



Clinical outcomes of infection-related hospitalization in incident peritoneal dialysis patients

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Background: Infection is the second leading cause of death in patients undergoing long-term dialysis. Peritoneal dialysis (PD) is associated with an increased risk of infection-related hospitalization (IRH) when compared with hemodialysis. In this study, we investigated the influence of IRH on clinical outcomes in incident PD patients.

Methods: In total, 583 incident PD patients were selected from the Clinical Research Center Registry for End-Stage Renal Disease, a nationwide multicenter prospective observational cohort study in Korea. Incident PD patients who had been hospitalized for infection-related diseases were defined as the IRH group. The primary outcome was all-cause mortality and the secondary outcome was technical failure. The median follow-up period was 29 months.

Results: Seventy-three PD patients (12.5%) were categorized in the IRH group. Multivariable logistic regression analysis showed that diabetes mellitus was a significant independent predictor for IRH (odds ratio, 2.43; 95% confidence interval [CI], 1.12 to 5.29; $P = 0.007$). The most common causes of IRH were peritonitis (63.0%) and respiratory tract infection (9.6%). Multivariable Cox proportional hazard model analysis showed that IRH was a significant independent risk factor for all-cause mortality (hazard ratio [HR], 2.51; 95% CI, 1.12 to 5.62; $P = 0.026$) and for the technical failure of PD (HR, 3.23; 95% CI, 1.90 to 5.51; $P < 0.001$).

Conclusion: Our data showed that after initiation of PD, IRH was significantly associated with higher risk of all-cause mortality and technical failure.

Keywords: Hospitalization, Infections, Mortality, Peritoneal dialysis, Peritonitis

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Introduction

Mortality and morbidity rates of dialysis patients are much higher than those of the general population worldwide [1–3]. Infection-related diseases are the second leading cause of all-cause mortality in end-stage renal disease (ESRD) with dialysis, and a common cause of hospitalization [4].

Peritoneal dialysis (PD) has a higher risk of all-cause mortality from infection-related diseases compared with hemodialysis (HD) [5]. Fatal peritonitis may contribute to a higher risk of infection-related mortality in PD patients compared with those undergoing HD [6]. PD is also associated with an increased risk of infection-related hospitalization (IRH) compared with HD [7]. Hospitalization is a marker of disease severity and considered the most clinically important event [5–12]. Thus, IRH may be a significant prognostic indicator of clinical outcomes in PD patients.

IRH in PD patients may not only affect clinical outcomes but also increase the financial burden due to the emergence of multidrug-resistant organisms associated with a long hospitalization period and rehospitalization shortly after discharge [5,10].

Despite the clinical importance of IRH in PD patients, there are limited data on the direct relationship between IRH and clinical outcomes in PD patients. Most studies on the association of IRH with clinical outcomes in PD patients have focused on comparison outcomes based on dialysis modality or age. Furthermore, they have been retrospective observational cohort studies or single-center experiences [5–10,13,14]. There are few data from multicenter prospective cohort studies for the association of IRH with clinical outcomes, especially all-cause mortality and technique failure in incident PD patients.

Considering that a prospective cohort study can assess temporal sequences and eliminate survival bias such as recall bias, a prospective study may provide more information on the relationship of IRH and clinical outcomes compared with a retrospective study.

In this nationwide multicenter observational prospective cohort study, we determined the impact of IRH on all-cause mortality and technical failure in incident PD patients.

Methods

Study population

All patients included in this study were enrolled in the Clinical Research Center (CRC) registry for ESRD, which is an ongoing observational prospective cohort study of patients with ESRD from 31 medical centers in Korea. The cohort was initiated in April 2009 and ended in April 2015. The cohort included adult (> 18 years of age) dialysis patients. A total of 598 patients incidentally undergoing PD were enrolled in this cohort. Patients with incomplete follow-up data or other missing values were excluded from this study. Finally, a total of 583 patients were enrolled.

Because our aim was to evaluate the impact of IRH on clinical outcomes after initiation of PD with a long-term follow-up period, we restricted the IRH group to PD patients who had been hospitalized for infection-related diseases within one year of the initiation of PD. IRHs were defined as an admission with an infection as a primary diagnosis according to the CRC for ESRD study classification system.

