



ISPD Asia-Pacific Chapter Newsletter, December 2021

VOLUME 19, ISSUE 3

Prepared by Chia-Te LIAO and Cheuk-Chun SZETO

News from the ISPD

International Society for Peritoneal Dialysis 2022 Congress

11-14 August 2022

Suntec, Singapore

Abstract Submission Open: 1 October 2021

Abstract Deadline: 1 February 2022

Early Registration: 29 April 2022

Website: <https://ispd2022.com/>

10th International Society for Peritoneal Dialysis Asia Pacific Chapter meeting

22-24 September 2023, New Delhi, India

ISPD Call for Research Proposals now open!

ISPD endorses and supports research projects requiring international cooperation and focusing on global PD issues.

You can [download here the guidelines for this call for projects](#).

ISPD 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 31 December 2021.** Details and application procedures can be found under the Regional Chapters – Asia-Pacific Chapter, at the ISPD website.

Renew your membership !

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

Upcoming Meetings

ISN World Congress of Nephrology 2022

24-27 February 2022

Kuala Lumpur, Malaysia

Website: <https://www.theisn.org/wcn22/>

- Application for ISPD Scholarships and Grants

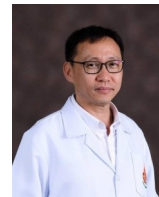
Membership for developing countries can be done at advantageous rates, by grouping members by institution or region geographical area. Write to admin@ispd.org for more information.

Guideline Update

Summary of Anemia Management in Peritoneal Dialysis: Perspectives from the Asia Pacific Region

(left) Phongsak Dandecha, M.D., Division of Nephrology, Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Thailand

(right) Talerngsak Kanjanabuch, M.D., Division of Nephrology, Department of Medicine and Center of Excellence in Kidney Metabolic Disorders, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.



Anemia is a common complication in patients with chronic kidney disease (CKD), particularly requiring dialysis. Anemia is diagnosed when hemoglobin (Hb) is less than 12 g/dL in women and 13 g/dL in men. Anemia is associated with a reduced quality of life (e.g., fatigue, reduced productivity) and increased risks of hospitalization, hospital length of stay, morbidity, and mortality, principally due to cardiac disease and stroke. In addition, direct healthcare costs are higher in CKD patients with anemia. The main cause of anemia in CKD is a loss of endogenous kidney erythropoietin (EPO) production capacity, which may be aggravated by a derangement in oxygen sensing. The other causes are iron deficiency, nutritional deficiency, blood loss, inflammation, and hemolysis.

There are 2 primary medicines in anemia correction, ESA (shorter and longer-acting agents) and iron supplementation. Shorter-acting ESAs, including epoetin alpha and beta, have a half-life of 6.8 hours for intravenous (IV) administration. Longer-acting ESAs include darbepoetin alfa with a half-life approximately 2 to 3 times longer than epoetin alfa and methoxy polyethylene glycol-epoetin beta, which has a significantly increased serum half-life of 130 hours with IV administration. Iron can be supplemented either via oral or IV routes. Several factors may reduce oral iron effectiveness, including gastrointestinal side effects and a reduction in enteral absorption due to its interaction with food, phosphate binders, and reduced gastric acidity. Standard formulations used for IV iron include iron dextran, iron sucrose, ferric gluconate, ferumoxytol, ferric carboxymaltose, and iron isomaltoside. There have been very few randomized controlled trials using IV iron in PD patients. The Kidney Disease Outcome Quality Initiative guidelines do not recommend a preferred route of iron administration for PD patients. A recent Cochrane database analysis found with low certainty of evidence that IV iron increased Hb, ferritin, and transferrin levels in patients with CKD as compared with oral iron. IV iron also helped more patients achieve target Hb levels and reduced their need for ESAs compared with oral iron. However, the review did not find sufficient evidence to determine whether the route of iron administration affects all-cause mortality, cardiovascular death, or quality of life. A paramount concern is the high possible risk for iron overload in dialysis patients treated with IV iron at doses recommended by current anemia management guidelines. An overload of iron in the liver can lead to an increase in hepcidin production and elevated plasma levels, which can activate macrophages of atherosclerotic plaques.

The third generation of ESA, a hypoxia-inducible factor (HIF) inhibitor, has been launched recently. These agents work by stabilizing the HIF complex and stimulating endogenous EPO production even in patients with CKD and hemodialysis. At least 3 HIF stabilizers are currently commercially available, including roxadustat, vadadustat, and daprodustat. Although there is no available study verifying the effectiveness of these agents in PD patients, these drugs are attractive as an oral form and could maintain Hb levels within 10 to 12 g/dL in patients receiving HD and are non-inferior to darbepoetin alfa.

