

## Retrospective Cohort Study

# Comparison of clinical features and outcomes in peritoneal dialysis-associated peritonitis patients with and without diabetes: A multicenter retrospective cohort study

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## Abstract

### BACKGROUND

The number of end-stage renal disease patients with diabetes mellitus (DM) who are undergoing peritoneal dialysis is increasing. Peritoneal dialysis-associated peritonitis (PDAP) is a serious complication of peritoneal dialysis leading to technical failure and increased mortality in patients undergoing peritoneal dialysis. The profile of clinical symptoms, distribution of pathogenic organisms, and response of PDAP to medical management in the subset of end-stage renal disease patients with DM have not been reported previously. Discrepant results have been found in long-term prognostic outcomes of PDAP in patients with DM. We inferred that DM is associated with bad outcomes in PDAP patients.

### AIM

To compare the clinical features and outcomes of PDAP between patients with DM and those without.

### METHODS

In this multicenter retrospective cohort study, we enrolled patients who had at

Individual informed consent was waived given that the study was retrospective and non-interventional by design.

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least one episode of PDAP during the study period. The patients were followed for a median of 31.1 mo. They were divided into a DM group and a non-DM group. Clinical features, therapeutic outcomes, and long-term prognostic outcomes were compared between the two groups. Risk factors associated with therapeutic outcomes of PDAP were analyzed using multivariable logistic regression. A Cox proportional hazards model was constructed to examine the influence of DM on patient survival and incidence of technical failure.

## RESULTS

Overall, 373 episodes occurred in the DM group ( $n = 214$ ) and 692 episodes occurred in the non-DM group ( $n = 395$ ). The rates of abdominal pain and fever were similar in the two groups ( $P > 0.05$ ). The DM group had more infections with coagulase-negative Staphylococcus and less infections with *Escherichia coli* (*E. coli*) as compared to the non-DM group ( $P < 0.05$ ). Multivariate logistic regression analysis revealed no association between the presence of diabetes and rates of complete cure, catheter removal, PDAP-related death, or relapse of PDAP ( $P > 0.05$ ). Patients in the DM group were older and had a higher burden of cardiovascular disease, with lower level of serum albumin, but a higher estimated glomerular filtration rate ( $P < 0.05$ ). Cox proportional hazards model confirmed that the presence of diabetes was a significant predictor of all-cause mortality (hazard ratio = 1.531, 95% confidence interval: 1.091-2.148,  $P < 0.05$ ), but did not predict the occurrence of technical failure ( $P > 0.05$ ).

## CONCLUSION

PDAP patients with diabetes have similar symptomology and are predisposed to coagulase-negative Staphylococcus but not *E. coli* infection compared those without. Diabetes is associated with higher all-cause mortality but not therapeutic outcomes of PDAP.

**Key Words:** Diabetes mellitus; Mortality; Peritoneal dialysis; Peritoneal dialysis-associated peritonitis; Technical failure

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**Core Tip:** We for the first time confirmed that the symptoms of peritoneal dialysis-associated peritonitis in the diabetes mellitus group were the same as those in the non-diabetes mellitus group. This is the first multicenter retrospective cohort study to examine the relationship between diabetes mellitus and long-term outcome in peritoneal dialysis-associated peritonitis patients. It is also the first study to analyze the profile of distribution of pathogenic organisms and response of peritoneal dialysis-associated peritonitis to medical management in the subset of end-stage renal disease patients with diabetes mellitus. We found that diabetes mellitus was inclined to infection with coagulase-negative Staphylococcus but not *Escherichia coli*. Diabetes mellitus was associated with higher all-cause mortality but not with adverse therapeutic outcome of peritoneal dialysis-associated peritonitis.

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## INTRODUCTION

The prevalence of diabetes mellitus (DM) in the general population is increasing so rapidly that diabetic nephropathy is now the leading cause of end-stage renal disease (ESRD) worldwide<sup>[1,2]</sup>. ESRD patients with DM who are undergoing renal replacement therapy in the form of dialysis pose certain group specific challenges to the overall

well-being of these patients<sup>[3,4]</sup>. Adequate vascular access for hemodialysis is often a concern in ESRD patients with diabetes, consequently many patients may have to opt for peritoneal dialysis.

