

## Optimising small solute clearances in peritoneal dialysis

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### GUIDELINES

- a. Aim to maintain residual renal function (RRF). Consider the use of ace inhibitors (Level II evidence) to preserve residual renal function and avoidance of nephrotoxins.
- b. With automated peritoneal dialysis (APD), consider the use of icodextrin for the long dwell. (Level II evidence)

### SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

- Aim to maintain RRF. It is a significant contributor to dialysis adequacy. (Level III evidence) Increasing clearance by an increase in peritoneal clearance cannot make up for loss of RRF. (Level III evidence)
- In general, increasing the dialysis volume or increasing the number of daily exchanges will increase the prescribed dialysis dose. The use of APD has not yet been shown to offer a clear advantage in small solute clearances. (Level III evidence)
- Peritoneal dialysis (PD) prescribing should be individualised to the patient, taking into account their body size, peritoneal transport status, RRF and personal preferences. (Levels III and IV evidence)

#### Optimising small solute clearances:

- Increasing the fill volume, the number of exchanges or the amount of ultrafiltration should increase clearances in most patients. Some patient populations may not tolerate increasing dwell volumes in CAPD, especially small patients. Even larger patients often cannot achieve targets set despite the increase in dialysis dose on CAPD. Use of APD should be considered in this group.
- Individualised PD prescriptions are essential, taking into account:
  - peritoneal transport
  - RRF
  - body surface area.
- Aim to provide the most dialysis possible to a patient given the constraints of lifestyle and quality of life, cost and clinical setting.

- **Aim to preserve RRF.**
- **An increase in peritoneal clearance will be needed as RRF diminishes. Adequate PD should be achievable in nearly all patients, even low-low average transporters as long as they retain some RRF.**
- **APD patients generally require wet days except some with high transport properties or considerable RRF.**
- **Low-low average transport patients generally achieve better clearances with continuous regimens such as continuous ambulatory peritoneal dialysis (CAPD) and continuous cyclic peritoneal dialysis (CCPD) whereas high-high average transport patients achieve better small solute clearances with short dwell techniques such as nocturnal peritoneal dialysis (NPD), and nocturnal tidal peritoneal dialysis (NTPD).**
- **Use of icodextrin will usually increase ultrafiltration and therefore solute removal and should be considered for the long daily dwell.**
- **Soon after each prescription change, total (renal and peritoneal) clearances should be measured.**

## **Background**

Small solute clearance has been emphasised historically as one of the most important factors determining dialysis adequacy. Studies have suggested that the greater the adequacy, the better the patient outcome, particularly survival. However, this has recently been refuted (Paniagua et al 2002) There is now renewed interest in small solute clearance particularly regarding preservation of RRF, and its place with other elements of dialysis adequacy such as nutritional status, quality of life, cardiovascular outcomes and fluid control.

Peritoneal dialysis does not deliver adequate small solute clearance when compared with native kidneys. Ideally, PD treatment should aim to deliver the most dialysis possible in patients given time, personal preferences and financial constraints. This should minimise uraemic symptoms, lead to better blood pressure control and hopefully, improve nutrition and quality of life. Possible negative consequences of interventions to improve small solute clearances include increased cost and time, potential for volume overload and abdominal distension and greater peritoneal exposure to glucose with local and metabolic effects. Increasingly, patients are using automated dialysis methods in order to enhance the amount of dialysis delivered as well as quality of life. Difficulties persist in certain subgroups such as low transporters and those without RRF.

The aim of this guideline is to summarise the current knowledge of methods to optimise small solute clearance in PD delivery.

## Search strategy

**Databases searched:** Medline (1966 to October Week 3 2003). MeSH terms and text words for peritoneal dialysis were combined with MeSH terms and text words for small solute clearance and kidney function. The search strategy was not limited by study type in order to maximise the number of relevant articles obtained. The Cochrane Renal Group Specialised Register of randomised controlled trials was also searched for relevant trials not indexed in Medline.

