by switching to HD for 4 weeks demonstrated a significant decrease in creatinine mass transfer coefficient (19 ± 5 to 15 ± 2, \( P < 0.05 \)) and a significant increase in UF (498 ± 278 to 881 ± 388 ml, \( P < 0.001 \)) (51). Similar results were found in CAPD patients who underwent peritoneal resting by changing to daytime ambulatory PD with a nocturnal “empty belly” (52); peritoneal resting improved the UF capacity and decreased the use of hypertonic solutions. Peritoneal resting appears to improve UF by decreasing peritoneal thickening and hyperpermeability to glucose (53).

**Dialysis Fluids and PM Integrity**

High glucose exposure has been directly implicated in the development of a high transport state because of the production of RCOs, a GDP. In a prospective study of 22 PD patients followed for 5 years, those who had increasing solute transport were exposed to significantly more hypertonic glucose (3.86% dextrose) during the first 4 years than did the patients with stable solute transport (54). However, the high transporters also had much less RRF, which is another reason they were exposed to more hypertonic fluid. Low-glucose solutions or more biocompatible solutions may preserve PM integrity and prevent the development of a high transport status. Icodextrin is a
glucose polymer developed to enhance UF in patients with increased solute transport. The high molecular weight of icodextrin creates colloid oncotic pressure that promotes UF at a much lower rate, but for a more extended time than does dextrose. When used for a long (≥8 hours) dwell, the UF obtained exceeds that possible with even 3.86% dextrose. Icodextrin use may be associated with preservation of PM function. In EAPOS (55), longitudinal changes in membrane function were least apparent in the patients using icodextrin from the start of PD. Patients using icodextrin had no change in UF capacity whereas patients using 2.27% or 3.86% dextrose had a significant decrease in UF capacity at 2 years. Similarly, solute transport at 2 years was unchanged in the icodextrin group (solute transport ratio at baseline: 0.72, at 24 months: 0.73; P > 0.05) compared with the group treated with glucose in which the ratio increased (solute transport ratio at baseline: 0.74, at 24 months: 0.84; P < 0.001).

The effects of biocompatible PD solutions other than icodextrin on membrane integrity have also been evaluated. The Euro-Balance trial (27) demonstrated that PM integrity was preserved, as indicated by an increase in CA125, reflecting increased mesothelial cell homeostasis, but peritoneal UF was decreased with Balance solution. There was also a significant decrease in the levels of circulating AGEs and inflammatory cytokines. In contrast, Fan et al. (28) found no difference in PM function between patients using biocompatible solutions (Physioneal or Balance) or conventional dialysis solutions. A recent study by Lee et al. (56) also found no significant improvement in PD technique survival with biocompatible solutions. Only one observational study has found an improvement in patient survival with biocompatible solutions, but the two groups being compared were inherently different and the difference in survival could therefore be due to patient characteristics, including genetic factors, rather than to the dialysis solutions (57).

To date there has been no randomized trial to examine a difference in patient survival with biocompatible solutions. The data regarding the effect of these low-GDP solutions on membrane integrity and preservation of RRF are contradictory, but there are more positive than negative studies. These biocompatible solutions may yet prove to have long-term clinical benefits, but longer and larger randomized trials are needed. Currently, only one biocompatible solution, icodextrin, is approved in the United States.

