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Risk Factors and Pathogen Spectrum in Continuous Ambulatory Peritoneal Dialysis-Associated Peritonitis: A Single Center Retrospective Study

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Background: To investigate the incidence, risk factors, pathogen distribution, and drug resistance patterns in continuous ambulatory peritoneal dialysis-associated peritonitis (CAPDP).

Material/Methods: Clinical data for 248 patients who underwent continuous ambulatory peritoneal dialysis (CAPD) treatment in a single center in China from March 2018 to January 2021 were retrospectively collected. The patients were divided into the CAPDP group (n=40) and the non-CAPDP group (n=208) according to whether peritonitis occurred. The incidence rate, risk factors, bacterial distribution, and drug sensitivity of CAPDP were analyzed.





Results: The incidence of CAPDP was 16.13%, and 87.5% of patients with CAPDP continued CAPDP treatment after anti-infection treatment. Patients with and without CAPDP were clearly distinguished, on the basis of their clinical characteristics, by using principal component analysis (PCA) methods. Logistic regression analysis found that body mass index (BMI; $P=0.0095$), albumin ($P=0.016$), albumin/globulin ratio ($P=0.018$), C-reactive protein ($P=0.0001$), and rapid transport ($P=0.034$) were independent risk factors for CAPDP. The main pathogens causing the CAPDP were *Staphylococcus epidermidis* (50.00%), *Staphylococcus capitis* (13.33%), and *Escherichia coli* (10.00%).

Among the pathogenic bacteria, the main drugs to which gram-negative cocci were sensitive were imipenem, meropenem, piperacillin/tazobactam, cefoperazone/sulbactam, ceftazidime, and tigecycline. The main drugs to which gram-positive cocci were sensitive were vancomycin, teicoplanin, and linezolid. The drug resistance rate of pathogenic bacteria to penicillin G, ampicillin, compound trimethoprim, cefepime, ceftriaxone, and amoxicillin-clavulanic acid drugs was 36.26-100%.

Conclusions: BMI, albumin, albumin/globulin ratio, C-reactive protein, and rapid transport are independent risk factors for CAPDP. Gram-positive bacteria are the main pathogens of CAPDP and are sensitive to vancomycin, teicoplanin, and linezolid.

Keywords: Peritoneal Dialysis • Peritonitis • Risk Factors

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Background

Current research points out that continuous ambulatory peritoneal dialysis (CAPD) is one of the main alternative therapies for patients with end-stage renal disease, which has proven to be an important method for peritoneal dialysis (PD) [1-3]. CAPD has obvious advantages in reducing the occurrence of peritonitis, improving the adequacy of dialysis, protecting residual renal function, and improving the quality of life of patients [2,3].

Peritoneal dialysis-associated peritonitis is an important complication of PD that can cause nearly 20% of PD failures and 3.5-10.0% of patient deaths [4-7]. With the development of dialysis equipment, disinfection measures, and increased awareness of aseptic practice, the infection rate of continuous ambulatory peritoneal dialysis-associated peritonitis (CAPDP) patients has decreased significantly [4-7]. However, CAPDP is still an independent risk factor that affects the efficacy and mortality of CAPD patients [4-7]. CAPDP can lead to an increase in hospitalization rate, loss of peritoneal function, and decline of residual renal function, which seriously affects the quality of life of patients [4-7]. CAPDP is also the direct and main reason for patients to withdraw from PD treatment for a short time or permanently [4-7]. Studies have shown that for every 0.5 times/year increase in the incidence of CAPDP, the risk of death increases by 4% to 11% [4-9]. At the same time, in recent years, with the wide application of antibiotics, antibiotic resistance in pathogens and, consequently, difficulty in clinical treatment of CAPDP have increased significantly [8,9]. Systematic research on the risk factors for CAPDP, along with the characteristics of the pathogenic bacteria seen in CAPDP and their drug resistance, is of great significance for preventing the occurrence of CAPDP and guiding clinical drug use. Therefore, this retrospective study from a single center in China aimed to study the factors associated with the development of peritonitis and the causes of infection in patients treated with CAPD between 2018 and 2021.

Material and Methods

Patient Selection and Clinical Data

A retrospective study design was conducted in the current investigation. Sample size was calculated using the website (<http://powerandsamplesize.com/Calculators/>) in line with the Strengthening the Reporting of Observational Studies in Epidemiology (STROPE) statement for observational studies. The parameter setting of the calculated sample size needed to test the odds ratio was the following: power ($1 - \beta$, 90%), type I error (α , 0.05), and odds ratio (OR, 1.3). The sample sizes necessary for the main factor were 285. Clinical data from 248 patients who underwent CAPD in our hospital from March

