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Impact of glycemic control on residual kidney function and technique failure associated with volume overload in diabetic patients on peritoneal dialysis

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Background: It is unclear whether poor glycemic control contributes to residual kidney function (RKF) decline and consequent volume overload in diabetic patients on peritoneal dialysis (PD).

Methods: This retrospective analysis included 80 diabetic patients who started PD at a single center. The first 2 years of patient data were collected to investigate the impact of glycemic control on RKF and volume overload in the early stages of PD. We used the time-averaged glycated hemoglobin (HbA1c) levels to estimate glycemic control. RKF loss was measured as the slope of RKF decline and time to anuria. To assess the association between glycemic control and volume overload, we examined technique failure (TF) associated with volume overload (TFVO), defined as TF due to excessive fluid accumulation. Multivariable linear regression and Cox regression analysis were performed to assess how glycemic control affects RKF and TFVO.

Results: Over the first 2 years, the mean rate of RKF decline was −3.25 ± 3.94 mL/min/ 1.73 m^2 per year. Multivariable linear regression showed that higher time-averaged HbA1c was associated with a rapid RKF decline (β = −0.95; 95% confidence interval [CI], −1.66 to −0.24; p = 0.01). In the adjusted Cox regression analysis, higher time-averaged HbA1c increased the risk of progression to anuria (adjusted hazard ratio [HR], 1.97; 95% CI, 1.29–3.00; p = 0.002) and TFVO (adjusted HR, 2.88; 95% CI, 1.41–5.89; p = 0.004).

Conclusion: Poor glycemic control is associated with rapid RKF decline and leads to volume overload in diabetic patients on PD.

Keywords: Anuria, Blood glucose, Diabetes mellitus, Peritoneal dialysis, Treatment failure

Introduction

Glycemic control is important in diabetes mellitus (DM); however, research on the goals and implications of glycemic control in end-stage kidney disease is lacking. DM is the leading cause of end-stage kidney disease, and South Korea has the highest increase in the morbidity of diabetic kidney disease [1,2]. Peritoneal dialysis (PD) typically uses a glucose-based dialysate that is absorbed by the peritoneum, which can lead to hyperglycemia. On the other hand, the intensive treatment required to maintain euglycemia during the dwell time increases the risk of hypoglycemia. Therefore, glycemic control in diabetic patients on PD remains challenging.

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PD is cost-effective, has fewer activity restrictions, and its clinical outcomes are not inferior to those of hemodialysis (HD) [3]. Despite these benefits, PD remains underutilized globally [1]. This trend suggests that many challenges remain in PD maintenance. Many factors have been reported to affect technique survival of PD or mortality: age, socioeconomic status, race, comorbidities such as DM, coronary artery disease (CAD) and congestive heart failure (CHF), and residual kidney function (RKF) [4,5]. Of these, RKF plays an important role in improving dialysis adequacy, volume status, quality of life, technique survival, and mortality [5–7].

Factors known to influence the RKF decline include age, DM, higher proteinuria, high glucose exposure, peritonitis, automated PD (APD), higher serum phosphate levels, and the use of aminoglycosides [8–10]. In particular, DM significantly contributes to the decline in kidney function, and poor glycemic control has been reported to accelerate this decline in the predialytic diabetic population [11,12]. However, in diabetic patients on PD, although a previous observational study showed no association between glycemic control and RKF decline [13], this remains unclear.

In addition, the RKF decline is related to volume overload, which can compromise technique survival in patients on PD. Volume overload in PD has been reported to increase the risk of technique failure (TF), peritonitis, cardiovascular events, left ventricular hypertrophy, and all-cause mortality [14,15]. Compared with HD, PD allows patients to freely take food by slow and continuous ultrafiltration (UF) over 24 hours. Despite this advantage, volume overload may occur more frequently in PD than in HD [16]. The risk of volume overload can be elevated in patients with inadequate peritoneal UF, increased dietary salt and fluid intake, reduced cardiac function, and decreased RKF [17,18]. Notably, DM may exacerbate these risk factors, increasing susceptibility to volume overload.