Peritoneal dialysis-associated peritonitis (PDAP) is a common and serious complication that not only leads to technical failure<sup>[5,6]</sup>, but is also associated with increased mortality in patients undergoing peritoneal dialysis (PD)<sup>[7]</sup>. Moreover, PDAP-related death constitutes a major chunk of all-cause mortality in patients undergoing PD<sup>[8]</sup>. Some studies suggest that DM is a risk factor for PDAP<sup>[9,10]</sup>, therefore, PDAP in patients with both ESRD and DM should draw careful attention. We hypothesized that there may be some differences in clinical features (symptoms and pathogens) and prognosis of PDAP between DM and non-DM patients. However, only few studies have analyzed the long-term prognostic outcomes of PDAP in patients with DM, often with discrepant results. Some studies concluded that DM was not a risk factor for death or technical failure<sup>[11,12]</sup> while others found DM to be a risk factor for all-cause death<sup>[13]</sup>, yet again some researchers like Tsai *et al*<sup>[14]</sup> found DM to be a significant risk factor for a combined outcome of death and catheter removal. More importantly, as far as we know, the profile of clinical symptoms, distribution of pathogenic organisms, and response of PDAP to medical management in the subset of ESRD patients with DM has not been reported previously.

To clarify the above issues, a large multicenter retrospective cohort study was performed to compare the clinical features (symptoms and pathogens) and outcomes (therapeutic outcomes and long-term prognostic outcomes) of PDAP in ESRD patients with DM with those without.

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## MATERIALS AND METHODS

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### **Participants**

This multicenter study was performed in Northeast China; the participating centers were The Second Hospital of Jilin University, The First Hospital of Jilin University-Eastern Division, Jilin FAW General Hospital, and Jilin Central Hospital. All PD patients who developed PDAP during the study period from January 1, 2013 to June 30, 2019 were recruited and followed until December 31, 2019. Patients with incomplete records, patients younger than 18 years, and those with chronic liver disease at initiation of PD were excluded from the study. Patients on immunosuppressant medications or steroids or with a history of intake of the same within the last 3 mo were also excluded from the study. We adhered to all the ethical requirements for retrospective observational studies at our center. Individual informed consent was waived given that the study was retrospective and non-interventional by design. We used a de-identified dataset. Diabetes was diagnosed according to American Diabetes Association criteria 2014<sup>[15]</sup>. According to the status of diagnosis of DM at initiation of PD, the patients were divided into a DM group and a non-DM group. They were followed until any of the following events: Death, a change to HD, renal transplantation, dropout, transfer to other centers, diagnosis with DM after initiation of PD, or until 31 December 2019.

### **Main clinical management**

Double-cuff Tenckhoff straight catheters and integrated Y-sets were used for PD treatment. PD trainings were conducted by experienced and educated physicians and nurses. The patients were asked to report back if they experienced cloudy effluent or abdominal pain. PD effluent was sent for bacterial and fungal culture by inoculation into blood culture media, and observed for at least 72 h to document pathogens. The diagnosis of PDAP required any two of the following features: (1) Clinical features consistent with peritonitis, *i.e.*, abdominal pain and/or cloudy dialysis effluent; (2) dialysis effluent white cell count  $> 100/\mu\text{L}$  or  $> 0.1 \times 10^9/\text{L}$  (after a dwell time of at least 2 h), with  $> 50\%$  polymorphonuclear cells; and (3) positive dialysis effluent culture<sup>[16]</sup>. All patients suspected of having PDAP were managed as per the International Society for Peritoneal Dialysis recommendation, which includes treatment with empiric intra-peritoneal antibiotics at presentation covering both Gram-positive and Gram-negative organisms, after taking culture samples<sup>[16]</sup>. Subsequent choice of antibiotics was directed by the effluent culture and sensitivity results.

### Data collection

Baseline data collected at the time of first episode of PDAP encompassed demographic data [age, gender, presence of DM, and history of cardiovascular disease (CVD)], timing of PDAP episodes, clinical and biochemical data, fever, abdominal pain, PD cell count on admission, 24 h urine output, serum white cell count, hemoglobin, serum albumin, blood urea nitrogen, serum creatinine, and estimated glomerular filtration rate (eGFR). Biochemical measurements were performed by standard laboratory techniques. The culture results of effluent samples were subcategorized into mono-microbial (Gram-positive, Gram-negative, fungal, and mycobacterial organisms), polymicrobial, culture-negative, and no culture. Patients with  $\geq 2$  cultured pathogens were considered to have polymicrobial peritonitis.

### Definitions of study outcomes

Therapeutic outcomes of medical management of PDAP included complete cure, catheter removal, PDAP-related death, and relapse. Complete cure was defined as complete resolution of PDAP by antibiotics alone without relapse or recurrence within 4 wk of completion of therapy<sup>[17]</sup>. PDAP-related death was defined as patient's death with peritonitis occurring within 30 d<sup>[8]</sup>. Relapse was defined as an episode occurring within 4 wk of completion of therapy with the same organism being isolated in effluent culture as in the previous episode<sup>[16]</sup>.

