ISPD Asia-Pacific Chapter Newsletter, Spring 2020

VOLUME 18, ISSUE 1

Chapter News

Meeting and conference

We are pround to announce the 10th Asia Pacific Chapter Meeting of the International Society of Peritoneal Dialysis (APCM-ISPD 2021) will held at the Bali Nusa Dua Convention Center (BNDCC), Bali, Indonesia, on 21 to 23 October 2021. The meeting will be hosted by the Indonesian Society of Nephrology. Professor Aida Lydia Sutranto, President of Indonesian Society of Nephrology, will be in charge of the organziation.

Call for further meeting

The ISPD Asia Pacific Chapter will call the bidding for hosting the 11th Asia Pacific Chapter Meeting of the International Society of Peritoneal Dialysis, which is expected in 2013.

Scholarship and fellowship

Dr. Vaishnavi Raman from India has just completed her ISPD fellowship program hosted by the Royal Brisbane & Women's Hospital and Queensland Children's Hospital, both at Queensland, Australia, under the supervision of Dr. Dwarakanathan Ranganthan and Dr. Peter Trnka, respectively. We look forward to seeing her other contribution to the International Society for Peritoneal Dialysis in the near future.

Prepared by: CC Szeto, Coordinator, ISPD Asia Pacific Chapter

News from the ISPD

Join the ISPD !

Visit https://ispd.org/memberships/ to join the ISPD or renew your membership.

Membership benefits of the International Society for Peritoneal Dialysis include:

- print and/or online subscription to Peritoneal Dialysis International
- Receipt of PD News
- Online access to ISPD Guidelines
- Special registration fees at ISPD Congress, Chapter Meetings and the Annual Dialysis Conference
- Application for ISPD Scholarships and Grants

Membership for developing countries can be done at advantageous rates, by grouping members by institution or region geographical area. Write to admin@ispd.org for more information.

Asia-Pacific Chapter Scholarship

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 2020.** Details and application procedures can be found under the Regional Chapters – Asia-Pacific Chapter, at the ISPD website.

Upcoming Meetings

10th Asia Pacific Chapter Meeting of International Society for Peritoneal Dialysis

21-23 October 2021

Bali Nusa Dua Convention Center (BNDCC)

Bali, Indonesia

ISPD / EuroPD Joint Congress

27-30 March 2021

Scottish Event Campus (SEC), Glasgow, Scotland

Website: http://ispd-europd2020.com/

Bidding for the 11th ISPD Asia-Pacific Chapter Meeting

Proposed timing

2023Q3-4

Deadline for bidding

30 September 2020

Submission of application

A soft copy of the bid application should be sent to the ISPD APC coordiator:

CC Szeto, c/o Department of Medicine & Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong.

Email: ccszeto@cuhk.edu.hk

Content of the bid application

- The name of president of the local organizing committee
- Support from the national or regional society of nephrology
- The proposed timing and venue of conference
- The convention facilities with preferably a venue hotel in the convention complex.
- The strength and experience of the local organizing committee, national or regional society of nephrology in relation to PD practice, development, research, and organization of conferences
- Rationale why Asia Pacific Chapter meeting should be hosted in that country
- Transportation information
- Accommodation details (at different budgetary levels)
- The proposed budget to host the meeting
- Local attractions for visitors

Financial Arrangement

Any profits arising from the Meeting will be split 50-50 between the Local Organization Committee and the ISPD. Majority of the profit going to ISPD will be designated for promotion and development of PD in the Asia Pacific region. Under extraordinary circumstances, ISPD APC will back up the organizing committee for financial deficit up to a maximum of USD$10,000. Any further financial loss will be the responsibility of the organizing committee.

Decision making body

All bid applications will be reviewed by the ISPD APC Executvie Group. A final decision would be made in close consultation with the ISPD President. The ISPD APC will convey the decision to the ISPD Council. The process will be completed and result announced around 18 months before the conference.

Research News from Asia-Pacific Region

Effect of Liver Cirrhosis on the Outcomes of Peritoneal Dialysis

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Peritoneal dialysis (PD) as a treatment option for patients with end-stage renal disease (ESRD) is an attractive therapy, providing greater cost-effectiveness and less hemodynamic stress with a lower bleeding tendency than hemodialysis [1]. Another advantage of PD is less travelling for dialysis maintenance, which may appeal to patients lacking adequate transportation or living long distances from dialysis facilities [2]. Despite advantages of peritoneal dialysis (PD), only 10%–15% of the dialysis population receive PD worldwide. Therefore, the potential indication of PD

may need to be expanded to patients with ESRD who have previously been unsuitable for this modality.

Liver cirrhosis (LC) is a common comorbidity in patients with chronic kidney disease. Catheter-related complications, such as peritonitis or leakage of peritoneal fluid, may be potential barriers to start PD in patients with LC [3]. However, ascites may sometimes be well controlled by PD [4]. Data on the usefulness of PD in patients with LC are scarce.

Among four hospitals, we followed 45 patients who had been diagnosed with LC before dialysis (LC-PD). Using a matching algorithm, we matched LC-PD patients with non-LC patients on PD (non-LC-PD) at a 1:1 ratio for age, sex, catheter insertion date, and diabetes mellitus. Concurrently, we screened 184 patients who had started HD in the same hospitals over the same period of 2000 to 2015 and had been diagnosed with LC before dialysis. Among the total patients, 45 were selected as the LC-HD group using the same propensity score matching.

The risks of technical failure, infection (exit-site infection and peritonitis), and all-cause mortality were similar between the LC-PD and non-LC-PD patients (Figures 1–3). These trends remained consistent irrespective of adjusting multiple covariates.

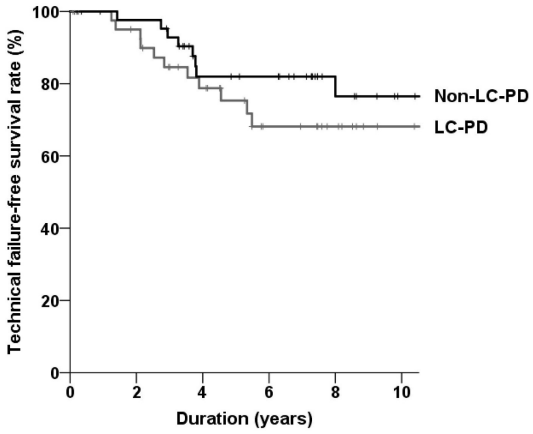

Figure 1. Technical failure-free survival curves between patients with LC and those without LC who underwent PD.