In this observational study, we investigated whether RKF declines more rapidly with poor glycemic control and whether poor glycemic control adversely influences several risk factors associated with volume overload, subsequently leading to TF.

Methods

Study population

We reviewed the clinical records of 90 patients with DM who started PD at our center between 2008 and 2022. The patients underwent PD for at least 90 days with PD modalities, including continuous ambulatory PD (CAPD) and APD. Of these, eight patients who exhibited anuria (a urine output of less than 100 mL/day) before PD and two without at least two consecutive RKF data were excluded. As a result, 80 patients were enrolled in this study, and the first 2 years of each patient's data were collected to investigate the impact of glycemic control, particularly in the early stages of PD.

This study was approved by the Institutional Review Board of Pusan National University Hospital (No. 2308-032-131). Written informed consent was waived because the retrospective design of the study.

Data collection

Demographic and clinical data were collected, including age, sex, body surface area, and comorbidities such as hypertension, dyslipidemia, CAD, CHF, and episodes of peritonitis during the follow-up period. Laboratory test results included glycosylated hemoglobin (HbA1c), hemoglobin, serum albumin, serum calcium, and phosphate levels. Medication history was also recorded, including beta-blockers, renin-angiotensin system (RAS) blockers, calcium channel blockers (CCB), and diuretics with their doses. In this study, we defined the use of high-dose loop diuretics as an oral dose greater than 250 mg daily furosemide equivalent [19].

We investigated the prescriptions for PD, including the use of icodextrin and high glucose exposure, defined as the use of 2.5% glucose dialysate exceeding 75% of the total use or the use of 3.85% or 4.25% glucose dialysate exceeding 25% of the total use [20]. The modified peritoneal equilibrium test (PET) using a 4.25% glucose solution was performed 2 months after the start of PD as a baseline test and was repeated every 4 to 6 months or more frequently as clinically indicated. The characteristics of peritoneal transport, as determined by the dialysate to plasma creatinine ratio at 4 hours on PET, were classified into four

groups: low (<0.50), low average (0.5–0.64), high average (0.65–0.80), and high (>0.81). Diagnosis of UF failure (net UF <400 mL/4 hr on modified PET) during the follow-up period was also investigated [21]. Additionally, we included 24-hour urine volume, 24-hour urine creatinine and urea clearance, renal Kt/V urea, peritoneal Kt/V urea, and weekly Kt/V urea to assess dialysis adequacy along with PET.

Assessment of glycemic control and residual kidney function

We defined the degree of glycemic control as the average of all HbA1c levels measured every 3 months during the follow-up [22]. RKF (mL/min/1.73 m^2) was determined by the average clearance of 24-hour urine urea and creatinine, normalized to the standard body surface area of 1.73 m^2. Twenty-four-hour urine analysis was performed every 4 to 6 months before and after the start of PD and was stopped when anuria developed. In the case of anuria, the RKF value was calculated as zero. We assessed RKF loss in two ways: the slope of RKF decline estimated by simple linear regression and the time to anuria [8].

Technique failure associated with volume overload

TF was defined as any transition from PD to HD lasting 30 days or more [23]. We investigated various causes leading to TF by chart review. To assess the volume overload in patients on PD, we examined TF associated with volume overload (TFVO). TFVO was defined as cases in which patients were permanently switched to HD due to excessive fluid accumulation, as determined by evidence of pleural effusion or pulmonary edema on imaging studies along with dyspnea or edema.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 23 (IBM Corp.) and R ver. 4.3.1 (R Foundation for Statistical Computing). We used the Kolmogorov-Smirnov test to assess the normality of the data distribution. Continuous variables are expressed as mean ± standard deviation if normally distributed and as median (interquartile range, IQR) if skewed. Categorical variables are presented as frequencies and percentages.