Asian Pacific (AP) region is diversified, with different ethnic groups, cultures, and medical practices. Although there are a gradually increasing number of dialysis patients, particularly PD, standard clinical practice guidelines specific to this

region are essential because they consider the diversified socioeconomic structures. A roundtable discussion among nephrologists and opinion leaders from mainland China, Hong Kong, Japan, Malaysia, Singapore, South Korea, and Thailand on the management of anemia in PD patients in the AP region was organized in November 2019. The roundtable set out to describe the current status of anemia in PD patients and the management issues concerning ESA and iron therapy to improve the current management of anemia in the AP region. The meeting report is summarized in the article entitled "Anemia Management in Peritoneal Dialysis: Perspectives From the Asia Pacific Region" and has been published in the *Kidney Medicine* 2021;3(3):405-411. This narrative aims to highlight critical points of the report.

- The difference in PD population is observed across different AP countries varying from 3% in Japan to 75% in Hong Kong (Table 1). These could be the results of different government policies and cultures.

Table 1. Comparison of Percentage of Prevalent Dialysis Patients Receiving PD in Asia Pacific Region

	No. of prevalent dialysis patients	Percentage of dialysis patients on PD
China	610,881	14.1%
Hong Kong	6,094	74.6%
Japan	339,841	2.8%
Malaysia	44,136	9.9%
Singapore	7,405	13.7%
South Korea	83,867	7.4%
Thailand	94,406	31%

- The most acceptable target of Hb level is more than 10 g/dL, besides Japan sets a higher goal at a level of between 11 to 13 g/dL. PD populations in mainland China, Singapore, and Thailand achieve the target Hb level of 10 gm/dL in 58%, 66%, and 58%, respectively. The other countries did not declare their performance.
- Variation in ESA treatment practice is observed. The proportion of PD patients on ESA varies from 82% in Hong Kong to 96% in Thailand. The most common uses of ESA in almost all AP countries are short-acting ESAs, while longer-acting ESAs are commonly used in Hong Kong and South Korea (Table 2).

Table 2. Use of ESAs Among Patients Receiving PD in the Asia Pacific Region

	Proportion of PD patients on ESA	most commonly used ESA
China	89%	short-acting ESA
Hong Kong	82%	darbepoetin alfa or methoxy polyethylene glycol-epoetin beta
Japan	NA	darbepoetin alfa
Malaysia	83%	short-acting ESA
Singapore	86.3%	epoetin beta
South Korea	84%	darbepoetin alfa or methoxy polyethylene glycol-epoetin beta
Thailand	96%	epoetin alfa

Abbreviations: ESA, erythropoiesis-stimulating agent; NA, not available

- Only Malaysia, South Korea, and Thailand present the data of iron therapy in their PD populations. In Malaysia, 65% and 15% of the PD population receive oral and IV iron supplementations, respectively, intending to achieve TSAT $\geq$ 20% and ferritin $\geq$ 100 ng/mL. The majority of the Malaysian PD population (89% and 93%) reaches these targets. South Korea issues a specific guideline of IV iron for PD patients. IV iron can be prescribed if an oral iron medication is not feasible or inadequate as supplementation and serum ferritin level is <100 ng/mL or TSAT is $<20\%$. However, they did not show the magnitude of success in iron therapy. IV iron therapy was used in only 8% of the Thai PD population. Intriguingly, a substantial number of PD patients have high serum ferritin levels (801-1,200 ng/mL). The postulated causes are related to chronic inflammation and high proportions of thalassemia traits and diseases in Thailand.

Anemia is a well-recognized complication of CKD. The number of patients with PD and HD is multiplying in the AP region, which poses a tremendous financial burden to many countries. Iron supplements and ESAs remain the cornerstone of anemia treatment. However, the overall penetration of PD and anemia treatment practices and patterns are greatly affected by individual governments' health care reimbursement policies and cultural differences. A pooled kidney registry program across the region may be established to compare the epidemiologic data and clinical practice to improve anemia care in PD patients in the AP region.

References

1. Li PKT, Choy ASM, Bavanandan S, Chen W, Foo M, Kanjanabuch T, Kim YL, Nakayama M, Yu X. Anemia Management in Peritoneal Dialysis: Prospectives from the Asian Pacific Region Perspectives. *Kidney Med* 2021 Apr 20;3(3):405-411.

Research News from Asia-Pacific Region

Assisted Peritoneal Dialysis: A Feasible KRT Modality for Frail Older Patients With End-Stage Kidney Disease (ESKD)

Qianhui Song [1,2] and Wei Fang [1,2]

[1] Department of Nephrology, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

[2] Shanghai Center for Peritoneal Dialysis Research, Shanghai, China



Correspondence to: Dr. Wei Fang M.D., Ph.D.

Email: fangwei_sh@126.com

Photo: Wei Fang

Compared with in-center hemodialysis, peritoneal dialysis (PD) offers many potential benefits to older patients, such as less intervention in lifestyle, no need for vascular access, fewer hemodynamic variations and cost-effective, etc. [1]. However, barriers to self-care PD including multimorbidity, physical disabilities and psychosocial problems often emerged with increasing age [2]. Assisted PD is used as an alternative option for the growing group of frail, older ESKD patients unable to perform their own PD. Several studies have showed that the use of assisted PD could increase the utilization of PD among older patients [3,4]. However, whether assisted PD achieved similar outcomes to self-care peritoneal dialysis still remained controversial [5].