Long-term prognostic outcomes of PDAP included continued PD, technical failure, and all-cause mortality. All-cause mortality was the primary endpoint in the patient survival analysis. If a patient died within 4 wk after switching over to hemodialysis, the death was attributed to PD because these early deaths are considered to reflect the health status of the patient during PD therapy<sup>[18]</sup>. Technical failure was defined as a switch to HD for at least 3 mo due to any reason<sup>[19]</sup>.

### Statistical analysis

Normally distributed parametric continuous variables are represented as the mean  $\pm$  standard deviation, and were compared by Student's *t*-test. Continuous variables with a non-normal distribution are represented as medians (Q1-Q3), and were compared using Wilcoxon's rank-sum test. Categorical variables are represented as frequencies (percentages) and were compared using the chi-square ( $\chi^2$ ) test. The risk factors associated with therapeutic outcomes of PDAP were analyzed using multivariable logistic regression. Kaplan-Meier survival curves were constructed to evaluate cumulative hazard of all-cause mortality and technical failure between the two groups, and differences in the survival distribution was assessed by log rank test. Cox proportional hazard analysis was used to analyze the relationship between DM and all-cause mortality. Data were analyzed using SPSS (version 22.0, IBM, New York, United States). A *P* value  $< 0.05$  was considered statistically significant. All the artworks were created using GraphPad Prism (version 8.0).

The statistical methods of this study were reviewed by Su-Yan Tian from the First Hospital of Jilin University.

## RESULTS

### Study population and baseline characteristics of 1065 PDAP episodes

A total of 1145 episodes of PDAP occurred in 660 patients from four PD centers in Northeast China during the study period. Finally, 1065 episodes of peritonitis in 609 patients were included in this study (Figure 1). Patients in the DM group had significantly lower levels of serum albumin and serum phosphorus, but a higher level of eGFR ( $P < 0.05$ ). There was no difference in the frequency or distribution of symptoms such as fever and abdominal pain between DM group and non-DM group ( $P > 0.05$ ) (Table 1).

### Causative organisms of 1065 PDAP episodes

Among the 1065 PDAP episodes, 373 (35%) episodes occurred in the DM group. The differential distribution of causative organisms of PDAP between the two groups is shown in Table 2. The incidence of infection by Gram-positive bacteria, especially coagulase-negative Staphylococcus (CNS), was significantly higher in patients in the DM group ( $P < 0.05$ ) while the incidence of *E. coli* and *Pseudomonas aeruginosa* infection was significantly higher in the non-DM group ( $P < 0.05$ ). No significant difference was found in other organisms between the two groups ( $P > 0.05$ ).

**Table 1 Clinical manifestations and laboratory parameters of 1065 peritoneal dialysis-associated peritonitis events**

Index	DM (n = 373)	Non-DM (n = 692)	P
Clinical manifestation			
Fever	115 (30.8)	253 (36.6)	0.061
Abdominal pain	300 (80.4)	552 (79.8)	0.797
PD cell count on admission(/ $\mu$ L)	1920 (620, 5350)	1847 (613, 4974)	0.791
Laboratory test			
WBC ( $10^{12}$ /L)	8.27 (6.57, 10.98)	8.29 (6.09, 11.43)	0.903
Hb (g/L)	97 (84, 109)	99 (85, 113)	0.128
Alb (g/dL)	28.24 $\pm$ 6.24	29.42 $\pm$ 6.29	0.003
BUN (mmol/L)	14.85 (10.79, 20.16)	15.68 (12.01, 19.92)	0.090
Scr ( $\mu$ mol/L)	672.66 (511.00, 854.50)	735.60 (511.00, 954.35)	0
eGFR	6.29 (4.68, 8.38)	5.70 (4.35, 7.28)	0

DM: Diabetes mellitus; PD: Peritoneal dialysis; WBC: White cell count; Hb: Hemoglobin; Alb: Albumin; BUN: Blood urea nitrogen; Scr: Serum creatinine; eGFR: Estimated glomerular filtration rate.