We used a multivariable linear regression model to evaluate the linear relationship between time-averaged HbA1c and the slope of RKF decline. In addition, a multivariable Cox proportional hazards model was used to examine the association between time-averaged HbA1c and the time to anuria. To construct multivariable linear and Cox regression models, we included independent variables that showed a substantial association ($p < 0.1$) with each outcome in the univariate analysis. Furthermore, a time-dependent receiver operating characteristic (ROC) curve was used to estimate the cut-off level of HbA1c for the risk of time to anuria, and the Kaplan-Meier analysis was performed using the HbA1c cut-off level.

A multivariable Cox model was established to investigate the association between glycemic control and TFVO. We used potential risk factors for volume overload as independent variables in the multivariable models, because there were no significant independent variables in the univariate model. We also performed multivariable logistic regression analysis to identify risk factors for TFVO. The time-dependent ROC curve was used to estimate the cut-off level of HbA1c for the risk of TFVO, and the Kaplan-Meier analysis was performed using the HbA1c cut-off level.

We further analyzed the patients to investigate whether the impact of glycemic control on RKF decline differs according to the baseline RKF. Patients were divided into two groups based on the mean RKF value. We performed multivariable linear regression with the slope of RKF decline as the dependent variable for each group. All probabilities were two-tailed, and a p-value of less than 0.05 was considered statistically significant.

Results

We enrolled 80 diabetic patients with incident PD, including 50 (62.5%) with CAPD and 30 (37.5%) with APD. Baseline demographic, biochemical, and clinical information is presented in Table 1. The median follow-up duration was 24.0 months (IQR, 16.3–24.0 months), and the mean age was 51.3 ± 10.9 years. A total of 61 patients (76.3%) were male, and hypertension (n = 56, 70.0%) was the commonest comorbidity. During the study period, the mean time-averaged HbA1c was 7.15% ± 1.05%.

Table 1. Baseline characteristics of the study population

Characteristic	Total
No. of subjects	80
Age (yr)	51.3 ± 10.9
Male sex	61 (76.3)
Body surface area (m^2)	1.75 ± 0.17
Follow-up duration (mo)	24.0 (16.3–24.0)
Comorbidities	
Hypertension	56 (70.0)
Dyslipidemia	13 (16.3)
Coronary artery disease	22 (27.5)
Congestive heart failure	13 (16.3)
Episodes of peritonitis	7 (8.1)
Laboratory tests	
Time-averaged HbA1c (%)	7.15 ± 1.05
Hemoglobin (g/dL)	10.82 ± 1.44
Albumin (g/dL)	3.65 ± 0.44
Serum calcium (mg/dL)	8.85 ± 0.71
Serum phosphorus (mg/dL)	4.50 ± 1.30
Medications	
RAS blockades	58 (72.5)
Beta-blockers	41 (51.2)
Calcium channel blockers	52 (65.0)
Diuretics	64 (80)
High-dose loop diuretics[a]	25 (31.3)
PD prescriptions	
PD exchange type, CAPD	50 (62.5)
Use of icodextrin	50 (62.5)
High glucose exposure[b]	32 (40)
PET data	
D/P creatinine at 4 hours	0.67 ± 0.13
Higher solute transport, high and high average	40 (50.0)
Diagnosed with ultrafiltration failure	29 (36.3)
Dialysis adequacy	
Baseline urine volume (mL)	1,030 (700–1,650)
RKF (mL/min/1.73 m^2)	6.09 ± 4.05
Total Kt/V urea	2.38 ± 0.71
Peritoneal Kt/V urea	1.43 ± 0.43
Renal Kt/V urea	0.94 ± 0.63

Data are expressed as number only, mean ± standard deviation, number (%), or median (interquartile range).
CAPD, continuous ambulatory peritoneal dialysis; D/P, dialysate to plasma; HbA1c, glycosylated hemoglobin; PD, peritoneal dialysis; PET, peritoneal equilibrium test; RAS, renin-angiotensin system; RKF, residual kidney function.
[a]Defined as an oral dose greater than 250 mg daily furosemide equivalent.
[b]Defined as the use of 2.5% glucose dialysate exceeding 75% of the total use or the use of 3.85% or 4.25% glucose dialysate exceeding 25% of the total use.