**Date of searches:** 28 October 2003.

## What is the evidence?

There are no prospective, randomised, multicentre controlled trials directly examining this issue. Evidence regarding improved small solute clearance is largely based on Level III and IV evidence.

## Residual renal function

### *Small solute clearance*

There is now evidence that RRF contributes significantly to total small solute removal. In the CANUSA study, 30% of total solute clearance was attributable to RRF. An RRF of 1 mL/min contributes around 10 L to total weekly creatinine clearance (Gahl & Jorres 2000, Harty & Gokal 1996). Loss of RRF cannot be entirely compensated by increasing peritoneal clearances. In the CANUSA study, the improvement in patient survival with higher weekly Kt/V and creatinine clearance measurements was entirely explained by the level of RRF (Churchill et al 1996). This study was reanalysed to investigate whether or not renal and peritoneal clearances were additive. They found that with each 5 L/week/1.73 m<sup>2</sup> increment in GFR, there was a 12% decrease in the relative risk of death; that is, RRF predicted patient survival on PD independent of PD dose (Bargman et al 2001).

A cross-sectional study of 68 patients that prospectively looked at increased prescription via an increased dwell volume versus control, found that the peritoneal Kt/V at 1 year had increased by only 12% despite an increased prescription of 22.4%. The total clearance at 1 year was not significantly changed, suggesting that renal and peritoneal clearances are not equivalent (Harty et al 1997). Similar conclusions were made in the cross-sectional study by Diaz-Buxo and colleagues (1999). Thus, while considerable attention in the literature and published guidelines has been devoted to maximising peritoneal dialysis dose, it is now realised that it is as important to ensure optimal preservation of RRF to optimise small solute clearances.

### *Medications*

The effect of medications on RRF has now been studied in patients who have commenced dialysis.

A randomised, open label, controlled single centre study of 60 prevalent PD patients examined the effect of Ramipril 5 mg daily in preserving RRF, over a 12-month

period. They found that the Ramipril group had a smaller decline in RRF than controls (2.07 mL/min per 1.73 m<sup>2</sup> versus 3 mL/min per 1.73 m<sup>2</sup>). Fewer patients in the intervention group developed anuria by the end of the study. Limitations of the study included the small sample size, no placebo-controlled group and no double blinding (Li et al 2003). A USRDS prospective cohort study of 2211 patients followed for 8–18 months examined predictors of loss of RRF. They found that the use of ACE inhibitors and calcium channel blockers was associated independently with a decreased risk of loss of RRF, thus showing an ongoing benefit of these agents after starting dialysis (Moist et al 2000). This finding is consistent with evidence that these medications slow progression of renal disease at higher levels of GFR (Maschio et al 1996). In some clinical situations renal function may worsen, such as renovascular disease and the overall risk in a particular patient must be assessed.

Furosemide has been shown to maintain urine volume but does not affect RRF or solute clearance (Medcalf et al 2001).

Aminoglycosides impact on RRF with a more rapid decline in urine volume shown in an observational prospective cohort study of 72 PD patients (Shemin et al 1999). There are no studies in dialysis patients examining the use of radio contrast or NSAIDs. Theoretically, they should be avoided in the post-dialysis setting given their known nephrotoxicity in patients with advanced kidney disease (Chandna & Farrington 2004). It is also reasonable to avoid other renal insults such as hypotension.

#### *Other benefits*

Patient survival:

30% of a patient's solute clearance was attributable to RRF at the start of the CANUSA study (Churchill et al 1996). A retrospective study of CAPD patients by Chung et al found that decreased 24h fluid removal was associated with decreased small solute clearance and inflammation. A high CRP and loss of RRF were associated with poorer survival (Chung et al 2003).