2018 to January 2021 were retrospectively collected for analysis. The patients were divided into the CAPDP group (n=40) and the non-CAPDP group (n=208) according to whether peritoneal dialysis-associated peritonitis (PDAP) occurred. The inclusion criteria were as follows: 1) patients who were followed up for CAPD; 2) patients who were older than 18 years old; 3) patients who met the inclusion criteria for chronic renal failure [10]; 4) patients who met the indications for PD; 5) patients who use CAPD for PD. Bearing in mind that the main purpose of exclusion is to avoid factors that may cause bias and error in the research results, the exclusion criteria included the following: 1) peritonitis caused by other diseases, such as gastrointestinal perforation; 2) patients who cannot cooperate with follow-up and use of CAPD; 3) People with hematological diseases prone to bleeding, such as leukemia, lymphoma, hemophilia, aplastic anemia; 4) patients who have mental system diseases and cannot complete CAPD. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All patients voluntarily participated in this study and signed an informed consent agreement. This study was approved by the Committee of The Second Affiliated Hospital of Chongqing Medical University and was carried out in accordance with the Declaration of Helsinki.

CAPDP Diagnostic Criteria and Efficacy Judgement

The diagnosis of CAPDP is based on the 2016 International Society for Peritoneal Dialysis standards, and CAPDP was diagnosed if it met 2 of the following 3 criteria: 1) presence of symptoms and signs of peritonitis, turbid dialysate, and/or abdominal pain/fever; 2) white blood cell count in the exudate $>100 \times 10^6/L$ and the proportion of neutrophils $>50\%$; and 3) positive culture of PD fluid [11]. Criteria for treatment outcomes included: 1) cure: clinical symptoms are completely relieved, laboratory indicators return to normal, no need to remove the PD catheter, no antibiotic treatment, and no recurrence within 30 days; 2) recurrence: peritonitis that recurs within 4 weeks after the peritonitis is cured, with the same pathogenic bacteria, or peritonitis with a negative culture; 3) withdrawal: the peritonitis leads to removal of the PD catheter, transfer to hemodialysis, and cessation of treatment; 4) death: the patient dies of active peritonitis or dies within 2 weeks of the onset of peritonitis [11,12].

Bacterial Culture, Identification and Drug Sensitivity Testing Methods

All the peritoneal fluid samples were collected when patients were admitted to the hospital and sent to the laboratory of the hospital for routine examination and bacterial culture. Bacterial

culture was performed with a Bact/ALERT3D360 automatic culture instrument from the French Mérieux Company (Lyon, France). The identification of positive specimens and drug susceptibility tests were completed by the VITEK 2 COMPACT automatic microbial identification system of the French Mérieux Company (Lyon, France). The results were determined in accordance with the American National Clinical Laboratory Standards.

Clinical Data Collection

The clinical data for the CAPDP and non-CAPDP groups were collected for analysis immediately after admission. The parameters that were compared and analyzed included sex, age, primary disease, education level, body mass index (BMI), catheterization time, complications, routine blood tests, liver and kidney function, blood glucose, blood lipids, electrolytes, transport type, pathogenic bacteria culture results, drug sensitivity test results, and prognosis.

Statistical Analysis

SPSS 20.0 software was used for statistical analysis of the data. The Kolmogorov-Smirnov single sample test was used to calculate the normal distribution of continuous variables before performing further comparisons. Normally distributed measurement data were expressed as the mean±standard deviation, and comparisons between groups were performed by *t* tests. Categorical variables were described by frequency or rate (%), and compared by chi-square test or Fisher test. Risk factor analysis was performed using univariate and multivariable logistic regression analysis-forward selection. Principal component analysis (PCA) was used to distinguish CAPDP patients from non-CAPDP patients on the basis of their clinical characteristics. Statistical modeling was done using random forest analysis. $P<0.05$ indicates that the difference was statistically significant.

Results

Clinical Data and Outcome Analysis of Patients with CAPDP

A total of 248 patients with CAPD were included in the current study, including 40 patients in the CAPDP group and 208 patients in the non-CAPDP group. The incidence of CAPDP was 16.13%. In the CAPDP group, 35 patients (87.5%) with CAPDP were able to continue on CAPD after treatment of the infection, and 5 (12.5%) patients withdrew from treatment due to poor infection control. There was no death or recurrence. As shown in **Table 1**, single factor analysis showed that there were no significant differences in age, sex, education level, diabetes, primary disease, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin, direct bilirubin, uric acid, blood creatinine, urea, blood lipids,

blood potassium, blood calcium, blood sodium, blood chlorine, total bile acid, unconjugated bilirubin, white blood cell count, red blood cell count, hemoglobin concentration, percentage of neutrophils, neutrophil count, lymphocyte percentage, or parathyroid hormone between the CAPDP group and the non-CAPDP group ($P>0.05$). There were significant differences in BMI (19.74 ± 2.22 vs 21.79 ± 2.96 , $P<0.001$), albumin (33.81 ± 4.19 vs 37.89 ± 5.02 , $P=0.008$), albumin/globulin ratio (1.42 ± 0.29 vs 1.79 ± 0.74 , $P=0.012$), platelet count (132.49 ± 53.67 vs 170.75 ± 69.90 , $P=0.031$), C-reactive protein (13.01 ± 8.82 vs 5.60 ± 4.95 , $P<0.001$), and rapid transport (32.50% vs 12.98%, $P=0.014$) between the CAPDP group and the non-CAPDP group.