The slope of residual kidney function decline

Over the first 2 years, the mean rate of RKF decline was –3.25 ± 3.94 mL/min/1.73 m^2 per year, and the mean baseline RKF was 6.09 ± 4.05 mL/min/1.73 m^2. To identify the independent predictors of RKF decline, we performed a univariate linear regression analysis using the following independent variables: age, body surface area, baseline RKF, hypertension, CHF, CAD, dyslipidemia, PD exchange types, high glucose exposure, use of icodextrin, episodes of peritonitis, and medications, including RAS blockers, beta-blockers, CCB, and diuretics. We included variables with $p < 0.1$ from the univariate analysis for multivariable linear regression (Table 2). Higher time-average HbA1c (β = –0.95; 95% confidence interval [CI], –1.66 to –0.24; $p = 0.01$) and higher baseline RKF (β = –0.33; 95% CI, –0.48 to –0.18; $p < 0.001$) were independent predictors of rapid RKF decline. The history of CHF showed significant associations (β = –2.85; 95% CI, –5.24 to –0.45; $p = 0.02$) in the univariate analysis; however, it did not remain significant in the multivariable analysis (β = –1.83; 95% CI, –3.99 to 0.33; $p = 0.10$).

Progression to anuria

A total of 24 patients (30.0%) developed anuria during the 2-year study period. The mean time of progression to anuria was 11.8 ± 6.1 months. The median baseline urine volume was 1,030 mL (IQR, 700–1,650 mL), and 25 patients (31.3%) were on high-dose loop diuretics at baseline. During the same period, two patients died before the development of anuria, seven transitioned to permanent HD, two underwent kidney transplantation and one recovered kidney function. Table 3 shows the univariate and multivariable Cox proportional hazards models for the possible factors associated with the time to anuria. In adjusted models, each 1% increase in time-averaged HbA1c was significantly associated with about a two-fold increased risk of progression to anuria (adjusted hazard ratio [HR], 1.97; 95% CI, 1.29–3.00; $p = 0.002$), and the use of high-dose loop diuretics was associated with 3.36-fold increased risk of progression to anuria (adjusted HR, 3.36; 95% CI, 1.27–8.88; $p = 0.02$). Additionally, a higher baseline urine volume was related to a lower risk of progression to anuria (per 0.1 L urine volume: adjusted HR, 0.88; 95% CI, 0.81–0.95; $p = 0.001$). The time-dependent ROC curve for the risk of

Table 2. Linear regression models for possible factors associated with the slope of RKF decline

Variable	Univariate		Multivariable[a]	
	β (95% CI)	p-value	β (95% CI)	p-value
Time-averaged HbA1c (%)	−0.86 (−1.62 to −0.10)	0.03	−0.95 (−1.66 to −0.24)	0.01
Baseline RKF (mL/min/1.73 m^2)	−0.39 (−0.54 to −0.23)	<0.001	−0.33 (−0.48 to −0.18)	<0.001
Use of icodextrin	−1.63 (−3.45 to 0.20)	0.08	−0.86 (−2.43 to 0.72)	0.28
Congestive heart failure	−2.85 (−5.24 to −0.45)	0.02	−1.83 (−3.99 to 0.33)	0.10

R^2 = 0.345; adjusted R^2 = 0.30.
CI, confidence interval; HbA1c, glycosylated hemoglobin; RKF, residual kidney function.
[a]Including variables that showed a substantial association (p < 0.1) with the slope of RKF decline in the univariate model.