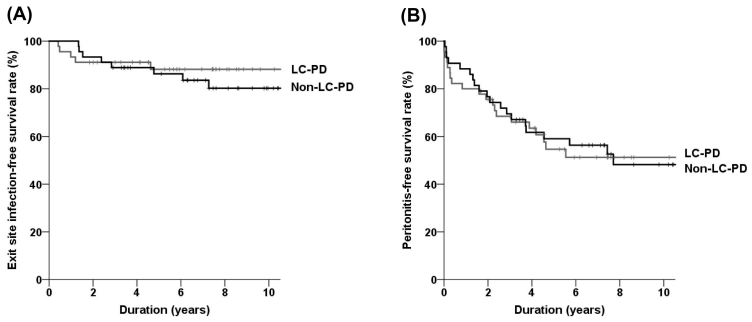

Figure 2. Exit site infection-free (A) and peritonitis-free (B) survival curves between patients with LC and those without LC who underwent PD.

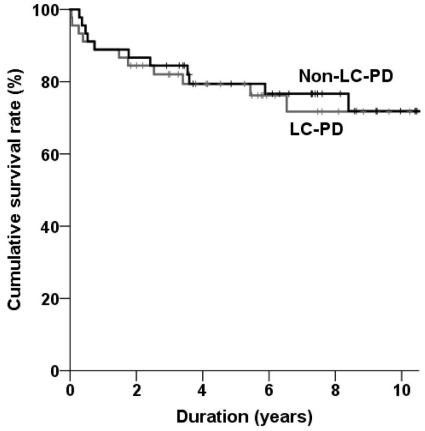

Figure 3. Death-free survival curves between patients with LC and those without LC who underwent PD.

The mortality curves of the LC-PD and LC-HD groups are shown in Figure 4. There seemed to be survival benefit in LC-PD patients compared with LC-HD patients (P = 0.034). However, when multiple covariates were adjusted, the LC-PD group had a similar risk of mortality to the LC-HD group (hazard ratio, 1.61 [0.714 – 3.610]; P = 0.252).

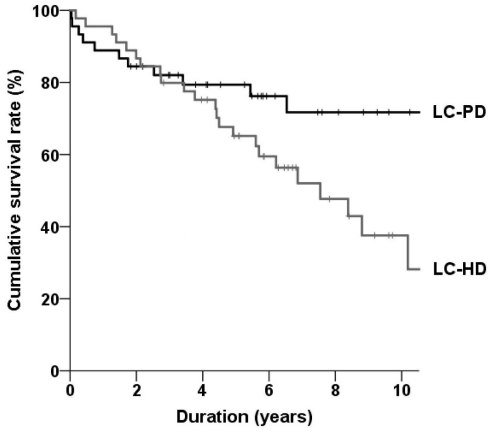

Figure 4. Death-free survival curves between patients with LC-PD and LC-HD.

Previous studies have shown a variety of conclusions: that LC did not worsen the outcome of PD (5), or that LC led to poor survival (6). In this study, there was no difference in the PD outcomes between the LC-PD group and the non-LC-PD group. In the real clinical situation, physicians predict that LC patients will visit the hospital frequently because of regular inspections for screening hepatocellular carcinoma. Excellent accessibility to hospitals in the LC-PD group might improve the overall outcomes comparable to the non-LC-PD group.

The present study has some limitations. First, the observational study design limited the application of causal relationships. Second, factors such as residual renal function or peritoneal function and sufficient information on nutritional and volume status could not be obtained in some patients, which might have affected our results. However, our study had a modest sample size, but matching analysis was performed to increase the power of analysis.

Overall, our study suggests that the presence of LC is not a critical factor for patient choice of dialysis modality. The results will make it easier for patients to choose PD as a long-term plan for ESRD with LC, which could help patients to experience and enjoy the benefits of PD. In addition to preserved residual renal function and lower cost, PD has many advantages in patients with ESRD and LC. Patients with LC have a hemorrhagic tendency. Anti-coagulant drugs used in HD aggravate bleeding. However, anti-coagulant drugs are not involved in PD, and thus PD may not aggravate bleeding. PD may also slowly clear up solutes, which could explain the previous finding that the prevalence of hypotension is relatively lower in PD than in HD (6). Therefore, PD could be an important therapeutic option in patients with ESRD and LC, and efforts to increase its use should be continued.

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Proton Pump Inhibitor Use Increases the Risk of Peritonitis in Peritoneal Dialysis Patients

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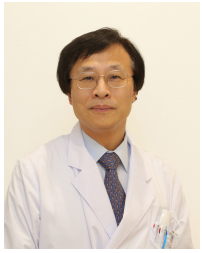

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Peritonitis is a major and the most significant complication of peritoneal dialysis (PD), which is associated with significant morbidity, catheter loss, transfer to hemodialysis, permanent membrane damage, and occasionally death[1]. Therefore, it is important to prevent and reduce the risk for developing peritonitis in patients on PD. Although proton pump inhibitors (PPIs) are among the top 10 most widely used drugs in the world. A meta-analysis showed a significant association between H2-receptor

antagonist (H2RA) use and "enteric peritonitis"; peritonitis was caused by enteric bacteria, but PPI use was not identified as a risk factor [2]. However, the study sample size was small, which might have led to the underestimation of the influence of PPIs. Therefore, the result remains to be elucidated and should be validated. We conducted and reported the study to examine whether PPI use might be a risk factor for peritonitis [3].

