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Authors

Khawar, Osman
Kalantar-Zadeh, Kamyar
Lo, Wai Kei
et al.

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Is the Declining Use of Long-Term Peritoneal Dialysis Justified by Outcome Data?

Osman Khawar,^{*,†} Kamyar Kalantar-Zadeh,^{*,†} Wai Kei Lo,[‡] David Johnson,[§] and Rajnish Mehrotra^{*,†}

^{*}Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, and [†]David Geffen School of Medicine at UCLA, Los Angeles, California; [‡]Tung-Wah Hospital, Hong Kong; and [§]University of Queensland at Princess Alexandra Hospital, Brisbane, Australia

In the past decade, peritoneal dialysis use among patients with end-stage renal disease has declined in many countries. Studies from the United States indicate that many academic centers do not have adequate resources to train fellows, most incident dialysis patients are not offered peritoneal dialysis, and more than half of dialysis clinics do not have the infrastructure to support peritoneal dialysis. Some are concerned that the outcomes of peritoneal dialysis and maintenance hemodialysis patients may not be equivalent, a notion that is not supported by outcome studies. Given the effect of modality selection on patients' lifestyle, attempts to conduct a randomized, controlled comparison of maintenance hemodialysis and peritoneal dialysis have been unsuccessful. Most observational studies showed that peritoneal dialysis is associated with a survival advantage that diminishes over time; it is unclear whether any of the differences over time are attributable to the modality. Between 1996 and 2003, the early outcomes of peritoneal dialysis patients further improved, whereas those for maintenance hemodialysis patients remained unchanged. Differences in outcomes may be due to residual statistical confounding; however, several biologic mechanisms can be postulated: The early survival advantage may be related to the better preservation of residual renal function with peritoneal dialysis, and the diminution of the survival advantage may be related to worsened volume control. There is a need for large observational and interventional studies among peritoneal dialysis patients to sustain and enforce the improvements in both dialysis therapies.

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In the past 30 yr, the number of patients with treated ESRD has progressively increased. Given the paucity of organ donors, maintenance dialysis is the dominant form of treatment for ESRD, and it is estimated that in 2004, more than 1.3 million patients were undergoing some form of dialysis treatment worldwide (1). The incidence and prevalence rates for treated ESRD vary widely among various parts of the world; these differences seem to be, in large part, a reflection of the availability of financial support for renal replacement therapies (1). The United States and Japan account for almost one half of all of the maintenance dialysis patients worldwide (2). Renal replacement therapies are provided at an enormous financial cost. In 2003, the ESRD program cost US Medicare approximately \$18.3 billion, and the total ESRD costs exceeded \$30 billion (2). These costs are likely to continue to go up: In the United States, the ESRD population is projected to exceed 700,000 by 2015 (3). In Australia, the cumulative discounted total cost of renal replacement therapy (RRT) for all current and new patients with ESRD will be approximately \$3.4 billion in today's currency by the end of this decade, rising to almost \$5.1

billion by 2019 (4). Despite these high costs, these individuals experience poor rehabilitation, high hospitalization rates, and increased mortality (2). In the United States, approximately two thirds of all dialysis patients die within 5 yr of initiation of dialysis treatment, a 5-yr survival that is worse than that experienced by many patients with cancer (2).

More than 80% of dialysis patients are treated with maintenance hemodialysis (MHD), and peritoneal dialysis (PD) is the dominant modality for home dialysis (1). Since the introduction of continuous ambulatory PD, studies have explored the question of whether dialysis modality *per se* independently affects patient outcomes, including an early attempt at a randomized, controlled trial (5–7). In this review, we present our analysis of the current state of knowledge about the effects of dialysis modality on patient outcomes in context of the declining proportion of patients who undergo PD in many parts of the world.

Declining Use of PD

The striking variation in the proportion of patients who undergo PD in various parts of the world has been repeatedly analyzed (8–10). The relative use of different dialysis modalities has substantial cost implications. Studies have repeatedly shown that the payor costs for PD are lower than that for MHD. In a recent analysis of a random sample of Medicare recipients (11), even after adjustment for the younger age and lower

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Correspondence: Dr. Rajnish Mehrotra, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, 1124 West Carson Street, Torrance, CA 90502. Phone: 310-222-3891; Fax: 310-782-1837; E-mail: rmehrotra@labiomed.org

comorbidity, the annual cost for PD patients were \$12,000 lower than that for MHD patients. When a switch from PD to MHD was made in the first 3 yr, cost savings decreased to \$10,000 but increased to \$20,000 when no switch was made. Overall, the cost advantage of PD persisted even when the higher probability of transfer of PD patients to MHD was accounted for. Similar cost advantages have been demonstrated in Australia, where the annual cost for home HD was \$38,028, for long-term PD was \$48,303, and for hospital MHD was \$70,349 (4). Thus, a higher use of PD has the potential to result in substantial cost savings, and understanding the causes of varying PD use has potentially significant public health implications (12). In addition to the cost advantages, patients who select PD report a greater satisfaction with care; this is very likely to be a result of education and training that go with the selection of the dialysis modality (13). These observations strengthen the case for greater use of PD.