Preserved nutritional status:

Mak et al (2000) in a prospective randomised trial, noted increased protein intake and peritoneal and total clearances in CAPD patients treated with an increased volume (8 L vs 6 L/day) although serum albumin was unchanged. A cross-sectional study of 242 Chinese patients was done to determine dietary intake and differential contributions of RRF and peritoneal Kt/V. Dietary caloric intake was greater in those with more RRF but not PD solute clearances (Wang et al 2001). In another study, 168 prevalent CAPD patients from a single centre were studied over 12 months with no difference observed between the dialysis-dependent and RRF patients (Szeto et al 1999).

Gender is likely to have no impact on preservation of RRF although in some (Moist et al 2000), but not all studies, there has been an association (females). There is some observational evidence that race (non-white), the presence of congestive cardiac failure and the presence of diabetes may affect the rate of loss of RRF (Moist et al 2000).

## **Automated peritoneal dialysis**

There are no randomised, double-blind controlled trials to confirm that the use of APD accelerates the loss of RRF. Theoretical reasons why APD might accelerate the loss include rapid changes in fluid volume resulting in an ischaemic insult to the kidney or the use of icodextrin or hypertonic glucose.

The effect of APD on loss of RRF has been examined in prospective trials. In the USRDS trial, no difference was seen between the use of APD and CAPD, although ultrafiltration rates were not reported (Moist et al 2000). In contrast to this, a prospective, non-randomised study of 53 new CAPD and 51 APD patients followed for at least 1 year, found a faster rate of loss of RRF and worse sodium removal in the APD group, despite controlling for PET results. This difference may be negated by the role of ultrafiltration in determining loss of RRF and may have been influenced by prescription alterations once PET results were known (Rodriguez-Carmona et al 2004). Further, in a prospective, small non-randomised trial of 36 consecutive unmatched (except for age) new PD patients followed over 12 months, there was a faster rate of decline in the APD group. The monthly decrease in clearance was  $-0.1$  mL/min versus  $-0.28$  mL/minute at 6 months and  $-0.13$  versus  $-0.26$  mL/min at 1 year in the APD versus CAPD groups, respectively. The APD group consisted of both CCPD and NIPD patients without any difference in the rate of loss for each therapy, although the numbers were small (Hufnagel et al 1999). A small, non-randomised prospective study over 6 months in new patients also found that those on APD (NIPD and CCPD) had a more rapid decline than the CAPD patients (Hiroshige et al 1996). At present, it is recommended that RRF should be reviewed every few months after the commencement of APD and the prescription adjusted accordingly.

## **Peritoneal dialysis prescription**

Increasing the fill volume and thus increasing the dialysis flow rate, is theoretically most effective in terms of clearance since it reduces the number of drain-fills. The use of short cycles causes dissociation between small and large molecule clearances (Durand et al 1996, Krediet et al 1998).

There is validation for the accuracy of computer modelling of PD prescriptions in CAPD patients (Vonesh et al 1996) and APD patients. Vonesh et al (1996) reported on a multinational prospective longitudinal study examining PD Adequest in CAPD and APD patients and found agreement between clinical and computer-modelled measurements. There is no evidence that this is better than empiric prescribing. Robertson and colleagues (1995) demonstrated that in 100 patients (CAPD 75, APD 25) computer models were on average, 10% different to clinical data (Robertson et al 1995). Best practice would still use clinical data to validate a particular prescription.

## **Automated peritoneal dialysis versus CAPD**

Use of APD has been recommended to increase small solute removal. More permeable peritoneal transport membrane types have more options to achieve clearance by using APD (Durand et al 1996). There are no RCTs that directly

compare APD (CCPD and NPD) with currently used (2.5–3 L) fill volumes in CAPD.

