Comparison Population Outcome

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By Ankur Shah and Natasha Dave

Dialysis Adequacy History of and quality of life. This was a prospective cohort study

Later, in 2003, the same group evaluated the significance of lean body mass, and past episodes of underhydration. affected by low residual GFR (rGFR), lower percentage
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ered dialysis dose (7). This study showed that PD symp

One year later, Lo et al. (9) published the results of the Hong Kong study, another randomized controlled trial of adequacy in the CAPD population. Enrolled inci
dent CAPD patients (n = 320) were randomized to three groups: Kt/V 1.5–1.7, Kt/V 1.7–2.0, and Kt/V >2.0. Of note, only peritoneal clearance, not residual kidney func
tion, contributed to the difference in Kt/V. The results showed no difference in survival among any of the groups; however, there was significantly higher dropout in the group achieving Kt/V 1.5–1.7, as a result of hyperglycemia, uremia, and worse anemia.

Both the ADEMEX trial and the Hong Kong study helped pave the way to re-address previous adequacy goals in patients using PD. In 2005 the ISPD and in 2006 KDOQI endorsed a weekly Kt/V target of 1.7 (2, 3). Additionally, if patients are reliant on residual kidney function, or rGFR, to achieve adequacy, those guidelines recommend frequent monitoring of 24-hour creatinine clearance (every 1–2 months).

In the context of these recommendations, it is important to note that the concept of adequate dialysis is, of course, not limited to a single solute. Assessments of adequacy should consider quality of life, volume status, nutrition, eukalaemia, acid–base disturbances, and uremic symptoms. The quantity of delivered dialysis should be adjusted regardless of Kt/V for patients in whom the above factors are not controlled. This can be achieved by increasing dwell volume, changing dwell time, or adding exchanges (4).

Among other considerations nephrologists must take into account are the implications of increased clearance on the patient. Increasing clearance requires the use of additional dialysate, which increases the risk for hyperglycemia and for advanced glycosylation end products, and also increases the risk for complications associated with blood pressure and volume. Furthermore, additional clearance may require manual exchanges, which may affect quality of life. Reduction of PD clearance minimizes these risks for patients and can improve patient-reported outcomes (4).

Congruous with a more comprehensive approach to dialysis adequacy, the ISPD has released 2020 guidelines recommending against a specific Kt/V goal. Instead, the ISPD advocates for a more holistic approach, including close monitoring of patient-reported outcome measures, fluid status, nutritional status, and toxin removal (4).

Over the past few decades, the recommendations for PD adequacy have evolved from numeric targets to a comprehensive assessment. The initial shift toward less stringent guidelines resulted from two randomized controlled

Figure 1. Landmark trials in peritoneal dialysis

**Table 1. Summary of randomized controlled trials assessing adequacy in peritoneal dialysis**

<table>
<thead>
<tr>
<th>Trial</th>
<th>Population</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADEMEX (RCT)</td>
<td>Enrolled 965 incident and prevalent PD patients</td>
<td>Peritoneal creatinine clearance of 60 L/wk per 1.73 m²</td>
<td>Preexisting PD prescriptions (this is about 45 L/wk or 4 daily 2L exchanges)</td>
<td>No difference in mortality at 2 years</td>
</tr>
<tr>
<td>Hong Kong Study (RCT)</td>
<td>Enrolled 320 incident CAPD patients</td>
<td>Kt/V 1.5–2.0 or Kt/V &gt;2.0</td>
<td>Kt/V 1.5–1.7</td>
<td>No difference in mortality at 2 years, more uremia and volume overload in group with Kt/V of 1.5–1.7</td>
</tr>
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</table>

Abbreviations: ADEMEX = Adequacy of PD in MEXico; CANUSA = Canada-USA; NECOSAD = Netherlands Cooperative Study on the Adequacy of Dialysis

### History of Adequacy Trials in Peritoneal Dialysis

By Ankur Shah and Natasha Dave

In the day-to-day jargon of a nephrologist, the word "adequate" is unique in its usage in this profession. Conversely the Merriam-Webster definition of "adequate" is "sufficient for a specific need or requirement," nephrologists use this term to reflect the quality of the dialysis prescription.