Studies from Europe and North America indicate that more than two thirds of incident patients do not have a medical contraindication for either MHD or PD (14–17). These findings are consistent with the notion put forth more than a decade ago that modality selection is dictated largely by nonmedical factors (8). In the United States, the initiation of PD has historically been low and has never exceeded 15 to 16% of incident or prevalent maintenance dialysis patients (18). Surveys (19) of US academic medical centers indicated that many training programs do not have sufficient number of patients or devote enough time for fellows to develop expertise in the care of PD patients; more than half of practicing nephrologists in the United States reported that they were trained mainly in providing care for MHD patients (20,21). Similarly, most incident dialysis patients reported that PD was not offered to them as a RRT (17,22). Surprising, the probability of offering PD as a method of treatment for ESRD was not related to the presence of medical contraindications to the therapy (17). Finally, more than half of the dialysis units in the United States do not have the infrastructure to support PD. Paradoxical, geographic areas that are likely to benefit the most from availability of home dialysis—rural and remote rural areas—are the least likely to have the infrastructure for home dialysis (23). Furthermore, industry experts estimate that 20% of nephrologists provide care to 80% of PD patients in the United States; PD became and has remained a “niche” rather than a “mainstream” RRT (18). These observations point to an overall substantial lack of enthusiasm for PD among providers in the United States and probably explains the low initiation rate for the therapy.

Against this background of low use, the proportion of patients who undergo PD has declined further in the past decade in the United States (Figure 1) (2,18), and a >50% decline in the proportion of incident patients who commence treatment with PD has occurred (24). The United States is not the only country with declining use of PD. It is a phenomenon seen in North America and Australia and New Zealand; trends in Europe are more varied (Figures 2 and 3) (2). The reasons for this decline remain speculative, and some of the proposed hypotheses are summarized in Table 1. Of the proposed hypotheses, only the relationship of increasing age, body size, and comorbidity bur-

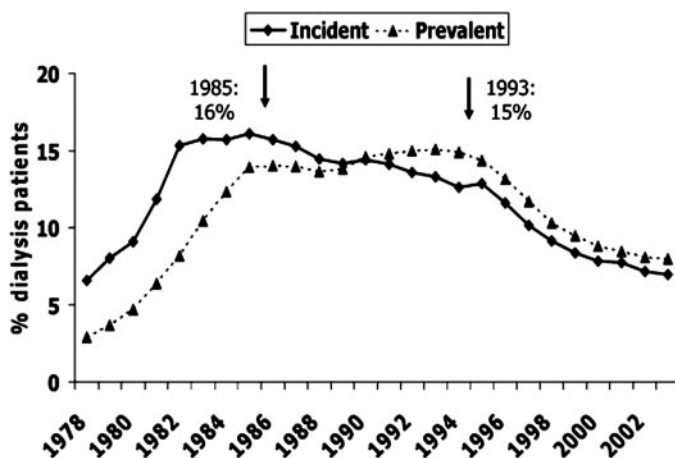


Figure 1. Trends in the proportion of incident and prevalent maintenance dialysis patients who underwent peritoneal dialysis (PD) in the United States from 1978 through 2003.

den of incident dialysis patients has been studied. During an 8-yr period, starting from 1996, the age and body size of the incident dialysis patient in the United States increased, but the burden of coexisting illnesses did not change (24). Furthermore, PD use declined in every age group and strata of body size and coexisting illnesses (24); therefore, the change in age, body size, and coexisting disease burden are insufficient to explain the decrease in PD use in the United States. The systematic decline in use is likely a result of system-wide factors in the delivery of care (Table 1). Rapid increase in the number of MHD facilities; expansion of the preexisting clinics by increasing the number of HD stations; and increase in the number of HD shifts, including adding early morning, late evening, or overnight shifts, all may have translated into greater use of MHD. There is a need to test each of these hypotheses to explain the continuing decline in PD use in many parts of the world.