Table 3. Cox proportional hazards model for possible factors associated with time to anuria

Variable	Univariate		Multivariable	
	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Age	0.97 (0.93–1.00)	0.16		
Male sex	0.51 (0.22–1.16)	0.11		
PD exchange type, CAPD	0.84 (0.36–1.95)	0.68		
Hypertension	1.26 (0.46–3.44)	0.65		
Congestive heart failure	0.93 (0.32–2.74)	0.90		
Coronary artery disease	0.63 (0.24–1.69)	0.36		
Time-averaged HbA1c (%)	1.94 (1.35–2.79)	<0.001	1.97 (1.29–3.00)	0.002
Baseline RKF (mL/min/1.73 m^2)	0.90 (0.75–1.10)	0.31		
Baseline urine volume (/0.1 L)	0.87 (0.80–0.94)	0.001	0.88 (0.81–0.95)	0.001
High glucose exposure	2.02 (0.89–4.62)	0.09	1.17 (0.44–3.11)	0.75
Use of icodextrin	1.21 (0.52–2.82)	0.67		
Episodes of peritonitis	0.37 (0.05–2.71)	0.32		
Use of RAS blockades	1.35 (0.53–3.40)	0.53		
Use of high-dose loop diuretics[a]	3.13 (1.40–7.01)	0.005	3.36 (1.27–8.88)	0.02
Use of beta-blockers	1.87 (0.82–4.27)	0.14		
Use of CCB	1.80 (0.71–4.55)	0.21		

CCB, calcium channel blocker; CAPD, continuous ambulatory peritoneal dialysis; CI, confidence interval; HbA1c, glycosylated hemoglobin; HR, hazard ratio; PD, peritoneal dialysis; RAS, renin-angiotensin system; RKF, residual kidney function.
[a]Defined as an oral dose greater than 250 mg daily furosemide equivalent.

progression to anuria in the first 2 years revealed that the cut-off HbA1c level was 7.2% (area under the curve [AUC] = 0.782, C-index = 0.709) (Fig. 1), and the Kaplan-Meier curve showed the validity of the HbA1c cut-off level of 7.2% (log-rank p < 0.001) (Supplementary Fig. 1A, available online).

Technique failure associated with volume overload

Over the first 2 years, 14 patients (17.5%) experienced TF. Among them, eight were attributed to volume overload. The mean time to TFVO was 12.4 ± 6.1 months. During the same period, six patients were censored due to TF from other causes, two died, one recovered kidney function, and four underwent kidney transplantation. Multivariable Cox proportional hazards models showed that an increase in the time-averaged HbA1c level was associated with a higher risk of TFVO (Table 4). In the fully adjusted model 3, which included age, sex, hypertension, CHF, CAD, CAPD, episodes of peritonitis, high glucose exposure, and higher transport type at baseline, the adjusted HR for TFVO was 2.88 (95% CI, 1.41–5.90; p = 0.004) for each 1% increase in time-averaged HbA1c. Multivariable logistic regression analysis was conducted to further evaluate the potential