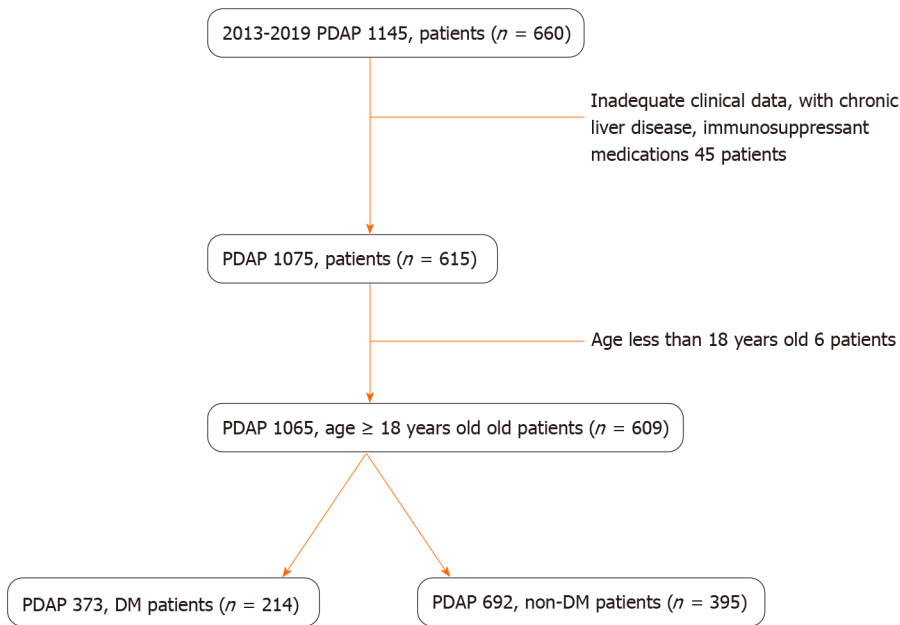
**Table 2 Causative organisms of 1065 peritoneal dialysis-associated peritonitis**

Organism (n, %)	DM (n = 373)	Non-DM (n = 692)	P
Gram-positive	172 (46.1)	259 (37.4)	0.006
<i>Coagulase-negative staphylococcus</i>	103 (27.6)	130 (18.8)	0.001
<i>Staphylococcus aureus</i>	22 (5.9)	26 (3.8)	0.108
<i>Streptococcus species</i>	30 (8.0)	59 (8.5)	0.786
<i>Enterococcus species</i>	8 (2.1)	11 (1.6)	0.514
Other gram-positive	9 (2.4)	33 (4.8)	0.060
Gram-negative	74 (19.8)	170 (24.6)	0.080
<i>Escherichia coli</i>	26 (6.7)	73 (10.5)	0.038
<i>Klebsiella species</i>	6 (1.6)	20 (2.9)	0.196
<i>Acinetobacter baumannii</i>	7 (1.9)	17 (2.5)	0.543
<i>Pseudomonas aeruginosa</i>	5 (1.3)	27 (3.9)	0.020
Other gram-negative	31 (8.3)	32 (4.6)	0.015
Fungi	13 (3.5)	30 (4.3)	0.501
<i>Mycobacterium tuberculosis</i>	2 (0.5)	8 (1.2)	0.508
Polymicrobial	24 (6.4)	55 (7.9)	0.369
Culture-negative	84 (22.5)	163 (23.6)	0.703
No culture	4 (1.1)	7 (1.0)	1.000

DM: Diabetes mellitus.

### Therapeutic outcomes of 1065 PDAP episodes

There was also no significant difference in the outcomes including rates of complete cure, catheter removal, PDAP-related death, and relapse of PDAP between the two groups ( $P > 0.05$ ) (Figure 2A). By using a multivariable logistic regression model, we did not find diabetes to be a significant risk factor for adverse therapeutic outcomes of PDAP ( $P > 0.05$ ) (Figure 2B).



**Figure 1** Flowchart of cohort establishment. PDAP: Peritoneal dialysis-associated peritonitis; DM: Diabetes mellitus.

### Baseline characteristics of 609 patients with PDAP

The patients were followed for a median of 31.1 mo (interquartile range, 16.5-49.6 mo). Baseline demographic characteristics and laboratory test parameters of patients with and without DM were compared and are presented in Table 3. Compared with patients without DM, the patients with DM were older and had a higher burden of CVD ( $P < 0.05$ ). Patients in the DM groups had a lower level of serum albumin, but a higher level of eGFR ( $P < 0.05$ ).

### Long-term prognostic outcomes of 609 patients with PDAP

One hundred and fifty (24.6%) patients died during the study period, of whom 71 belonged to the DM group and 79 to the non-DM group. The reasons for death included PDAP, cardiovascular death, cerebrovascular death, and others. Compared to the non-DM group, the all-cause mortality rate in the DM group was significantly higher, and correspondingly the rate of continuing on dialysis was significantly lower ( $P < 0.05$ ). One hundred and thirty-four (22.0%) patients experienced technical failure, of whom 42 were in the DM group and 92 in the non-DM group. There was no significant difference in the rates of technical failure between the two groups ( $P > 0.05$ ) (Figure 3A).

Kaplan-Meier survival curves showed that the DM group had a higher all-cause mortality rate compared to the non-DM group ( $P < 0.05$ ) (Figure 3B). There was no significant association between the occurrence of diabetes and incident rates of technical failure ( $P > 0.05$ ) (Figure 3C).

