

7 Adequacy of peritoneal dialysis

Guidelines

A. Adequacy targets for dialysis should include both urea removal and fluid removal.

(Evidence level C)

B. These targets should be based on those achieved by peritoneal dialysis only. Urine production and renal urea clearance can be subtracted from the targets.

(Evidence level C)

C. The minimum peritoneal target for Kt/V_{urea} in anuric patients is a weekly value of 1.7 (Evidence level A); the minimum peritoneal target for net ultrafiltration in anuric patients is 1.0l/day. (Evidence level B)

The presence of residual renal function can compensate when these peritoneal targets are not achieved.

(Evidence level C)

D. When the targets are not achieved, patients should be monitored carefully for signs of overhydration, uraemic complaints and malnutrition. Appropriate therapy changes might be considered.

(Evidence level C)

E. Some APD patients who use frequent short exchanges and have a slow transport status can fulfil the above targets, but may have a low peritoneal creatinine clearance. In these patients, an additional target of 45l/week/1.73 m² for peritoneal creatinine clearance should be aimed at in addition to achieving the Kt/V_{urea} target of 1.7.

(Evidence level C)

Commentary to Guideline 7: adequacy of peritoneal dialysis

Guideline A

The objectives of any dialysis treatment are the removal of accumulated waste products and/or excess fluid. Consequently, adequacy targets should include both solute and fluid removal by dialysis. Accumulation of uraemic waste products occurs both for low molecular weight solutes and for the so-called ‘middle molecules’, including low molecular weight proteins such as β_2 -microglobulin. Theoretically, targets for solute removal by dialysis should include various solutes covering a mol. wt range from 60 to

20 000 Da. This is impossible from a practical point of view. Therefore, studies have focused especially on the clearance of urea (60 Da), expressed as Kt/V_{urea} , and of creatinine (113 Da). A slight beneficial effect of a low serum β_2 -microglobulin concentration on patient survival has been reported in the CANUSA study, but this effect could be ascribed entirely to the magnitude of residual glomerular filtration rate (GFR) [1].

Clearances are usually normalized according to the size of the patients. Creatinine clearance is expressed per 1.73 m² body surface area, and the urea distribution volume (V) is given as Kt/V_{urea} . V cannot be measured easily in peritoneal dialysis (PD) patients and is therefore usually estimated either using a fixed percentage of body weight or using Watson’s formula [2]. The estimation of V, that has a large impact in the Kt/V equation, can be inaccurate in individual patients [3]. Overestimates of V are present in obese patients, and underestimates in those who are underweight. These inaccuracies must be taken into consideration when Kt/V targets are interpreted.

A number of prospective cohort studies have been published analysing the effects of the combined renal and peritoneal clearances of either urea or creatinine on mortality, morbidity and quality of life. The first prospective cohort study by Blake *et al.* was unable to find an effect of total Kt/V_{urea} on patient survival [4]. This study used a fixed percentage of body weight to assess V. Only after reanalysis of the data using Watson’s formula to estimate V did it appear that a significant excess number of deaths was present when total Kt/V_{urea} was <1.5 per week [5]. In a single-centre study from Italy, the effects of solute clearances on risk of death were analysed dichotomously [6]. It appeared that $Kt/V_{\text{urea}} \geq 1.96$ per week and creatinine clearance ≥ 501 per week were associated with the best survival. The CANUSA study, performed in 680 incident continuous ambulatory peritoneal dialysis (CAPD) patients in Canada and the USA with a mean follow-up of 1.2 years per patient, showed a 6% reduction in the relative mortality risk for every 0.1 increase in Kt/V_{urea} per week and 7% reduction for every 5l/week/1.73 m² increase in creatinine clearance [1]. The results of these studies [1,3] were the basis for the recommendations made by the peritoneal dialysis working group of the National Kidney Foundation Dialysis Outcomes Quality Initiative (DOQI) on the minimum dose for adequate CAPD [7]: a Kt/V_{urea} of 2.0 per week and a creatinine clearance of

601/week/1.73 m². The results of the CANUSA study with regard to the associations of total Kt/V_{urea} and creatinine clearances with mortality have been confirmed in the majority of subsequent prospective observational studies [8–11]. It should be noted, however, that this was only the case when total Kt/V_{urea} was analysed. A reanalysis of the CANUSA study [12] and also others (see commentary to Guideline B) showed that the associations of solute clearances with mortality were only caused by the magnitude of residual GFR.

Ultrafiltration failure is an important complication of PD [13], potentially leading to overhydration and an excess number of deaths [14]. Prospective observational cohort studies have found associations of fluid removal, especially by residual GFR, with mortality [12,15,16]. The effects of peritoneal fluid removal were equivocal.

Guideline B

Analysis of the effects of total solute clearances on mortality assumes equivalency of renal and peritoneal clearances. This ignores possible effects of tubular secretion and of endocrine renal function. Furthermore, only peritoneal solute clearances can be influenced by changing the dialysis dose. When the prospective observational studies on adequacy and determinants of mortality were analysed for the effects of peritoneal clearances only, no effect on mortality could be established [6,8–11,12,15,16]. Also, the analysis of a large clinical database by Diaz-Buxo *et al.* showed no effect of peritoneal clearance on patient survival [17]. Five studies have been published about possible effects of peritoneal solute clearances in anuric PD patients [18–22], although two of them only in abstract form [20,21]. With the exception of the study from Hong Kong [19], all the others were unable to find a relationship between peritoneal solute clearances and survival. In the only retrospective analysis of anuric PD patients [18], a Kt/V_{urea} <1.85/week was non-significantly associated with an increased mortality, but this was not reproducible in the prospective studies [20,22].