Logistic Regression Analysis of Risk Factors in Patients with CAPDP

As shown in **Table 2**, both univariate and multivariate analysis found that BMI, albumin, albumin/globulin ratio, C-reactive protein, and rapid transport are independent risk factors for CAPDP. Multivariate logistic regression analysis found that BMI ($\beta=-0.5919$, OR=0.554, $P=0.0095$), albumin ($\beta=-0.474$, OR=0.985, $P=0.016$), albumin/globulin ratio ($\beta=-3.253$, OR=0.874, $P=0.018$), C-reactive protein ($\beta=0.294$, OR=1.342, $P=0.0001$), and rapid transport ($\beta=-2.134$, OR=0.876, $P=0.034$) were independent risk factors for CAPDP.

PCA and Random Forest Analysis of Risk Factors in Patients with CAPDP

Except for logistical regression analysis, the unsupervised learning method of PCA was employed to distinguish CAPDP from non-CAPDP patients. However, we could not find any effects that were discernable with such methods (**Figure 1**). Random forest, another frequently used classification algorithm, was employed in the current data analysis. The classification accuracy of the random forest method depends on user-defined parameters *N* and *m*, where $N=100$ and $m=3$ are selected for optimal CAPDP and non-CAPDP classification. The out-of-bag estimate of error rate 0.34 was used to measure the variance importance of patients who developed CAPDP. Mean decreased accuracy and Gini's test are shown in **Figure 2A and 2B**. The most important source of variance for detecting patients who developed CAPDP was C-reactive protein. The analysis revealed that, at the optimal cut-off value of 1.5 for the random forest model, the sensitivity was 92.5% and the specificity was 98.3%, with an area under the curve (AUC) of 0.929 (95% confidence interval, 0.857-1) (**Figure 2C**).

Analysis of Bacterial Distribution and Drug Resistance Rate in Patients with CAPDP

As shown in **Table 3**, specimens from 40 patients with CAPDP were submitted for examination, of which 30 specimens were

Table 1. Comparative analysis of clinical data for patients with automated peritoneal dialysis-associated peritonitis.

Parameter	PDAP group (n=40)	Non-PDAP group (n=208)	P value
Age (year)	47.05±10.25	51.34±13.23	0.491
Gender			
Male	30 (75.00%)	137 (65.86%)	
Female	10 (25.00%)	71 (34.14%)	0.259
Level of education			
≥Undergraduate	8 (20.00%)	49 (23.56%)	
<Undergraduate	32 (80.00%)	159 (76.44%)	0.624
Diabetes (n, %)			
Yes	7 (17.50%)	25 (12.02%)	
No	31 (77.50%)	183 (87.98%)	0.281
Primary disease			
Chronic glomerulonephritis	28 (70.00%)	149 (71.63%)	
Nephrotic syndrome	2 (5.00%)	6 (2.88%)	
Diabetic nephropathy	3 (7.50%)	7 (3.65%)	
Hypertensive nephropathy	1 (2.50%)	8 (3.85%)	
IgA nephropathy	2 (5.00%)	13 (6.25%)	
Other	4 (10.00%)	25 (12.02%)	0.81
BMI (kg/m ²)	19.74±2.22	21.79±2.96	<0.001*
Alanine aminotransferase (U/L)	13.55±8.52	16.35±10.53	0.414
Aspartate aminotransferase (U/L)	14.74±6.94	17.44±12.31	0.32
Total protein (g/L)	56.58±11.80	61.30±10.56	0.052
Albumin (g/L)	33.81±4.19	37.89±5.02	0.008*
Albumin/globulin ratio	1.42±0.29	1.79±0.74	0.012*
Alkaline phosphatase (U/L)	72.07±29.22	77.74±36.75	0.385
Total bilirubin (μmol/L)	8.18±2.21	8.12±2.51	0.877
Direct bilirubin (μmol/L)	1.24±0.52	1.25±0.57	0.923
Uric acid (μmol/L)	505.50±134.28	473.32±135.59	0.17
Blood creatinine (μmol/L)	978.19±287.90	960.79±341.84	0.763
Urea (μmol/L)	50.26±94.92	50.39±106.82	0.994
Triglycerides (mmol/L)	1.86±1.58	1.57±0.96	0.117
Total cholesterol (mmol/L)	4.27±1.23	4.25±1.03	0.916
High-density lipoprotein (mmol/L)	0.99±0.27	1.06±0.28	0.197
Low-density lipoprotein (mmol/L)	2.18±0.91	2.20±0.70	0.91
Serum potassium (mmol/L)	4.52±0.83	4.56±0.82	0.825
Serum calcium (mmol/L)	2.05±0.25	2.03±0.34	0.751

Table 1 continued. Comparative analysis of clinical data for patients with automated peritoneal dialysis-associated peritonitis.