Measuring the adequacy of hemodialysis (HD) and peritoneal dialysis (PD) has long been a topic of intense interest and debate. Currently, we measure adequacy using the fractional urea clearance equation known as Kt/V, whereby K is the clearance of urea, t is time during dialy-
sis, and V is volume of distribution of urea.

Over three decades, the goal Kt/V range has evolved from a numeric value to a patient-centric approach. The initial recommendation of total Kt/V of 2.0 and total creatinine clearance of 60 L/week per 1.73 m² was made by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (KDOQI) in 1997 (1). Later, between 2005 and 2006, both the International Society for Peritoneal Dialysis (ISPD) and the KDOQI recommended a total kidney and peritoneal Kt/V of 1.7 (2, 3). The most recent ISPD guideline update, made in January 2020, now recommends against treating to a specific Kt/V (4). To understand the evolution of Kt/V recommendations, it is imperative to review the history of adequacy trials (Figure 1).

One of the first large trials to evaluate PD adequacy was a prospective observational cohort study, "Adequacy of Dialysis and Nutrition in Continuous Peritoneal Dialysis: Association with Clinical Outcomes," also known as the CANUSA trial (5). From 1990 to 1993, 680 patients using continuous ambulatory peritoneal dialysis (CAPD) were enrolled in Canada and the United States to evaluate the relationship of dialysis adequacy and nutritional status to mortality, morbidity, and technique failure. The analysis of this study led to the target weekly Kt/V of 2.0 for patients using CAPD. In addition, every 0.1 decrease of Kt/V resulted in an increased risk of death by 5%. These findings assumed that PD clearances and residual kidney function were equivalent and therefore additive (5). Years later, a repeated analysis was done to address this assumption and revealed that there was no association between increased peritoneal creatinine clearance and risk of death; instead, the mortality benefit was due to residual kidney function, not to increased dialysis dose (6).

Independently in 1999, the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) considered patient-reported outcomes in the context of delivered dialysis dose (7). This study showed that PD symptom burden was not caused by dialysis dose; rather, it was affected by low residual GFR (rGFR), lower percentage of lean body mass, and past episodes of underhydration. Later, in 2003, the same group evaluated the significance of rGFR and PD clearance in relation to patient survival and quality of life. This was a prospective cohort study of 413 incident PD patients in the Netherlands and was known as NECOSAD-2. The result revealed that for every milliliter per minute of rGFR, there was a relative decrease in mortality of 12%; furthermore, no significant effect of PD clearance on mortality was found. The combined findings of CANUSA and NECOSAD-2 inspired others to conduct randomized controlled trials evaluating this association (Table 1).

In 2002, a prospective randomized controlled trial in Mexico, the ADEMEX trial, sought to study the effects of increased peritoneal clearances on mortality rates in PD (8). This study randomized 965 patients to receive four daily 2-L exchanges or to be dosed to achieve a peritoneal creatinine clearance of >60 L/week per 1.73 m², through either increased volumes or exchanges. The average Kt/V of the intervention group was 2.27, and that of the control group was 1.8. At 2 years, the percentage of survival was no different between treatment groups. Predictors of patient survival in this trial included age, presence of diabetes, albumin concentration, and residual kidney function. Several secondary outcomes were also evaluated; only serum albumin and total peritoneal ultrafiltration were significantly higher in the intervention group. Despite the higher serum albumin in that group, the change from baseline was not statistically significantly different. Hospitalization rates were also similar for both groups in both unadjusted and adjusted analyses.

This article is the first in a series about peritoneal dialysis. Additional articles will be published in upcoming issues.