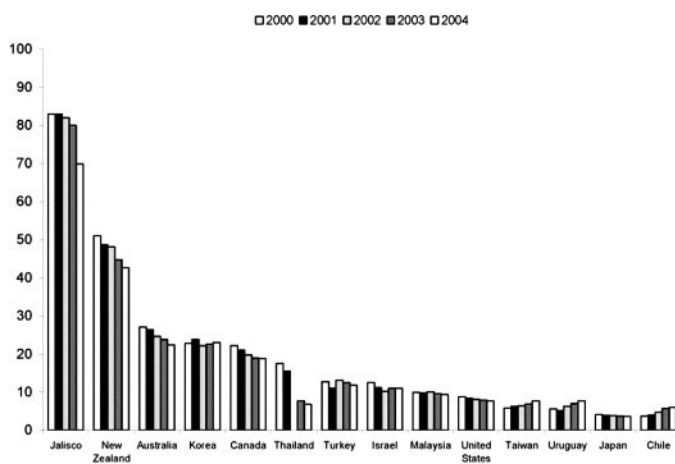


Figure 2. Trends in the proportion of prevalent maintenance dialysis patients who underwent PD in the Americas, Asia, and Australia and New Zealand from 2000 through 2004.

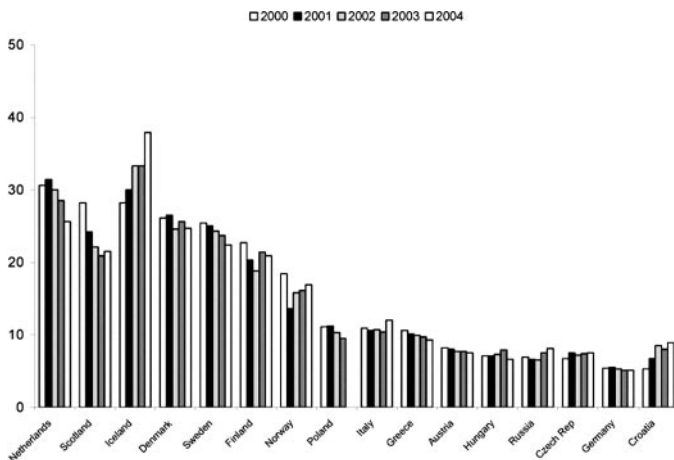


Figure 3. Trends in the proportion of prevalent maintenance dialysis patients who underwent PD in Europe from 2000 through 2004.

Table 1. Several hypotheses that have been proposed to explain the decrease in use of PD^a

Hypotheses invoking medical causes
increasing age and comorbidity of ESRD population
concern about inferior outcomes with PD
belief about better outcomes with high-frequency hemodialysis
inability of inadequately trained nephrologists to prescribe complex regimens required to implement small solute clearance guidelines
Hypotheses invoking "system issues"/nonmedical causes
increasing density of hemodialysis units
corporatization of delivery of dialysis care, particularly in the United States
changing patterns for reimbursement for delivery of dialysis care

^aPD, peritoneal dialysis.

Comparative Survival Data between MHD and PD

The best study design to determine whether the dialysis modality has an independent effect on survival is a randomized, controlled trial; however, to randomly assign patients to two therapies with such disparate effects on their lifestyle is an uphill task. This was aptly demonstrated by the recent attempt undertaken as a part of the Netherlands Co-operative Study on Dialysis (NECOSAD); when patients were educated about the two dialysis modalities, more than 90% of the eligible patients wanted a choice in the selection of the RRT and refused to be randomly assigned (25). It is unlikely that another randomized, controlled trial will be attempted any time soon; therefore, one has to depend on observational studies for intermodality comparisons.

For the first 20 yr after the introduction of continuous ambulatory PD, numerous single-center and regional studies attempted to compare the outcomes in PD and MHD (26). Although the results of these studies were variable, the emerging consensus seemed to be that the outcomes with both of the modalities were similar; however, a study from the US Renal Data System raised questions about this assumption: In that analysis of comparative outcomes of prevalent MHD and PD patients with 170,700 patient-years of follow-up, the death rate for PD patients was 19% higher than that for MHD patients (27). Studies that were conducted in the past decade clearly demonstrated that there is a significant interaction between dialysis vintage and modality (28,29). In other words, the risk for death for PD patients, relative to that for MHD patients, changes over time. It follows, then, that using a prevalent cohort of patients, as used in this study, may have been inappropriate, and an optimal comparison would entail a prospective study of incident dialysis patients.

Several large studies (28,30–37) of incident dialysis patients have since been conducted, and the key studies are summarized in Table 2. Even though some of the findings differed between the various studies, intermodality comparisons using registries from various parts of the world may allow one to conclude that patients who undergo PD may have a survival advantage during the first few years of RRT; the magnitude and duration of time for this advantage seems to be affected by the patient's age, diabetic status, and the presence or absence of other coexisting illnesses. Generally, the lower the disease burden (*viz*, young patients without diabetes or other coexisting illnesses), the greater the apparent survival advantage seen with PD. Conversely, the greater the disease burden (*viz*, older patients with diabetes and other coexisting illnesses), the lower the apparent benefit with PD; however, it must be emphasized yet again that these registry comparisons are fraught with significant limitations: The assignment of patients to modality is nonrandom, and the comorbidity or laboratory data in large registries are often limited. The registries with more detailed data, such as the Danish registry, generally have the smallest number of patients (35); therefore, it remains unclear whether any of the outcome differences are causal and attributable to the dialysis modality. Nevertheless, in the context of this discussion, the data from registry studies summarized in Table 2 suggest that PD is associated with outcomes that are at least equivalent for most subgroups of incident patients.