To investigate the outcomes of assisted PD in ageing patients, we conducted a study that included all patients aged 70 and above who started on PD in our hospital from 2009 to 2018. Patients were divided into assisted PD group (PD exchanges performed by a family member or a domestic helper) and self-care PD group according to the independence of bag exchange, and followed up until death, PD cessation or to the end of the study (December 31, 2019). Outcome measures in our study included patient survival, peritonitis-free survival and technique survival.

A total of 180 patients were enrolled in this analysis, including 106 (58.9%) males with a median age of 77.5 (77.2–81.2) years. Among the 180 patients, 62 patients (34.4%) were assisted. Patients in the assisted PD group were older (80.7 (76.9–84.0) vs 75.6 (72.5–79.2) years, $P<0.001$), less likely to be male (48.4% vs 64.4%, $P<0.05$), more prevalent in diabetics (48.4% vs 33.1%, $P<0.05$) and CVD (46.8% vs 29.7%, $P<0.05$), with a higher Charlson score (7.0 (6.0–8.0) vs 6.0 (5.0–7.0), $P<0.001$) than those in the self-care PD group. Other demographic and laboratory data were similar between the two groups. Our findings indicated that patients requiring assistance were often frail and older individuals, with physical disability or cognitive impairment, and had multiple comorbidities.

After a median follow-up of 32.5 months, 100 (55.6%) patients died. We found that cardiovascular disease remained the leading cause of death in older PD patients, accounted for up to 32.0% of deaths. However, infection was also a major cause of death in our study, accounted for up to 26.0% of deaths, and the majority of which was due to non-peritonitis infections, most being pulmonary infection. In concordance with our study, another analysis of elderly PD patients aged 70 and above found that infection constituted 26.6% of the causes of death [6]. These results indicated that older PD patients were prone to non-peritonitis infection, this might be a result of a high prevalence of DM, physical disabilities,

poor nutrition and immunodeficiency. Therefore, aggressive prevention and treatment of infection is essential for older PD patients. In our study, assisted PD patients had comparable patient survival to self-care PD patients (see Figure 1A). After adjustment for important demographic and clinical variables, assisted PD was not associated with patient survival either in the Cox or in the Fine–Gray (FG) models. We also identified that advanced age, comorbid with CVD and low RRF were independent predictors for mortality in the FG model (see Table 1), which were well-recognized prognostic factors for mortality in older PD patients demonstrated by numerous studies [7,8].

In total, there were 101 peritonitis episodes recorded. The peritonitis rate was 0.155 episode per patient-year in the assisted PD group and 0.216 episode per patient-year in the self-care PD group, respectively. In our cohort, peritonitis-free survival was comparable between assisted patients and self-care patients (see Figure 1B). After adjusted for age, gender, BMI, diabetes, CVD, hemoglobin, albumin and RRF, the use of assisted PD was not associated with peritonitis-free survival for both models, and no variables were found to be significantly associated with peritonitis-free survival.

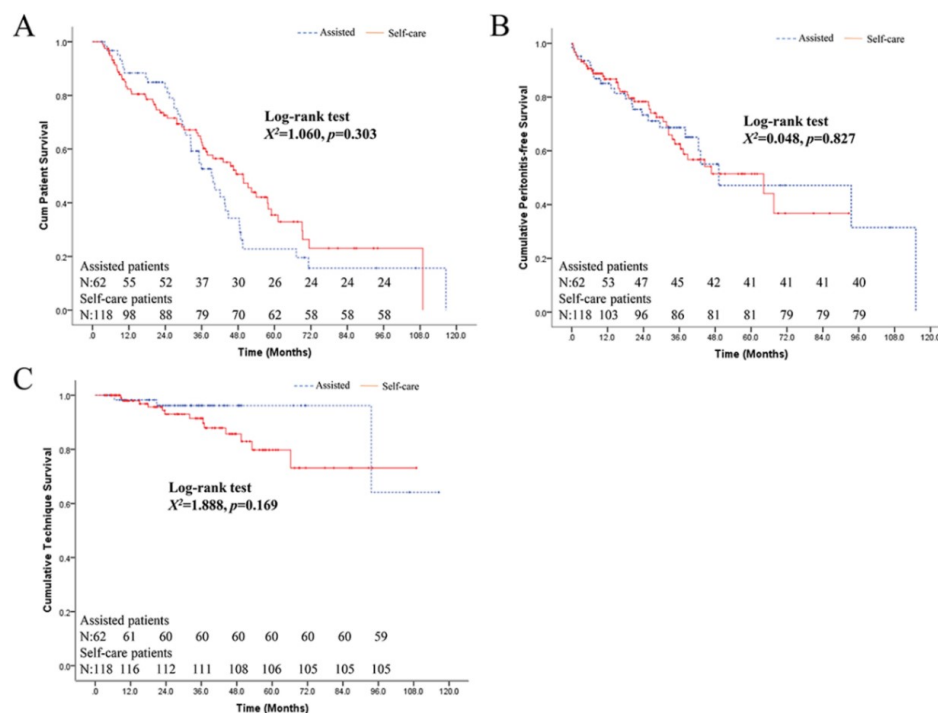


Figure 1. Kaplan-Meier curves by assistance for (A) patient survival, (B) peritonitis-free survival; and (C) technique survival.