The present study included 230 Japanese PD patients, with 73 (31.7%) patients in the PPI group and 157 (68.3%) patients in the non-PPI group. The baseline characteristics of the two groups were not significantly different between the two groups. During the follow-up period (median, 36 months; interquartile range, 19–57 months), 86 patients (37.4%) developed at least one episode of peritonitis. Forty-one (56.2%) and 45 (28.7%) patients in the PPI and non-PPI groups, respectively, developed peritonitis at least once (P<0.001). Among the total of 41 patients who developed peritonitis in the PPI group, 36 (87.8%) developed peritonitis during the period of PPI use. The proportion of recurrent episodes of peritonitis (more than 2 episodes) was higher in the PPI group than in the non-PPI group (19 [26.0%] patients vs 24 [15.3%] patients, P = 0.041). The incidence of peritonitis was 0.30 and 0.18 person-year in the PPI and non-PPI groups, respectively. The cumulative probabilities of the first episode of peritonitis at 1, 3, and 5 years were 0.22, 0.43, and 0.63, respectively, in the PPI group and 0.14, 0.22, and 0.39, respectively, in the non-PPI group, indicating that the PPI group had a higher risk for developing peritonitis than did the non-PPI group (logrank test: P = 0.003; Fig. 1).

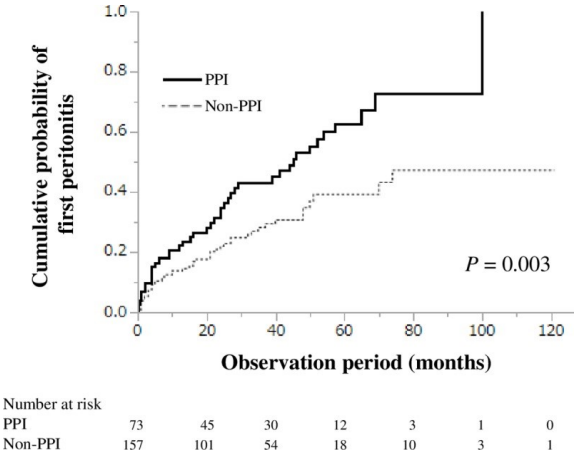

Figure 1. Cumulative probability of the first episode of peritonitis

In the univariate models, low serum albumin level and PPI use were significantly associated with overall peritonitis. Multivariate adjustment for clinically relevant factors attenuated the association between low serum albumin (per 1 g/dl adjusted HR = 0.59, 95% CI): 0.39–0.90; P = 0.014), PPI use (HR, 1.73; 95% CI, 1.12–2.68; P = 0.013), and peritonitis (Table 3). H2RA use was not identified as a risk factor for peritonitis in the univariate and multivariate models. PD withdrawal occurred in 57 (78.1%) and 122 (77.7%) patients in the PPI and non-PPI groups, respectively. During the observation period, 10 (13.7%) and 19 (12.1%) patients in the PPI and non-PPI groups, respectively, had mortality events of all causes, indicating that the cause of death was not different between the two groups (P = 0.434). The organisms isolated from the PD effluent were not different between the groups (P = 0.808).

In this retrospective study of single center cohort of 230 consecutive Japanese PD patients, we found that PPI use was associated with increased risk of peritonitis. PPIs are used worldwide, and PPI usage was higher in PD patients because of various gastrointestinal conditions, such as gastroesophageal reflux disease, peptic ulcer, and ulcer prophylaxis for anti-platelet therapy. PPI use was reported to be associated with increased risk of enteric infections, such as *Clostridium difficile* infection and spontaneous bacterial peritonitis in cirrhosis patients [4, 5]. This is probably due to bacterial overgrowth within the gastrointestinal tract and translocation across the epithelial barrier by usage of acid-suppressive therapy [4, 5]. Regarding PD patients, the relationship between PPIs and peritonitis has not been extensively studied.

Some in vitro studies showed that PPIs affect the inflammatory cells, including lymphocytes, neutrophils, or natural killer cells, directly. Other studies have indicated that PPIs inhibit the oxidative burst in human neutrophils and disturb the response by dendritic cells to microbial ligands [6,7]. These impaired functions of the immune cells might promote the translocation of intestinal bacteria, thereby leading to peritonitis. All of these effects may cause changes in the natural gut microbial environment, which subsequently leads to increased bacterial colonization in the gastrointestinal tract. Overall, PPIs may predispose patients to bacterial overgrowth within the gastrointestinal tract and translocation across the impaired epithelial barrier [8], which increases the risk for peritonitis development.

Only one recent meta-analysis consisting of 6 small sized observational studies involving 378 PD patients has evaluated the relationship between PPI, H2RA, and

enteric peritonitis [2]. Although the results showed that H2RA use in PD patients was associated with an increased risk of enteric peritonitis (odds ratio [OR] = 1.27; 95% CI: 1.02-1.57), PPI use was not identified as a risk factor (OR = 1.13; 95% CI: 0.72-1.77); the results should be interpreted cautiously in the following points. As for the methodological point, the meta-analysis included a small number of patients, which may have underestimated the influence of PPI on peritonitis development. In one study when taking into account the data on H2RA use during the follow-up period in the time-dependent Cox proportional hazard models, a significant association between H2RA and peritonitis was not found. In some studies, H2RA was not used by current recommended does. In a different point of view, most of the previous studies in PD patients had evaluated the association between PPI or H2RA and "enteric" peritonitis, which was caused by the enteric organisms [2, 9]. However, the definition of "enteric" organisms was different in each study, namely, enteric bacteria included in each study was different.

Contrary to the previous studies, the present study showed that H2RA was not a risk factor for peritonitis development. The reason was unclear, but it might be that bacterial colonization of the small intestine and bacterial overgrowth might occur more easily in subjects using PPIs, because PPIs are associated with stronger acid suppression than H2RA even in PD patients with kidney dysfunction, as previously reported in patients with normal kidney function [10]. Given that the effect of both PPI and H2RA for gut microbial environment was not directly compared, it is unknown which drug has a stronger influence on the intestinal environment in PD patients. Therefore, further studies should be undertaken in the future to clarify the mechanism.

In summary, PPI use was independently associated with PD-related peritonitis. The results suggest that nephrologists should pay attention when prescribing PPI in PD patients.