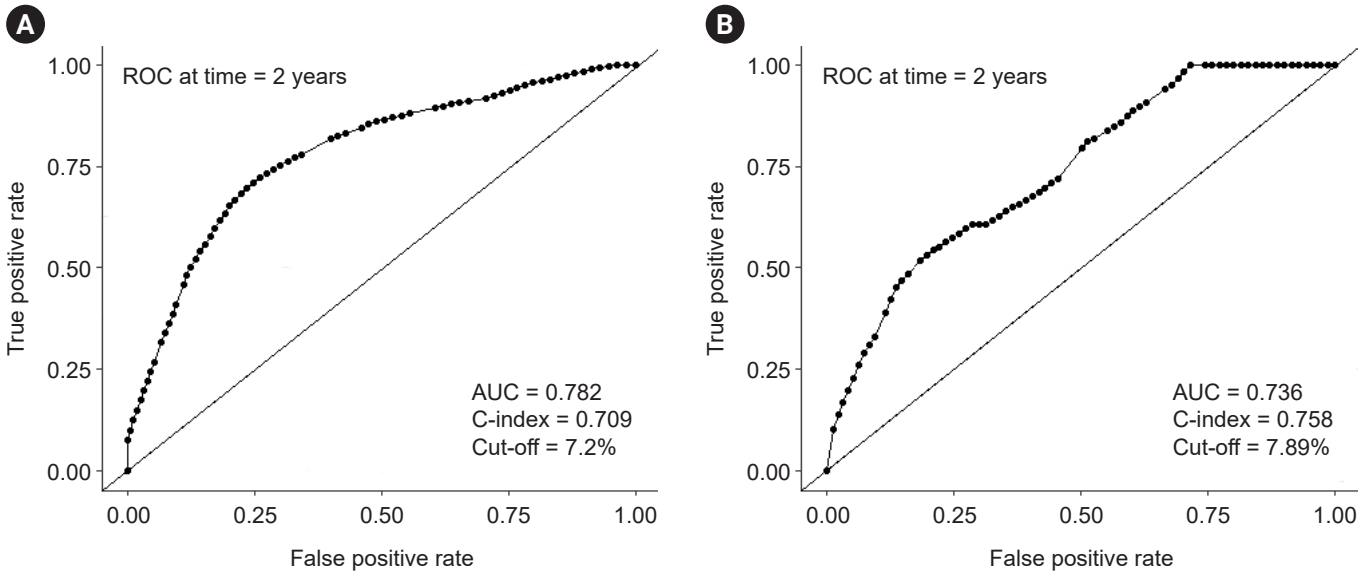

Figure 1. Time-dependent ROC curve for glycosylated hemoglobin in predicting time to the renal complications at first 2 years. (A) To anuria. (B) To technique failure associated with volume overload.
AUC, area under the curve; ROC, receiver operating characteristic.

Table 4. Cox proportional hazards models for the association of time-averaged HbA1c with TFVO

	Adjusted HR (95% CI)[a]	p-value
Crude[b]	2.27 (1.20–4.29)	0.01
Model 1	2.62 (1.35–5.11)	0.005
Model 2	2.79 (1.35–5.78)	0.006
Model 3	2.88 (1.41–5.89)	0.004

CI, confidence interval; HbA1c, glycosylated hemoglobin; HR, hazard ratio; TFVO, technique failure associated with volume overload.
Model 1: adjusted for age, sex; Model 2: Model 1 + hypertension, congestive heart failure, coronary artery disease; Model 3: Model 2 + continuous ambulatory peritoneal dialysis, episodes of peritonitis, high glucose exposure, higher solute transport type (high and high average).
[a]Each 1% increase in time-averaged HbA1c. [b]Unadjusted.

risk factors associated with TFVO. After adjustment for age, sex, CAPD, CHF, and diagnosis with UF failure during the study period, patients who progressed to anuria showed a significant association with the risk of TFVO (OR, 5.51; 95% CI, 1.09–27.96; p = 0.04) (Supplementary Table 1, available online). Furthermore, the time-dependent ROC curve for the risk of TFVO in the first 2 years revealed that the cut-off HbA1c level was 7.89% (AUC = 0.736, C-index = 0.758) (Fig. 1), and the Kaplan-Meier survival curve showed the validity of the HbA1c cut-off level of 7.89% (log-rank p < 0.001) (Supplementary Fig. 1B, available online).

Subgroup analysis

In a subgroup analysis, patients were classified into two groups according to the mean baseline RKF value of 6.09 mL/min/ 1.73 m^2: higher RKF group and lower RKF group. Multivariable linear regression analysis showed that time-averaged HbA1c (β = –1.620; 95% CI, –2.506 to 0.200; p = 0.020) and CHF (β = –4.427; 95% CI, –7.706 to –0.962; p = 0.016) were significantly associated with a rapid RKF decline in the higher RKF group (Table 5). Whereas, in the lower RKF group, time-averaged HbA1c was not related to the slope of RKF decline (β = –0.465; 95% CI, –3.957 to 7.543; p = 0.173).

Discussion

This study investigated whether poor glycemic control accelerates RKF decline and affects the risk of TFVO in patients with diabetic PD. In the predialytic population with DM, intensive glycemic control has been demonstrated to reduce albuminuria, preserve kidney function, and reduce major macrovascular and microvascular events [24,25].