During the study period, a total of 16 (8.9%) patients switched to HD. Our study showed that assisted PD patients had comparable technique survival to self-care PD patients (see Figure 1C). Furthermore, according to a Cox model, a significant technique survival benefit was demonstrated in assisted patients compared to self-care patients (cs-HR 0.20, 95% CI 0.04-0.76), but the association lost its statistical significance in the FG model (see Table 1). Higher BMI was the only predictor that was associated with technique survival in the FG model. In concordance with our study, report from the RDPLF which analyzed 9822 incident patients starting PD between January 2002 and December 2010 suggested that assisted patients had a lower risk for transfer to HD compared with self-care patients [9]. Querido et al. also found that technique survival was better in assisted PD patients compared with self-care patients [10]. As older patients who engaged independently in PD usually suffer from poor physical strength, cognitive dysfunction, vision impairment and deafness, which are all conditions that may affect the PD procedure, we suggested that for frail older patients unable to perform ideal self-dialysis, proper assistance should be provided to reduce the risk of PD technique failure, thereby prolong technique survival.

Table 1. Adjusted cs-HRs (Cox model) and sd-HR (Fine and Gray model) for each event

Variable	Death		Peritonitis		Transfer to HD	
	cs-HR (95% CI)	sd-HR (95% CI)	cs-HR (95% CI)	sd-HR (95% CI)	cs-HR (95% CI)	sd-HR (95% CI)
Age	1.09 (1.04-1.14)***	1.05 (1.01-1.09)*	1.05 (0.99-1.11)	1.01 (0.95-1.09)	1.15 (1.02-1.31)*	1.05 (0.89-1.24)
Male	1.22 (0.78-1.91)	1.26 (0.80- 1.98)	1.16 (0.68-1.99)	1.07 (0.61-1.86)	0.30 (0.07-1.36)	0.39 (0.11-1.34)
BMI	0.99 (0.93-1.06)	0.94 (0.89-1.00)	1.07 (0.99-1.16)	1.06 (0.96-1.17)	1.31 (1.11-1.55)**	1.25 (1.02-1.54)*
Diabetes	0.85 (0.55-1.32)	1.06 (0.68-1.64)	0.95 (0.55-1.64)	1.02 (0.59-1.76)	0.35 (0.11-1.10)	1.64 (0.67-4.05)
CVD	1.87 (1.23-2.83)*	1.59 (1.05-2.41)*	0.85 (0.48-1.51)	0.62 (0.35-1.11)	1.17 (0.30-4.48)	0.40 (0.09-1.78)
Hemoglobin	0.99 (0.97-0.99)*	0.99 (0.98-1.00)	0.99 (0.97-1.00)	0.99 (0.98-1.01)	0.99 (0.96-1.03)	1.00 (0.97-1.03)
Albumin	1.00 (0.97-1.03)	0.99 (0.96-1.02)	1.00 (0.96-1.03)	0.99 (0.96-1.02)	1.05 (0.96-1.16)	1.06 (0.97-1.15)
Low RRF ^a	1.78 (1.18-2.71)**	1.81 (1.21-2.72)**	0.70 (0.41-1.21)	1.22 (0.69-2.13)	1.79 (0.43-7.38)	0.43 (0.08-2.20)
Assisted-PD ^b	1.40 (0.88-2.21)	1.08 (0.70-1.65)	1.34 (0.73-2.46)	1.22 (0.69-2.13)	0.20 (0.04-0.76)*	0.40 (0.14-1.15)

Abbreviations: cs-HR, cause-specific hazard ratio; sd-HR, subdistribution hazard ratio; CI: confidence interval; BMI: body mass index; CVD: cardiovascular disease; RRF: residual renal function.

a Low Residual Renal Function (RRF), defined as RRF below median, as compared to high RRF group.

b As compared to self PD group

*P<0.05, **P<0.01, ***P<0.001

Overall, our study revealed that in a cohort of patients aged 70 and above, assisted PD patients had comparable patient survival and peritonitis-free survival to self-care PD patients. Moreover, assisted PD might protect older patients incapable of self-care from technique failure. Therefore, we suggested that poor self-care ability alone should not be used as a barrier to PD treatment and assisted PD could be a safe and effective modality of KRT for older patients incapable of self-care.