Renin-Angiotensin Aldosterone System Inhibition and PM Integrity

Experimental studies have demonstrated that ACE inhibitors protect the PM from hypertonic glucose-induced alterations (fibrosis and neoangiogenesis). This appears to be due to the effect of ACE inhibitors on angiotensin II (57). Acting as a growth factor, angiotensin II stimulates the release of inflammatory cytokines such as TNF-α and IL-6 and the pro-fibrotic factor TGF-β (58). When human peritoneal mesothelial cells are exposed to high glucose concentrations in vitro, angiotensin II upregulates TGF-β1 (59). In a study of rats exposed to high-glucose solutions (3.86%), rats receiving oral enalapril had reduced TGF-β1 levels, reduced peritoneal thickness, and improved UF and solute transport compared with rats receiving placebo (60). In humans, a small cohort study of PD patients over 2 years found that small solute transport was decreased in patients treated with ACE inhibitor/ARBs, suggesting that these drugs prevent the increase in mass transfer area coefficients that occur in long-term PD (61). A recent prospective study of 217 CAPD patients from NECOSAD also found that treatment with ACE inhibitors/ARBs prevented the increase in small solute transport in long-term PD (P = 0.01) (62), although no statistically significant effects on patient or technique survival were observed. In a small, randomized trial of patients assigned to valsartan or placebo, valsartan significantly increased creatinine clearance (P < 0.05) and Kt/V urea (P < 0.01) compared with placebo (23). Thus, protection of the PM may be yet another reason for prescribing ACE inhibitors and ARBs to PD patients, but large randomized trials are needed to confirm these potential membrane protective effects.

The effects of aldosterone antagonists on peritoneal fibrosis have recently been evaluated in rats. Nishimura and colleagues (63) developed a new rat model of peritoneal fibrosis and evaluated the effects of oral spironolactone on peritoneal structure and function. Spironolactone resulted in significant suppression of peritoneal thickening, macrophages, and TGF-β. Furthermore, peritoneal function was significantly improved by spironolactone. The role of spironolactone in the preservation of peritoneal structure and function has not yet been evaluated in humans.

Preventing Infections

Background

Infections are the most frequent and important complication of PD and often result in catheter removal and discontinuation of PD. PD-related infections include peritonitis and infections of the PD catheter, including exit-site and tunnel infections. Peritonitis is associated with adverse patient outcomes including decreased technique and patient survival. For every 0.5-per-year increase in peritonitis rate, the risk of death increases by 4% (64). In a recent study in PD patients in the United States and Canada, the rate of peritonitis was 1 per 30 patient-months. Eighteen percent of the episodes resulted in removal of the PD catheter and 3.5% resulted in death (65).

General approaches targeted to minimizing the occurrence of peritonitis have been extensively reviewed elsewhere and will therefore be reiterated only briefly herein. Suffice it to say that the roles of prophylactic antibiotic administration with anti-Staphylococcal coverage before catheter placement, patient training of adequate duration, exit-site care, and treatment for Staphylococcus aureus nasal carriage have all been well established and use of each of these measures should now be “standard of care” for every PD patient. A single dose of an intravenous antibiotic (first-generation cephalosporin or vancomycin) should be given at the time of catheter insertion (66,67).

The ISPD recommends the use of prophylactic antibiotics for patients undergoing a dental procedure or a colonoscopy, and it also recommends that the abdomen be emptied of fluid before any procedure involving the abdomen or pelvis (35). Although this is indeed our standard practice, it is important to
recognize that, as the authors of the ISPD guidelines acknowledge, there are in fact no studies demonstrating the efficacy of this approach. The PD community may wish to examine these practices more critically, perhaps with a randomized clinical trial.

All patients must be trained in aseptic techniques and in the proper response to contamination. The duration of patient training regarding PD is also important. Patients receiving enhanced training (mean training time of 29 hours) have significantly fewer exit-site infections (1 every 31.8 months) compared with patients receiving standard training (mean training time of 22.6 hours; exit-site infection rate of 1 every 18 months, \( P = 0.003 \)) (68). Enhanced training also results in a trend toward a decrease in the rate of peritonitis compared with standard training (1 infection every 36.7 months versus 1 every 28.2 months, \( P = 0.098 \)). The exit site should be washed daily with antibacterial soap or an antiseptic. Daily application of topical antibiotics should be performed; although not demonstrated in all centers, there are some data suggesting that topical gentamicin may be the preferred agent. In a randomized, double-blind trial of 0.1% gentamicin cream versus 2% mupirocin cream, catheter infection rates (0.23/yr versus 0.54/yr, \( P = 0.005 \)) and peritonitis rates (0.35/yr versus 0.52/yr, \( P = 0.03 \)) were significantly lower with gentamicin cream (69).