Parameter	PDAP group (n=40)	Non-PDAP group (n=208)	P value
Serum sodium (mmol/L)	138.71±3.48	138.85±3.25	0.797
Serum chlorine (mmol/L)	104.20±6.25	105.72±5.67	0.128
Total bile acid (µmol/L)	2.29±1.57	2.68±2.61	0.364
Indirect bilirubin (µmol/L)	6.48±1.96	6.22±2.30	0.508
White blood cell count (10 ⁹ /L)	8.22±5.54	6.45±2.54	0.08
Red blood cell count (10 ⁹ /L)	2.70±0.53	2.84±0.63	0.197
Hemoglobin concentration (g/L)	76.80±18.95	82.81±17.35	0.169
Platelet count (10 ⁹ /L)	132.49±53.67	170.75±69.90	0.031*
Percentage of neutrophils (%)	74.11±10.46	70.77±8.99	0.127
Neutrophil count (10 ⁹ /L)	5.42±2.64	4.66±2.34	0.245
Lymphocyte percentage	15.97±8.21	18.87±7.06	0.082
Lymphocyte count (10 ⁹ /L)	1.02±0.48	1.25±1.69	0.393
Parathyroid hormone (mmol/L)	526.47±342.84	472.81±288.62	0.298
C-reactive protein (mg/L)	13.01±8.82	5.60±4.95	<0.001*
Erythrocyte sedimentation rate (mm/h)	30.80±14.27	25.69±16.78	0.071
Total urea clearance index	2.17±0.65	2.31±0.65	0.193
Rapid peritoneal transport	13 (32.50%)	27 (12.98%)	0.014*
	27 (67.50%)	181 (87.02%)	

PDAP – peritoneal dialysis-associated peritonitis; BMI – body mass index.

Table 2. Logistic regression analysis of risk factors in patients with continuous ambulatory peritoneal dialysis-associated peritonitis.

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	p value	HR	95% CI	p value
BMI	0.627	0.31-1.23	0.001	0.554	0.319~0.807	0.0095
Albumin	0.994	0.12-2.05	0.042	0.985	0.114~2.020	0.016
Albumin/globulin ratio	0.852	0.85-1.03	0.030	0.874	0.769~0.966	0.018
Platelet count	1.08	0.95-1.04	0.052	0.982	0.958~0.998	0.107
C-reactive protein	1.286	0.904-1.83	0.003	1.342	1.208~1.578	0.0001
Rapid peritoneal transport	0.972	1.3-3.29	0.024	0.876	1.308~5.007	0.034

HR – hazard ratio; CI – confidence interval; BMI – body mass index.

positive for infection (the positive rate was 75.00%). In the present study, multiple infections and repeated infections were not found. Twenty-one positive specimens (70.00%) were infected with gram-positive bacteria, 8 positive specimens (26.67%) were infected with gram-negative bacteria, and 1 positive specimen (3.33%) was infected with a fungus (*Aspergillus*). Among the positive strains, *Staphylococcus*

epidermidis (50.00%), *Staphylococcus capitis* (13.33%), and *Escherichia coli* (10.00%) were the main species. As shown in **Table 4**, in the drug sensitivity analysis of pathogenic bacteria, we found that the main drugs to which the gram-negative bacteria were sensitive were imipenem, meropenem, piperacillin/tazobactam, cefoperazone/sulbactam sodium, and ceftazidime, and the main drugs to which the gram-positive bacteria

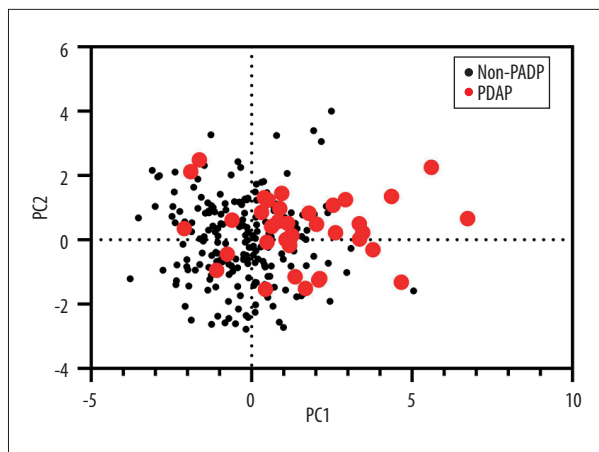


Figure 1. Principal component analysis (PCA) of clinical characteristics between patients with peritoneal dialysis-associated peritonitis (PDAP) and without PDAP.

were sensitive were vancomycin, teicoplanin, linezolid, and tigecycline. In this study, patients with CAPDP showed strong resistance to penicillin G, ampicillin, compound trimethoprim, cefepime, ceftriaxone, amoxicillin-clavulanic acid, and other drugs (the resistance rate was 36.26-100%).