References

1. Sinnakirouchenan R, Holley JL. Peritoneal dialysis versus hemodialysis: risks, benefits, and access issues. *Adv Chronic Kidney Dis* 2011;18:428-432.
2. Brown EA, Johansson L. Epidemiology and management of end-stage renal disease in the elderly. *Nat Rev Nephrol* 2011;7:591-598.
3. Boyer A, Solis-Trapala I, Tabinor M, et al. Impact of the implementation of an assisted peritoneal dialysis service on peritoneal dialysis initiation. *Nephrol Dial Transplant* 2020; 35:1595-1601.
4. Oliver MJ, Quinn RR, Richardson EP, et al. Home care assistance and the utilization of peritoneal dialysis. *Kidney Int* 2007;71:673-678.
5. Hofmeister M, Klarenbach S, Soril L, et al. A Systematic Review and Jurisdictional Scan of the Evidence Characterizing and Evaluating Assisted Peritoneal Dialysis Models. *Clin J Am Soc Nephrol* 2020;15:511-520.
6. Lamping DL, Constantinovici N, Roderick P, et al. Clinical outcomes, quality of life, and costs in the North Thames Dialysis Study of elderly people on dialysis: a prospective cohort study. *Lancet* 2000;356:1543-1550.
7. Bargman JM, Thorpe KE, Churchill DN, et al. Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. *J Am Soc Nephrol* 2001;12:2158-2162.
8. Genestier S, Meyer N, Chantrel F, et al. Prognostic survival factors in elderly renal failure patients treated with peritoneal dialysis: a nine-year retrospective study. *Perit Dial Int* 2010;30:218-226.
9. Lobbedez T, Verger C, Ryckelynck JP, et al. Is assisted peritoneal dialysis associated with technique survival when competing events are considered? *Clin J Am Soc Nephrol* 2012;7:612-618.
10. Querido S, Branco PQ, Costa E, et al. Results in Assisted Peritoneal Dialysis: A Ten-Year Experience. *Int J Nephrol* 2015;2015:712539.

Association of Blood Pressure After Peritoneal Dialysis Initiation With The Decline Rate Of Residual Kidney Function In Newly-Initiated Peritoneal Dialysis Patients

Yusuke Kuroki [1] and Toshiaki Nakano [2]

[1] Nephrology & Dialysis Center, Japanese Red Cross Fukuoka Hospital, Fukuoka, Japan

[2] Department of Medicine and Clinical Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan



Correspondence to Yusuke Kuroki, M.D.

Email: kuroki.yusuke.ge@mail.hosp.go.jp

Photo: Yusuke Kuroki (left),
Toshiaki Nakano (right)

The preservation of residual kidney function (RKF) is an independent predictor of survival in patients with chronic kidney disease (CKD) G5D [1, 2]. Even a slight decline in RKF impacts a PD patient's survival, and it is thus important to be able to predict a decline in RKF. Hypertension is a strong risk factor for the progression of CKD [3], and thus treatment of hypertension is the basis of the control of CKD progression. However, there are limited data on this association in PD patients. We conducted the present retrospective cohort study to evaluate the association between BP levels and the decline rate of RKF.

We enrolled 228 patients whose PD was initiated between 1998 and 2014. RKF was measured as the mean urea and creatinine clearance values of a 24-hr urine collection after correcting for the patient's body surface area. Urine collections of <100 ml were excluded from the analysis. RKF was prospectively measured within 3 months of PD initiation, and at 4–6-month intervals thereafter. We calculated the annual rate of the decline of RKF from serial RKF measurements by creating regression lines for individual patients. RKF is considered to decline exponentially, therefore the decline rate of log RKF was also calculated in the same manner as the decline rate of RKF. Subjects were categorized into the following four groups according to the 2018 European Society of Cardiology and European Society of Hypertension Guidelines for the management of arterial hypertension [4]: Optimal (O; <120/80 mmHg), Normal & High normal (N; 120–139/80–89 mmHg), Grade 1 hypertension (G1; 140–159/90–99 mmHg), and Grade 2 & 3 hypertension (G2–3; $\geq 160/\geq 100$ mmHg). Patients whose systolic and diastolic BP indicated different categories were categorized into the higher category.

The overall median (IQR) decline rate of RKF and that of log RKF were -1.09 (-1.93 – -0.59) ml/min/1.73m²/year and -0.54 (-1.08 – -0.23) log(ml/min/1.73m²/year), respectively. The median age of patients was 62 (52–72) years. There were 147 males (64.5%) and 78 diabetics (34%). There were 27, 57, 75 and 69 subjects in the O, N, G1 and G2–3 groups, respectively. The mean eGFR, hemoglobin, frequency of icodextrin use, diuretics use and peritonitis rate were significantly decreased with higher BP3M levels.

