Delivering High-Quality Peritoneal Dialysis
What Really Matters?

Isaac Teitelbaum

Introduction
In much of the world, assessment of the quality of peritoneal dialysis (PD) has focused largely on the measurement of small solute clearance, usually in the form of Kt/Vurea. It must be recognized, however, that the evidence linking patient survival to achieving a given Kt/Vurea is weak at best. Furthermore, the measurement of small solute clearance, usually in the form of Kt/Vurea, is weak at best. The need to take a more holistic view of the patient by focusing on the patient’s desires and quality of life and by monitoring a variety of biochemical and clinical parameters (1). The methods used to assess health-related quality of life (HRQOL), factors influencing HRQOL in patients on PD, and the relation between HRQOL and patient outcomes in these patients have recently been reviewed in detail and will therefore not be discussed herein (2). This article will focus on the biochemical levels and physical parameters that are associated with better survival. I will briefly review the data for these parameters, indicating the desired range or value to target for each (Box 1).

Acid-Base Status
Chang et al. (3) analyzed survival of patients on PD as a function of their time-averaged serum bicarbonate. Compared with the reference range of 24 to <26 meq/L, patients with a lower time-averaged serum bicarbonate had higher all-cause and cardiovascular mortality, which worsened as bicarbonate fell. In contrast, higher levels of bicarbonate had no effect on mortality. Thus, I suggest that patients should achieve a serum bicarbonate of at least 24 meq/L. It remains to be determined whether patients residing at altitude—where a normal serum bicarbonate may be as low as 22 meq/L (as is the case for my patients in Colorado)—fare equally well if they achieve that value.

Albumin
A number of studies have demonstrated a relationship between higher serum albumin and survival in PD. Although true of baseline serum albumin at the initiation of PD, the more important relationship may be that between survival and time-averaged serum albumin during performance of PD. Mehrotra et al. (4) demonstrated that, compared with a cohort with time-averaged albumin 4–4.19 g/dl, those with time-averaged serum albumin <3.8 g/dl had higher all-cause mortality; the hazard ratio for mortality was progressively higher with lower serum albumin. Thus, the higher serum albumin attained, the better survival. Trends in the change of serum albumin are important as well. Compared with those in whom serum albumin remained level over a 6-month period, those patients in whom serum albumin increased by ≥0.3 g/dl during that period enjoyed significantly lower all-cause, cardiovascular, and infection-related mortality. Conversely, those in whom serum albumin decreased by ≥0.2 g/dl experienced higher mortality.

Blood Pressure
Surprisingly, few studies have analyzed the relationship between BP and survival in patients on PD. Using systolic BP 111–120 as a reference, a 2-year study from the United States Renal Data System database demonstrated higher mortality with lower BP but no effect of higher pressures up to a systolic BP ≥180. In contrast, a larger and longer study from the United Kingdom demonstrated a protective effect of higher BP in the first 6 months of PD and no effect through year 5 but higher mortality thereafter (5).

Hypotension in patients on dialysis is due largely to intrinsic cardiac disease. To the extent that it may relate to zealous antihypertensive therapy, it seems that we should not allow BP to fall to a systolic level below 111. The upper limit of acceptable BP is uncertain; at least for the first 5 years of PD, it would appear that we may relax control somewhat—I would...
propose keeping systolic BP ≤159—and not require patients to increase their already high pill burden for what seems to be little to no benefit.

Electrolytes

Hypokalemia is far more common in PD than hyperkalemia. Several studies have demonstrated progressively higher all-cause, cardiovascular, and infection-related mortality as serum potassium falls below 4 meq/L (6). Thus, even mild hypokalemia warrants attention as to causation and possible adverse effects. In contrast, mild hyperkalemia up to 5.4 meq/L has no adverse effect. Similarly, although mild hypernatremia has no discernible effect on mortality, even mild hyponatremia of 135 or below (and in some studies, levels of 137–138 that would usually be considered normal) is associated with higher all-cause and infection-related mortality (7). It is unclear whether the mild dilutional hyponatremia induced by icodextrin metabolites (usually just 2–3 meq/L) is equally deleterious; this will require examination. A serum potassium target in the range of 4–5.4 meq/L and serum sodium ≥135 meq/L are advised.