In a prospective, sequential study comparing the techniques of CAPD, CCPD, tidal peritoneal dialysis (TPD) 25% and 50% across a range of peritoneal transport groups, clearances were similar between the CCPD and TPD groups, although the 50% TPD and CCPD groups had the best creatinine clearances. Urea clearance was greatest in the CPPD group. Clearances were consistently better in APD versus CAPD, even in low transporters, achieved with a daytime exchange (Rodriguez et al 1998). In contrast, CCPD and CAPD were shown to have similar small solute clearances in a small study of 18 CAPD and 11 CCPD patients although 2 L or less fill volumes were used in the CAPD group. Ultrafiltration was not statistically different between the groups (Gao et al 1999). The use of short cycle modalities in nightly APD makes it more difficult to achieve creatinine clearance targets than Kt/V urea targets (Rodriguez et al 1997, Durand et al 1996). Use of the 'dry day' in NIPD reduces clearance by up to 10%–15% compared with CAPD or CCPD (Gahl & Jorres 2000). Therefore, a daytime exchange is often necessary.

Tidal modalities have been proposed to more efficiently increase small solute clearances in APD, in part by reducing the impact of drain–fill multiplication but at higher cost (Gahl & Jorres 2000). This is due to an effective increase in dialysis flow rate. There is a maximal effective flow rate for different peritoneal transport types, beyond which no extra clearance is achieved. The optimal tidal exchange volume remains in question but less than 50% has given worse clearances to date (Rodriguez et al 1997, Durand et al 1996). Vychytil et al (1999) compared the effect of low- and high-flow TPD on peritoneal small solute clearances in low- and high-peritoneal transport patients (n = 30). In the low-low average group, IPD improved urea and creatinine clearances compared with TPD at low flow rates with similar volumes and length of treatment, but not once flows were increased. In high transporters, urea and creatinine clearances were greater than in low-low average transporters, with no difference between the PD modalities at low and high flow rates. Ultrafiltration did not improve with increasing volumes in this study. In two small cohort studies, Juergensen and co-workers compared TPD with conventional APD and found that no clearance advantage was found with fill volumes up to 24 L for TPD compared with conventional APD, but that clearances could be improved by increasing the frequency and fill volume in all transport types (Juergensen et al 2000, Juergensen et al 2002). Anuric, low peritoneal membrane transport patients have difficulty achieving adequate small solute clearances with TPD.

At present, there is no high level evidence that the use of TPD enhances small solute clearance. APD prescriptions should be individualised in terms of volumes and number of exchanges, body size, transport status, RRF and patient preference. PET tests should be repeated to ensure adequacy targets are met once this modality is introduced.

### **Ultrafiltration**

The use of icodextrin has been advocated for enhanced fluid removal, particularly for high transporters during the long daytime dwell, as well as increasing 24 hr creatinine clearance. An open, randomised prospective study of the daytime dwell with icodextrin versus glucose was performed in 23 APD (CCPD) patients followed for 2

years. They found that the dialysis creatinine clearance/1.73 m<sup>2</sup> increase in the icodextrin group could be fully explained by an increase in ultrafiltration (Posthuma et al 1997). Wolfson et al (2002) reported on 2 RCTs comparing the safety (n = 287, 210 CAPD, 77 APD) and efficacy (n = 175 CAPD) of icodextrin and glucose for the long daily dwell in APD and CAPD patients. They found that in the short-term efficacy study, icodextrin gave greater small solute clearance, which was explained by the higher ultrafiltration in that group, especially in high transporters. Icodextrin use has been associated with culture-negative peritonitis, allergy and increased maltose blood levels.

The use of alternative osmotic agents has been investigated including glycerol-based solutions (Smit et al 2000) in a small non-randomised study of short dwells or bicarbonate-based solutions (Plum et al 1999). No added effect was seen on small solute clearance. An amino acid-based solution in a small long-term retrospective study was associated with a decreased small solute clearance when used in one bag per day, although ultrafiltration rates were unreported (Taylor et al 2002).