Demographic and clinical data were collected at the time of study enrollment. Dialysis characteristic were assessed and measurements were performed every six months until follow-up was completed. Dates and causes of death were reported throughout the follow-up period.

Ethics

This study was approved by the Institutional Review Boards at each of the following centers (in alphabetical order): The Catholic University of Korea, Bucheon St. Mary's Hospital; The Catholic University of Korea, Incheon St. Mary's Hospital; the Catholic University of Korea, Seoul St. Mary's Hospital; the Catholic University of Korea, Yeouido St. Mary's Hospital; The Catholic University of Korea, St. Vincent's Hospital; The Catholic University of Korea, Uijeongbu St. Mary's Hospital; Cheju Halla General Hospital; Jeonbuk National University Hospital; Chonnam National University Hospital; Chung-Ang University Hospital; Chungbuk National University Hospital; Chungnam National University Hospital; Dong-A University Medical Center; Ehwa Womans University Medical Center; Fatima Hospital, Daegu; Gachon Uni-

versity Gil Medical Center; Inje University Busan Paik Hospital; Kyungpook National University Hospital; Kwandong University College of Medicine, Myongji Hospital; National Health Insurance Corporation Ilsan Hospital; National Medical Center; Pusan National University Hospital; Samsung Medical Center, Seoul; SMG-SNU Boramae Medical Center; Seoul National University Hospital; Seoul National University Bundang Hospital; Yeungnam University Medical Center; Yonsei University, Severance Hospital; Yonsei University, Gangnam Severance Hospital; Ulsan University Hospital; and Wonju Severance Christian Hospital. The study was performed in accordance with the tenets of the Declaration of Helsinki and written informed consent was collected from all patients before study inclusion.

Clinical and dialysis parameters

In the CRC registry for ESRD, baseline demographic and clinical data including age, sex, body mass index (BMI), primary causes of ESRD, comorbidities, including cardiovascular disease with complications and diabetes mellitus (DM), laboratory values, and death rate were recorded. Cardiovascular disease was defined as the presence of coronary artery disease, congestive heart failure, peripheral vascular disease, cerebrovascular disease, or atrial fibrillation. Hemoglobin, serum albumin level, creatinine, calcium, phosphate, total CO₂ content (tCO₂), uric acid, total cholesterol, intact parathyroid hormone (iPTH), ferritin, and high-sensitivity C-reactive protein (hsCRP) were measured. Dialysis solute clearance was assessed based on the Kt/V parameter (amount of dialysis delivered: K, clearance of urea; t, time on dialysis; V, estimated total body water) using urea kinetic modeling. The adequacy of solute clearance was assessed based on the weekly total Kt/V (the sum of peritoneal Kt/V and renal Kt/V). Timed 24-hour urine collection was performed at the time of enrollment and urine volume was recorded at 24-hour intervals.

Outcomes

The clinical outcomes of this study were planned all-cause patient mortality as the primary outcome and technical survival of PD as the secondary outcome. For each death and drop-out from PD, the principal investigator

at that given institution completed a form that included the cause of death and cause of drop-out according to the CRC registry for ESRD study classification. Follow-up of the patients was censored at the time of death, kidney transplantation, patient withdrawal from the study, or patient transfer to a nonparticipating hospital. The follow-up period was calculated after the initiation of PD.

Statistical analyses

Data with continuous variables and normal distributions are presented as mean ± standard deviation, while those without a normal distribution are presented as a median with range. Student's *t* tests and Mann–Whitney *U* tests were used to determine the differences among continuous variables. Categorical variables were presented as percentages. Pearson's chi-squared test was used to determine the differences in categorical variables.

Univariable and multivariable logistic regression analysis were used to assess the clinical factors associated with IRH in PD patients. Multivariable logistic regression analysis was adjusted for significant or nearly significant ($P < 0.05$) predictors of IRH in univariate logistic regression analysis, including DM, cardiovascular disease, systolic blood pressure (BP), and diastolic BP. To achieve an adequate confounder control, important covariates known to be influential based on previous studies and clinical insight were retained in the multivariable logistic regression model, regardless of their statistical significance. These covariates included age, sex, BMI, serum levels of albumin, calcium, phosphate, iPTH, ferritin, and hsCRP.