Hemoglobin

Studies examining the relationship between hemoglobin and survival of patients on PD have yielded mixed results. Two small studies found no relationship between hemoglobin and survival. In contrast, two more robust studies had very similar results: in erythropoiesis stimulating agent-treated patients, compared with those with hemoglobin 11–12 g/dl, patients with lower hemoglobin exhibited statistically significant higher mortality (8), whereas higher levels had no adverse effect. It seems, therefore, that one should target a hemoglobin ≥11 g/dl.

Minerals

In a large study of a DaVita database, Rivara et al. (9) demonstrated higher all-cause mortality with either high (≥10.2 mg/dl) or low (<8.5 mg/dl) albumin-corrected calcium. Interestingly, hyperphosphatemia was not associated with higher mortality unless the phosphorus was ≥6.4 mg/dl. The relationship between serum magnesium and survival in patients on PD was examined in a small Chinese study; hypomagnesemia (<0.7 mmol/L; 1.68 mg/dl) was associated with higher mortality. Because there were very few patients with hypermagnesemia (>1.2 mmol/L; 2.88 mg/dl), its effects could not be defined. I propose that each of these—the proper range of calcium, phosphorus below 6.4 mg/dl, and magnesium ≥1.7 mg/dl—be targeted in this multidimensional assessment of PD quality.

Volume Status

The role of volume homeostasis in survival of PD patients has been extensively studied, though the best manner to assess it remains uncertain. It is clear, however, that euvolemia is associated with enhanced survival compared with volume overload. Using bioimpedance spectroscopy, Van Biesen et al. (10) demonstrated that volume overload >17.3% above predicted is associated with higher mortality. Similarly, using N-terminal pro-brain natriuretic peptide as a surrogate marker for volume status, Wang et al. (11) found that patients with the lowest levels enjoy the best survival. An assessment of volume status should be included in this multidimensional analysis of patient well-being. I would suggest that, at minimum, we seek to have patients be devoid of overt signs of volume overload (i.e., no rales or lower extremity edema on physical examination).

Conclusion

Although the studies cited are associational and not interventional—it has yet to be demonstrated that intervening to “correct” one of these variables is associated with benefit—it seems nevertheless that there are a number of biochemical and clinical parameters that correlate with patient survival. Admittedly, a derangement in one of these markers may be secondary to an underlying problem that must itself be addressed (e.g., hypokalemia due to severe vomiting or excessive diuresis). Furthermore, the factors that determine the achieved value for some of these parameters are complex and are not entirely in the nephrologist’s control. Examples are adherence with diet,

<table>
<thead>
<tr>
<th>Acid-base</th>
<th>Bicarbonate ≥ 24 meq/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>Albumin (BCG) ≥ 3.8 g/dl</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>Systolic BP 111 – 159 mmHg</td>
</tr>
<tr>
<td>Electrolytes</td>
<td>Potassium 4 – 5.4 meq/L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>≥ 11 g/dl</td>
</tr>
<tr>
<td>Minerals</td>
<td>Calcium (albumin-corrected) 8.5 – 10.1 mg/dl</td>
</tr>
<tr>
<td>Volume status</td>
<td>Absence of rales and lower extremity edema</td>
</tr>
</tbody>
</table>

Box 1. | Proposed clinical and biochemical targets for high-quality peritoneal dialysis.
medications, and dialysis treatments and the presence or absence of inflammation. Nevertheless, knowledge of the values or ranges for these various parameters that are associated with superior outcomes will help guide the nephrologist as she or he works jointly with individuals performing PD, assisting them in achieving their personal life goals.

Disclosures
The author reports receiving personal fees from Zytoprotec and personal fees and nonfinancial support from liberDi, outside the submitted work.

Funding
None.

Acknowledgments
The content of this article does not reflect the views or opinions of the American Society of Nephrology (ASN) or CJASN. Responsibility for the information and views expressed herein lies entirely with the author(s).

References

Published online ahead of print. Publication date available at www.cjasn.org.