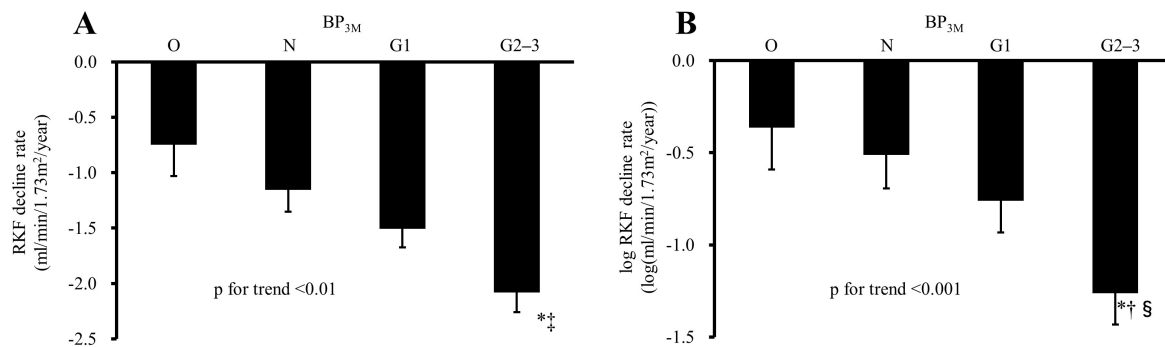
The differences in the decline rates of RKF and log RKF among the BP3M levels were analyzed. The multivariable-adjusted rate of the decline in RKF gradually decreased with higher BP3M levels (p for trend <0.0001; Figure 1A). The multivariable-adjusted rate of the decline in RKF was significantly lower in the G2–3 group compared to the O group, and in the G2–3 group compared to the N group (both p <0.05).

The multivariable-adjusted decline rate of log RKF also decreased with higher BP3M levels (p for trend <0.001; Figure 1B). The multivariable-adjusted decline rate in log RKF was significantly lower in the G2–3 group compared to the O group, and in the G2–3 group compared to the N group (all p <0.05).

We assessed the OR for a faster decline in RKF, which we defined as the faster side separated by the median decline rate of RKF. The multivariable-adjusted ORs gradually and significantly increased with higher BP3M levels (p for trend <0.05). The OR for a faster decline in RKF was 4.04 (95% CI: 1.24–13.2) in the G2–3 group compared to the O group. We performed the same analysis for a faster decline in log RKF. The OR for a faster decline in log RKF was 5.50 (1.58–19.2) in the G2–3 group compared to the O group.

Figure 1. The decline rate of RKF and log RKF according to the graded BP3M groups. A: The multivariable-adjusted decline rate of RKF among the BP3M groups. B: The multivariable-adjusted decline rate of log RKF among the BP3M

groups. * $p < 0.01$ vs. O, † $p < 0.01$ vs. N, ‡ $p < 0.05$ vs. N, § $p < 0.05$ vs. G1. Adjusted for age, sex, diabetes mellitus, previous history of cardiovascular disease, eGFR, hemoglobin, serum albumin, dialysate-to-plasma creatinine ratio at 4 hr, BMI, renin-angiotensin system inhibitors use, icodextrin use, high glucose fluid use, diuretics use, dosage of PD fluid, and peritonitis rate. Error bars indicate the standard error. BP_{3M}: blood pressure after 3 months of PD initiation; G1: Grade 1 hypertension; G2–3: Grade 2 & 3 hypertension; N: Normal & High normal; O: Optimal; RKF: residual kidney function.



Our analyses revealed that the decline rate of RKF was negatively correlated with BP_{3M} levels. In the multivariable-adjusted logistic regression analysis, the OR for a faster decline of RKF gradually increased with higher BP_{3M} levels. The same relationship was observed between the OR for a faster decline of log RKF and higher BP_{3M} levels. This indicates that the higher the BP_{3M} level is, the faster the decline of RKF is. We therefore speculate that optimal BP control is important for the preservation of kidney function not only before dialysis therapy but also after PD initiation.

We used the parameter of blood pressure after 3 months of PD initiation as a predictor of RKF decline. However, blood pressure just before PD initiation was not associated with the decline rate of RKF. Other studies have noted that PD patients displayed blood pressure variations related to dynamic changes in their fluid volume status for the first 2 months after the start of PD [5, 6]. We suspect that those patients' blood pressure changed greatly in 3 months, and that after 3 months of PD initiation these changes impacted the RKF decline.

In conclusion, our study revealed for the first time that a higher blood pressure level, not just before PD initiation but after 3 months of PD initiation was associated with a slower RKF decline. Appropriate blood pressure control might be important for maintaining RKF not only before dialysis therapy but also after PD initiation.

