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INTERNATIONAL SOCIETY FOR PERITONEAL DIALYSIS (ISPD)
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FROM THE EDITORIAL OFFICE

Dear All,

Welcome back from the ISPD Asia-Pacific Chapter meeting at Guangzhou. It has over 5000 delegates and was a great success.

In this issue, we are delighted to have Dr. Wei Fang from China to discuss the relation between PD exchange volume and residual renal function. In addition, Dr. Rachael Walker from New Zealand will share her experience of starting PD, while Dr. Ryu from Korea will present the data of technique failure in his country.

You are most welcome to distribute this newsletter electronically or in printed form to your colleagues or other people interested. If you or your colleagues want to receive this newsletter directly from our editorial office, please send your e-mail address to: ccszeto@cuhk.edu.hk

Sincerely,
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Opening Ceremony of the ISPD Asia-Pacific Chapter meeting at Guangzhou on 22 March 2017

Peritoneal dialysis exchange volume and residual kidney function

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The importance of residual kidney function (RKF) to survival and quality of life for dialysis patients has been well established. Both renal solute clearance, which is usually named as residual renal function (RRF), and urine output are important aspects of RKF. It has been shown that in peritoneal dialysis (PD) patients, for every 1 ml/min increase in glomerular filtration rate (GFR) there was a 50% reduction in the risk of death (1) and that a 250-ml increase in daily urine output was associated with a 36% reduction in mortality (2). Unfortunately, factors affecting RKF deterioration in PD are still not completely understood.

Only few studies have reported the association between PD exchange volume and RKF. A cohort study found that larger PD fluid volume per day was a strong independent predictor of a steep decline in RRF (3), but causality between large PD volume and fast RKF loss cannot be identified due to the observational study design. Recently, a randomized controlled trial (RCT) showed that the reduction in residual Kt/Vurea and urine output were associated with increases in PD volume, however, RKF was only a secondary outcome in that study (4).

We conducted a randomized controlled trial to compare the effects of 3 exchanges CAPD (6 liters of conventional PD fluids per day) and 4 exchanges CAPD (8 liters of conventional PD fluids per day) on RKF in 139 incident patients (5). We found that after 24-month follow up, subjects undergoing these two regimens had similar GFR, urine output, decline rates of GFR and urine output, and anuria-free survival rates. However, it is far from drawing the conclusion that these regimens have identical impacts on RKF since our study was of limited sample size which might lead to underpowered results. Actually, we observed that decrements in urine output (628 ± 646 vs. 941 ± 610 ml/d, p = 0.011) and GFR (2.8 ± 3.0 vs. 3.9 ± 3.0 ml/min, p = 0.066) were less dramatic in patients dialyzed with 3 exchanges CAPD after 12 months on PD (data unpublished). On the other hand, less susceptive to peritonitis, similar patient survival and technique survival were observed in patients on 3 exchanges CAPD when compared with their counterparts dialyzed with 4 exchanges.

Ultrafiltration achieved by different PD exchange volume may lead to diversity in RKF deterioration. There is a conflict between achieving euvolemia and risking episodes of hypovolemia and loss of RKF when concerning ultrafiltration in dialysis. An interventional study by Gunal

et al reported that increased ultrafiltration optimized body weight and blood pressure control but at the same time led to significant reduction in RRF and urine output (6). Jansen et al found that the presence of intravascular dehydration contributed to accelerated RRF loss in a retrospective study (7). Our results also support the competition relationship between ultrafiltration and urine output. Though lower PD exchange volume does not inherently stand for inferior ultrafiltration capacity, our study showed that patients dialyzed with 3 exchanges CAPD had considerably less ultrafiltration in contrast to their counterparts undergoing 4 exchanges CAPD during most of the study period. That means low PD exchange volume is less likely to yield aggressive amount of ultrafiltration, and subsequently there may be less opportunities to develop intravascular volume depletion. Though previous studies did not support the benefit of extracellular volume expansion in preserving RKF, what the situation will be if "moderate" volume status is achieved is not clear, particularly when given that it is difficult to define even by using novel techniques such as bioimpedance. We believe that maintaining appropriate ultrafiltration avoiding both hypovolemia and hypervolemia is critical to RKF preservation.

Glucose exposure from PD fluid may be another factor influencing RKF. In our study, dextrose concentrations were chosen according to patients' individual condition, and we did not restrict the use of hypertonic PD fluid, but even so, 3 exchanges CAPD regimens still rendered significantly less glucose load compared to 4 exchanges CAPD all through the study period. That may be a hint that in majority of cases more PD exchange volume means more glucose exposure. Szeto et al reported in a retrospective analysis that every 10 g/day higher glucose exposure was associated with a 2.5% increase in the risk of progressing to anuria (8), and later a sub-study of balANZ trial also showed that every 10 g/day increase in dialysate glucose exposure was associated with 4% and 10% worse RRF and urine output preservation respectively (9). High glucose exposure may exert adverse effect on RKF via excessive ultrafiltration as mentioned above. Another possible explanation may be more glucose-degradation-product (GDP) burden accompanying high glucose exposure. However, GDP induced apoptosis and toxicity in renal tubular cells is only demonstrated in animal study and there has not been evidence from clinical studies. This hypothesis can only be speculated from studies investigating protective benefit of low GDP PD fluids to RKF.

