



FROM THE EDITORIAL OFFICE

Dear All,

In this issue we are delighted to have Dr. Li Lin, from Shanghai, share her experience of using peritoneal dialysis in ESRD patients with polycystic kidney disease. In addition, Dr. Sunjay Gupta, from New Delhi, will share his experience of handling compliance problems in PD patients.

You are most welcome to distribute this newsletter electronically, or in printed form to your colleagues or others who may be interested. If you or your colleagues would like to receive this newsletter directly from our editorial office, please send your e-mail address to: ispd@multi-med.com.

The 14th Congress of the ISPD will be held in September, in Kuala Lumpur! See you there!

Sincerely,

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Peritoneal Dialysis as the First-line Renal Replacement Therapy in Patients with Autosomal Dominant Polycystic Kidney Disease

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Autosomal dominant polycystic kidney disease (ADPKD), as the most common genetic kidney disease in the world, accounts for 3-10% of all patients currently treated for end-stage renal disease (ESRD) in Western countries ^(1,2). According to the latest statistics of the US Renal Data System (USRDS), cystic kidney disease (mostly ADPKD) is the fourth leading cause of ESRD. ESRD patients caused by cystic kidney disease rose by 2.4 percent, to 83 per million population in 2009, compared with that in 2008. Haematodialysis was more likely utilized as the renal replacement therapy in this group of patients, and the haematodialysis to peritoneal dialysis (PD) ratio was 6:1 (8999 vs. 1421).

Despite a rapid increase in the utilization of PD in China under the 'PD First' policy, there is a general perception that PD is not preferred as the renal replacement modality for patients with ADPKD because of the possible limited abdominal space which may restrict dialysis volume, possible peritoneum structural abnormalities which may alter the properties of dialysis membrane, and disposition of peritonitis secondary to potential colon diverticulitis or cyst infection. However, in our experience, PD is a valid option for the dialysis of patients with ADPKD.

Recently, we conducted a retrospective study enrolling 42 patients with ADPKD and 84 matched controls to analyze the clinical outcome of PD in a large unselected group of patients with ADPKD. Total duration of follow-up was 5,429 patient months; average follow-up was 43.2±33.9 months for the ADPKD group and 41.5±32.0 months for the control group. We found that survival of patients with ADPKD receiving PD was essentially the same as that for other non-diabetic PD patients. During the study period, 47 patients died. At 5 years, overall survival using the Kaplan-Meier estimate was 71.0% and 69.7% for the ADPKD and control groups ($P=0.4$; Figure 1), whereas technique survival was 51.6% and 37.3%, respectively ($P=0.3$; Figure 2). For complications, we also found that the risk of developing peritonitis was similar between patients with and without ADPKD. During the study period, 82 and 152 episodes of peritonitis were observed in the ADPKD and control groups, respectively. There was no significant difference in overall rates of peritonitis and peritonitis-free survival between groups ($P>0.05$). The major difference between the ADPKD and control groups was a higher incidence of hernia in the former. During the period of PD, 14 patients in the ADPKD group and 6 in the control group developed abdominal wall hernias ($P=0.001$). In our experience, patients with hernia could resume PD therapy after surgical repair, and there was no recurrent hernia. It is also noted that patients with ADPKD were more likely to develop recurrent blood-stained effluent than other PD patients, which we believe most were caused by the rupture of renal or liver cysts and had no discernible effect on the outcome of PD.