Abbreviations: ADEMEX = Adequacy of PD in MEXico; CANUSA = Canada-USA; NECOSAD = Netherlands Cooperative Study on the Adequacy of Dialysis
trials, the ADEMEX trial and the Hong Kong Study. This paved the way for the 2006 KDOQI recommendations for a weekly Kt/V target of 1.7. The 2020 ISPD guidelines have taken this a step further, advocating for a more holistic approach rather than the specific targeting of a single clearance metric. It is imperative for us as nephrologists to understand the evolution of adequacy in PD and the implications of increased clearance in patients using PD. Studying this evolution allows clinicians to be better equipped to understand current practice guidelines while also providing a foundation for the development of future studies. Furthermore, this article highlights the importance of considering the patient in context to the guideline instead of achieving a numeric goal.

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References

@RenalFellow, #NephTwitter Wants YOU

By Tiffany Truong

Fellows Corner

Tiffany Truong

Love it or hate it, social media has become an ever-pervasive presence in nearly every aspect of our lives, and no sphere has been spared, especially nephrology. We may postulate that this is perhaps because nephrology, by its very nature, provides such a rich soil for academic discourse; that fluid physiology demands a blog post, electrolyte puzzles make great tweets, and regardless of all that we just cannot help posting salty jokes. That may be true, but certainly the world of nephrology on social media provides many benefits.

To start, social media can be fun. At first glance, “fun” may sound trivial, but that enjoyment becomes enthusiasm, which can lead to passion, drive, and initiative. In a time when physician burnout is a recurring headline and is being rebranded as “moral injury,” remembering that our work is creative, intriguing, and rewarding is arguably as vital as any duty hour regulation. It spills over into patient care. It has been my experience that most physicians who use social media are not there to represent any financial interest; they maintain a presence because being a part of this virtual community, deemed “NephTwitter,” is just making the room that much bigger. To be a nephrologist, let alone any discourse on social media. Now, as a first-year fellow, my days on service can be invariably busy and dedicated to patient care, but in those few minutes between clinic and grand rounds or after a hectic day on consultations, I find that some time spared to follow the world of nephrology on social media provides many benefits.

Besides the feel-good value, however, the blogs, websites, and Twitter accounts of these nephrologists/social-media guru pioneers are brimming with educational dialogue that can enrich one’s professional growth. There is much to learn, from the tweetorials on physiology to journal clubs on current research to lively debates on how management should or should not change after a study. This virtual community, deemed “NephTwitter,” is an academic gathering place for nephrologists around the world, who can share their unique experiences while still speaking in the common tongue of nephrology. One of the most successful social media experts in medicine, Dr. Anthony Bux, has emphasized that social media’s major impact is not just the dissemination of information but a shift in the entire clinical perspective from that trap of anchoring; from asking “What is the answer?” to “Why is there a problem?” and “Why does this work?”

The funny thing about online discourse is that it is a great equalizer, particularly for fellows. Although we are all identified professionally, the hierarchy of attendings, fellows, residents, and students does not translate into rigid roles. We are all simply teachers and students, with things to say and things to learn.

Last but not least, social media is an avenue for patient advocacy. The American Medical Association and other professional societies, notably in pediatrics, agree that physicians have a responsibility to advocate for public health and address the root causes of threats to the public well-being. Although civic engagement among physicians is easily touted, many of us have no formal training to advocate for healthcare beyond our individual patients. In a field as institutionalized as nephrology, this is remarkable. Social media provides a platform, accessible to everybody, that if used judiciously can inform our patients and our communities about even the sociopolitical barriers to health that we know intimately.

In the Netflix show Diagnosis, Dr. Lisa Sanders uses the web to connect patients with difficult diagnoses to experts across the world. She states, “One of the tools that doctors use are the other doctors in the room. . .what we’re doing is just making the room that much bigger.” To be a nephrology fellow in this day and age is to train in an enormous room, one with very smart little blue “Twitter birds who spout Free Open Access Medical education (FOAMed). That is the sound of the NephTwitterverse calling. Consider yourself recruited.

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