In an apparent attempt to overcome some of the limitations of the registry studies, the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) study was launched as a prospective, cohort study of comparisons of outcomes between MHD and PD patients (34). The CHOICE investigators reported no difference between outcomes during the first year, but in the second year, PD patients had a significantly increased risk for death (34). Although the efforts of these investigators were laudable, the study included only 1041 patients, substantially lower than the registry studies. Because the PD patients were selected from relatively fewer dialysis programs than the MHD patients, some have questioned the external validity of the study (38). Furthermore, concern has been raised that the mul-

Table 2. Selected registry or multicenter studies comparing the survival of incident MHD and PD patients^a

Country	Publication Year (Reference)	Sample Size		Cohort Period	Follow-Up	Key Findings	
		HD	PD				
North America Canada	1997 (28)	7792	2841	1990 to 1994	Up to 5 yr	27% lower mortality with PD; survival advantage with PD in all subgroups except older (>65 yr) patients with diabetes (equal risk to HD); PD advantage concentrated to first 2 yr	
	2000 (31)	248	93	1993 to 1998	Maximum of 6 mo (through January 1, 1998)	No significant survival advantage for either modality or in any major subgroups defined by age, gender, or diabetic status.	
United States	1994 (30)	3376	681	1986 to 1987	Through April 1, 1990	NS survival advantage for PD among patients without diabetes; significantly higher (26%) mortality among patients who had diabetes and underwent PD compared with HD	
	1999 (32)	99,048	18,110	1994 to 1996	Through June 30, 1997	For patients who survived at least 90 d, PD was associated with a survival advantage in all sub-groups except older (>55 yr) patients with diabetes; increased risk seen among female patients with diabetes; survival advantage with PD seen during first 3 to 12 mo	
	2004 (33)	352,706	46,234	1995 to 2000	Maximum of 3 yr (through September 2001)	Analyses for patients who survived at least 90 d; for patients with no additional baseline comorbidity, PD was associated with better survival among patients without diabetes and younger patients with diabetes (<45 yr) but similar survival among older patients with diabetes; for patients with at least one baseline comorbidity, similar survival among patients without diabetes and younger patients with diabetes but higher mortality among older patients with diabetes	
	2005 (34)	767	274	1995 to 1998	Mean 2.4 yr; up to 7 yr	Dialysis modality defined as therapy on an average of 10 wk after first dialysis; similar survival during the first year, significantly higher mortality among PD patients during second year; no significant interaction among age, diabetic status, and cardiovascular comorbidity	
Europe Denmark	2002 (35)	3281	1640	1990 to 1999		PD was associated with 35% lower mortality on as-treated analysis; better survival seen in all subgroups on the basis of age and diabetic status; advantage limited to first 2 yr	
	Netherlands	2003 (36)	742	480	1996 to 1998	Through September 2002	Analyses restricted to patients who survived 90 d; no significant differences in survival during the first 24 mo; PD associated with higher risk for death between 24 and 48 mo, especially among individuals \geq 60 yr of age.
		2006 (37)	10,841	5802	1987 to 2002	Through December 2002	Analyses restricted to patients who survived 90 d; in younger patients, PD was associated with superior survival during first 15 mo, irrespective of diabetic status; in older patients, survival advantage only among those without diabetes

^aMHD, maintenance hemodialysis.

tivariate models in the study may be overadjusted. Using over-adjusted models is not a trivial problem, because systematic differences in laboratory parameters may be the result of the dialysis modality itself. For example, serum C-reactive protein was measured after an average of 5 mo after the first dialysis treatment (34). The serum C-reactive protein was higher among MHD patients, and it is possible that this difference may be a function of the dialysis modality (*viz*, greater systemic inflammation arising from the use of tunneled venous catheters). Finally, the findings of this study are inconsistent with virtually all registry studies of incident patients (Table 2).