### **Special groups**

In special groups such as diabetics and children, there is little data to date. In children, prescriptions are generally empirical and based on evidence extrapolated from adult studies. In a prospective cohort study of 51 children followed for 18 months, with the dialysis prescription left to the physician, Kt/V urea was greater in the APD (Kt/V 2.23) versus CAPD (Kt/V 1.68) patients but weekly creatinine clearance was similar. Loss of RRF was compensated by an increase in fluid turnover. High transporter status was a risk factor for impaired growth (Shaefer et al 1999). No additional recommendations regarding small solute clearance can be made for this subpopulation.

Studies of small solute clearance in diabetic patients on PD have shown conflicting results. Peritoneal membrane transport characteristics have been found to be unaltered (Graff et al 1999) in some studies but in others, higher peritoneal creatinine clearances on CAPD using a standard 2 L exchange schedule were found due to higher transport status (Tzamaloukas et al 1999). At this time, there is not enough evidence to suggest any different interventions to optimise small solute clearance for this subgroup of patients.

### **New techniques**

There is currently limited clinical experience with continuous flow PD although early experience has found increases in small solute clearance. Currently, the technique is in its experimental stages and technical difficulties still need to be overcome particularly relating to the type of catheter (ideally double lumen) inserted, to avoid recirculation (Amerling et al 2001). Continuous flow PD was compared with NIPD and NTPD in a crossover trial in 5 stable APD patients. This study confirmed the effectiveness of small solute clearance using a single pass, increasing dialysate flow rate protocol. They found that the creatinine clearance doubled that of the control APD patients and was five times greater than the mean CAPD value. Additionally, in low transporter patients, small solute removal was increased. Phosphate and urea clearances were enhanced as well as ultrafiltration (Freida & Issad 2003). Computer

simulations have also predicted improved small solute clearances (Leyboldt & Burkart 2002) with this therapy.

## **Summary of the evidence**

Evidence regarding optimisation of small solute clearance is largely based on studies of Level III evidence. There is increasing evidence for maintaining RRF as long as possible to enhance small solute clearance and emerging evidence of the effect of medications and nephrotoxins. Also, there is some evidence that there are other beneficial effects of preserved renal function to patient well-being. The use of APD has not been shown to hasten the loss of renal function and its use can improve small solute clearance in some patient groups such as high transporters. Increasing the fill volume or frequency of dialysis exchanges will generally improve clearances. Tidal peritoneal dialysis has no added advantage to small solute clearances at present. Icodextrin use can enhance clearance via increased ultrafiltration.

## **What do the other guidelines say?**

**Kidney Disease Outcomes Quality Initiative:** Ensure that staff are knowledgeable about PD prescribing; patient compliance is encouraged by reinforcing the appropriateness and benefit of treatment and regular updates regarding the importance of technique and the prescription (Guidelines 19, 20). Dialysis dose can be increased by increasing the instilled volume or increasing the number of exchanges per day, maintaining the maximal dwell (Guideline 18). NIPD dose must be 8% greater than CAPD to achieved prescribed dose (Guideline 16).

**British Renal Association:** Three clinical parameters that are essential are: residual renal function, patient size and peritoneal solute transport status. Residual renal function should be expressed as the mean urea to creatinine clearance. PET testing should be performed to assess transport status and individualise the dialysis prescription. A change in prescription should be checked for clinical efficacy by repeating clearance studies. Use of icodextrin is recommended for the daytime dwell in APD to optimise solute clearance and achieve ultrafiltration.

**Canadian Society of Nephrology:** (Opinion). Remeasure patient's total clearances soon after each alteration in prescription. Discusses the "incremental versus maximal" and "empiric versus modelled" approaches in dialysis prescription. If the empiric is used, take into account body size, residual renal function and transport status. Suggests minimal volumes instilled according to BSA, use of daytime dwells if on APD unless very small size, high transporters or good residual renal function. In APD, clearances are best increased by: increasing dwell volumes or cycler time or adding a second daytime dwell. Individualise prescription taking into account individuals preferences and lifestyle to minimise non-compliance.