Cox regression analysis was used to analyze the relationship between DM and all-cause mortality. It was found that DM was a significant independent risk factor for all-cause mortality (hazard ratio = 1.531, 95% confidence interval: 1.091-2.148,  $P < 0.05$ ) (Figure 3D).

## DISCUSSION

The present study aimed to explore differences in the clinical features and outcomes in PDAP patients with and without diabetes as we hypothesized. We found that the symptoms of PDAP between the DM group and non-DM group were similar; the DM group had more infections with CNS and less infections with *E. coli* as compared to the non-DM group; the therapeutic outcomes of PDAP including complete cure, catheter removal, PDAP-related death, and relapse were comparable between the two groups; DM was an independent risk factor of all-cause mortality but not technique failure in PDAP patients.

**Table 3 Demographic characteristics and clinical data of 609 peritoneal dialysis-associated peritonitis patients**

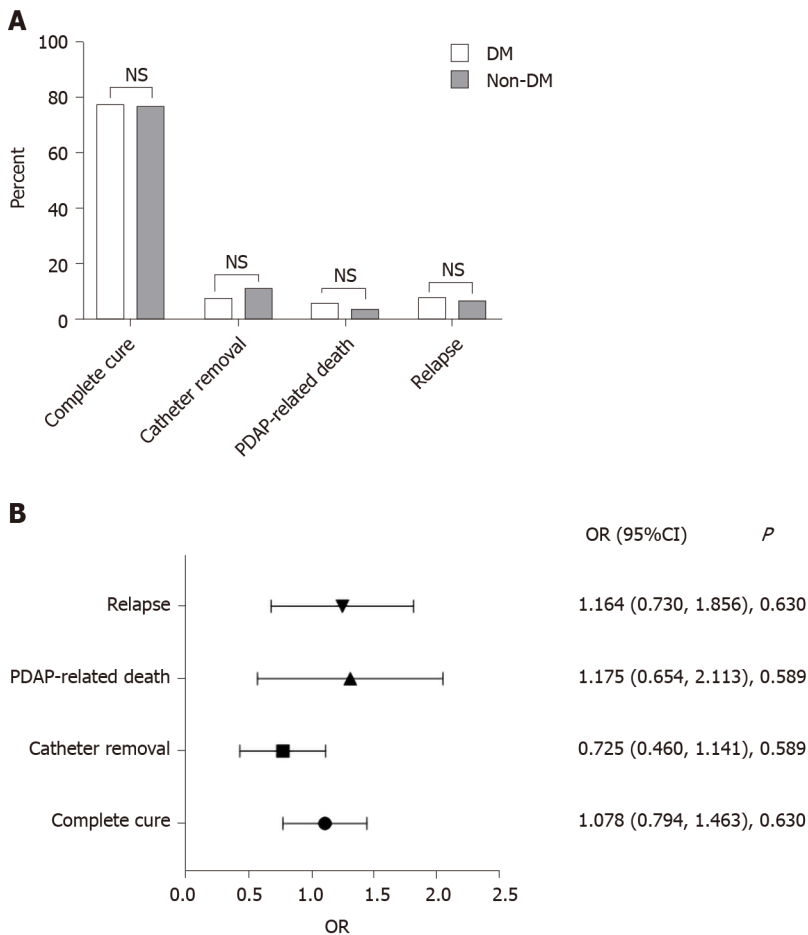
Variable	DM (n = 214)	Non-DM (n = 395)	P
Demographic characteristics			
Age (yr)	61 (54, 68)	55 (42, 68)	0
Gender (male, n, %)	117 (54.7)	185 (48.6)	0.065
No. of PDAP episodes, n (%)			0.596
1	127 (59.3)	230 (58.2)	
2	51 (23.8)	86 (21.8)	
≥ 3	36 (16.8)	79 (20.0)	
CVD	77 (36.0)	104 (26.3)	0.013
Laboratory test			
WBC (10 <sup>12</sup> /L)	8.41 (6.90,10.62)	8.26 (5.99,11.29)	0.411
Hb (g/L)	96 (80, 108)	98 (83, 111)	0.089
Alb (g/dL)	28.34 ± 6.74	29.60 ± 5.88	0.017
BUN (mmol/L)	14.9 (10.2, 20.5)	16.0 (12.5, 20.2)	0.062
Scr (μmol/L)	654.7 (480.0, 858.0)	745.3 (575.2, 972.2)	0.001
eGFR	6.46 (4.61, 8.55)	5.51 (4.23, 7.17)	0
PD cell count on admission(/μL)	1799.5 (571.0, 5040.0)	2040 (739.0, 5219.5)	0.330

DM: Diabetes mellitus; PDAP: Peritoneal dialysis-associated peritonitis; CVD: Cardiovascular disease; WBC: White cell count; Hb: Hemoglobin; Alb: Albumin; BUN: Blood urea nitrogen; Scr: Serum creatinine; eGFR: Estimated glomerular filtration rate; PD: Peritoneal dialysis.