The survival curves were estimated using the Kaplan–Meier method and compared by log-rank tests between patients in the IRH and non-IRH groups. A Cox proportional hazards regression model was used to calculate the hazard ratio (HR) with a 95% confidence interval (CI) for all-cause mortality. Analyses were adjusted for potential confounders including age, sex, DM, cardiovascular disease, systolic BP, and diastolic BP. A value of $P < 0.05$ was considered to be statistically significant. All statistical analyses were performed using the IBM SPSS 21.0 software program (IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

A total of 583 patients with incident PD from the CRC were included in this study. The mean dialysis duration of all patients was 29 months (interquartile range, 16 to 42 months). A total of 73 patients (12.5%) were included in the IRH group, whereas 510 patients were included in the non-IRH group. The median period from the initiation of PD to the IRH event in the IRH group was 4 months (interquartile range, 1 to 8 months). The baseline characteristics of the study population are shown in Table 1. The IRH group had more underlying comorbidities such as cardiovascular diseases and DM compared with the non-IRH group. Systolic and diastolic BP were significantly increased in the IRH group compared with the non-IRH group. There were no significant differences in age, sex, BMI, hemoglobin level, serum levels of creatinine, al-

bumin, alkaline phosphatase, calcium, phosphate, uric acid, iPTH, total cholesterol, tCO₂, ferritin, hsCRP, 24-hour urine volume, or residual renal function between the IRH and non-IRH groups.

Determinants of IRH

Next, we evaluated the clinical parameters to predict IRH. Table 2 shows the clinical and laboratory risk factors that influence the IRH in the entire patient cohort. In the univariable logistic regression analysis, DM (odds ratio [OR], 1.68; 95% CI, 1.12 to 5.29; *P* = 0.031), cardiovascular disease (OR, 1.88; 95% CI, 1.11 to 3.19; *P* = 0.019), systolic BP (OR, 1.02; 95% CI, 1.00 to 1.03; *P* = 0.006), and diastolic BP (OR, 1.03; 95% CI, 1.01 to 1.04; *P* = 0.008) significantly influenced the prevalence of IRH. In the multivariable logistic analysis, DM was a significant independent risk factor for IRH in model 1 (OR, 2.26; 95% CI, 1.08 to 4.72; *P* = 0.031) as well as model 2 (OR, 2.43; 95% CI, 1.12 to 5.29; *P* =

Table 1. Baseline characteristics of the study population

Characteristic	IRH group (n = 73)	Non-IRH group (n = 510)	<i>P</i> value
Age (yr)	53.9 ± 13.1	51.0 ± 13.1	0.075
Male	48 (65.8)	306 (60.0)	0.346
Body mass index (kg/m ²)	23.1 ± 3.1	22.7 ± 3.4	0.434
Comorbidities			
Diabetes mellitus	43 (58.9)	231 (45.3)	0.039
Cardiovascular diseases	25 (34.2)	116 (22.7)	0.018
Systolic blood pressure (mmHg)	143 ± 26	135 ± 21	0.006
Diastolic blood pressure (mmHg)	84 ± 16	79 ± 13	0.007
Serum creatinine (mg/dL)	8.3 ± 3.4	8.7 ± 4.2	0.377
Hemoglobin (g/dL)	9.1 ± 1.5	9.3 ± 1.7	0.172
Serum albumin (g/dL)	3.4 ± 0.7	3.5 ± 0.6	0.347
Serum alkaline phosphatase (IU/L)	125 ± 85	116 ± 96	0.427
Serum calcium (mg/dL)	7.8 ± 1.1	7.9 ± 1.0	0.306
Serum phosphorus (mg/dL)	5.5 ± 1.7	5.5 ± 1.9	0.723
Serum uric acid (mg/dL)	8.0 ± 2.5	8.2 ± 2.5	0.535
Serum total cholesterol (mg/dL)	163.2 ± 46.6	162.8 ± 50.7	0.949
Serum tCO ₂ (mmol/L)	18.9 ± 5.6	19.7 ± 5.6	0.268
Serum iPTH (pg/mL)	225 (113–395)	210 (119–372)	0.934
Serum ferritin (ng/mL)	212 (106–357)	161 (88–336)	0.177
hsCRP (mg/dL)	0.16 (0.04–0.86)	0.24 (0.05–1.18)	0.918
24-hour urine volume (mL)	775 (470–1,515)	990 (430–1,500)	0.884
Weekly total Kt/V	3.56 ± 7.96	3.58 ± 6.64	0.982

Values for continuous variables are given as mean ± standard deviation and variables without a normal distribution are given as median (interquartile range); values for categorical variables are given as number (%).

hsCRP, high-sensitivity C-reactive protein; iPTH, intact parathyroid hormone; IRH, infection-related hospitalization; K, clearance of urea; t, time on dialysis; tCO₂, total CO₂ content; V, estimated total body water.