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Liposome-Supported Peritoneal Dialysis: A New Approach for the Removal of Protein-Bound Toxins

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There is growing evidence that accumulations of protein-bound uremic toxins (PBUTs) contribute significantly to the high cardiovascular morbidity and mortality observed in patients with chronic kidney disease (CKD) and those who are on renal replacement therapy [1]. Because PBUTs-albumin complex is not permitted through the traditional dialyzer, which has an approximate molecular weight cut-off of 20 KDa, and only the unbound or free fraction of PBUTs drives diffusion across the dialysis membrane during hemodialysis (HD). The clearance of PBUTs is therefore much lower than that of the water-soluble solutes [2]. Hemodialysis and hemofiltration provide insufficient clearance of PBUTs [3], and the clearance of PBUTs is even lower for peritoneal dialysis (PD) than for HD, as the removal of PBUTs in patients on PD depends heavily on the residual renal function [4].

Liposomes have long been customized as therapeutic nano-carriers to deliver diverse bioactive agents [5], and have also recently shown promising potential in blood purification interventions. With the hydrophobic structure of the lipid bilayer and the kinetic property of the phospholipid molecules, liposome is a material that has the quality to produce indirect adsorption. Because of this unique structure, liposomes can capture hydrophobic agents within the lipid bilayers and encapsulate hydrophilic agents inside the center of the aqueous core. Moreover, liposome can easily be customized and functionalized in diverse ways to display various sizes, trans-membrane pH gradients, and surface electric potential, among other properties.

In 2014, Forster *et al.* developed a PD medium, supported by liposomes with basic or acidic aqueous cores, which was able to enhance the removal of ammonia and several drugs from rats and therefore to be useful in the treatment of hyperammonemia and drug overdose [6]. Liposomes containing alcohol metabolizing enzymes were subsequently developed, and the liposome-supported enzymatic PD successfully enhanced ethanol metabolization and accelerated ethanol intoxication in rat models [7]. The addition of liposome to the dialysate also significantly improved the removal of the representative PBUTs in both the rat model that used HD and the one with PD [8,9]. The *in vitro* PD experiments showed that the uptake capacity of liposome was comparable with that of albumin for PCS and 3-IAA, though slightly inferior for IS. PD treatment in uremic rats also demonstrated that liposome-supported peritoneal dialysis (LSPD) resulted in more total mass removal for PBUTs than the conventional glucose-based PD, which suggested that LSPD might be a promising alternative to albumin PD. These findings highlight the versatility and advantages of LSPD for the blood purification treatment of a variety of pathological conditions. LSPD has a unique strength in comparison to other forms of

blood cleansing therapies, because this functionalized liposome-supported dialysis can be designed specifically for the removal of certain toxins.

Although using liposome-supported dialysis with great efficiency and decent biocompatibility showed potential as a novel technique for blood purification, it was only a good idea until the following concerns had been addressed. Batch production of liposome-contained dialysis media was necessary to ensure that LSPD could be a cost-effective strategy for blood detoxification. Also, since the liposomes are produced for medical purposes, those in the dialysate must be designed to be very stable with strict compositions and nano sizes, among other physical and chemical properties that need to be at room temperature for a certain period of time. A major concern over the use of LSPD is the retention of liposomes in the peritoneal cavity. Even though using liposomes with large nano sizes (> 500 nm) resulted in fewer amounts remaining in the peritoneal cavity or systemic circulation than with smaller-sized liposomes [9], the residual amount would still be considerable for long-term and regular LSPD treatments. Therefore, the liposomes should be functionalized to possess supreme clearing efficiency, and the PD sessions for the removal of PBUTs should be restricted. Since liposome-supported HD has been proven to significantly increase the extraction of cholestasis toxins in rats with acute liver failure [10], LSPD could also be applied as a novel artificial liver support system. With specifically functionalized and biocompatible liposomes, LSPD could be most useful as a PD therapy for the detoxification of numerous endogenous and exogenous protein-bound toxins.

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An Early Experience of Check-List to Improve Patient Self-Care and Product Defect

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An increase in number of peritoneal dialysis (PD) patients and demand for PD products following implementation of "PD first policy in Thailand [1] has led to logistics supply chain challenges and inherent product quality problems. Available evidences suggested that defective PD products may predispose the patients to peritonitis [2]. Although not included in the international guidelines, Thailand Clinical Practice Guideline for PD 2017 recommends the patients to check PD products themselves before use. Thus this narrative highlights an early experience from an implementation of the guideline which has been recently published in Int J Artif Organs 2019; September 27, entitled "An early experience of check list to improve patient self-care and product defect report in continuous ambulatory peritoneal dialysis (CLIP-SP) study" [3]. The study was a cluster randomized trial conducting in 22 PD centers in Thailand. Patients from 11 randomly selected sites were asked to use the Check List to report any product quality defects. The PD product Check List required patients to check the expiration date, glucose concentration, clarity, color, and integrity of inner and outer bags of PD fluid as well as the PD connectors prior to each use. Patients were also asked to report their findings in the report form by filling check or cross marks in the table and writing their complaint in the space provided (Figure 1). The PD solution product was considered defective if it had been expired on the day of use, had incorrect glucose concentration, abnormal clarity or abnormal color. Other potential defects such as abnormality of the boxes and/or PD bags, containing air bubbles/abnormal spots inside the bag, presenting fluid inside plastic sleeves, or loosened PD connector were also taken into account.

Patient Study ID #: ..... Date: .....

Mode of Shipment: O Pick-up O Thai Post BOX Lot #: .....

Glucose Concentration: O Correct O Incorrect

Box Defect: O None O Defect (describe): .....

Box Contamination: O None O Contamination (describe): .....

Please mark ✓ if no problem and mark ✕ if there is a problem then describe in the space below

	Expiration Date	Glucose Conc.	Clarity	Color	Outer Bag	Inner Bag	Connector
BAG 1							
BAG 2							
BAG 3							
BAG 4							

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Figure 1: Peritoneal dialysis (PD) product Check List

In the report, 28 out of 338 patients, who had received the Check List from 5 participating centers, returned the reports. Eight defects out of 3,960 products in total (0.2%) were detected. According to the written reports by patients, most patients concerns about the sterilization of PD product. One stated that “every box and the outer bag have numerous black-colored particles staining on it, but not on the inner bags”. Another patient even reported that “there was a lack of antiseptic in the catheter cap.” Some patients expressed their concern about the quality of a bag. “There are three leaky inner bags, but they contain clear peritoneal fluid.”