**European Best Practice Guidelines:** No recommendation.

**International Guidelines:**

**International Society of Peritoneal Dialysis Guidelines:** Individualise the prescription according to patient's body surface area, amount of residual renal function and peritoneal membrane characteristics. Use of 2.5–3L fill volume, adding an extra exchange, using a “wet day” for those on APD should be considered when increasing the weekly Kt/V or creatinine clearance. Aim to provide the most dialysis possible to the patient, given financial, social and clinical constraints.

**Implementation and audit**

The ANZDATA registry should be used to determine small solute clearances in the Australian and New Zealand dialysis populations by mode of peritoneal dialysis, including details of and the rate of loss of residual renal function as well as associated clinical events. Suggest inclusion of details regarding how clearances were achieved; fill volume used, ultrafiltration achieved and dialysis prescription. Document any adverse outcomes from achieved small solute clearances such as degree of inflammation, cost, and concurrently report other relevant dialysis outcomes such as cardiovascular events.

**Suggestions for future research**

1. Conduct prospective observational cohort studies, such as via the ANZDATA registry, looking at the rate of loss of residual renal function in incident peritoneal dialysis patients by reporting exposure to events such as: medications such as ACE inhibitors, non steroidal anti-inflammatory drugs or nephrotoxic antibiotics, radio contrast media, hypotensive episodes or sepsis. The peritoneal dialysis technique used, age and other comorbidities should be recorded.
2. Conduct a multinational prospective cohort study of peritoneal dialysis in children measuring small solute clearances, residual renal function, the dialysis regimen used and clinical endpoints.
3. Conduct a prospective national randomised controlled trial of CAPD and APD in adult peritoneal dialysis patients including subgroup reporting e.g. diabetics, the elderly, obese and underweight patients, assessing small solute clearances obtained, dialysis prescription and clinical outcome.
4. Conduct controlled clinical studies of continuous flow through peritoneal dialysis compared with standard peritoneal dialysis techniques in larger numbers of patients reporting outcomes such as ease of technique, cost, patient preference, quality of life and cardiovascular morbidity and mortality.
5. New osmotic peritoneal dialysis solutions should be studied in a randomised controlled trial setting comparing small solute clearances achieved, volume control, technique survival and adverse reactions.

6. Any new therapeutic intervention affecting peritoneal membrane vasculature attempting to enhance solute removal should be part of a clinical trial rather than a small case series.

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## Appendices

**Table 1 Characteristics of included studies**

Study ID (author, year)	N	Study Design	Setting	Participants	Intervention (experimental group)	Intervention (control group)	Follow up (months)	Comments
Li, 2003	60	Randomised controlled clinical trial	Single centre	60 adult patients, PD	Ramipril 5 mg/day	No treatment	12	None
Mak, 2000	82	Randomised controlled clinical trial	Single centre	82 CAPD patients	3 daily 2 L exchanges (6 L of exchanges)	4 daily 2 L exchanges (8 L of exchanges)	12	None
Maschio, 1996	583	Randomised controlled clinical trial	Multicentre 49 European hospitals	583 patients with chronic renal insufficiency	Benazepril 10 mg/day	Placebo	36	None
Medcalf, 2001	61	Randomised controlled clinical trial	Single centre	61 new CAPD patients; $\geq 16$ yrs	Furosemide 250 mg/day	No treatment	12	None
Paniagua, 2002	965	Randomised controlled clinical trial	24 dialysis centres in 14 Mexican cities	865 CAPD patients; 18–70 yrs	Modified OD regimen. Achieve pC <sub>Cr</sub> value of 60 L/wk per 1.73 m <sup>2</sup>	Standard PD regimen. 4 daily exchanges of 2 L PD solution.	24	None
Plum, 1999	10	Randomised cross-over, intra-individual clinical trial	University medical centre	10 non-diabetic CAPD patients	1% amino acid with 34 mmol/L bicarbonate in 6 hr dwell for 1–3 wks.	1.5% glucose anhydrous, 24 mmol/L bicarbonate or conventional solution with 1.5 glucose anhydrous, 35 mmol/L lactate	15–72	3-arm study