Discussion

In this study, we found that the incidence of CAPDP was 16.13%. Logistic regression analysis found that BMI, albumin, albumin/globulin ratio, C-reactive protein, and rapid transport were independent risk factors for CAPDP. Gram-positive bacteria, especially *S. epidermidis*, are the main pathogens of CAPDP. Gram-positive bacteria are sensitive to vancomycin, teicoplanin, and linezolid. PDAP is a common serious complication of PD. PDAP is a major cause of death (16% mortality) and termination of PD and permanent conversion to hemodialysis [13-16].

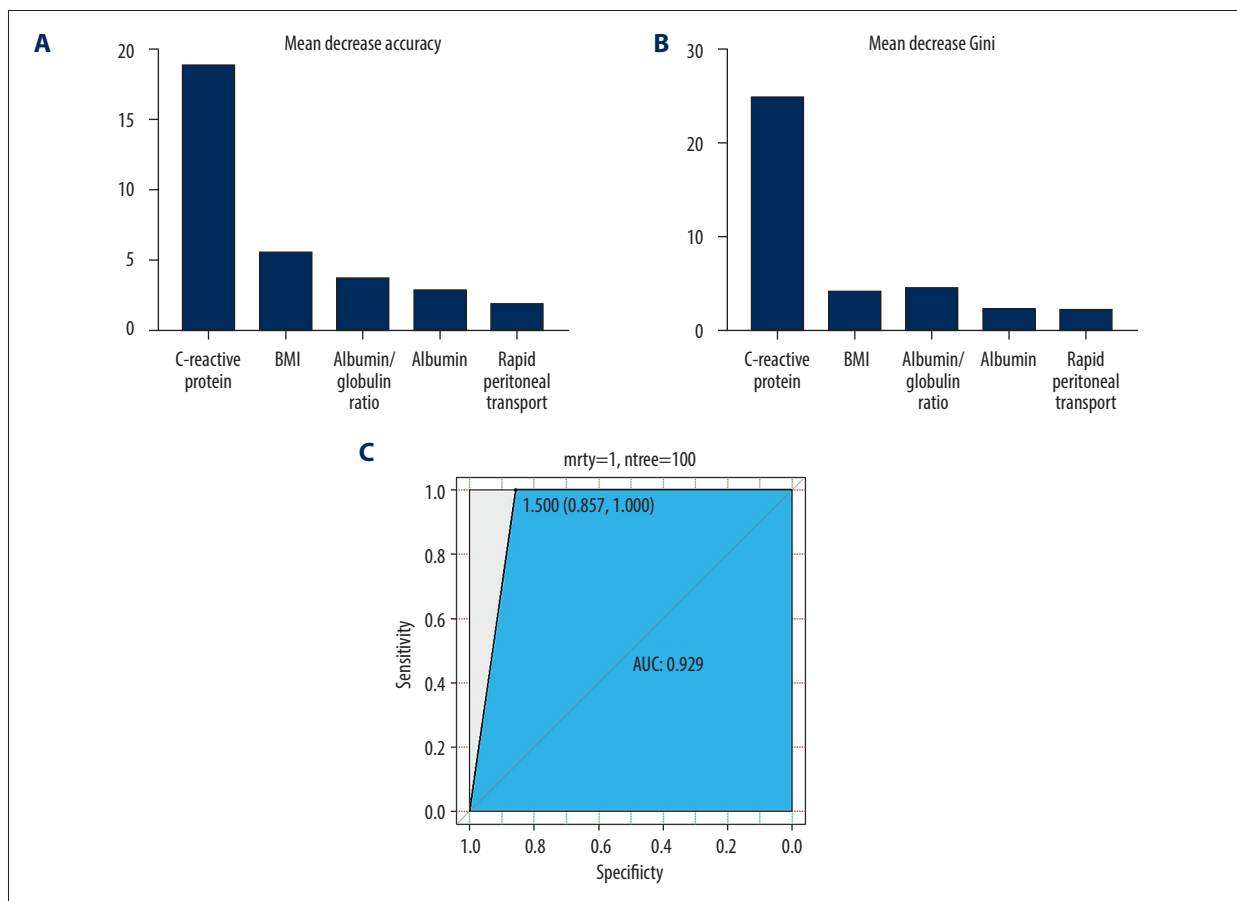


Figure 2. (A) Mean decrease in accuracy in predicting the occurrence of peritoneal dialysis-associated peritonitis (PDAP) when using the random forest model. (B) Mean decrease in the Gini coefficient in predicting the occurrence of PDAP when using the random forest model. (C) The results of the receiver operating characteristic curve (ROC) analysis, using random forest prediction value to detect the occurrence of PDAP.

Table 3. Bacteria culture and distribution of peritoneal fluid.