Some further prospective investigations are being conducted in our centre aiming to illuminate factors contributing clinical outcome of PD in patients with ADPKD. For example, intraperitoneal pressure (IPP) in ADPKD patients with reduced intraperitoneal space is potentially an important factor influencing the incidence of PD-related complications. IPP is not recommended by K/DOQI guidelines ⁽³⁾ and is rarely performed during current daily. Data of IPP in ADPKD and its relationship with clinical outcome of PD are rarely known in literature. In newly enrolled eligible ESRD patient with ADPKD as well as in the

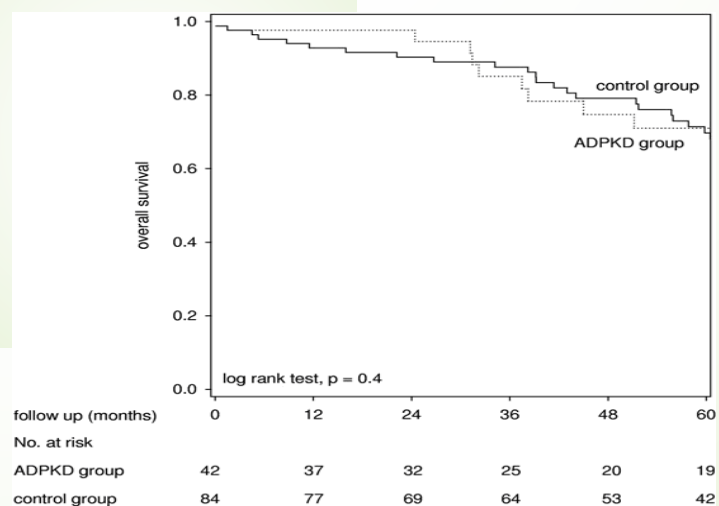


Figure 1 Kaplan-Meier plot of patient survival. Abbreviation: ADPKD, autosomal dominant polycystic kidney disease.

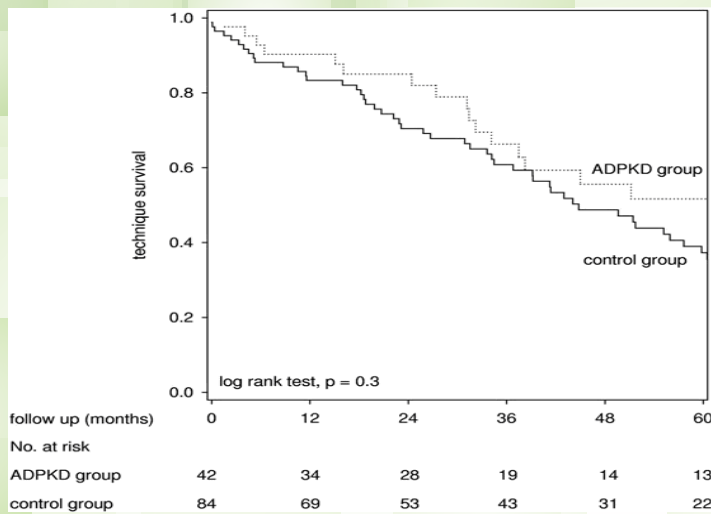


Figure 2 Kaplan-Meier plot of technique survival. Abbreviation: ADPKD, autosomal dominant polycystic kidney disease.

matched non-ADPKD patients receiving PD, IPP was measured as previously described by Durand *et al.*⁽⁴⁾. Briefly, a graduated column (cm), the zero level of which was placed on the medial axillary line of the patient in a supine position on a horizontal plane, was bound to the completely emptied abdominal cavity through the PD catheter before the test. IPP was measured on non-deep expiration (IPP exp) and non-deep inspiration (IPP insp) with a drained peritoneal cavity (time 0) and then for inflow volumes of 2000 ml, respectively with a 1.25% glucose dialysate solution. The results were read in centimetres of water (cm H₂O). IPP used in this study was the mean value between IPPs measured at expiration and inspiration: (IPP exp + IPP insp)/2. Our unpublished raw data showed that the IPP in ADPKD patients is significantly higher than that in non-ADPKD patient in a supine position with emptied peritoneal cavity, with 7.53 ± 3.49 cm H₂O and 13.29 ± 5.46 cm H₂O ($P < 0.05$), respectively. Similarly, IPP with 2000 ml of 1.25% glucose dialysate solution in peritoneal cavity in ADPKD patients was higher than that in non-ADPKD patient in a supine position, with 11.63 ± 4.54 cm H₂O and 19.02 ± 6.41 cm H₂O ($P < 0.05$). Cardiac doppler ultrasound was applied in the ADPKD and non-ADPKD patients with ESRD before and after drainage of PD fluid in our centre to test the influence of increased IPP on the heart function and clinical prognosis. However, there is no data showing significant difference between ADPKD patient and their counterparts concerning IPP impact on heart function until now. More data is needed to test whether higher IPP tends to increase the incidence of subsequent PD-related complications, such as hernias, late leakage, gastroesophageal reflux (GOR) and enteric peritonitis (EP).