This was the first study guiding and empowering PD patients to systematically examine their PD product under a simple supervision of the provided Check List. Check List has been used to promote quality improvement in many areas of health including PD but how to achieve most benefits from such approach still needs a lot of consideration [4]. Anyway, we have learnt from the report that PD product defect does exist and if guided properly patients can detect the defect by themselves. Moreover, the Check List was designed to be simple enough for patients, and/or caregivers to follow as all the returned reports were written in a way that the investigators and all PD staffs could easily comprehend. The effects of the Check List intervention on patients’ outcomes particularly reduction of peritonitis rate has yet to be answered hopefully at the end of the CLIP-SP study.

In conclusion, despite low response rate and incomplete report in the early phase report, the Check List provided important information on product defects while an impact of the defects on PD primary outcomes requires a further investigation.

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Health Economic Evaluation of Peritoneal Dialysis Based on Cost-Effectiveness in Japan

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Peritoneal dialysis (PD) had been shown to have clinical superiority over hemodialysis (HD) in several areas, including the minimal strain on the cardiovascular system and maintenance of residual renal function (RRF; i.e., urine volume) [1]. The “PD first” concept accounts for these advantages and is the basis for recommending PD therapy [2]. In other words, a therapy that has advantages on the quality of life (QOL), patient prognosis, and reduced medical cost burden potentially forms the basis of a comprehensive medical treatment for renal failure. In Japan, the medical expenditures associated with dialysis have garnered considerable interest; however, a cost-effectiveness evaluation of peritoneal dialysis (PD) is yet to be evaluated. In particular, the health economics of the “PD first” concept, which can be advantageous for clinical practice and healthcare systems, must be evaluated. Under these circumstances, there were 37,983 renal replacement therapies in patients who underwent HD, 1,946 in those who underwent PD, and 1,648 in those who underwent transplantation during 2016 in Japan. Therefore, we performed a prospective observational study on the health economics for PD, especially APD, as a spreading medical technology in recent years in Japan [2].

This multicenter study investigated the cost-effectiveness of PD. The major effectiveness indicator was quality-adjusted life year (QALY), with a preference-based utility value based on renal function, and the cost indicator was the amount billed for a medical service at each medical institution for qualifying illnesses. In comparison

with hemodialysis (HD), a baseline analysis of PD therapy was conducted using a cost-utility analysis (CUA). Continuous ambulatory PD (CAPD) and automated PD (APD) were compared based on the incremental cost-utility ratio (ICUR) and propensity score (PS) with a limited number of cases. The mean duration since the start of PD was 35.0±14.4 months. The overall CUA for PD (179 patients) was USD 55,019/QALY, which was more cost effective (USD/monthly utility) compared with that for HD for 12–24 months (4,367 vs. 4,852; $p<0.05$). The CUA reported significantly better results in the glomerulonephritis group than in the other diseases, and the baseline CUA was significantly age sensitive. The utility score was higher in the APD group (mean age, 70.1±3.5 years) than in the CAPD group (mean age, 70.6±4.2 years; 0.987 vs. 0.860; $p<0.05$). Compared with CAPD, APD had an overall ICUR of USD 126,034/QALY.

The effectiveness index (utility) of PD was statistically superior to that of HD ($p<0.05$), but there was no difference in the cost index. In addition, the CUA for PD was slightly better than that for HD although there was no statistical difference. Although there were restrictions on the observation period (≥6 months), our study results suggested that the baseline cost-effectiveness of PD was satisfactory and that the primary disease, renal function, and other factors influenced the medical economics. A previous study [3] showed that the etiology of chronic kidney disease (CKD) had a major influence on the cost-effectiveness of HD treatment; in particular, diabetic nephropathy, which is one of the most common etiologies of CKD, resulted to lower cost-effectiveness, when compared with that for glomerulonephritis. The present study showed similar results. The difference in the cost-effectiveness between the two diseases was nearly the same for PD treatment in the present study and for HD treatment in previous studies, which showed that the diabetic nephropathy group, compared with the glomerulonephritis group, had approximately 20% lower performance.

A previous research identified several classic factors, such as low HDL cholesterol, as risk factors in HD patients [4]. In recent years, abnormalities in serum K and P metabolism have been identified as cardiovascular mortality risk factors in patients on dialysis [5]. The present study also identified serum P, K, HDL, and TG as factors that influenced the cost-effectiveness. Future research focused on this topic is essential for interpreting these results, but the main reasons for these factors may be related to the cost of medications and hospitalizations, such as those for anemia, hyperphosphatemia treatment, and secondary hyperparathyroidism treatment. For example, in the AURORA study [6] and 4D study [7], the initiation of rosuvastatin and atorvastatin treatment had no significant effect on the primary clinical endpoint in patients undergoing HD. Based on these data, we recognized that the adequate

management of dialysis using relevant indices was extremely important in improving the socioeconomic burden of ESRD therapy.

The results also suggested that the cost-effectiveness of PD was potentially good in the elderly and patients with less than 24 months on dialysis. In addition, comparison of the ICUR between CAPD and APD suggested that, in the early stage of initiation, APD may be a superior PD technique, and the major determinants were utilities. However, the number of patients in the APD and HD groups was very small, so it was difficult to draw conclusions. The findings of cost-effectiveness might be related to the high utility level with home medical care, and the possible reasons for the low long-term performance were the factors related to encapsulating peritoneal sclerosis. The maintenance of the RRF after the initiation of dialysis is considered to vary widely among patients, depending on the underlying disease, drugs administered, and dialysate used. A recent study estimated the speed of RRF decline to be approximately −1.5 mL/min/1.73 m2/year [8]. Although a Japanese population was not targeted, a related study indicated that the mean duration of PD was 30 months [9]. In this case, after reaching the objectives of optimal dialysis [i.e., dialyzer clearance of urea, dialysis time/volume (spKt/V) urea of 1.7 per week], uremic toxin management can be achieved by PD alone in approximately three years.