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Posthuma, 1997	23	Randomised controlled clinical trial	Single centre	23 CCPD patients	Icodextrin daytime dwell (14–15hrs) for 2 yrs	Glucose daytime dwell (14–15 hrs) for 2 yrs	24	None
Wolfson, 2002	175 for efficacy study; 287 for safety study	Randomised controlled clinical trial	36 centres in USA and Canada	Adult CAPD patients for efficacy study; 210 CAPD and 77 APD patients for safety study	7.5% Icodextrin in long daily dwell (8–16 hrs)	2.5% dextrose in long daily dwell (8–16 hrs)	1 month for efficacy study; 12 months for safety study	2 randomised studies

Table 2 Quality of randomised trials

Study ID (author, year)	Method of allocation concealment	Blinding			Intention-to- treat analysis	Loss to follow up (%)
		(participants)	(investigators)	(outcome assessors)		
Li, 2003	Computer generated	No	No	No	Yes	0.0
Mak, 2000	Adequate, sealed envelopes	No	No	No	No	19.5
Maschio, 1996	Not specified	Yes	Yes	Yes	No	22.1
Medcalf, 2001	Not specified	No	No	No	Unclear	23.0
Paniagua, 2002	Central	No	No	No	Yes	18.0
Plum, 1999	Not specified	No	No	No	Yes	0.0
Posthuma, 1997	Not specified	No	No	No	No	39.5
Wolfson, 2002	Computer generated	Yes	Yes	Yes	Unclear	6.9

**Table 3 Results for continuous outcomes**

Study ID (author, year)	Outcomes	Intervention group (mean [SD])	Control group (mean [SD])	Difference in means [95% CI]
Li, 2003	Residual GFR (mL/min per 1.73m <sup>2</sup> )	3.55 (2.13)	3.74 (1.84)	-0.19 (95%CI: -1.20, 0.82)
Mak, 2000	Total urea clearance after 1 year (wKt/V)	1.67 (0.32)	2.02 (0.51)	-0.35 (95%CI: -0.54, -0.16)
	Peritoneal urea clearance after 1 year (wKt/V)	1.56 (0.32,)	1.92 (0.44)	-0.36 (95%CI: -0.53, -0.19)
	Renal urea clearance after 1 year (wKt/V)	0.11 (0.19)	0.10 (0.25)	0.01 (95%CI: -0.09, 0.11)
	Total creatinine clearance after 1 year (L/1.73 m <sup>2</sup> )	54.60 (12.96)	61.90 (12.65)	-7.30 (95%CI: - 12.84, -1.76)
	Peritoneal creatinine clearance after 1 year (L/1.73 m <sup>2</sup> )	48.40 (9.72)	56.0 (6.32)	-7.60 (95%CI: -11.13, -4.07)
	Renal creatinine clearance after 1 year (L/1.73 m <sup>2</sup> )	6.20 (11.02)	5.30 (12.65)	0.90 (95%CI: -4.25, 6.05)
Medcalf, 2001	Urine volume after 1 year (mL/24 hrs)	1070.00 (1074.58)	733.00 (679.18)	337.00 (95%CI: -112.62, 786.62)

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Plum, 1999	Glucose and lactate: Average serum glucose after 30 and 60 min dwells (mg/dL)	102.00 (15.00)	82.00 (8.00)	20.00 (95%CI: 9.46, 30.54)
	Glucose and bicarbonate: Average serum glucose after 30 and 60 min dwells (mg/dL)	93.00 (15.00)	82.00 (8.00)	11.00 (95%CI: 0.46, 21.54)
	Glucose and lactate: Average insulin over 6 hrs ( $\mu$ U/mL)	20.20 (10.50)	17.90 (9.00)	2.30 (95%CI: -6.27, 10.87)
	Glucose and bicarbonate: Average insulin over 6 hrs ( $\mu$ U/mL)	19.90 (9.10)	17.90 (9.00)	2.00 (95%CI: -5.93, 9.93)