Another limitation of present studies is the lack of information about kidney volume in ADPKD patient and their counterparts receiving PD. We have established a mature technique and procedure to measure kidney volume with Magnetic Resonance Image (MRI) as previously described (Figure 3)⁽⁵⁾, in cooperation with the division of nephrology of the University Hospital in Switzerland, to find whether kidney volume weighs in the clinical outcome of PD in patients with ADPKD. Larger sample sizes and longer follow-up periods are still needed to have sufficient statistical power to identify certain clinically meaningful differences between these subgroups.

In conclusion, our experience is that PD is a feasible treatment option for most ADPKD patients with ESRD. However, further evidence is needed and more prospective clinic trials are required.

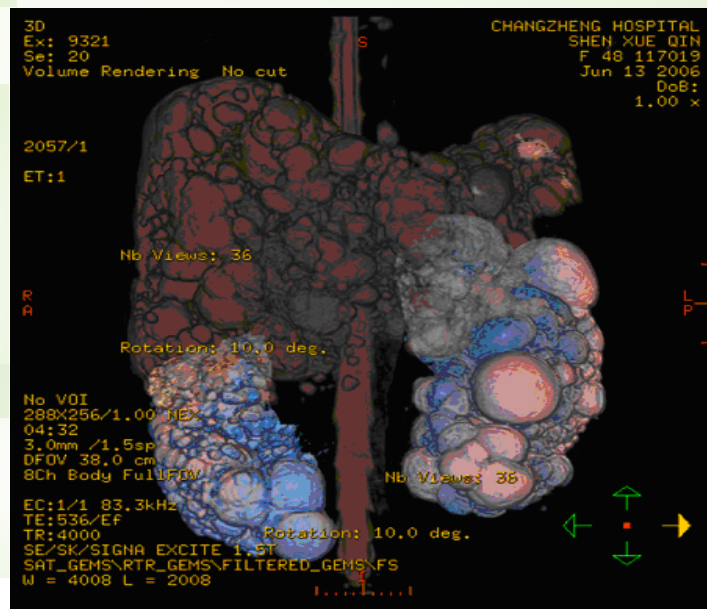


Figure 3 Representing image of MRI for kidney volume measuring.

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Non-compliance to the Continuous Ambulatory Peritoneal Dialysis Procedure Increases the Risk of Peritonitis

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Peritonitis is the most distressing complication of Continuous Ambulatory Peritoneal Dialysis (CAPD) treatment. Amongst the causes of technique failure, peritonitis is the most common (56%). Other causes are ultra filtration failure (14.7%), exit site and tunnel infections (13.2%), inadequate dialysis (10.2%), and mechanical malfunction (5.8%)⁽¹⁾. Peritonitis is responsible for 30-80% of permanent transfer to hemodialysis and 1-6% of death.

For any clinician, it is a goal to keep patients free of peritonitis, thus achieved by decreasing its risk factors. Risk factors such as diabetes, hypoalbuminemia and obesity are non-modifiable. Modifiable risk factors for peritonitis were investigated in our study, viz adherence to the procedure. The question we asked was, "Do the patients modify the procedure at home, and if they do, is the

modification detrimental in increasing peritonitis?"