In this prospective observational study on the health economics of PD, we show that the cost-effectiveness of PD is potentially good in the elderly and in patients on dialysis for <24 months, although the number of HD groups assessed was limited. Therefore, the prevalence of PD use may affect the public health insurance system, particularly when applying the “PD first” concept.

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Use of PD for Children In Developing Countries

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Peritoneal dialysis (PD) offers distinct advantages for patients with end-stage kidney disease (ESKD), especially in children from developing world [1]. In our long follow-

up study of children on continuous ambulatory PD (CAPD) from India, it was encouraging to see a good school attendance ratio, lower peritonitis episode, and fewer incidence of technique failure due to social reasons or inadequate dialysis [1]. The study also gave an insight into the changing patterns of catheter configuration, connection system, and the effectiveness of PD infection control programs in reducing the incidence of peritonitis and improvement in PD outcomes1. The long-term outcome data is encouraging to opt-in PD as RRT for ESKD children in the Asia-Pacific region, which is a mix of the nation of both developed and developing countries.

Children with chronic kidney disease (CKD) and ESKD have relatively high mortality rates [2]. Renal replacement therapy (RRT) is lifesaving but associated with high treatment costs. The use of hemodialysis, peritoneal dialysis (PD) in particular continuous ambulatory peritoneal dialysis (CAPD) or transplantation, varies widely across countries [3]. In developing countries, access to RRT and provision for pediatric renal care are important determinants for this variability. CAPD should be the preferred modality of RRT for children in developing countries as it offers home-based therapy with minimal infrastructure requirements, especially in rural areas where access to power and clean water supply are lacking [4]. Other inherent advantages include fewer prerequisites for highly trained personnel, freedom from serious infections (hepatitis B and C), superior rehabilitation, and school attendance [1,4].

There are few renal registries and clinical studies from developing countries related to long term children on PD. An electronic survey conducted by the International Society of Nephrology showed only 45% of countries in Africa had access to long-term PD compared to 75% of countries across the globe [3]. Also, only 35% and 27% of countries in Africa and 20% of countries in South Asia received complete public (Government) funding for chronic and acute PD, respectively. Overall the study reported an extremely poor or poor/below average infrastructure for AKI and CKD care in Africa and South Asia [3]. In an international survey to estimate the trend for pediatric dialysis modalities in children with AKI, 40 of 48 centers in developing countries, mainly from Asia, used acute rigid PD catheters over a pointed stylet to gain access to peritoneum [5]. Acute PD as an option for RRT was available in all participating centers from developing countries. However, only 68.5% and 29.1% of the institutes from Asia preferred PD as a dialysis modality for AKI in infants and older children (>12yr), respectively [5].

For chronic PD, the higher cost of CAPD has been a major deterring factor to its popularity in developing countries. The need to import supplies, additional taxes and

duties, and transportation costs contribute to the increased cost of PD. Most children on chronic PD are on three to four manual exchanges/day, and cycler-assisted PD is rarely practiced [1]. Short-term grants have achieved hands-on training for nurses and physicians from developing countries to visit established dialysis centers. The primary focus has been to train them on basic principles of PD, techniques of PD catheter placement, and training algorithms for PD [6]. PD is often promoted where dialysis is primarily government-funded. The government of Thailand has adopted a "PD-first" policy, and all eligible patients are offered PD [6].

In contrast, despite rapid economic growth and improved ability to provide pediatric nephrology services, the prevalence of children receiving RRT is only 0.5 and 1 per million age-related population (pmarp) in China and India, respectively [7]. Improvement in PD techniques over the years, such as switching to a double bag system and emphasis on implementation of "Consensus Guidelines for the Prevention and Treatment of Catheter-related Infections and Peritonitis in Pediatric Patients Receiving Peritoneal Dialysis" has resulted in significant improvement in peritonitis rates and survival among pediatric PD patients, especially among infants [1,8]. In a longitudinal study of the International Pediatric Peritoneal Dialysis Network Nutritional Status in children undergoing chronic PD, underweight was most prevalent among children starting PD in developing countries of South and Southeast Asia (20%), and underweight was associated with increased mortality among older children [9].

One of the best models to improve the uptake of PD as an RRT modality among children from developing countries is noticeable in Sudan. With efforts of renal societies such as the International Pediatric Nephrology Association (IPNA) and the International Society of Nephrology (ISN), in establishing a center linked with a university hospital in the United Kingdom plus a combination of a state-funded program and a private donation, all forms of RRT are provided for children in Khartoum, Sudan, with an annual incidence of around three pmarp [7]. Careful selection of patients, methods to preserve residual renal function, improving availability of small dialysate bags, provision of cheaper dialysis supplies by manufacturing PD fluids locally or in a neighboring country, and establishment of publicly supported RRT programs can facilitate access to, and success of pediatric PD in developing countries.

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Retraining via Operation Inspection or Verbal Education Vs Usual Care On The Prevention Of Peritonitis In Peritoneal Dialysis: A Randomized Controlled Trial

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Although a proper performance of bag exchanges is generally emphasized during the initial training for new learners, post-training test score is actually not related to the risk for peritonitis [1]. The afterward bag exchange procedure seems to be of importance. Our previous study has found that above 50% of patients had problems of improper procedure during bag exchange at 6th month on PD, which predicted a higher risk of peritonitis during the follow up [2]. These clues support that PD patients training should be repeated periodically as recommended by ISPD guideline and systematic reviews [3-5]. It is hypothesized that retraining on bag exchange to ensure a standardized procedure would be helpful to reduce the risk of contact contamination. We therefore explored whether retraining every other month via operation inspection or verbal education can reduce the risk for peritonitis as compared to usual care in PD patients.

This is a randomized controlled trial conducted in the center of Peritoneal Dialysis, Peking University First Hospital. All participants meeting the inclusion and exclusion criterion were randomly assigned 1:1:1 by a computer- generated random number table to retraining every 2 months for the following 2 years via operation inspection, retraining via verbal education or usual care (control group). The Primary outcome was time to first-episode peritonitis including non-enteric and enteric organism peritonitis. The secondary outcomes were time to transfer to hemodialysis and all-cause mortality.