Table 2. Logistic regression analysis for predicting infection-related hospitalization

Characteristic	Univariable		Multivariable			
	OR (95% CI)	P value	Model 1 ^a		Model 2 ^b	
			OR (95% CI)	P value	OR (95% CI)	P value
Age (per 10 years)	1.02 (0.99–1.04)	0.100	1.01 (0.99–1.04)	0.231	1.02 (0.99–1.05)	0.231
Sex (male vs. female)	1.28 (0.77–2.14)	0.347	1.17 (0.68–2.02)	0.575	1.12 (0.61–2.27)	0.625
Body mass index (per 1 kg/m ²)	1.03 (0.96–1.11)	0.414	1.02 (0.94–1.11)	0.616	1.02 (0.93–1.12)	0.641
DM (vs. non-DM)	1.68 (1.12–5.29)	0.031	2.26 (1.08–4.72)	0.031	2.43 (1.12–5.29)	0.007
Cardiovascular diseases	1.88 (1.11–3.19)	0.019	1.41 (0.78–2.57)	0.259	1.09 (0.53–2.25)	0.821
Systolic blood pressure (per 1 mmHg)	1.02 (1.00–1.03)	0.006	1.01 (0.99–1.02)	0.581	1.02 (0.97–1.01)	0.641
Diastolic blood pressure (per 1 mmHg)	1.03 (1.01–1.04)	0.008	1.03 (0.99–1.05)	0.081	1.02 (0.99–1.06)	0.219
Serum creatinine (per 1 mg/dL)	0.97 (0.91–1.04)	0.375	0.97 (0.91–1.05)	0.476		
Hemoglobin (per 1 g/dL)	0.90 (0.77–1.05)	0.171	0.89 (0.75–1.05)	0.153		
Serum albumin (every 1 g/dL)	0.82 (0.55–1.23)	0.824	0.93 (0.59–1.48)	0.767	0.87 (0.50–1.52)	0.619
Serum alkaline phosphatase (per 1 IU/L)	1.00 (0.99–1.01)	0.427	1.00 (0.99–1.01)	0.589		
Serum calcium (per 1 mg/dL)	0.89 (0.70–1.12)	0.305	0.89 (0.69–1.15)	0.371	0.97 (0.69–1.35)	0.840
Serum phosphorus (per 1 mg/dL)	0.98 (0.85–1.12)	0.976	0.98 (0.85–1.15)	0.829	1.00 (0.84–1.20)	0.976
Serum uric acid (per 1 mg/dL)	0.98 (0.89–1.09)	0.726	0.98 (0.88–1.09)	0.672		
Total cholesterol (per 1 mg/dL)	1.00 (0.99–1.01)	0.880	0.99 (0.99–1.01)	0.848		
iPTH (per 1 pg/mL)	1.00 (0.99–1.01)	0.884	1.00 (0.99–1.00)	0.641	1.00 (0.99–1.01)	0.567
Serum ferritin (per 1 ng/mL)	1.00 (1.00–1.00)	0.530	1.00 (1.00–1.00)	0.569	1.00 (0.99–1.01)	0.526
hsCRP (per 1 mg/dL)	0.94 (0.85–1.04)	0.201	0.94 (0.86–1.04)	0.219	0.96 (0.89–1.04)	0.348
24-hour urine volume (per 1 mL)	1.00 (1.00–1.00)	0.992	1.00 (1.00–1.00)	0.950		

CI, confidence interval; DM, diabetes mellitus; hsCRP, high-sensitivity C-reactive protein; iPTH, intact parathyroid hormone; OR, odds ratio.

^aMultivariable model including age sex, DM, cardiovascular disease, systolic blood pressure, and diastolic blood pressure. ^bMultivariable model including age and sex (model 1) as well as body mass index, cardiovascular disease, systolic blood pressure, diastolic blood pressure, serum levels of albumin, calcium, phosphate, iPTH, ferritin, and hsCRP.