It is agreeable that a break in the aseptic technique leads to peritonitis. The independence that CAPD allows patients is an advantage, but it may also predispose some patients to poor compliance to the procedure. Many patients may resort to convenient exchange procedure, which may be incorrect and detrimental by increasing the peritonitis rate. For convenience, patients may choose unhealthy steps or miss an infection-preventing step. Fortunately non-adherence to the protocol is correctable by adequate education.

We visited CAPD patients to assess compliance to the procedure. We observed the CAPD exchange procedure in home and assessed it as per the structured checklist. The procedure was then categorized into poor, average and good compliance. The compliance was correlated with the episodes of peritonitis.

In our study, only 16.5% patients were in good compliance, 67% in average compliance and 16.5% were in poor compliance. Poorly compliant patients uniformly defaulted in all domains, and as a result their attitudes must be improved by aggressive training. The most common improperly performed steps were: face mask not worn by 68%, tubing not flushed by 60%, all articles not gathered before starting by 42%, work surface not cleaned by 42% and hands not washed by 24%. Poor adherence to procedure was independent of age, gender, education and duration of dialysis⁽²⁾. All of the above steps are important in decreasing the risk of peritonitis, especially wearing a face mask, as many studies have shown this to be a cause of peritonitis⁽³⁾.

Ten episodes of peritonitis occurred in five patients over a one-year period. Interestingly, peritonitis occurred in 60% of the poorly compliant patients, where the fully compliant patients had no peritonitis episodes. Moreover 40% of the poorly compliant patients had multiple episodes of peritonitis. The Relative Risk (RR) of peritonitis between poorly compliant and good/average compliant patients was 7.5 (95% CI 1.8 to 30.7).

Amongst 10 peritonitis episodes, coagulase-negative staphylococci was the causative organism in 3 (30%), *Staphylococcus aureus* was the etiologic agent in 3 (30%) episodes and *E. coli* was detected in one (10%) only. Three (30%) episodes of peritonitis were culture negative. This implies the role of touch contamination in peritonitis.

The fact that nearly 84% of patients failed to adhere to the bag exchange procedure as taught, points to the need of retraining. Preparing patients to perform home dialysis safely is an intimidating task⁽⁴⁾. PD patients undergo a training process that enables them to perform PD exchange in a safe and effective way independently. Due to the chronic nature of CAPD, patients tend to progressively alter the CAPD procedure by skipping mandatory steps, thereby decreasing their attention to hygiene, while continuing to believe to be an expert and safe.

High prevalence of poorly compliant patients emphasizes the need for proper training and retraining after some interval to reinforce the procedure. Home visits to assess the adherence to the procedure is extremely important, which was suggested earlier⁽⁵⁾. The risky modifications of the procedure in our study were detected during home visits, thus highlighting the importance of home visits in the PD program.

Jie Dong *et al*⁽⁶⁾ study reported similar results; improper hand washing by 51%, failure to check expiration date or bag leakage by 46% and face mask and cap not worn by 11%. They reported that by not wearing a face mask and cap (hazard ratio (HR): 7.26; 95% confidence interval (CI): 2.6 to 20.1; $P < 0.001$) was an independent

predictor for a first episode of peritonitis.

Our study demonstrates an independent effect of non-compliance to CAPD procedure on the risk of peritonitis. Those who performed the CAPD procedure properly remained free of peritonitis and the poorly compliant patients were having a higher incidence and frequency of peritonitis.

The good association between compliance and peritonitis free patients, as demonstrated in the current study, verifies our hypothesis that patients who do not adhere to the procedure, as per their convenience, is injurious to their well-being. Although our data showed association between non-compliance with peritonitis, our study cannot verify a causal link between the two.