**Table 3a Results for dichotomous outcomes**

Study ID (author, year)	Outcomes	Intervention group (number of patients with events/number of patients exposed)	Control group (number of patients with events/number of patients not exposed)	Relative risk (RR) [95% CI]	Risk difference (RD) [95% CI]
Li, 2003	Anuria	14/30	22/30	0.64 (95%CI: 0.41, 0.99)	-0.27 (95%CI: -0.51, -0.03)
Maschio, 1996	Primary endpoint reached in 3 yrs (doubling of baseline serum creatinine concentration or dialysis)	31/300	57/283	0.51 (95%CI: 0.34, 0.77)	-0.10 (95%CI: -0.16, -0.04)
	Mortality	8/300	1/283	7.55 (95%CI: 0.95, 59.96)	0.02 (95%CI: 0.00, 0.04)
	Withdrawn due to hyperkalemia	5/300	3/283	1.57 (95%CI: 0.38, 6.52)	0.01 (95%CI: -0.01, 0.02)
	Cough	25/300	10/283	2.36 (95%CI: 1.15, 4.82)	0.05 (95%CI: 0.01, 0.09)
Medcalf, 2001	All-cause mortality	3/31	1/30	2.90 (95%CI: 0.32, 26.38)	0.06 (95%CI: -0.06, 0.19)
	Anuria	3/31	2/30	1.45 (95%CI: 0.26, 8.09)	0.03 (95%CI: -0.11, 0.17)
	Fatal CV events	2/30	2/30	1.00 (95%CI: 0.15, 6.64)	0.00 (95%CI: -0.13, 0.13)

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	Hospitalisation	14/30	13/30	1.08 (95%CI: 0.62, 1.89)	0.03 (95%CI: -0.22, 0.28)
Paniagua, 2002	All-cause mortality	159/481	157/484	1.02 (95%CI: 0.85, 1.22)	0.01 (95%CI: -0.05, 0.07)
Posthuma, 1999	Peritonitis (1 or more episodes)	3/19	0/19	7.00 (95%CI: 0.39, 126.92)	0.16 (95%CI: -0.06,0.34)
	All-cause mortality	0/19	4/19	0.11 (95%CI: 0.01, 1..93)	-0.21 (95% CI: -0.41, -0.02)
Wolfson, 2002	Death	19/175	9/112	1.35 (95%CI: 0.63, 2.88)	0.03 (95%CI:-0.04, 0.10)
	Peritonitis	57/175	41/112	0.89 (95%CI: 0.64, 1.23)	-0.04 (95%CI: -0.15, 0.07)
	Upper respiratory tract infection	41/175	25/112	2.92 (95%CI: 1.48, 5.76)	0.01 (95%CI: -0.09, 0.11)
	Hypertension	40/175	21/112	1.22 (95%CI: 0.76, 1.95)	0.04 (95%CI: -0.05, 0.14)
	Anaemia	39/175	26/112	0.96 (95%CI: 0.62, 1.48)	-0.01 (95%CI: -0.11, 0.09)
	Rash	33/175	13/112	1.62 (95%CI: 0.89, 2.95)	0.07 (95%CI: -0.01, 0.16)
	Pain	30/175	18/112	1.07 (95%CI: 0.63, 1.82)	0.01 (95%CI: -0.08, 0.10)
	Exit-site infection	28/175	24/112	0.75 (95%CI: 0.46, 1.22)	-0.05 (95%CI: -0.15, 0.04)

**Dialysis Adequacy – Peritoneal Dialysis  
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	Hypotension	25/175	27/112	0.59 (95%CI: 0.36, 0.97)	-0.10 (95%CI: -0.19, 0.00)
	Headache	25/175	9/112	1.78 (95%CI: 0.86, 3.67)	0.06 (95%CI: -0.01, 0.13)