We found no difference in the symptomatology of PDAP between the two groups. Theoretically, the symptoms of PDAP in diabetic patients may be atypical due to the presence of concomitant peripheral and autonomic neuropathy<sup>[14]</sup>. However, we confirmed that the symptoms of PDAP in the DM group were the same as those in the non-DM group for the first time.

To the best of our knowledge, no prior study has compared differences in microbial isolates on culture of effluent fluid between PDAP patients with and without diabetes. Our study characterized the microbiological etiology of PDAP in patients with DM over a period of 7 years. We found important differences in the distribution of organisms responsible for PDAP between the two groups, with a higher propensity for infection with Gram-positive bacteria, especially CNS in the DM group. One plausible reason for greater number of peritonitis episodes caused by CNS in diabetic population is due to higher risk of touch contamination and incorrect operation of peritoneal fluid exchange consequent to impaired vision due to diabetic retinopathy. The identification of an increased CNS peritonitis rate in this population suggests that more extensive training and more frequent review of operations might be beneficial. In addition, *Staphylococcus epidermidis* is the most common CNS, which can cause disease under certain circumstances. A study showed that the *Staphylococcus epidermidis* causing PDAP had low immunogenicity, which makes it more easily establish an infection since it cannot be immediately recognized by the immune system<sup>[20]</sup>. Meanwhile, DM is related to impaired immunity<sup>[21]</sup>. We consequently infer that CNS is inclined to colonize in PD patients with DM. Moreover, DM patients are more susceptible to infection especially in poorly controlled diabetics<sup>[22]</sup>. The impairment of neutrophil oxidative burst in individuals with poorly controlled diabetics may explain this phenomenon. A negative correlation was observed between neutrophil oxidative burst and hemoglobin A1c levels in the study by Osar *et al*<sup>[23]</sup>. And reduced neutrophil respiratory burst activity in diabetic patients could be restored to almost normal by blood glucose control<sup>[24]</sup>. However, our findings contrast with a previously published study, which showed that the development of CNS PDAP was not associated with DM<sup>[25]</sup>. A possible explanation for this discrepancy may be varying microbiological flora over geographical area and time.

*E. coli* is one of the most frequent causes of PDAP caused by Gram-negative bacteria. In our study, *E. coli* peritonitis was less common in patients with diabetes