0.007). Model 1 was adjusted for age, sex and significant factors found in univariate analysis such as DM, cardiovascular diseases, systolic BP and diastolic BP and model 2 was adjusted for the factors included in model 1 and BMI, serum levels of albumin, calcium, phosphate, iPTH, ferritin, and hsCRP.

Causes of IRH

Table 3 shows the distribution of causative infectious diseases in the IRH group. The most common cause of IRH was peritonitis (63.0%) and the second leading cause of IRH was respiratory tract infections, including pneumonia and bronchitis (9.6%). Other causes identified included skin and soft tissue infection, abscess, urinary tract infection, gastrointestinal tract infection, military tuberculosis, fungal infection, and viral infections.

Table 3. Infection-related diseases in the infection-related hospitalization group

Variable	Value
Peritoneal dialysis-related peritonitis	46 (63.0)
Respiratory tract infection	7 (9.6)
Soft tissue infection	7 (9.6)
Abscess	2 (2.7)
Fungal infection	2 (2.7)
Gastrointestinal tract infection	1 (1.4)
Urinary tract infection	1 (1.4)
Viral infection	1 (1.4)
Miliary tuberculosis	1 (1.4)
Other infection not recorded in category	5 (6.8)
Total	73 (100.0)

Data are presented as number (%).

Association between IRH and all-cause mortality in PD patients

During the median follow-up period of 29 months, nine patients died in the IRH group (12.3%) and 21 deaths occurred in the non-IRH group (4.1%). The median period from the event of IRH to a death in the IRH group was 23 months (interquartile range, 13 to 37 months). The causes of death in the study population are shown in Table 4. Cardiovascular disease was the most common cause of death (36.7% of all death), followed by infectious diseases

(30.0% of all deaths).

We determined the association between IRH and all-cause mortality in this study cohort. Fig. 1A shows the Kaplan–Meier survival curve for all-cause mortality. The log-rank test showed that all-cause mortality was significantly increased in the IRH group compared to the non-IRH group ($P = 0.007$).

Univariable and multivariable Cox proportional hazards model analysis of all-cause mortality are shown in Table 5. In the crude model, the HR for all-cause mortality of the IRH group was 2.81 (95% CI, 1.29 to 6.14; $P = 0.010$)

Table 4. Causes of death in the study population

Cause of death	Total	IRH group	Non-IRH group	P value
Cardiovascular disease	11 (36.7)	2 (22.2)	9 (42.9)	0.066
Infectious disease	9 (30.0)	2 (22.2)	7 (33.3)	0.323
Unknown	10 (33.3)	5 (55.6)	5 (23.8)	0.145
Total	30 (100.0)	9 (100.0)	21 (100.0)	

Data are presented as number (%).

IRH, infection-related hospitalization.