PD modality might be also worthy of note. Automated PD (APD) calls for higher daily PD fluid volume than CAPD does to achieve same goal of solute clearance. Though it remains controversial, there have been evidences that APD might result in greater decline in RKF (10). Its uncontinuous fluid removal is akin to that of hemodialysis, and that makes fluid status less stable and possibly causes faster RKF loss.

In summary, our study suggested that 3 exchanges CAPD did not preserve RKF better than did 4 exchanges CAPD within a 2-year period in incident patients except alleviated decline of urine volume during the first year on PD. Clearly more clinical evidences are needed to elucidate the association between PD exchange volume and RKF. Our study also indicates that initiating PD therapy with lower dose, then incrementally increasing dialysate volume according to individual conditions, could be a safe and cost-effective strategy of PD therapy.

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News from the ISPD

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This is a scholarship to support up to 3 months training in clinical PD for doctors and nurses from Asia-Pacific region. Deadline for application for each round: twice a year at 30 June or 31 December. **The next deadline is 30 June 2017.** Details and application procedures can be found under the Regional Chapters – Asia-Pacific Chapter, at the ISPD website.

Upcoming Meetings

ISN World Congress of Nephrology
21-25 April 2017
Mexico City, Mexico
Web site: http://www.wcn2017.org/

23rd Annual Meeting
Japanese Society of Peritoneal Dialysis
7-8 October 2017
Kitakyushu, Fukuoka, Japan
Web site: http://www.congre.co.jp/jspd2017/

17th Congress of International Society for Peritoneal Dialysis
5-9 May 2018
Vancouver, Canada
Website: http://ispdvancouver2018.org/

Where to start? Educating patients and their families about Peritoneal Dialysis

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Nephrology units face a dialysis decision-making paradox. As we encourage choice of peritoneal dialysis (PD) for numerous reasons including preservation of vascular access, reducing hospital admissions, and promoting independence and flexibility, as well as reducing the large financial burden on renal units of facility haemodialysis, the patient experience informs us we are not adequately preparing or supporting them in these areas. The most effective and patient-centered way to educate people with end stage kidney disease (ESKD) remains poorly understood and researched. Despite international guidelines recommending patients are fully educated about all treatment options and are able to choose the most preferred renal replacement therapy (RRT) according to lifestyle preferences, there currently exist no guidelines, recommendations or even convincing data that offers advice on what constitutes effective RRT education nor on how we best meet patients' educational needs.

A recent systematic review and meta-analysis which summarizes the findings of 15 studies exploring the influence of pre-dialysis educational interventions for both patients' pre-dialysis choice and commencement of PD identified only one randomised control trial (RCT) in this area (1). The authors report in the RCT, receiving an educational intervention was associated with a 4.6-fold increase in the odds of patients choosing PD, in 4 observational studies a patient-targeted intervention increased the odds of choosing PD by 2-fold increase and a 3.5-fold increase in the odds of patients receiving PD as their initial dialysis modality, compared to standard education. However, the individual components within the educational interventions that influence patient decision-making were unclear and so the "best" strategy to educate patients about PD remains poorly understood. Despite not completely understanding the optimal components of educational programs, evidence suggests that patient choice of PD is associated with better long-term PD survival (2) and therefore we should focus on how to positively influence patient education and confidence in PD decision-making.

Compounding the challenge to adequately educate patients is the low health literacy and numeracy of the general adult population (3). This is intensified in the ESKD patient population who are generally more disadvantaged than the general population many with ESKD as a result of previously uncontrolled diabetes, hypertension and obesity. We are asking an enormous task of these patients to be educated, and make an "informed decision" in such a short space of time, often after only one time-limited education session. Our previous research has indicated that patients themselves acknowledge they reach ESKD scared and unprepared for what lies ahead despite having had formal pre-dialysis education (4) and pre-dialysis nurses themselves delivering the education feel they do not have adequate time to educate patients (5). Services that are committed to increasing PD uptake must therefore invest in ensuring they are delivering high quality pre-dialysis programs. Previous research has shown that nephrologists are influential figures in renal departments (6) and their recommendation of PD to nursing staff, patients and their families is important. This recommendation is usually based on the nephrologists own previous experience and exposure to successful PD programs.