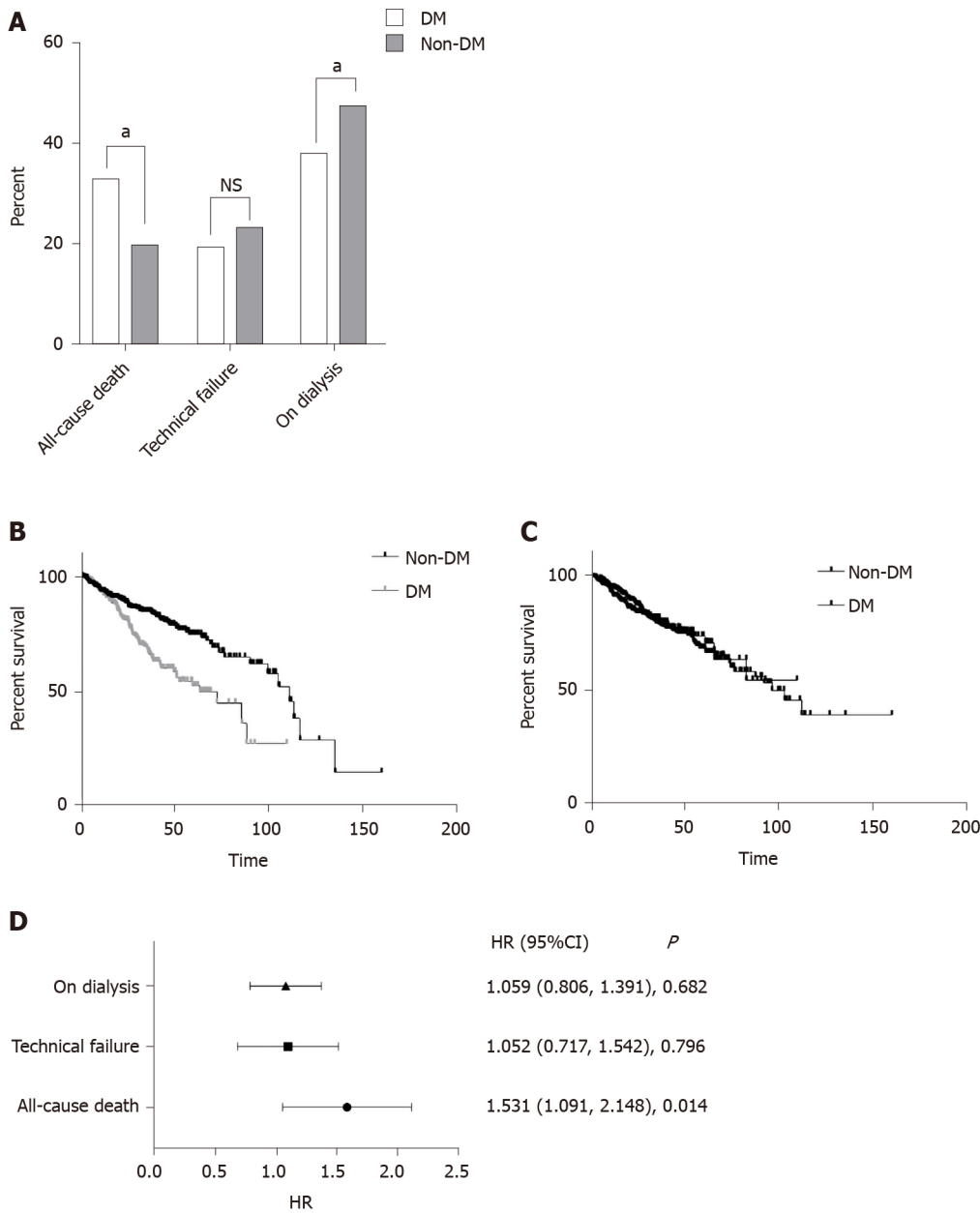
**Figure 2 Association between diabetes mellitus and therapeutic outcomes of peritoneal dialysis-associated peritonitis.** A: Therapeutic outcomes of peritoneal dialysis-associated peritonitis (PDAP), including complete cure, catheter removal, PDAP-related death, and relapse of PDAP, between the two groups; B: Multivariable logistic regression analysis of relationship between diabetes mellitus and therapeutic outcomes of PDAP. Covariates with  $P < 0.05$  in the univariate model and conventional confounders related to therapeutic outcomes (history of diabetes mellitus, age, gender, number of peritonitis episodes, history of cardiovascular diseases, basic hemoglobin, albumin, and estimated glomerular filtration rate) were included in the multivariate regression model. NS: Not significant; PDAP: Peritoneal dialysis-associated peritonitis; DM: Diabetes mellitus; OR: Odds ratio.

with no apparent explanation. Both *E. coli* virulence characteristics and host factors contribute to the development of PDAP. Previous studies showed that the PDAP *E. coli* isolates exhibited a superior virulence capability<sup>[26,27]</sup>. However, *E. coli* obtained from patients with PDAP did not show a common virulence profile and exhibited diverse serotypes<sup>[28]</sup>. Difference in virulence patterns of *E. coli* may explain a differential distribution frequency of infection between the DM group and non-DM group.

A noteworthy finding of our study is that the therapeutic outcomes of peritonitis between the DM group and non-DM group are comparable. More importantly, our results were further confirmed by using a multivariable logistic regression model. Our observation had both similarities and differences with previous data from ANZDATA registry study, which included 11122 episodes of peritonitis in 5367 patients in Australia during the period of 2004-2014<sup>[29]</sup>. Our study demonstrated that the complete cure rates were comparable between DM group and non-DM group, which was similar to the study by Htay *et al*<sup>[29]</sup>. DM was not associated with PDAP-related death in our study. In contrast, Htay *et al*<sup>[29]</sup> showed that DM correlated with PDAP-related death. Regional differences may account for this discrepancy.

The effect of DM on long-term prognostic outcomes of PDAP is controversial. A previous study found that DM is a risk factor for all-cause death<sup>[13]</sup>. Additionally, the study by Tsai *et al*<sup>[14]</sup> in a single Taiwan center also found a positive relation between DM and PDAP treatment failure, which was defined as death or catheter removal. However, in another study involving 483 patients (69 DM patients) diagnosed with PDAP, patients with DM had similar patient survival with those without DM<sup>[11]</sup>. In our study, we found a significantly higher all-cause mortality rate in the DM group than in the non-DM group. Higher burden of CVD could explain greater all-cause mortality in patients with diabetes. Patients with diabetes also had a lower level of serum albumin,