Table 5. Multivariable linear regression for possible factors associated with the slope of RKF decline according to the baseline RKF

Variable[b]	Higher RKF[a] (n = 37)		Lower RKF (n = 43)	
	β (95% CI)	p-value	β (95% CI)	p-value
Time-averaged HbA1c (%)	−1.62 (−2.97 to −0.28)	0.02	−0.47 (−1.15 to 0.21)	0.17
Use of icodextrin	−1.24 (−4.38 to 1.90)	0.25	−0.41 (−2.05 to 1.23)	0.62
Congestive heart failure	−4.43 (−7.96 to −0.89)	0.02	0.48 (−2.22 to 3.19)	0.72

R^2 = 0.289 in the higher RKF group and 0.055 in the lower RKF group.
CI, confidence interval; HbA1c, glycosylated hemoglobin; RKF, residual kidney function.
[a]Divided by the mean baseline RKF value of 6.09 mL/min/1.73 m^2. [b]Including variables that showed a substantial association ($p < 0.1$) with the slope of RKF decline in the univariate model.

Chronic hyperglycemia damages the kidney and vascular cells through several pathways, including glucose auto-oxidation, polyol and hexamine pathways, production of advanced glycan end-products (AGEs), nicotinamide adenine dinucleotide phosphate oxidase synthesis, protein kinase C stimulation, and RAS hyperactivity [26]. These mechanisms of damage also apply to patients on PD, and indeed DM has been reported to be associated with an RKF decline in patients on PD [9]. However, there is a lack of research on the degree of glycemic control and its effect on the decline in RKF in patients on PD.

The current study showed that an increase in time-averaged HbA1c levels was significantly associated with a rapid RKF decline. By contrast, the previous study by Sung et al. [13] showed no association between mean HbA1c and the changes in RKF during the first 1-year observation period in diabetic patients on PD ($r^2 < 0.001$, $p = 0.880$). There are probable reasons for the difference in results between the two studies. First, Sung et al. [13] assessed the changes in RKF using the ratio of ΔRKF (ΔRKF/baseline RKF) between baseline and 1 year. This accurately indicates the change in RKF between two points in time and ensures the consistency and completeness of the data. However, it may not reflect the trend and dynamic process of RKF decline over time compared to the slope of RKF decline estimated by linear regression used in our study. Second, the observation period is different. In this study, 14 patients (17.5%) developed anuria within 1 year, which is comparable to that reported by Sung et al. [13] (17%), and 10 (12.5%) additionally developed anuria between 1 and 2 years. Given that the incidence of anuria within 1 year and between 1 and 2 years is similar, a 2-year observation period with a higher incidence of events may be appropriate for a more accurate analysis. These differences may have contributed to the conflicting results.

We further identified that more intensive glucose control could be beneficial in patients with higher RKF compared with those with lower RKF. Although we divided patients into two groups based on the mean RKF value for comparison, this finding suggests that more attention should be paid to blood sugar control in the early stages of PD, when RKF is relatively high.

In this study, we demonstrated that an increase in time-averaged HbA1c was associated with the risk of anuria. Furthermore, we found that lower baseline urine volume and the use of high-dose loop diuretics were independent risk factors for anuria. In general, patients on PD who have a low urine volume at baseline are at potential risk of progression to anuria. However, because the need for high-dose diuretics to maintain adequate urine volume also reflects the reduced RKF, this should be considered in addition to urine volume to predict the risk of anuria.

DM is also associated with volume overload in patients on PD [27]. Hyperglycemia leads to the accumulation of AGEs and glucose degradation products in the peritoneum, which causes peritoneal fibrosis and vasculopathy and subsequently increases peritoneal permeability [28]. As a result, diabetic patients are at high risk of UF failure and require higher glucose dialysate to maintain their peritoneal UF, which can also lead to hyperglycemia and additional peritoneal damage [20,29]. This vicious cycle can, in turn, reduce the peritoneal UF capacity over time. Furthermore, DM increases the risk of CHF [30] and increases fluid intake by exacerbating thirst distress [31]. These factors may account for the increased risk of volume overload in diabetic patients on PD.