Positive rate and bacteria	Percentage	Positive rate and bacteria	Percentage
Total positive rate	30/40 (75.00%)	<i>Escherichia coli</i>	3/30 (10.00%)
Total negative rate	10/40 (25.00%)	<i>Serratia liquefaciens</i>	2/30 (6.67%)
Gram-positive bacteria	21/30 (70.00%)	<i>Salmonella enteritidis</i>	1/30 (3.33%)
Gram-negative bacteria	8/30 (26.67%)	<i>Streptococcus gordonii</i>	1/30 (3.33%)
Fungus	1/30 (3.33%)	<i>Streptococcus mitis</i>	1/30 (3.33%)
<i>Staphylococcus epidermidis</i>	16/30 (50.00%)	<i>Staphylococcus ludunensis</i>	1/30 (3.33%)
<i>Staphylococcus capitis</i>	4/30 (13.33%)	<i>Aspergillus</i>	1/30 (3.33%)

Table 4. Analysis of drug susceptibility and drug resistance rate of common bacteria with positive peritoneal fluid (%).

Drug names	<i>Escherichia coli</i>	<i>Staphylococcus epidermidis</i>	<i>Staphylococcus capitis</i>	<i>Serratia liquefaciens</i>
Penicillin G	–	100.00%	94.42%	–
Ampicillin	100.00%	100.00%	74.56%	–
Compound trimethoprim	80.51%	87.82%	77.35%	–
Cefepime	71.86%	82.32%	81.42%	62.84%
Ceftiofur	72.86%	80.32%	64.42%	78.84%
Ceftriaxone	62.12%	84.58%	79.56%	56.61%
Ciprofloxacin	45.64%	71.52%	54.03%	61.28%
Norfloxacin	79.86%	67.56%	76.16%	65.28%
Ofloxacin	87.86%	78.06%	80.86%	70.67%
Amoxicillin-clavulanic acid	41.96%	47.46%	36.26%	55.38%
Amikacin	37.16%	32.77%	36.14%	33.47%
Piperacillin/tazobactam	18.62%	20.62%	23.62%	21.08%
Cefoperazone and sulbactam sodium	29.52%	30.70%	29.31%	28.75%
Meropenem	6.74%	10.60%	4.65%	2.23%
Imipenem	2.23%	6.25%	4.44%	4.44%
Ceftazidime	10.53%	20.47%	19.27%	11.08%
Linezolid	0.00%	0.00%	0.00%	0.00%
Teicoplanin	0.00%	0.00%	0.00%	0.00%
Levofloxacin	0.00%	0.00%	0.00%	0.00%
Vancomycin	0.00%	3.30%	0.00%	0.00%
Tigecycline	0.00%	0.00%	0.00%	0.00%

Therefore, early detection of peritonitis and effective prevention and treatment strategies are the keys to successful PD treatment. Studies have shown that the incidence of peritonitis in CAPD patients varies among different races, and the incidence of PDAP in Asian races is approximately 17.67-47% [17]. In the present study, we found that the incidence of CAPDP was 16.13%. The decrease in the incidence of CAPDP may be due to the strengthening of regular follow-up and nursing facilities for patients in our clinic. In the present study, we found that 87.5% of patients with CAPDP were cured after treatment of the infection, 12.5% of patients withdrew, and no death or recurrence occurred in patients.

Previous studies have shown that risk factors for peritonitis associated with PD include hypoalbuminemia, nasal *S. aureus* carriers, diabetes, serum parathyroid hormone, high calcium, low phosphorus, and other factors [17-20]. In this study, we found that education level, sex, age, kidney function, electrolytes, total urea clearance index, primary disease, bilirubin, erythrocyte sedimentation rate, white blood cell count, red blood cell count, hemoglobin concentration, alkaline phosphatase, blood lipids, and other factors had no effect on the incidence of CAPDP. In the present study, we found that BMI, albumin, ratio of albumin to globulin, C-reactive protein, and rapid transport were independent risk factors for CAPDP. BMI, plasma albumin level, and albumin/globulin ratio are important predictors of body condition and malnutrition [21]. Studies have shown that the incidence of malnutrition in PD patients is 53.2%, and loss of appetite, insufficient energy intake caused by digestive disorders, and protein loss during dialysis are important factors [21]. Studies have confirmed that hypoproteinemia is the main risk factor for peritonitis after CAPD [22,23]. In the present study, we found that the albumin level and albumin/globulin ratio were significantly reduced in the CAPDP group, and the albumin level and albumin/globulin ratio were independent risk factors for CAPDP. PD patients have long-term malnutrition, reduced immune function, increased susceptibility to pathogenic microorganisms, and increased incidence of peritonitis. In addition, after the occurrence of peritonitis, due to changes in the permeability of the peritoneal blood vessels, macromolecular proteins are more likely to be lost from the PD exchange fluid, which is likely to cause progressive malnutrition. Therefore, rationally adjusting the diet, increasing the intake of protein and amino acids, and actively improving the malnutrition status of CAPD patients may be of great significance for alleviating and preventing the occurrence of CAPDP. Troidle et al showed that the serum CRP level was significantly increased within 48 h of the onset of peritonitis in CAPD patients, especially in patients with gram-negative bacilli peritonitis. Similar to the study by Hind et al, CRP levels in all CAPD patients were significantly increased during peritonitis [24,25]. However, the increase in serum CRP level is not highly specific; it is reported to be only 55%. As a result, it cannot be used

as a standard for the diagnosis of peritonitis, but the level and duration of CRP increase are related to the severity and prognosis of infection [26,27]. In the present study, we found that CRP levels in PDAP patients caused by CAPD were significantly increased. In logistic regression analysis, we found that a serum CRP > 10 mg/L was an independent risk factor for CAPDP. Previous studies have suggested that diabetes is an independent risk factor for PDAP [28]. However, in our study, we did not find that diabetes was an independent risk factor for CAPDP. Possible reasons for this result include race and having fewer diabetic patients in the included population.