Patients themselves also report a number of barriers to PD uptake that require changes in service delivery to better align to patient priorities. A significant barrier throughout the available evidence is the need for increased nursing support at home to help alleviate the initial fear of commencing home dialysis. The evolution of assisted PD in some European countries may indicate that it is indeed achievable to meet this patient preference. Countries such as France and Norway where assisted PD is reimbursed have seen a dramatic rise in the uptake of this modality, particularly in the older population and from an economic perspective, this option appears to have comparable operational costs to facility dialysis and may also lead to improvements in the quality of life of the RRT population (7).

The recent awareness of shared-decision making encouragingly suggests that we are now heading in the right direction and starting to focus more on the importance of patient-centered care that incorporates patient values and preferences. Decision aids encourage people to consider information about all treatment options and their advantages and disadvantages, evaluate this information while considering their own values and goals and then make decisions based on this combined information. Recent evaluation of the Yorkshire Dialysis Decision Aid (YoDDA) booklet demonstrated pre-dialysis patients highly valued this decision-aid. The group who utilised YoDDA reported higher scores for understanding kidney disease, reasoning about options, feeling in con-trol, and sharing their decision with family than the conventional group (8). As well as encouraging the use of decision-aids to patients, clinicians can also use decision-aids to better understand patient preferences and values and therefore be guided in their discussions with patients.

We must also look to previous research that identifies the barriers to PD uptake. Nephrologists and renal nurses in New Zealand identified the most frequent barriers to uptake of PD as being the lack of information about PD, established misconceptions about patient suitability for PD, and late referrals to dialysis. An important enabler was early and frequent pre-dialysis education (9). A recent Canadian review suggests a step-wise process for successfully initiating a patient on PD. The first step is the need to identify all potential PD patients, including those who present with acute kidney failure, failed HD access, late referrals, and patients with failing transplants. The second step involves assessment of each patients' suitability to PD by an experienced multidisciplinary team. This assessment should consider challenges (such as limited dexterity) and how to alleviate these prior to PD initiation by determining whether PD could be performed by a family member or a healthcare professional (10).

In conclusion, although a number of challenges exist in educating patients about initiating PD, these challenges are not insurmountable. They do, however, require renal services and policy makers to actively consider patient values and priorities and focus on aligning services to better meet patients' educational and home support needs. There is still much research to do in this area and future clinical trials should focus on the evaluation of educational programs, and what components within these programs are best suited to the patient and are also most influential on modality choice and uptake of PD.

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Technique failure in Korean incident peritoneal dialysis patients: a national population-based study

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In Korea, the number of new patients on peritoneal dialysis (PD) has been decreasing since 2007, whereas more patients are selecting hemodialysis (HD) as the first dialysis modality (1). The plausible reasons are inferred to be increased number of HD centers, easy accessibility to the widespread HD centers, and concern for the complications of PD including PD peritonitis (2).

High technique failure rate of PD mainly due to peritonitis and peritoneal membrane failure is an important health issue to PD patients. In addition, it may affect a medical staff and a patient with chronic kidney disease who is about to select the first dialysis modality, thus it is partly related to low incidence of PD. As transference from one dialysis modality to another usually needs hospitalization and may be associated with mortality, it has been emphasized for nephrologists to recognize the causes and predictors for the technique failure, which may be helpful to prevent it. Although a population-based research regarding this issue was reported in a Western country (3), there is no similar study in Asia, where clinical characteristics of dialysis patients are quite different from Western countries. Therefore, we recently analyzed technique failure rate in detail and tried to determine the predictors for technique failure in Korea using the Korean Health Insurance Review and Assessment Service (HIRA) database (4).

Since all medical practices and related expenses are reviewed by HIRA for the reimbursement in Korea, we were able to identify all patients who had started PD between January 1, 2005, and December 31, 2008 using the HIRA database. In this analysis, a total of 7,614 PD patients was included. During the median follow-up of 24.9 months, 942 (12.4%) PD patients had experienced technique failure, and the crude incidence rate of technique failure in new Korean PD patients was 54.1 per 1,000 patient-years. Median time of technique failure after initiation of PD was 25.0 months (interquartile range, 15.3-39.0 months).

The cumulative 1-, 2-, and 3-year technique failure rates of PD patients were 4.9%, 10.3%, and 15.6%, respectively, by Kaplan-Meier analysis. However, those were higher than the values by competing risks analysis (1-, 2-, and 3-year technique failure rates; 4.6%, 9.1%, and 12.8%, respectively), and the differences increased with the follow-up period. Since there are several competing risks, such as death, transplantation, and technique failure in survival analysis of dialysis patients, Kaplan-Meier method, which does not count those competing risks, is likely to overestimate the incidence of technique failure. Therefore, we suggest that competing risk analysis should be performed and the results are presented together with those by Kaplan-Meier method.