Our findings showed that the increase in time-averaged HbA1c was significantly associated with an increased risk

of TFVO in diabetic patients on PD. Furthermore, patients who developed anuria during the study period were at high risk for TFVO. However, there was no association between the higher transport type at baseline and volume overload. This may be due to adjustments in PD prescriptions, such as the use of icodextrin or higher glucose dialysate to enhance UF. In addition, comorbidities such as CHF and CAD, which are potential risk factors of volume overload, did not show a statistically significant association. Nevertheless, inadequate glycemic control may exacerbate these risk factors, particularly RKF loss, and contribute to an increased risk of volume overload.

We used HbA1c levels as indicators of glycemic control. In patients on PD, it is unclear whether HbA1c is a reliable indicator of average glucose levels over the past 90 days [32]. Metabolic acidosis and uremia tend to increase HbA1c levels [33,34], whereas many factors, such as a reduced red blood cell lifespan, blood transfusions, and malnutrition, can lead to decreased HbA1c levels [35]. Therefore, this may overestimate or underestimate the average blood glucose levels of individuals based on their hemoglobin values. However, alternative glucose monitoring tests, such as glycated albumin and fructosamine, have been reported to correlate weakly with blood glucose levels in advanced chronic kidney disease; thus, current guidelines still recommend using HbA1c for glucose monitoring [36], which was acceptable in our study.

The optimal target HbA1c level in diabetic patients on PD has not been established. A retrospective cohort study [37] demonstrated a U-shaped association between HbA1c and all-cause mortality, suggesting that both poor and excessive glycemic control are associated with a high risk of mortality. For these reasons, current guidelines recommend an individualized HbA1c target ranging from 6.5% to 8.0% according to comorbidities and the risk of hypoglycemia [32,36]. In our results, the optimal HbA1c cut-off levels for the risk of progression to anuria and TFVO were 7.2% and 7.89%, respectively. Based on these results, strict glycemic control (HbA1c less than 7.2%) may be considered reasonable for patients with PD and a low risk of hypoglycemia to preserve RKF. This may also provide an additional rationale for the current guidelines.

RKF in patients on PD plays an important role in long-term survival. A previous large cohort study, CANUSA (Canada-USA) [7], reported that a 0.5 mL/min increase in glomerular filtration rate (GFR) was associated with a 9% lower risk of death. The NECOSAD (Netherlands Cooperative Study on the Adequacy of Dialysis) study group [5] identified a 12% reduction in the risk of death and a 10% reduction in the risk of combined death and TF per 10 L/wk/1.73 m^2 increase in GFR. Additionally, RKF is associated with multiple benefits, including improvements in long-term blood pressure control [38], dialysis adequacy [39], left ventricular hypertrophy [40], volume status, and quality of life [6]. Therefore, efforts to preserve RKF are necessary to ensure the long-term sustainability of PD, and appropriate glycemic control is one of the ways to preserve RKF in diabetic patients on PD.

This study has some limitations. First, this study involved a relatively small number of subjects from a single center. However, to the best of our knowledge, this is the first study to demonstrate the impact of glycemic control on RKF decline and volume overload in diabetic patients on PD. Therefore, further large-scale studies are required to confirm the reproducibility of these results. Second, we included patients who underwent both CAPD and APD. Whether the decline in RKF differs according to PD exchange type remains controversial [6]. In our study, although there was no difference in RKF decline between CAPD and APD (Table 3), the effect of the exchange type could not be completely excluded. Finally, in some cases, the RKF value was calculated to be zero when the 24-hour urine output was less than 100 mL. This may have resulted in an overestimation of the individual slope of RKF decline.

In conclusion, our study found that poor glycemic control was associated with a rapid RKF decline and a trend toward increased TFVO during the first 2 years in diabetic patients who started PD. Therefore, appropriate glycemic control in diabetic patients on PD is necessary to preserve RKF, particularly in those with higher RKF, which in turn reduces the risk of volume overload and may contribute to a favorable long-term outcome.

Conflicts of interest

All authors have no financial conflicts of interest to declare.

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Data sharing statement

The data presented in this study are available from the corresponding author upon reasonable request.

Authors' contributions

Conceptualization, Supervision: EYS, SHS
Data curation: DEK, DWK, YC
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