Of 150 participants, 50 were assigned to each group. During the median duration of four years, the incidence of all episodes of peritonitis were numerically lowest in the operation inspection group, as compared to verbal education group and usual care group, as 4.37, 5.72, and 6.06 /100 patient-year, respectively. However, the time to first-episode peritonitis was not significantly different between groups. As for the incidence of causative organisms examined for first-episode peritonitis, subjects in the usual care were more likely to develop peritonitis from non-enteric organisms

than those in the operation inspection group (2.36/100 patient-year vs 0.84/100 patient-year, $P<0.01$), but comparable to those in the verbal education group, 1.85/100 patient-year. After multivariate adjustment, the difference in the risk for non-enteric peritonitis between usual care and operation inspection group was weakened ($P=0.07$). The incidence of transfer to hemodialysis, death and kidney transplantation were not significantly different between groups.

Our results revealed that, although time to first-episode peritonitis was not significantly different between the retraining groups and control group, retraining via operation inspection could significantly reduce the risk of non-enteric peritonitis. The findings support the hypothesis that repeat operation inspection would be helpful to correct improper steps during bag exchange and thus reduce the risk for non-enteric peritonitis. This novel strategy should be included as an essential part of training and retraining program, especially for those at high-risk for peritonitis, such as elderly, malnourished, diabetic patients and those with low socioeconomic status [6-8].

In the present study, participants in operation inspection group were requested to repeat practice. The PD nurse supervised all procedures in order to give the patient/learner immediate feedback throughout the course, until they perform bag exchange correctly. This program provided chances for watching, listening and performing during a continuous learning process, followed by the nurse assessment checklist that is “fit for purpose” to ensure the efficacy of retraining. By contrast, retraining via verbal education is not helpful where patients were reviewing the standard exchange by reading and listening while the PD staff concentrated on the knowledge of patients pertaining to the bag exchange rather than their behavior habits. Our data did not support the efficacy of strengthening the knowledge solely by verbal education on the prevention of peritonitis.

Enteric and non-enteric peritonitis was analyzed separately in this study since non-enteric organisms originate from contact contamination in most part. Several studies on training in PD patients included peritonitis from gram-positive organisms as the primary outcome [9,10]. To evaluate the influence of a specific intervention on the procedure of bag exchange and risk for contact contamination, we suggest consider non-enteric peritonitis as a more suitable outcome.

Despite that operation inspection could reduce the risk for non-enteric peritonitis, 7 (14%) patients in the operation inspection group discontinued the retraining within the first year. The cause for withdraw was unwilling to be inspected repeatedly for all. By contrast, all patients in the verbal education group could keep on their retraining program. This finding indicated that retraining via operation inspection is not an easy task for our patients. We should develop more attractive learning tools during the

retraining program, such as step-by-step instructions on audiotape, computer-guided audio and visual cues or other multi-faceted educational approach.

In conclusion, this randomized controlled trial indicated that retraining via operation inspection every 2 months can reduce the risk for non-enteric PD-related peritonitis. This novel strategy can be recommended as a routine method for retraining bag exchange for PD patients. In the future, more strategies for retraining by multi-faceted educational approaches should be explored on the prevention of peritonitis, including patients' compliance as one of major measurements. We also need more evidences on how often and how soon retraining should be done after initial training.

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Key Performance Indicators for Peritoneal Dialysis in Thailand: The Importance of Provider Perspective

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Setting up goals or key performance indicators (KPIs) is the key to quality improvement in all healthcare services, including peritoneal dialysis (PD). [1,2]. Although standard guidelines have been published by the International Society for Peritoneal Dialysis (ISPD) covering almost every important aspect of PD, the PD Outcomes and Practice Patterns Study (PDOPPS) demonstrates that many centers limit their uptake of the guideline [3].

Unlike the guidelines, KPIs provide the targets that all care providers should aim to achieve. In PD, there has never been KPIs endorsed by all PD centers worldwide. However, in 2010, the Asian-Pacific chapter-ISPD proposed a set of 15 KPIs involving PD processes and patient outcomes [4]. While aiming toward target achievement for all of the KPIs seems to be a good practice, limitations may arise, particularly in the limited resource countries like Thailand. For instance, achieving the target of weekly Kt/V assures adequate small solute clearance, and the weekly Kt/V is one the KPIs proposed by ISPD. Unfortunately, this information might not even be available among many PD centers in Thailand, and, hence, setting it as a KPI is not going to allow inter/intracenter performance comparison.

In 2017, the Nephrology Society of Thailand aimed to launch the KPIs that suited the Thai PD community. In this regard, the initial set of 13 KPIs was proposed by the steering committee (Table 1). A national feasibility survey was then performed by distributing an online questionnaire to all PD centers in Thailand, asking their opinions on data availability and goal achievement anticipation for each KPI. Both questions were assessed by the 5-point Likert scale (1-strongly disagree, 2-disagree, 3-neither agree nor disagree, 4-agree, 5-strongly agree) [5]. There was also an open space for the respondents to express their points of view toward each respective KPI. By the time of the survey, there were 197 PD centers in Thailand, 119 (60%) of which responded to the questionnaire [6].

Concerning PD center's ability to acquire data for the proposed KPIs, "the percentage of PD patients with dialysis adequacy measured in the last 12 months", "the percentage of PD patients with a total weekly Kt/V > 1.7", and "the percentage of 3-year technique survival" were the three KPIs that most PD centers thought they could not afford to obtain the data (strongly disagree plus disagree 26%, 25%, and 23%, respectively). On the other hand, the three most agreeable KPIs as obtainable indicators were "exit-site infection rates," "peritonitis rate," and "PD nurse-to-patient ratios" (strongly agree plus agree 92%, 91%, and 91%, respectively). Because the PD nurse-to-patient ratio could be as low as 1:387 in some centers, regular Kt/V measurement was considered unattainable due to overburden of the nurse's workload. Parathyroid hormone (PTH) level was considered inappropriate as a KPI (strongly disagree plus disagree 17%) since most PD centers affiliated to community hospitals in the rural regions of Thailand could not afford to set up a laboratory for measuring PTH, and the cost of submitting patients' serum to private laboratories could not be reimbursed under the Universal Health Coverage Scheme. Reporting survival outcomes was also an issue. Many respondents complained that the commonly used data analysis software for PD outcomes was not user-friendly, which made calculating survival outcomes difficult, particularly in centers without full-time nephrologists.