References

1. Maiorca R, Brunori G, Zubani R, Cancarini GC, Manili L, Camerini C, et al. Predictive value of dialysis adequacy and nutritional indices for mortality and morbidity in CAPD and HD patients. A longitudinal study. *Nephrol Dial Transplant*. 1995; 10:2295-2305
2. Diaz-Buxo JA, Lowrie EG, Lew NL, Zhang SM, Zhu X, Lazarus JM. Association of mortality among peritoneal dialysis patients with special reference to peritoneal transport rates and solute clearance. *Am J Kidney Dis*. 1999; 33:523-534
3. Yamagata K, Ishida K, Sairenchi T, Takahashi H, Ohba S, Shiigai T, et al. Risk factors for chronic kidney disease in a community-based population: A 10-year follow-up study. *Kidney Int*. 2007; 71:159-166.
4. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *J Hypertens* 2018; 36:1953-2041
5. Saldanha LF, Weiler EW, Gonick HC. Effect of continuous ambulatory peritoneal dialysis on blood pressure control. *Am J Kidney Dis*. 1993; 21:184-188.
6. Lameire N. Cardiovascular risk factors and blood pressure control in continuous ambulatory peritoneal dialysis. *Perit Dial Int*. 1993; 13 Suppl 2:S394-S395

Effect of Weekly Chlorhexidine Impregnated Dressing For Exit-Site Care In Peritoneal Dialysis Patients: A Pilot Study

Htay Htay [1,2], David Johnson [3,4], Marjorie Foo Wai Yin [1,2]

[1] Department of Renal Medicine, Singapore General Hospital, Singapore;

[2] Duke-NUS Medical School, [3] Department of Nephrology, Princess Alexandra Hospital, Brisbane, Australia; [4] Australasian Kidney Trials Network, University of Queensland, Brisbane, Australia.

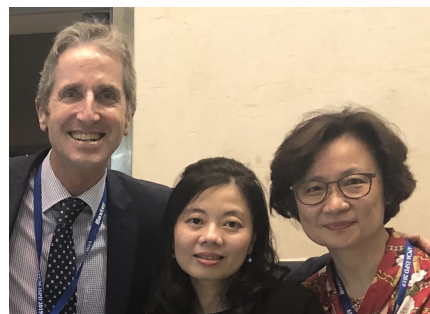


Photo (left to right): David Johnson, Htay Htay, Marjorie Foo

Correspondence to Dr. Htay Htay

Email: htay.htay@singhealth.com.sg

Peritoneal dialysis(PD)-related infection remains one of the main reasons why patients discontinue PD therapy [1,2]. Measures to prevent catheter-related infection in PD are of paramount importance to help retain patients on PD therapy and improve technique survival. One such measure is catheter exit-site care using topical antimicrobial agents. ISPD recommends the regular application of topical antibiotics at the exit-site to prevent exit-site infection [3,4]. In contrast to hemodialysis therapy, the majority of PD patients perform dialysis daily. In addition, they have to perform exit-site care regularly. Reducing the frequency of exit-site care from daily to weekly may enhance adherence to exit-site care, which potentially can reduce infection and also improve the quality of life of PD patients. The use of weekly chlorhexidine dressings for catheter exit-site care among patients requiring central venous catheters has been proven to be effective in the prevention of catheter-related bloodstream infection in randomized controlled trials and meta-analyses [5]. The role of chlorhexidine dressing in PD patients has not been examined before.

We conducted a pilot study of using weekly chlorhexidine impregnated sponge dressings for PD catheter exit-site care in 50 incident PD patients followed for one year at a single center in Singapore [6] Participants were trained to use chlorhexidine sponge dressings and were instructed to change the dressing weekly unless it was soaked with blood or fluid, in which case the dressing was changed immediately. The exit-site was first cleaned with 10% povidone-iodine, then dried with sterile gauze before applying a chlorhexidine sponge (2.5 cm x 0.7 cm) at the exit-site and securing it with transparent Tegaderm, 3M, I.V Advanced dressing (Figure 1).



Figure 1. Chlorhexidine impregnated sponge dressing at peritoneal dialysis catheter exit-site

The primary outcome of the study was exit-site/tunnel tract infection rate and secondary outcomes were peritonitis rate, time to first episode of exit-site/tunnel tract infection, time to first episode of peritonitis, PD infection-related hospitalization, technique survival, patient survival, and adverse events. These outcomes of the study cohort were compared with those of a historical cohort using daily topical gentamicin cream for exit-site care. In addition, the user

acceptability of weekly chlorhexidine sponge dressings was assessed at the 3rd month of study using treatment acceptability questionnaires [7]. The primary outcome, exit-site/tunnel tract infection rate, and the secondary outcomes of peritonitis rate and PD infection-related hospitalization were compared using multivariable Poisson regression. Time to first episode of PD infection, technique survival, and patient survival were analyzed using Kaplan-Meier survival analysis and log-rank tests, and multivariable Cox regression.