The failure of the majority of the above observational cohort studies to demonstrate an effect of peritoneal solute clearances on mortality may be due to the rather small range of achievable peritoneal clearances and the overwhelming effects of residual renal function.

Two large randomized controlled trials on the effects of peritoneal clearances on survival have been published; the ADEMEX study from Mexico [23] and the study by Lo *et al.* from Hong Kong [24]. Increasing the peritoneal creatinine clearance from an average 451/week/1.73 m² to 601/week/1.73 m² had no effect on patient survival [23]. Also, an increase of Kt/V_{urea} from 1.7/week to 2/week was not associated with decreased mortality [23,24]. However, patients with a Kt/V_{urea} <1.7/week had more clinical problems, and a

small percentage of them needed treatment with erythropoietin [24]. Associations between peritoneal fluid removal and survival have been found in a study from Turkey [15] in CAPD patients and in the EAPOS study, performed in anuric PD patients [22]. A significant association was absent in two cohort studies in which the majority of patients had residual renal function [14,16].

Despite the relatively small contribution of peritoneal clearances and fluid removal to survival in PD patients with residual renal function, the committee decided to formulate targets based on those achieved by dialysis only. These targets should be adequate for anuric PD patients. It follows from these considerations that the presence of residual renal function can compensate in situations where the peritoneal targets are not achieved.

Guidelines C

The two randomized controlled trials on the effects of peritoneal solute clearance on survival, both showing that an increase in peritoneal Kt/V_{urea} from 1.7/week to 2.0/week is not associated with a better patient survival [23,24], made the committee decide to formulate a minimum target of 1.7/week. This is a value that can be achieved on a conventional CAPD scheme in the majority of patients. This does not exclude that some patients may require higher clearances. The presence of clinical symptoms of underdialysis should be avoided, and when they occur the dialysis dose should be increased accordingly.

The committee discussed whether peritoneal urea clearance or creatinine clearance should be used as the target. Recognizing that renal creatinine clearance exceeds urea clearance, while peritoneal creatinine clearance is lower than urea clearance, and that the adequacy of the haemodialysis dose is usually expressed as Kt/V_{urea}, the committee decided on Kt/V_{urea}. The committee decided not to formulate a higher Kt/V_{urea} target for APD than for CAPD, because of the rapid diffusion of urea, also during short cycles.

The need to formulate a target for ultrafiltration was felt because of the clinical problem of overhydration that occurs especially in long-term PD patients who are often anuric. To increase the awareness of the maintenance of a euvolaemic state, the committee decided on an arbitrary target of 1.01/day. There was no published evidence on the accuracy of this value when it was formulated. In the study of Ates *et al.*, the dialytic fluid volume was only analysed as a continuous variable, the mean value being 1302 ml/24 h/1.73 m² [15]. The average contribution of peritoneal fluid removal was 78%. It appeared that the quartile with total fluid removal of <1265 ml/24 h/1.73 m² had the lowest survival. This would support the peritoneal target of 1.01. Recent analyses in the NECOSAD cohort also show that low ultrafiltration in anuric patients is associated with a decreased survival [25]. In anuric APD patients, a predefined

ultrafiltration target of <750 ml/day at baseline was associated with a decreased patient survival [22]. Therefore, patients below the 11 target need very careful attention.

Kt/V_{urea} is mainly dependent on the dialysate flow rate, i.e. the drained volume divided by the duration of the dwell. Therefore, relationships are present between Kt/V_{urea} and the amount of drained dialysis solution which is mainly dependent on the instilled volume and to a lesser extent on the ultrafiltered volume. The relationships between Kt/V and ultrafiltered volume are dependent on the volume of distribution of urea and peritoneal transport status. In conventional CAPD, using 41 exchanges and a drained volume of 9 l/24 h, a 60 kg patient with an average peritoneal transport status will have a Kt/V of ~ 1.6 . A 40 kg patient with a fast transport status will have a much higher Kt/V and an 80 kg patient with a slow transport status a much lower Kt/V than 1.6/week. This is caused by the normalization used in the expression of urea clearance.

Guideline D

The numbers given in the commentary on Guideline C and the potential inaccuracies in the calculation of V in the Kt/V equation as discussed in the commentary on Guideline A illustrate that the numerical targets should be interpreted cautiously. Failure to reach these targets should not be considered an absolute indication to change the dialysis prescription *a priori*, but should be a warning sign that must lead to careful clinical examination of the patients with special attention paid to signs of underdialysis and overhydration. The clinical status of the patient prevails over the numbers where adequacy is achieved. Potential benefits and drawbacks of an adaptation of therapy should be weighed against potential improvements of the condition of the patient by altering the dialysis schedule.

Guideline E

Creatinine diffuses more slowly than urea because of its higher molecular weight. The use of relatively long exchanges as in CAPD weakens this difference. Therefore, the committee decided not to formulate a separate guideline for CAPD. The average ratio between peritoneal creatinine clearance and Kt/V_{urea} in CAPD is 26 [26]. Consequently, peritoneal creatinine clearance is 44 l/week for a Kt/V_{urea} of 1.7/week.

The relationship between Kt/V and creatinine clearance decreases in APD patients using a large number of short exchanges, especially when they have a slow peritoneal transport status. They may have a disproportionately low peritoneal creatinine clearance. Because these patients are at risk for clinical signs of underdialysis, an additional target has been set based on peritoneal creatinine clearance. A minimum target of 45 l/week/1.73 m² is advised on top of the Kt/V_{urea} and ultrafiltration targets.

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