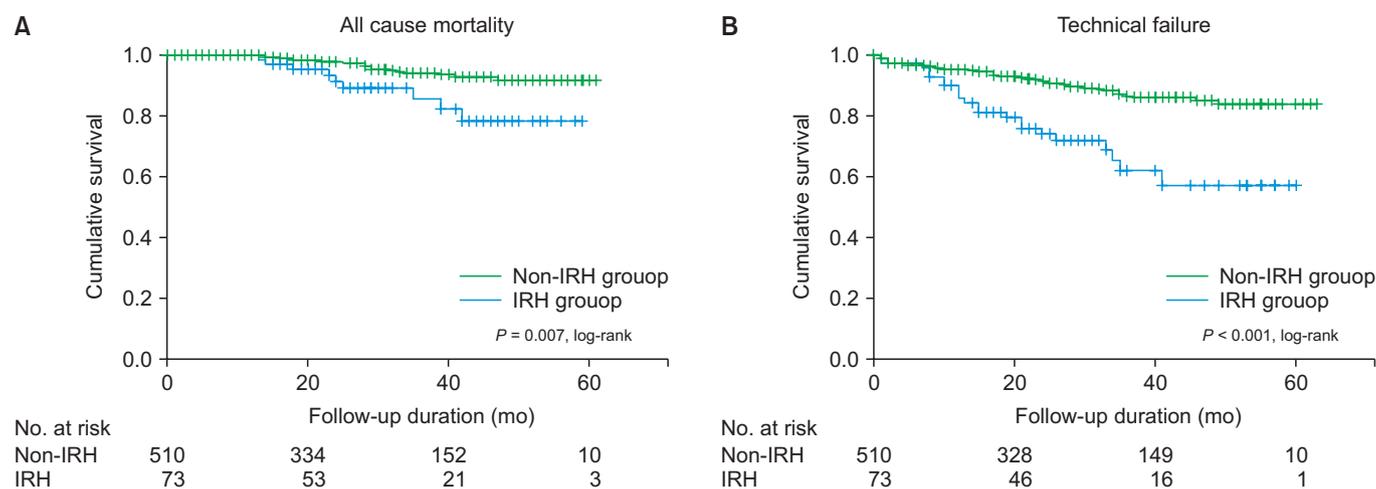


Figure 1. Kaplan–Meier survival curve for (A) all-cause mortality and (B) technical survival according to infection-related hospitalization (IRH).

Table 5. Univariable and multivariable Cox proportional hazards model analysis of IRH for all-cause mortality and technical failure

IRH	All-cause mortality			Technical failure		
	HR	95% CI	P value	HR	95% CI	P value
Crude model	2.81	1.29–6.14	0.010	3.11	1.89–5.12	< 0.001
Model 1 ^a	2.79	1.28–6.09	0.010	3.14	1.90–5.18	< 0.001
Model 2 ^b	2.51	1.12–5.62	0.026	3.23	1.90–5.51	< 0.001

CI, confidence interval; HR, hazard ratio; IRH, infection-related hospitalization.

^aMultivariable model including age and sex. ^bMultivariable model including age, sex (model 1) as well as cardiovascular disease, diabetes mellitus, systolic blood pressure, and diastolic blood pressure.

using the non-IRH group as the reference category. In multivariable Cox regression analysis, the IRH group had a significantly higher risk for all-cause mortality in model 1 (HR, 2.79; 95% CI, 1.28 to 6.09; $P = 0.010$) and model 2 (HR, 2.51; 95% CI, 1.12 to 5.62; $P = 0.026$). These findings indicate that the predictive power of the IRH for all-cause mortality was independent of the potential confounders, including age, sex, DM, cardiovascular diseases, systolic BP, and diastolic BP, and the IRH group had a 2.5-fold higher risk of death compared with the non-IRH group.

Association between IRH and technical survival in PD patients

During the follow-up period, 12.7% of enrolled patients in this study cohort ($n = 74$ of 583 patients) changed the modality of dialysis to HD from PD due to technical failure. Technical failure rates of PD in the IRH group and the non-IRH group were 30.1% ($n = 22$ of 73 patients) and 10.2% ($n = 52$ of 510 patients), respectively. The median period from the IRH event to a technical failure in the IRH group was 20 months (interquartile range, 9 to 31 months).

A Kaplan–Meier plot showed that the cumulative survival rate from technical failure was significantly lower in the IRH group compared with the non-IRH group ($P < 0.001$ by log-rank test) (Fig. 1B). Table 5 shows the results of univariable and multivariable Cox regression analysis for technical failure. In the crude model, the HR for technical failure in the IRH group was 3.11 (95% CI, 1.89 to 5.12; $P < 0.001$) using the non-IRH group as the reference category. In multivariable Cox regression analysis, the IRH group had a significantly independent higher risk for technical failure even after adjusting for demographics, laboratory data, and comorbid conditions (model 1: HR, 3.14; 95% CI, 1.90 to 5.18; $P < 0.001$; model 2: HR, 3.23; 95% CI, 1.90 to 5.51; $P < 0.001$).

Discussion

In this nationwide multicenter observational prospective cohort study, we found that the incident rate for IRH within 1 year after initiating PD treatment was 14.3% and that IRH in incident PD patients is independently associated with clinical outcomes such as all-cause mortality and technical failure. These findings highlight the burden

of IRH in the PD population and demonstrate that PD patients with IRH need greater attention from physicians.

For the IRH and clinical outcomes, Laurin et al [6] compared the mortality and overall readmission after IRH between PD and HD and found that PD was associated with a higher risk of infection-related overall readmission, compared with HD. There are limited data on the direct relationship between IRH and mortality in incident PD patients because most studies for IRH and clinical outcomes in dialysis patients included both HD and PD populations. Our study included only incident PD patients and was designed as a nationwide multicenter prospective cohort study, which demonstrates the clear association between IRH and all-cause mortality in PD patients.