Proposed Key Performance Indicators	Targets	Initial KPIs	Final KPIs
Infrastructure			
1. Nephrologist : Patient Ratio	1:100	X	X
2. PD Nurse : Patient Ratio	1:50	X	X
Process			
3. Percentage of PD patient with dialysis adequacy measured in the last 12 months	≥ 80%	X	-
	≥ 70%	X	X
4. Percentage of PD patient having Hb 10.0-12.5 g/dL or Hct 30.0-37.5%	≥ 70%	X	-
	≥ 90%	X	-
5. Percentage of PD patient with serum parathyroid levels within 150-500 pg/mL	> 50	X	X
	≤ 20%	X	X
6. Percentage of PD patient with total weekly Kt/V ≥ 1.7			
7. Exit-site Infection Rate (patient-month)			
8. Percentage of peritonitis with negative culture			
Clinical Outcomes			
9. Peritonitis Rate (patient-month)	> 24	X	X
10. Percentage of 1-Year PD Patient survival	≥ 90%	X	X
11. Percentage of 1-Year PD Technique survival	≥ 85%	X	X
12. Percentage of 3-Year PD Patient survival	≥ 60%	X	-
13. Percentage of 3-Year PD Technique survival	≥ 75%	X	-

Table 1: Summary of the initially proposed KPIs and the finally selected KPIs

Abbreviation: Hct, hematocrit; Hb, hemoglobin; KPIs, key performance indicators; PD, peritoneal dialysis.

Some KPIs were thought to be unachievable by over one-third of the PD centers, namely, “PD adequacy assessment target”, “the nephrologist-to-patient ratio of 1:100”, and the PD nurse-to-patient ratio of 1:50” (strongly disagree plus disagree 35%, 39%, and 40%, respectively) all of which confirmed the problem of work burden and the lack of medical personnel in the PD program in Thailand. In contrast, most centers agreed that “the target hemoglobin level”, “exit-site infection rates”, and “peritonitis rates” were achievable (strongly agree plus agree 63%, 77%, and 67%, respectively).

Considering all the responses from over 100 PD centers throughout Thailand, the initially proposed 13 KPIs were cut down to 8 KPIs. All of which were considered obtainable and achievable by most care providers (Table 1). This set of KPIs was announced 2 years ago and has been well accepted by the Thai PD community, with each PD center now consistently reporting the same 8 KPIs. This set of KPIs has been incorporated into the Thailand PD guidelines 2017 to ensure its uniform utilization in the country.

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Society News: Lesson Learned from Thailand Home Delivery of PD Bag

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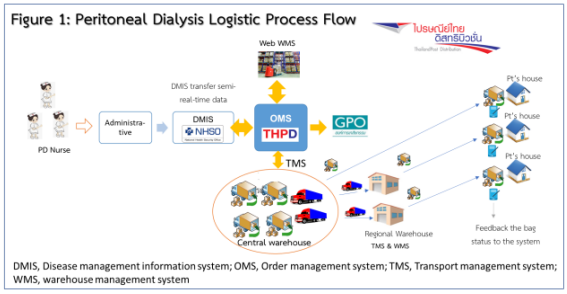
Since the launch of “PD First” policy in 2008, a number of active PD patients soar with increasing by 10 times from the last decade and tend to be rolling up [1,2] resulting in a PD bag distribution system targeting patient’s home delivery in Thailand is challenging. Not only does it need to deliver to the right condition, in the right place, and at the right time, but it also deals with a highly demanding situation. The right condition does not only mean a delivery of the bag filled with 2-L liquid with minimal

physical defects but also has to be thermal control and sunray protection during transportation. The right place means making the PD bag available for the patients at the pre-specified area while the right time is defined as making the product available not too early since most of the patients have limited supply room in their house and not too late until the patient's product is run out before arriving of new bags.

Under the policy, PD bags are international brands but locally or regionally manufactured. The Government Pharmaceutical Organization (GPO) is responsible for national procurement. The products are distributed by the Thailand Post Distribution Co., Ltd (THPD), whereas local logistic companies are subcontracted for delivery to the patients residing in rural areas. THPD has 10 distribution centers throughout the geographic region of the country [2]. Each hospital and PD clinics have to monthly key-in data for an amount of the PD requirement for each patient. The prescribed order is linked to the NHSO and the GPO, subsequently forwards to the suppliers and THPD. THPD connects multi-partners using a web-based system and adopts the mobile Global Positioning System (GPS) for tracking the bag during the distribution and informing the patients ahead of the delivery [3] (Figure 1). The distribution system has carried out beautifully and effectively over the past decade and was capable of handling the major flood in the central region of Thailand during 2011 without a significant shortage of the supply [3] (Figure 2). Nowadays, more than 27 million bags are delivered to patients' homes each year and still expanding.



Strength of this home delivery system over the traditional logistic system is reducing PD clinic/hospital burden and cost in management of the stock, particularly in Thailand where most of the public hospitals had a burgeoning workloads for health workforce in devoting to administrative and pharmaceuticals management as well as a limited hospital warehouse in storage the PD bag. However, there is still room for improvement. There are substantial reports of delay delivery, and most mistakes fall into problems in the administration system and subcontractors. Like other commercial goods, the PD solution delivered to the patients is reported to have physical damage during transportation, almost up to 0.2% [4]. Training of the

patients and caregivers to carefully check the product before use needs to be emphasized, and an improvement in the quality of the subcontracting chain in the bag delivery is mandated. In addition, integration of innovations and next-generation technology, including mobile application, robotic, artificial intelligence in the PD logistic, tracking, and chain supplier should be considered These all are the challenges and future opportunities for Thailand's PD home delivery.

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