**Other Considerations**

GDPs result in the release of AGEs that damage the PM, induce inflammation, and may thereby increase the risk of infection (70). Thus, the use of low-GDP dialysis solutions (biocompatible solutions) may result in a decrease in the incidence of PD-related infections. A recent small study evaluating 120 CAPD patients found significantly lower rates of peritonitis (\( P = 0.002 \)) and exit-site infections (\( P = 0.02 \)) in patients using low-GDP dialysis solutions compared with those using conventional solutions. The peritonitis-free interval was 47.6 months with the low-GDP dialysis solutions and only 20 months with the conventional solutions (70). The decrease in peritonitis rates may be a consequence of enhanced phagocytic activity of peritoneal macrophages and preserved dendritic cell differentiation and function as has been observed previously with the use of neutral \( \mathrm{pH} \) (7.4) dialysate solutions (71,72). Further studies are necessary to identify the potential role of low-GDP dialysate solutions in reducing the risk of peritonitis because, at this time, there is no strong evidence supporting one solution over another.

Is there a difference in peritonitis rates between continuous and intermittent modalities? Data regarding this question are unclear. Most studies have found that the rate of peritonitis is lower with CCPD than CAPD (presumably related to fewer connections and disconnections), but others have reported that the rate is higher or the same (73–75). At this time, neither modality can be recommended over the other to decrease the risk of peritonitis.

If a patient does experience peritonitis, what factors predispose him/her to catheter loss? In a large retrospective study of CAPD peritonitis, independent predictors of PD catheter loss included number of organisms cultured, organism type (\( P = 0.044 \), anaerobes \( P = 0.006 \), and fungi \( P < 0.001 \)), low serum albumin (3.4 versus 3.7 mg/dl, \( P = 0.004 \)), PD effluent leukocyte count remaining above 100 per \( \mu \)l after 5 days (\( P < 0.001 \)), and concomitant exit-site or tunnel infection (\( P = 0.005 \) and \( P < 0.001 \), respectively) (76). Knowledge of these predictors may help guide clinicians to best treat their patients and may lead to future therapeutic and preventive methods for peritonitis.

**Dialysis Center Size**

A dialysis center’s experience with and degree of specialization toward PD strongly affects patient outcomes. Studies have found that as the cumulative numbers of PD patients treated increases, technique failure decreases significantly (2,77). In a recent study of over 40,000 PD patients, center size correlated inversely with the frequency of catheter problems (\( P < 0.0001 \)), inadequate dialysis (\( P < 0.01 \)), and infectious complications (\( P < 0.01 \)) (2). The effect of PD center size on patient mortality has been evaluated in only one study. In a study of 17,900 PD patients, larger center size was associated with a significant decrease in mortality (RR 0.71 for a center with cumulative experience of >500 patients compared with a RR 0.95 for a center with 100 to 199 patients, \( P < 0.05 \)) (7). Center size may not be modifiable for an individual patient, but the data suggest that patient outcomes may be improved if units in the same geographic area were to combine into one large center. Further studies are needed to determine which center characteristics (e.g., physician or nurse experience, nurse-to-patient ratio, etc.) affect patient outcomes.

**Conclusions**

Although mortality rates in PD patients continue to decline, long-term survival remains poor. CVD accounts for most patient deaths, and unfortunately strategies aimed at reducing traditional and nontraditional cardiovascular risk factors have not been shown to be beneficial in dialysis patients. There are

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**Figure 1.** Flow diagram for strategies to improve long-term survival of PD patients.
several patient factors that affect survival that cannot be modified, such as age and diabetes status. Thus, attention needs to be placed on modifiable factors such as RRF, PM integrity, and PD-related infections, all of which are strongly associated with long-term survival in PD patients. Priority needs to be given to strategies aimed at the preservation of RRF and membrane integrity as well as the prevention and treatment of infections. ACE inhibitors and ARBs should be used in all hypertensive PD patients—and perhaps all PD patients if tolerated—because there is potential for preservation of RRF and membrane integrity as well as the prevention and treatment of infections. The use of biocompatible solutions may help preserve RRF and membrane integrity and may decrease the incidence of infections, but further studies are needed. A flow diagram depicting the various strategies to enhance long-term survival in PD patients is presented in Figure 1.

Disclosures
None.

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