Interestingly, DM was an independent predictor for IRH in this study population. In this study, incident PD patients with DM had a 2.43-fold higher risk of IRH than those without DM. DM is associated with increased infection-related events in HD patients as well as PD patients [15]. In PD patients, DM has been reported to be a risk factor for peritonitis [16,17]. Considering that hospitalization for infection-related disease reflects the severity of disease, in contrast to simple infection-related events, our findings that show the association between DM and IRH in incident PD patients support the importance of DM as a clinical predictor. To reduce IRH in incident PD patients, it is important to carefully monitor infection signs, especially in patients with DM.

In this study, the most common cause of IRH was PD-related peritonitis (63.0% of all IRH), which is similar to the rate reported in the study from the Canadian Organ Replacement Register and provincial health service administrative databases and the Peritoneal Dialysis Outcomes and Practice Patterns Study (PDOPPS) [6,18]. In the current study, we demonstrated that IRH is an independent risk factor for technical survival in incident PD patients. There are some explanations for these results. First, PD-related peritonitis is the leading cause of a permanent transition to HD and known as a PD technique failure [19,20]. A high proportion of PD-related peritonitis in the IRH group in this study may have contributed to the high incidence of PD technical failure. Second, Lee et al [21], reported in their national population-based study that DM is an independent risk factor for technical failure in Korean incident PD patients. In this study, the IRH

group had more underlying comorbidities, such as DM compared with the non-IRH group, which may have contributed to the increased incidence of technical failure in the IRH group.

PD technique failure is reported to be associated with mortality within two years of post-technique failure [22]. As shown in this study, the high incidence of PD technical failure in the IRH group may contribute to the increased all-cause mortality. Considering that the incidence of PD-related peritonitis is highest during the earliest months after the initiation of PD [19], our data suggest the importance of careful attention and education for PD-related peritonitis after initiation of PD, to reduce technique failure and all-cause mortality. Early nephrology referral for chronic kidney disease patients at the predialytic stage might be important for reducing IRH in incident PD patients. Patient education and training by nephrologists before initiation of PD decreases the likelihood of PD-related peritonitis, resulting in a reduction in all-cause mortality and technical failure.

There were some important strengths with the approach of this study. First, all analyses were performed on data from a large prospective nationwide multicenter cohort study, which regularly monitors clinical outcomes every six months using surveys to validate the quality of the data. This provides a clear causality between IRH and clinical outcomes. Second, we only enrolled incident PD patients, and excluded PD patients who previously received renal replacement therapy, which allowed the remnant effect of previous PD, HD, or kidney transplantation on clinical outcomes, such as all-cause mortality and technical failure, to be removed.

Our study also had several limitations. First, the design of our study was a prospective observational study and not a randomized controlled study. Therefore, potential biases such as confounding, informed, and selection biases should be carefully considered for interpretation of the results. Second, the number of patients with IRH included in this investigation was relatively small, which may limit the generalization of the results of this study. Third, rehospitalization rates could not be assessed as clinical outcomes. Fourth, infections that did not require hospitalization were not analyzed as prognostic factors for clinical outcomes. In addition, the mean follow-up period of 28 months was relatively short.

In conclusion, we found that IRH in patients with in-

cident PD presented significant risks for all-cause death and PD technical failure. Our findings suggest that implementing better education and surveillance to prevent IRH could reduce the risks for all-cause mortality and PD technique failure among patients that are receiving PD for maintenance.

Conflicts of interest

All authors have no conflicts of interest to declare.

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Authors' contributions

Youngdong Jeon, Hyung Duk Kim, and Yu Ah Hong participated in the data collection and wrote the manuscript. Hyung Wook Kim, Chul Woo Yang, Yoon-Kyung Chang, and Yong Kyun Kim participated in the study design and performed the statistical analysis. Yoon-Kyung Chang, Yu Ah Hong, and Yong Kyun Kim participated in the conception, analysis, and interpretation of data. Yoon-Kyung Chang and Yong Kyun Kim provided intellectual content of critical importance to the work and technical support. Youngdong Jeon, Hyung Duk Kim, Yoon-Kyung Chang, and Yong Kyun Kim participated in coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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