**Figure 3 Association between diabetes mellitus and long-term prognostic outcomes of peritoneal dialysis-associated peritonitis.** A: Long-term prognostic outcomes of PDAP, including all-cause death, technique failure, and on dialysis between the two groups; B and C: Kaplan-Meier analysis of cumulative patient survival and technique survival according to diabetes mellitus (DM); D: Cox regression analysis of relationship between DM and long-term prognostic outcomes. Covariates with  $P < 0.05$  in the univariate model and conventional confounders related to long-term prognostic outcomes (history of DM, age, gender, times of peritonitis episodes, history of cardiovascular diseases, basic hemoglobin, albumin, and estimated glomerular filtration rate) were included in the multivariate regression model. <sup>a</sup> $P < 0.05$ , compared between DM group and non-DM group. DM: Diabetes mellitus; HR: Hazard ratio.

which again has been associated with higher mortality in some studies<sup>[30,31]</sup>. Blood albumin is a marker of both ongoing inflammatory response and malnutrition, which is contained in the malnutrition inflammation score. High malnutrition inflammation score indicates malnourished status in patients undergoing PD<sup>[32]</sup>, which further leads to bad clinical outcomes<sup>[33]</sup>. Clinicians need to pay more attention to the serum albumin status of patients with diabetes to improve the prognosis of PDAP. The discrepancy between our study and previous studies may be explained by distinct patient characteristics and different covariates included in the Cox proportional hazards model. Similar to the previous study, we also did not find diabetes to be a risk factor for technical failure, further affirming that diabetes should not be considered a hurdle for instituting peritoneal dialysis<sup>[11-13]</sup>.

However, the present study has some limitations. Since it is a retrospective cohort study, potential bias and other confounding factors cannot be entirely excluded. Moreover, we did not consider the effect of indicators such as glycosylated

hemoglobin and fasting blood-glucose on the outcomes of the study.

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## CONCLUSION

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In conclusion, PDAP patients with DM have similar symptomology and are predisposed to CNS but not *E. coli* infection compared those without. DM is not associated with adverse therapeutic outcomes of PDAP. DM is associated with higher all-cause mortality but not technical failure in patients with PDAP.

## ARTICLE HIGHLIGHTS

### **Research background**

The number of end-stage renal disease patients with diabetes mellitus (DM) who are undergoing peritoneal dialysis is increasing. Peritoneal dialysis-associated peritonitis (PDAP) is a serious complication of peritoneal dialysis leading to technical failure and increasing mortality in patients undergoing peritoneal dialysis. The profile of clinical symptoms, distribution of pathogenic organisms, and response of PDAP to medical management in the subset of end-stage renal disease patients with DM has not been reported previously. Discrepant results have been found in long-term prognostic outcomes of PDAP in patients with DM. It is important to clarify the clinical features and outcomes of PDAP patients with DM.

### **Research motivation**

PDAP in DM patients is very common in the clinical practice, and treatment of PDAP in DM population is difficult and often with poor prognosis. Our research aimed to study the clinical manifestations, distribution of pathogenic organisms, and outcomes of PDAP in DM patients to provide a basis for future research of reasonable treatment and improvement of prognosis in this population.

### **Research objectives**

This study aimed to compare the clinical features and outcomes of PDAP between patients with DM and those without. We found that the distribution of pathogenic organisms of PDAP was different between the DM group and non-DM group, and DM was a significant predictor of all-cause mortality but not technical failure.

### **Research methods**

This is a multicenter retrospective cohort study. We enrolled patients who had at least one episode of PDAP during the study period. The patients were divided into a DM group and a non-DM group. Clinical features, therapeutic outcomes, and long-term prognostic outcomes were compared between the two groups. Risk factors associated with therapeutic outcomes of PDAP were analyzed using multivariable logistic regression. A Cox proportional hazards model was constructed to examine the influence of DM on patient survival.

### **Research results**

We confirmed that the symptoms of PDAP in the DM group were the same as those of the non-DM group ( $P > 0.05$ ). The DM group had more infections with coagulase-negative Staphylococcus and less infections with *Escherichia coli* (*E. coli*) as compared to the non-DM group. DM was not associated with therapeutic outcomes (complete cure, catheter removal, PDAP-related death, or relapse) of PDAP ( $P > 0.05$ ). The presence of DM was a significant predictor of all-cause mortality (hazard ratio = 1.531, 95% confidence interval: 1.091-2.148,  $P < 0.05$ ), but did not predict occurrence of technical failure ( $P > 0.05$ ). However, we did not consider the effect of indicators such as glycosylated hemoglobin and fasting blood-glucose on the outcomes of the study.

### **Research conclusions**

The symptoms of PDAP are similar in the DM group and non-DM group. Patients with diabetes are predisposed to coagulase-negative Staphylococcus but not *E. coli* infection. DM is associated with higher all-cause mortality but not therapeutic outcomes of PDAP.

### Research perspectives

Future research should focus on the effects of blood glucose control on PDAP outcomes, the mechanism of bacterial colonization, and ways to improve prognosis of PDAP in DM patients.

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