A review of Table 2 also demonstrates that most of the studies included cohorts largely from the 1980s and 1990s; only one included patients who were incident after 2000. There are data to suggest that the outcomes of MHD and PD patients may have differentially changed during this period (24). In an analysis of the US Renal Data System data during an 8-yr period (1996 to 2003), the 12-mo outcomes of 606,777 incident patients were studied. The hazards for either death or transfer to MHD during 12 mo progressively decreased from 1996 to 1997 to 2002 to 2003, largely as a reduction in mortality (24). This improvement in outcomes of long-term PD patients was confirmed on multivariate analyses; using 1996 to 1997 as a reference, the hazard ratio for technique failure progressively decreased (Figure 4). In contrast, the outcomes of MHD patients remained largely unchanged during the same period (Figure 4) (24). Given these differential change in outcomes among patients who were treated with the two dialysis modalities, the inter-modality comparisons need to be reexamined using a more contemporary cohort.

It is possible that the differential change in outcomes may be

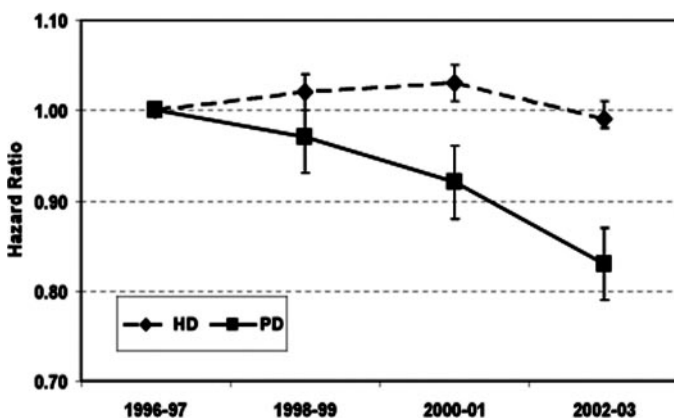


Figure 4. Hazard ratios for incident maintenance hemodialysis (MHD) and PD patients either to die or to transfer to MHD during the first 12 mo. Using 1996 to 1997 as the reference period and adjusting for demographics, case-mix, and laboratory data, the hazard ratios (confidence interval) for patients who started MHD were 1.02 (1.00 to 1.04) from 1998 to 1999; 1.03 (1.01 to 1.05) from 2000 to 2001; and 0.99 (0.98 to 1.01) from 2002 to 2003. The corresponding hazards ratio for patients who started PD were 0.97 (0.93 to 1.02) from 1998 to 1999; 0.92 (0.88 to 0.96) from 2000 to 2001; and 0.83 (0.79 to 0.87) from 2002 to 2003. Reprinted from reference (24), with permission.

a result of more stringent criteria used to select patients who embark on PD therapy in the United States; however, many changes could also account for a greater improvement in outcomes of PD patients. For example, there has been a progressive reduction in peritonitis rates, largely because of a greater use of disconnect systems and use of exit-site antibiotic prophylaxis (39,40). Furthermore, many more centers are using continuous quality improvement programs that may have led to these improvements. Finally, there has been a greater use of automated PD that may, in part, account for the better PD outcomes; however, the role of these and other changes in the improved outcomes remains speculative and needs to be tested in future studies.

Possible Biologic Explanations for Differences in Outcomes by Modality

If one is to accept the notion that treatment with PD may be associated with an early survival advantage in some patient subgroups, then an important question that follows is, “Is it biologically plausible?” The leading hypothesis to explain the lower mortality among PD patients in the first few years relates to its salutary effect on residual renal function.

The relationship between residual renal function and survival of prevalent PD patients, first reported by Maiorca *et al.* (41), has now been repeatedly confirmed (42–46). These findings were further corroborated by the re-analysis of the Canada-USA (CANUSA) study wherein each 5-L/wk per 1.73 m² higher mean of urea and creatinine clearances was associated with a 12% decrease in the relative risk for death (47). The remarkable consistency of these observations provides evidence for the importance of residual renal function to outcomes of PD patients.

The effect of residual renal function on outcomes for MHD patients is not as well studied. In a single-center study of 114 MHD patients, the presence of residual renal function was demonstrated to be protective during a 2-yr period (48). More recently, in a prospective study of 740 incident MHD patients, residual renal function was measured 3 mo after first dialysis treatment and then at 6-mo intervals. Using time-dependent models, during a median follow-up of 1.7 yr, every unit of residual renal Kt/V_{urea} was associated with 66% lower adjusted hazard for death (49). This magnitude of effect of residual renal function on survival is not unlike that seen among patients who undergo PD.