In this study, after adjustment with all eligible variables, Medical Aid (hazard ratio [HR], 1.28; 95% confidence interval [CI], 1.07-1.52; P = 0.007) and diabetes mellitus (HR, 1.42; 95% CI, 1.24-1.62; P < 0.001) were the independent predictors for technique failure in Cox proportional hazard analysis. In comparison, Medical Aid (subdistribution HR, 1.27; 95% CI, 1.07-1.52; P = 0.008), diabetes mellitus (subdistribution HR, 1.35; 95% CI, 1.19-1.54; P < 0.001), and cancer (subdistribution HR, 0.62; 95% CI, 0.41-0.93, P = 0.022) remained statistically significant in Fine and Gray analysis. In spite of slight difference in the results between the two analytic methods, we can draw a straightforward conclusion that we should pay more attention to PD patients on Medical Aid and/or with diabetes for the prevention of technique failure.

Considering the unique medical environment in Korea, we'd like to point out that Medical Aid was a significant predictor for technique failure as well as mortality (HR, 1.71; 95% CI, 1.53-1.90; P < 0.001) among incident PD patients (5). Although Medical Aid beneficiaries and patients covered by National Health Insurance are a crude dichotomous classification, complex and rigorous criteria are applied into the classification process in Korea, including lack of family support and/or incapability of labor as well as low income. If we can say that the type of health security system serves as a rough estimate for each patient's socioeconomic status in Korea, economic and functional status of PD patients and family support for them would generally affect the important clinical outcomes.

In addition, we found that there was no significant difference in the technique failure-free survival rate according to the dialysis initiation year between 2005 and 2008. Although the period is definitely not enough to investigate sequential changes, the survival rate among Korean PD patients initiating dialysis was significantly improved during the same period, as previously reported (5). We unfortunately could not evaluate the causes of technique failure in this study because there was neither clinical nor laboratory information in the HIRA database. However, we are aware of the fact that the most common cause (63.6%) of technique failure is still peritonitis in Korea from a

representative prospective cohort study (6), and we need to put more effort to prevent peritonitis in order to decrease high technique failure rate.

Conclusively, although a conventional method such as Kaplan-Meier analysis is likely to overestimate the risk of technique failure in PD patients, it is definitely a major concern in patients initiating PD in Korea, especially in diabetic patients and Medical Aid beneficiaries. In addition, peritonitis is a major cause of technique failure. Therefore, we suggest that the sustained effort to prevent PD peritonitis is an important strategy for the improvement in PD patient outcomes, especially among PD patients at high risk for the development of technique failure.

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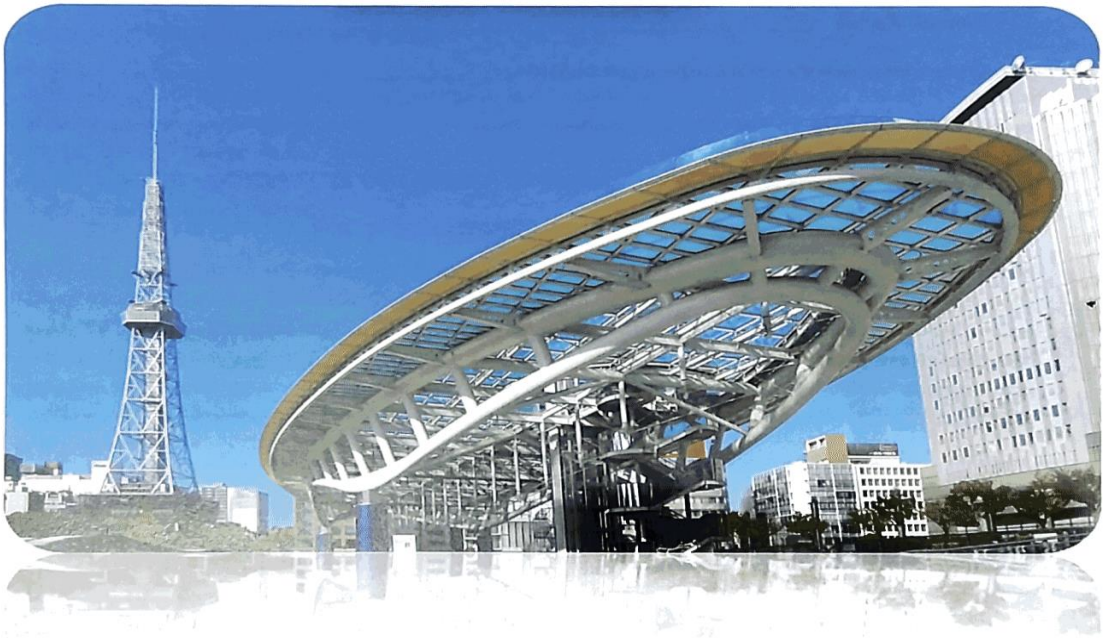

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