The study recruited 50 incident PD patients between March and August 2018 for chlorhexidine dressings. A total of 238 incident PD patients (using daily topical gentamicin cream for exit-site) between 2016 and 2017 were included as a historical control group [6]. The mean follow-up durations for the study and control groups were 45.8 and 212.1 patient-years, respectively. A total of 4 (8%) patients from the chlorhexidine group and 24 (10%) patients from the control group developed exit-site infection. The exit-site infection rates in the chlorhexidine and control groups were 0.09 (95% Confidence Interval [CI] 0.02 – 0.22) and 0.14 (95% CI 0.09 – 0.20), respectively. There was no significant difference in exit-site infection rates between the two groups (incidence rate ratio [IRR] 0.65, 95% CI 0.22 – 1.92). Time to first episode of exit-site infection was comparable between the two groups [6].

Peritonitis rates for patients in the chlorhexidine and control groups were 0.07 (95% CI 0.01 – 0.19) and 0.25 (95% CI 0.18 – 0.32) episodes per patient-years, respectively. Peritonitis rate was significantly lower in the chlorhexidine group compared with the control group (IRR 0.24, 95% CI 0.07 – 0.77). Time to first episode of peritonitis was comparable between the two groups. PD infection-related hospitalization was significantly lower in the chlorhexidine group compared with the control group (IRR 0.21, 95% CI 0.06 – 0.69). There were no significant differences in technique and patient survivals between the chlorhexidine and control groups. Six patients (12%) developed delayed localized contact dermatitis to chlorhexidine sponge dressing. The median time to dermatitis was 0.83 (interquartile range [QR] 0.73 – 0.91) years. Chlorhexidine dressing was rated by most participants as being very acceptable, very effective, unlikely to have negative side effects, and very trustworthy.

The novel finding of the study was that weekly use of chlorhexidine dressings was associated with reduced peritonitis rate and PD infection-related hospitalization compared with daily application of gentamicin cream at the exit-site among incident PD patients [6]. Another important finding from the study was that the majority of patients receiving chlorhexidine dressings expressed their satisfaction with the dressings. The majority of patients rated the chlorhexidine dressings as very acceptable for exit-site care. One of the concerns with the use of chlorhexidine dressings was the development of an allergic reaction. The study demonstrated that 12% of participants developed delayed localized contact dermatitis with chlorhexidine dressing. All patients who developed localized dermatitis resolved with medical therapy (topical steroid cream).

This study was the first to examine the effect of weekly chlorhexidine impregnated sponge dressings for the prevention of catheter-related infection in PD patients. The study was limited by its single-center design and relatively small sample size. Although patients receiving chlorhexidine dressings were followed up prospectively, a historical cohort was used for the control arm (gentamicin), which imposed a risk of recall bias, performance bias, and era effects. In addition, it was not a randomized controlled trial, such that there was a risk of selection bias.

In summary, the pilot study demonstrated that the use of chlorhexidine dressings was considered a very acceptable exit-site care option by incident PD patients. Though the use of chlorhexidine dressing was not associated with reduced exit-site infection, its use was associated with a lower peritonitis rate and PD infection-related hospitalization rate compared with the use of topical gentamicin cream in this study. These findings need to be confirmed in a randomized controlled trial.

References

1. Kavanagh D, Prescott GJ, Mactier RA. Peritoneal dialysis-associated peritonitis in Scotland (1999-2002). *Nephrol Dial Transplant*. 2004 Oct;19(10):2584-91.
2. Htay H, Cho Y, Pascoe EM, et al. Multicenter Registry Analysis of Center Characteristics Associated with Technique Failure in Patients on Incident Peritoneal Dialysis. *Clin J Am Soc Nephrol*. 2017;12(7):1090-1099.
3. Li PK-T, Szeto CC, Piraino B, et al. ISPD Peritonitis Recommendations: 2016 Update on Prevention and Treatment. *Perit Dial Int*. 2016;36(5):481-508.
4. Szeto C-C, Li PK-T, Johnson DW, et al. ISPD Catheter-Related Infection Recommendations: 2017 Update. *Perit Dial Int*. 2017;37(2):141-154.

5. Safdar N, O'Horo JC, Ghufraan A, et al. Chlorhexidine-impregnated dressing for prevention of catheter-related bloodstream infection: a meta-analysis*. Crit Care Med. 2014;42(7):1703-1713.
6. Htay H, Choo JCJ, Johnson DW, Pascoe EM, Jayaballa M, Oei EL, Ng LC, Wu SY, Foo MWY. Chlorhexidine-impregnated sponge dressing for prevention of catheter exit-site infection in peritoneal dialysis patients: a pilot study. Int Urol Nephrol. 2021 Apr;53(4):803-812.
7. Shen K, Cho Y, Pascoe EM, et al. The SIESTA Trial: A Randomized Study Investigating the Efficacy, Safety, and Tolerability of Acupressure versus Sham Therapy for Improving Sleep Quality in Patients with End-Stage Kidney Disease on Hemodialysis. Evidence-Based Complement Altern Med. 2017;2017:1-10.