The foregoing discussion underscores the importance of residual renal function on outcomes of maintenance dialysis patients, irrespective of dialysis modality. Numerous studies have compared the rate of loss of residual renal function in MHD and PD patients, and the key studies (50–56) are summarized in Table 3. All but one study (53) demonstrated the relative advantage of PD over MHD in the preservation of residual renal function, even when one accounts for informative censoring. The participants who were undergoing MHD and enrolled in the only study that demonstrated equivalent rates of loss of residual renal function were treated with ultrapure water, a therapy that is not widely available (56). Thus, the preponderance of evidence suggests that PD is associated with slower rate

Table 3. Results of some of the studies that compared the rate of decline of residual renal function among HD and PD patients^a

Author, Year (Reference)	No. of Patients (HD/PD)	Study Design	Baseline Measure	Index of Renal Function	% Decline/Mo (HD/PD)	PD Decline Rate (% of HD Rate)
Rottembourg <i>et al.</i> , 1983 (50)	25/25	Prospective	Before dialysis	Ccr	6.0/1.2	80
Cancarini <i>et al.</i> , 1986 (51)	75/86	Retrospective		Ccr	5.8/2.9	50
Lysaght <i>et al.</i> , 1991 (52)	57/48	Retrospective	Before and after dialysis	Ccr	7.0/2.2	69
Misra <i>et al.</i> , 2001 (53)	40/103	Retrospective	After dialysis	Mean	7.0/2.2	69
Lang <i>et al.</i> , 2001 (54)	30/15	Prospective	Dialysis start	Ccr	9.4/5.0	47
Jansen <i>et al.</i> , 2002 (55)	279/243	Prospective	Before dialysis	Mean	10.7/8.1	24
McKane <i>et al.</i> , 2002 (56)	300/175	Retrospective	Before or after dialysis	Urea CI	Rate of decline similar in HD and PD	Rate of decline similar in HD and PD

^aAll HD patients underwent dialysis with high-flux dialyzers and ultrapure water. Ccr, timed creatinine clearance; Mean, mean of timed urea and creatinine clearances; Urea CI, timed urea clearance. Reproduced, with permission, from: Teitelbaum I, Mohrotra R, Golper TA, Burkart JM, Piraino P: Peritoneal Dialysis. In *Diseases of the Kidney*, edited by Schrier RW, 8th Ed., Lippincott Williams & Wilkins, 2007, pp 2612–2647.

of loss of residual renal function, and this may explain the consistent, early survival advantage in favor of PD in many subgroups of incident patients; however, the practice of both MHD and PD has changed, and comparisons using a more contemporary cohort is needed.

Alternatively, the early survival advantage of PD patients may be a result of a higher risk for early death among MHD patients. Sicker patients are more likely to commence MHD rather than PD, and the differences in outcomes may be a result of residual confounding. Furthermore, in the past decade, the proportion of MHD patients with a tunneled venous catheter increased, and along with it has been an exponential increase in the hospitalization of these patients with septicemia (2,57). Moreover, patients who experience a single episode of septicemia have a higher risk for death, myocardial infarction, peripheral vascular disease, and stroke (58). During the same period, the risk for infectious complications among PD patients decreased. Given that most MHD patients in the United States begin maintenance dialysis with a venous catheter, the survival advantage for PD patients may be a result of the lower risk for serious, systemic infectious (59).

With increasing dialysis vintage, the survival advantage of PD diminishes, and some subgroups seem to experience a higher risk for death. This change in relative risk may result from a change in the characteristics of the two cohorts. Thus, the sickest MHD patients experience early mortality, which may be further exacerbated by the infectious risk imposed by venous catheters. Conversely, the transplantation rate of PD patients is more than twice as much as that of MHD patients in the early period after the start of RRT (24). This, in turn, may remove the healthiest patients from the PD cohort. These two processes may result in the change in relative risk over time between the two modalities.

The leading hypothesis to explain the increase in relative risk for death for PD patients postulates that with increasing dial-

ysis vintage, PD patients become volume overloaded (60,61). Single-center studies suggested that patients who were treated with continuous ambulatory PD had greater worsening of their volume status with increasing dialysis vintage than MHD patients. In addition to the loss of residual renal function, bioincompatible PD solutions may lead to alterations in the peritoneal membrane that further accentuate volume overload. The high concentrations of glucose in conventional peritoneal dialysis fluids, along with glucose degradation products that are generated during heat sterilization, damage the peritoneal membrane, either directly or through the formation of advanced glycosylation end products. The structural changes often include an increase in capillary density and, thus, the effective peritoneal surface area, leading to an increase in peritoneal transport rate (62). This, in turn, leads to reduced peritoneal ultrafiltration capacity, particularly with continuous ambulatory PD using conventional glucose-based fluids (62). These peritoneal changes, coupled with loss of residual renal function, probably underlie the high prevalence of volume overload seen in many PD patients. Several studies (63–65) have shown an inverse relationship between daily peritoneal ultrafiltration volume and mortality, data that are consistent with the notion that reduced ultrafiltration capacity and consequent hypervolemia with increasing dialysis vintage may reverse the early survival advantage with PD.

