Adequacy of peritoneal dialysis

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Introduction

As a renal replacement therapy, dialysis, at best, only approximates normal renal function (Table 1). Despite these deficiencies, however, dialysis has extended the lives of end-stage renal disease (ESRD) patients, some for over 20 years [1]. Although many patients do very well on dialysis, data compiled by the Health Care Financing Administration (HCFA) and analysed by the United States Renal Disease System (USRDS) have shown that the gross mortality rate for the United States ESRD population (predominantly haemodialysis (HD) patients) in 1990 was 24% [2]. The extent to which uraemia in the form of underdialysis contributed to this overall mortality rate in ESRD patients is unknown. Some have suggested that inadequacies in the prescribed dose of dialysis were contributing to these high mortality rates [3, 4]. As a result, more attention has been paid to patient outcome and to optimizing total solute clearance. The mean $Kt/V$ for Subpopulations of HD patients has increased from 1.0/Rx in patients starting dialysis during 1986–87 to 1.22/Rx in a random sample of prevalent HD patients in December 1993 [5]. Associated with this change there has been a gradual increase in the adjusted 1-, 2- and 5-year patient survival percentages for patients starting dialysis over the years 1979–73.

Although 'adequate' dialysis is crucial for the well-being of any ESRD patient, adequacy of peritoneal dialysis or any renal replacement therapy is difficult to define. The word 'adequacy' comes from the Latin word 'adequare' [6], which means 'to equalize'. Ideally, this would mean that adequate dialysis would return the patients' lifestyle and life-expectancy to what it would have been if the patient never had renal disease. 'Optimal' dialysis prescriptions are said to be those in which there is no further incremental improvement in patient outcome as the dose is increased further while also imparting minimal negative effects on the patient's quality of life.

One indisputable reason for the lower life-expectancy in ESRD patients is that they have at least one chronic medical condition and therefore are 'patients', and not healthy individuals. In addition, ESRD patients tend to have multiple comorbid diseases at initiation of dialysis that can also adversely influence outcome [7], the prevalence of which is increasing. We can influence the patient's total solute clearance. Nephrologists must do their best to provide enough renal replacement therapy so we are sure that the amount of dialysis delivered is not the rate-limiting step that determines whether the patient lives or dies. One example of this concept is the data by Charra et al. [8], who reported on long-term (20 years) follow-up for 445 unselected HD patients, all of whom received 24 hours/week of conventional HD using Kiil plate dialysers. The mean $Kt/V$ for these 445 patients was 1.67, much higher than the estimated average prescribed $Kt/V$ in the USA at that time ($Kt/V = 1.02$) [9]. Each gender subgroup was then split into two equal-numbered subgroups as a function of $Kt/V$ and mean arterial pressure (MAP). For these subgroups outcome was not a function of $Kt/V$, but was correlated with blood pressure, and age. The overall 20-year patient survival was 43%, approaching that for healthy individuals of the same age! This is an example of an optimal dialysis prescription — i.e. one in which patient outcome is dependent not on the amount of dialysis delivered, but on the other comorbid dis-

![Table 1. Solute removal by dialysis and the natural kidney](image)


eases that are present. Our goal as nephrologists is to provide this optimal dose of dialysis.

This chapter discusses adequacy issues for peritoneal dialysis (PD) in terms of total solute clearance and other issues related to the PD prescription. It acknowledges that adequacy of dialysis addresses more than just total solute clearance issues. Optimal treatment of a patient with ESRD must additionally address multiple issues such as blood pressure, volume control, treatment of acidosis, anaemia and prevention of metabolic bone disease, most of which are beyond the scope of this chapter.

**What yardstick for adequacy of dialysis should we use?**

Many of the known clinical manifestations of uraemia, such as decreased appetite, metallic taste, nausea, vomiting, pericarditis, pleuritis and encephalopathy, are obvious [10]. There is evidence to suggest that underdialysis may be associated with hypertension [11] and lipid abnormalities [12], both of which may increase the risk of atherogenesis, cardiovascular disease and mortality. Uraemic neuropathy may not be diagnosed until it is far advanced, at which time it may be irreversible [13]. Because of the insidious onset and potentially fatal or irreversible nature of some manifestations of uraemia, nephrologists needed a laboratory parameter that measures the delivered amount of solute clearance, while predicting patient outcome. There is no documented single substance that has been shown to be the 'uraemic toxin'. Undoubtedly, the clinical manifestations of the uraemic syndrome are the result of the synergistic effect of an entire family of uraemic toxins of both small and moderate molecular weights. Therefore, because there is no single uraemic toxin, we will have to rely on surrogate markers for uraemia. Currently, solutes such as urea nitrogen, creatinine and \( \beta_2 \)-microglobulin are commonly used.

There are data to suggest that the outcome for both HD and PD patients [14, 15] is related to total solute clearance. However, it would be appropriate to ask, whether protein intake, nutritional status or middle molecule clearance should be used as the yardstick for dialysis dose.

It has been suggested that dietary protein intake (estimated by obtaining the protein equivalent of nitrogen balance or PNA) tends to correlate with total solute clearance [16]. A higher \( Kt/V \) is generally associated with a higher protein energy intake, both in HD and in PD. Would it suffice to only monitor normalized PNA, and if it is stable and in an adequate range, assume that the dose of dialysis is 'adequate'? Anecdotal clinical data would suggest the answer is no. Furthermore, their relationship may be more mathematical than physiological. Our current practical ways to measure protein intake are estimations of protein intake [17] and can be very misleading when the patient is not in a steady state. The protein equivalent of nitrogen appearance or PNA will often overestimate dietary protein intake (DPI) in a catabolic state and may underestimate DPI when anabolic. The relationship between protein intake, solute clearance, and the manifestations of uraemia is likely to be different in each patient. Certainly, small molecular weight clearance is not the only factor that determines dietary protein intake. Comorbid diseases have a significant impact. Therefore, although PNA should be an adequacy target, it cannot be the only target used.

It is a common clinical experience that when PD patients manifest uraemic symptoms they improve after increasing the volume or number of exchanges/day. Figure 1 demonstrates the theoretical influence of the number of PD exchanges on the weekly solute clearance for a wide range of molecular weights. It is clear that increasing the number of exchanges per day results in only a minimal increase in large or middle molecule clearance, but a marked increase in small solute clearance (MW <500 Da). Therefore, based on Keshaviah’s theoretical projections [18] and the available clinical experience, it seems that overall small solute clearance, not middle or large molecular weight clearance, is most closely related to uraemic toxicity, and that small solute clearance

![Figure 1. The influence of the number of CAPD exchanges on the weekly solute clearance for a range of solute molecular weights derived from a computerized model of peritoneal transport. (Keshaviah P. Adequacy of CAPD: A quantitative approach. Kidney Int 1992; 42 (suppl. 38): S160–4.)](image-url)