How to improve the quality of PD therapy is a big challenge. In an attempt to address this we have initiated an education program to improve patient adherence to the procedure, thus leading to a decrease in the peritonitis rate. Presently initial aggressive training starts in the hospital, continues at home for a total of two weeks, followed by a compliance assessment and reinforcing the steps at six months intervals. Each episode of peritonitis is carefully investigated and followed by a reinforcement of the procedure technique of the patients and caregivers. We are yet to publish this data.

In summary, there is a significant prevalence of the improper bag exchange procedure. Non-compliance is significantly associated with the increased incidence and frequency of peritonitis. In other words, adherence to aseptic procedure as per the protocol prevents peritonitis. This study stresses the importance of adequate training and retraining. This practice is critical to the goal of decreasing the risk of peritonitis and maintaining the viability of the peritoneal membrane. As adherence of the procedure can be improved by retraining, compliance is a modifiable risk factor for peritonitis.

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Literature Update

Xie J, *et al*. Coiled versus straight peritoneal dialysis catheters: a randomized controlled trial and meta-analysis. *Am J Kidney Dis* 2011; 58: 946-955.

KEY POINTS: Which design of peritoneal dialysis catheter should we use? Variations in peritoneal dialysis catheter design include differences in numbers of cuffs, shapes of subcutaneous paths,

and shapes of intra-abdominal segments. The relative benefits of these designs are unknown. A recent randomized control trial of 80 patients compared coiled and straight catheters. Unexpectedly, the researchers found an insignificant increase in the risk of catheter tip migration with dysfunction in the coiled catheter group (hazard ratio, 1.96; $p = 0.09$). The same group went on and performed a meta-analysis of close to 500 patients from 4 trials, and, once again, they found that coiled catheters had an increased risk of catheter tip migration (relative risk, 2.08; $p = 0.002$).

Thirugnanasambathan T, et al. Repeated peritoneal dialysis-associated peritonitis: a multicenter registry study. Am J Kidney Dis 2012; 59: 84-91.

KEY POINTS: Although labelled as a distinct category under the contemporary ISPD guideline, very little is known about repeat peritonitis, defined as episodes occurring more than 4 weeks after treatment of a prior episode and caused by the same organism. Based on the Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) data from 2003 to 2007, a group of researchers reviewed 245 repeat peritonitis episodes. In short, they found that *Staphylococcus aureus* and coagulase-negative staphylococcus were distinctly more common in repeated peritonitis. Using multivariate logistic regression, repeated peritonitis was associated independently with higher relapse but a lower hospitalization rates. Contrary to common belief, the rates of catheter removal, hemodialysis transfer, and death were similar to the control group.

Rees L, et al. Growth in very young children undergoing chronic peritoneal dialysis. J Am Soc Nephrol 2011; 22: 2303-2312.

KEY POINTS: Peritoneal dialysis is the usual modality of renal replacement therapy for very young children, but very little is known about the nutrition and growth in this group of patients. A multinational group recently analyzed data from 153 children in 18 countries who received peritoneal dialysis at 24 months of age or less. The researchers found that body length decreased sharply during the first 6 to 12 months of life and then tended to stabilize. In terms of body weight, an interesting observation was noted: 26% of North American children were obese, while 50% of Turkish children were malnourished. Another important finding was, in addition to the administration of growth hormone, the use of biocompatible PD solution was associated with improved length.

Loureiro J, et al. Blocking TGF- β 1 protects the peritoneal membrane from dialysate-induced damage. J Am Soc Nephrol 2011; 22: 1682-1695.

KEY POINTS: TGF- β 1 plays an important role in the pathogenesis of peritoneal fibrosis, especially in the process of mesothelial-to-mesenchymal transition (MMT), a process associated with peritoneal-membrane dysfunction. A group of researchers from Spain recently reported the efficacy of TGF- β 1-blocking peptides in modulating MMT and ameliorating peritoneal damage in a mouse model of PD. In short, administration of TGF- β 1 blocking peptides significantly ameliorated fibrosis and angiogenesis, and improved peritoneal function. This form of local therapy seems an attractive approach and deserves further translational research.

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