It has also been argued that, in addition to local changes in the peritoneum, continued exposure to conventional PD solutions may have adverse systemic consequences. The continued absorption of glucose from PD solutions has been implicated in weight gain (generally fat), dyslipidemia, and hyperleptinemia. One recent study of 200 patients with stages 4 to 5 chronic kidney disease reported that PD was independently predictive of development of the metabolic syndrome (66). *Post hoc* analyses of the Euro-Balance trial (67) demonstrated that treatment with a new PD solution with very low concentrations of glucose

Table 4. Summary of some of the studies that evaluated the relationship of body size to outcomes in patients undergoing MHD or PD^a

Author, Year (Reference)	Data Source	Sample Size	Incident/Prevalent	Follow-up (Yr)	Nature of Relationship of Body Size to Mortality
MHD					
Degoulet <i>et al.</i> , 1982 (76)	French, multicenter	1453		5	Higher death rate with lower BMI
Leavey <i>et al.</i> , 1998 (77)	CMAS of USRDS	3607	Prevalent	5	Higher mortality with lower BMI
Fleischmann <i>et al.</i> , 1999 (78)	US, multicenter	1346	Prevalent	1	Higher mortality with lower BMI; lower death risk among overweight/obese
Kopple <i>et al.</i> , 1999 (79)	Fresenius US	12,965	Prevalent	1	Progressive decrease in mortality with increasing weight-for-height with lowest risk in obese patients
Wolfe <i>et al.</i> , 2000 (80)	CMAS and DMMS of USRDS	9165	Prevalent	2	Lower mortality among overweight and obese patients
Leavey <i>et al.</i> , 2001 (81)	DOPPS	9417	Prevalent	4	Progressive decrease in mortality with increasing BMI in both United States and Europe
Port <i>et al.</i> , 2002 (82)	Medicare-covered US	45,967	Prevalent	2	Lowest mortality observed in the highest tertile of BMI
Lowrie <i>et al.</i> , 2002 (83)	Fresenius US	43,334	Prevalent	1	Log risk decreased linearly for weight, weight-for-height, and body surface area; reverse J-shaped for weight/height and BMI
Glanton <i>et al.</i> , 2003 (84)	USRDS	151,027	Incident	2	Obesity associated with lower risk for death with the association stronger in black patients
Abbott <i>et al.</i> , 2004 (85)	DMMS Wave 2 of USRDS	1675	Incident	5	Lowest survival in patients with the lowest BMI, and best survival among obese patients
Stack <i>et al.</i> , 2004 (86)	USRDS	117,309	Incident	2	The relative risk for death was the greatest among patients with lowest BMI and decreased with increasing BMI such that obese patients had the best survival
Johansen <i>et al.</i> , 2004 (87)	USRDS	418,055	Incident	2	Larger body size associated with lower mortality, even at extremely high BMI, in all racial subgroups except Asian
Kalantar-Zadeh <i>et al.</i> , 2005 (88)	DaVita	54,535	Prevalent	2	Higher BMI at baseline, and weight gain over time was associated with the best all-cause mortality
PD					
Johnson <i>et al.</i> , 2000 (89)	Single Australian center	43	Prevalent	3	Higher BMI associated with a significantly better survival
Aslam <i>et al.</i> , 2002 (90)	US, multicenter	208	Incident	2	In a case-control study, patients with high BMI (>27) had outcomes that were similar to that of control subjects (BMI 20 to 27)
McDonald <i>et al.</i> , 2003 (91)	ANZDATA	9679	Incident	Up to 10	J-shaped relationship between BMI and mortality rates with increasing death risk with increasing body size; lowest mortality risk lowest for BMI of 20 kg/m ²
Snyder <i>et al.</i> , 2003 (92)	USRDS	418,021	Incident	3	Compared with those with normal BMI, for the first 2 yr, underweight patients had higher mortality, whereas overweight and obese patients had lower mortality; the third-year mortality was equivalent for underweight and overweight but higher for obese compared with those with normal weight
Abbott <i>et al.</i> , 2004 (85)	DMMS Wave 2 of USRDS	1662	Incident	5	Highest risk of death seen among patients with lowest BMI; equivalent survival among patients with BMI >22.4. No survival advantage seen for obese PD patients
Stack <i>et al.</i> , 2004 (86)	USRDS	17,419	Incident	2	Highest risk for death was seen among patients with the lowest BMI, and no survival advantage or disadvantage seen with higher BMI

^aAdapted from references (74,75). ANZDATA, Australia and New Zealand Registry; BMI, body mass index; CMAS, Case Mix Adequacy Study; DMMS, Dialysis Morbidity and Mortality Study; DOPPS, Dialysis Outcomes and Practice Patterns Study; USRDS, US Renal Data System.

degradation products may slow the rate of loss of residual renal function. Furthermore, a retrospective study (68) showed a survival advantage among PD patients who were treated with more physiologic dialysis fluids. In that study, the use of PD solutions was nonrandom, and there was lack of stratification or adjustment for cardiovascular disease, hypertension, socioeconomic status, and center. Finally, 305 patients who had a favorable prognosis and converted from conventional PD solutions to those with low concentrations of glucose degradation products were excluded from the analyses. Nevertheless, these observations are important in generating new hypotheses to be tested in clinical trials (69).

Relationship of Risk Factors to Outcomes May Differ among MHD and PD: Caution against Extrapolation

Notwithstanding the various risks that are observed over time with different dialysis modalities, the need for reducing cardiovascular risk among both MHD and PD patients is widely acknowledged; however, how to devise a risk reduction strategy remains undefined. This is related, in part, to numerous studies that demonstrated that the relationship of traditional cardiovascular risk factors to outcomes may be reversed in patients who undergo maintenance dialysis—the so-called “reverse epidemiology” (70). The confounding influence of inflammation can probably explain the reversal of association for some but not all of these risk factors that are deemed to be important in the general population (71). Moreover, interventions that have been consistently shown to be effective in the general population do not produce predictable results in maintenance dialysis patients: Whereas lipid-lowering therapy failed to improve outcomes among MHD patients with diabetes, treatment with carvedilol improved survival among MHD patients with dilated cardiomyopathy (72,73); therefore, although it may be prudent to use interventions that have been demonstrated to be consistently effective in the general population, it is possible that the same advantages may not accrue among maintenance dialysis patients.

Similarly, the relationship of risk factors to outcomes may differ between MHD and PD patients, exemplified by disparate results that were obtained in the studies that evaluated the relationship of body size to outcomes in MHD and PD patients (74,75). As summarized in Table 4, virtually all studies demonstrated that there is an inverse relationship between body size and patient outcomes in MHD patients, very likely a result of a higher body fat (76–88). Conversely, no such consistent findings have been reported among PD patients (85,86,89–92). Some studies have shown that obese patients have a survival advantage; others have shown an increased risk (91,92). Still other studies have shown no relationship between body size and outcomes of PD patients (85,86). These differences in relationship of body size to outcomes may be related to disparate metabolic conditions associated with the two modalities; therefore, one has to be careful in extrapolating data that were obtained from MHD patients to those who undergo PD.

Focus on the Future: Efforts to Continue to Improve Outcomes of Maintenance Dialysis Patients

On the basis of this discussion, it can be reasonably concluded that neither the differences in outcomes between PD and MHD patients are large enough nor are the data strong enough to implicate that these differences are causally related to the selected dialysis modality. It follows, then, that the outcome studies cannot be used to deny patients with ESRD a choice in the selection of dialysis modality. The processes discussed should, however, form the basis for devising future studies or management strategies with the potential to improve the outcomes of both MHD and PD patients; therefore, all efforts should be made to minimize the use of venous catheters or to reduce the risk for infections that are associated with use of catheters among patients who undergo MHD. Efforts to preserve residual renal function are likely to be beneficial for both MHD and PD patients. Randomized, controlled trials have demonstrated that angiotensin-converting enzyme inhibitors or angiotensin receptor blockers are renoprotective among PD patients (93,94). Even though there is no evidence that slowing the rate of decline of residual renal function translates into a survival benefit for maintenance dialysis patients, a controlled trial to test this hypothesis is probably unethical. Careful monitoring of volume status and achievement of euvolemia seem to be reasonable goals for both MHD and PD patients; however, numerous challenges remain in this field. Even though a large number of tools have been used to ascertain the volume status of maintenance dialysis patients, there is a paucity of controlled data to demonstrate that any of the noninvasive assessments can be used to guide therapy. There are significant ethical considerations, however, in the design of such a clinical trial, and attaining euvolemia should be attempted in all patients who undergo dialysis. Finally, numerous advances have been made in developing new PD solutions, but other than icodextrin, in the present regulatory environment, no other new PD solution is likely to be introduced in the United States at any time in the near future. The process for approval of new dialysis solutions needs to be re-evaluated. In addition, controlled clinical trials are needed to test the putative local peritoneal and systemic benefits of the new PD solutions in humans.

Conclusions

This discussion highlights the complexity of intermodality comparisons. Nevertheless, most studies demonstrate an early survival benefit among many subgroups of patients who are treated with PD, a benefit that likely is attributable to better preservation of residual renal function. Many studies also demonstrate an increase in relative risk for death among PD patients with increasing dialysis vintage, a risk that may be a result of worsening volume status. These observations allow us both to develop new hypotheses to be tested in clinical trials and to devise management strategies with the aim of improving outcomes of maintenance dialysis patients.

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