Pathogen detection is the key to guiding clinical PDAP treatment, and the proportion of culture-negative peritonitis, according to International Society for Peritoneal Dialysis (ISPD) guidelines, should not exceed 20% [29]. In the present study, the positive detection rate for pathogenic bacteria was 75.00%, which is slightly lower than the recommendations in the ISPD guidelines. In terms of the spectrum of pathogenic bacteria, this study found that gram-positive bacteria accounted for 70.00% of the CAPDP, gram-negative bacteria accounted for 26.67% of the CAPDP, and fungi accounted for 3.33% of the CAPDP. The most important pathogenic bacteria in this PD center are gram-positive bacteria, and *S. epidermidis* is the main pathogen, accounting for 50.00% of the positive bacteria. These results are similar to those in previous literature reports [30-32]. *S. epidermidis* is mostly related to skin contact and a lack of strict aseptic operation. On the other hand, infection with *S. epidermidis*, a member of the normal, healthy skin microbiota, may be related to the fact that PD patients are prone to malnutrition and decreased resistance, allowing *S. epidermidis* to act as an opportunistic pathogen [33]. Therefore, it is important to urge CAPD patients to increase their awareness of aseptic practice and strengthen their self-management ability. At the same time, giving patients nutrition and diet guidance has important clinical significance for preventing CAPDP. In recent years, with the application of antibiotics, drug resistance in pathogenic bacteria has increased year by year. ISPD recommends vancomycin or first-generation cephalosporins to cover gram-positive bacteria and third-generation cephalosporins or aminoglycosides to cover gram-negative bacteria. At the same time, it is recommended that each center select individualized antibacterial drugs based on the antibiotic sensitivity of pathogens infecting recent peritonitis patients [34, 35]. In the present study, we found that the resistance rate of gram-positive bacteria to cefepime and penicillin G in CAPDP patients was as high as 62.84-82.32%, but no strains were found to be resistant to vancomycin, teicoplanin, or linezolid. For gram-negative bacteria, the rate of resistance to ceftazidime reached 10.53-20.47%. In contrast, the resistance rates to carbapenem antibiotics, such as meropenem and imipenem, were 6.74% and 2.23%, respectively. This result is consistent with previous literature reports [34,35]. On

the basis of the recommendations of the ISPD guidelines combined with the results of the present study, we recommend vancomycin combined with piperacillin/tazobactam as initial treatment for CAPDP.

The present study has certain limitations. First, our study is a retrospective study, and the study design has inherent limitations and biases. Second, our study was a small-sample, single-center study, and the research conclusions therefore have limitations. Large-sample, multicenter studies are needed to confirm our results. Third, due to differences in the underlying disease, population, and living environment, the results of our study are subject to inherent errors and biases. Fourth, the observation time of our study was short, and long-term studies with large samples are needed to further explore the present findings. Fifth, our study has inherent limitations and risks of bias in research design.

References:

1. Li PK, Chow KM, Van de Luitgaarden MW, et al. Changes in the worldwide epidemiology of peritoneal dialysis. *Nat Rev Nephrol.* 2016;13(2):90-103
2. Woodrow G, Fan SL, Reid C, et al. Renal association clinical practice guideline on peritoneal dialysis in adults and children. *BMC Nephrol.* 2017;18(1):333
3. Jeloka TK, Abraham G, Bhalla AK, et al. Continuous ambulatory peritoneal dialysis peritonitis guidelines – consensus statement of Peritoneal Dialysis Society of India – 2020. *Indian J Nephrol.* 2022;31(5):425-34
4. Mujais S. Microbiology and outcomes of peritonitis in North America. *Kidney Int Suppl.* 2006;10(3):S55-62
5. Salzer WL. Peritoneal dialysis-related peritonitis: challenges and solutions. *Int J Nephrol Renovasc Dis.* 2018;11(2):173-86
6. Tian Y, Xie X, Xiang S, et al. Risk factors and outcomes of high peritonitis rate in continuous ambulatory peritoneal dialysis patients: A retrospective study. *Medicine (Baltimore).* 2016;95(49):e5569
7. Hsieh YP, Wang SC, Chang CC, et al. The negative impact of early peritonitis on continuous ambulatory peritoneal dialysis patients. *Perit Dial Int.* 2014;34(6):627-35
8. Andy Tang SO, Carolisna YI, Sakura D, et al. Demographic characteristics and outcomes of continuous ambulatory peritoneal dialysis related peritonitis in Miri General Hospital, Malaysia. *Med J Malaysia.* 2019;74(4):270-74
9. de Fijter CW, Jakulj L, Amiri F, et al. Intraperitoneal meropenem for polymicrobial peritoneal dialysis-related peritonitis. *Perit Dial Int.* 2016;36(5):572-73
10. Meersch M, Schmidt C, Zarbock A. Patient with chronic renal failure undergoing surgery. *Curr Opin Anaesthesiol.* 2016;29(3):413-20
11. Li PK, Szeto CC, Piraino B, et al. ISPD peritonitis recommendations: 2016 update on prevention and treatment. *Perit Dial Int.* 2016;36(5):481-508
12. Boudville N, Kemp A, Clayton P, et al. Recent peritonitis associates with mortality among patients treated with peritoneal dialysis. *J Am Soc Nephrol.* 2012;23(8):1398-405
13. Michaela CB, Keith S, Kerssens J, et al. Peritoneal dialysis-associated peritonitis rates and outcomes in a national cohort are not improving in the post-millennium (2000-2007). *Perit Dial Int.* 2011;31(6):639-50
14. Al Sahlawi M, Bargman JM, Perl J, et al. Peritoneal dialysis-associated peritonitis: Suggestions for management and mistakes to avoid. *Kidney Med.* 2020;2(4):467-75
15. Yekinni IO, Viker T, Hunter R, et al. Design and proof-of-concept evaluation of a touchless connector system for preventing peritoneal dialysis-associated peritonitis. *BMJ Innov.* 2022;8(2):98-104
16. Ghali JR, Bannister KM, Brown FG. Microbiology and outcomes of peritonitis in Australian peritoneal dialysis patients. *Perit Dial Int.* 2011;31(6):651-62
17. Liao CT, Zheng CM, Lin YC, et al. Aberrant serum parathyroid hormone, calcium, and phosphorus as risk factors for peritonitis in peritoneal dialysis patients. *Sci Rep.* 2021;11(1):1171
18. Ong LM, Ch'ng CC, Wee HC, et al. Risk of peritoneal dialysis-related peritonitis in a multi-racial Asian population. *Perit Dial Int.* 2017;37(1):35-43
19. Liakopoulos V, Nikitidou O, Kalathas T, et al. Peritoneal dialysis-related infections recommendations: 2016 update. What is new? *Int Urol Nephrol.* 2017;49(12):2177-84
20. Kotsanas D, Polkinghorne KR, Korman TM, et al. Risk factors for peritoneal dialysis-related peritonitis: Can we reduce the incidence and improve patient selection? *Nephrology (Carlton).* 2007;12(3):239-45
21. Cheng LT, Chen W, Tang W, et al. Does loss of residual renal function lead to malnutrition in peritoneal dialysis patients? *Clin Nephrol.* 2006;66(3):192-201
22. Contreras-Velázquez JC, Soto V, Jaramillo-Rodríguez Y, et al. Clinical outcomes and peritoneal histology in patients starting peritoneal dialysis are related to diabetic status and serum albumin levels. *Kidney Int Suppl.* 2008;8(108):S34-41
23. Wang X, Han Q, Wang T, et al. Serum albumin changes and mortality risk of peritoneal dialysis patients. *Int Urol Nephrol.* 2020;52(3):565-71
24. Laura T, Alan K, Nancy GB, et al. Course of C-reactive protein during continuous peritoneal dialysis-associated peritonitis. *Nephrology (Carlton).* 2005;10(5):442-45
25. Hind CR, Thomson SP, Winearls CG, et al. Serum C-reactive protein concentration in the management of infection in patients treated by continuous ambulatory peritoneal dialysis. *J Clin Pathol.* 1985;38(4):459-63
26. Yilmaz FM, Yilmaz G, Akay H, et al. Evaluation of a card test for procalcitonin in continuous ambulatory peritoneal dialysis peritonitis. *Ann Clin Biochem.* 2007;44(Pt 5):482-84
27. van Esch S, Krediet RT, Struijk DG. Prognostic factors for peritonitis outcome. *Contrib Nephrol.* 2012;178:264-70
28. Coronel F, Cigarrán S, Herrero JA, et al. Peritoneal protein losses in diabetic patients starting peritoneal dialysis: Is there a relationship with diabetic vascular lesions? *Adv Perit Dial.* 2009;25:115-18
29. Beth P, Judith Bi, Edwina B, et al. ISPD position statement on reducing the risks of peritoneal dialysis-related infections. *Perit Dial Int.* 2011;31(6):614-30
30. Trinh E, Hanley JA, Nadeau-Fredette AC, et al. A comparison of technique survival in Canadian peritoneal dialysis and home hemodialysis patients. *Nephrol Dial Transplant.* 2019;34(11):1941-49
31. Alwakeel JS, Alsuwaida A, Akram A, et al. Outcome and complications in peritoneal dialysis patients: A five-year single center experience. *Saudi J Kidney Dis Transpl.* 2011;22(2):245-51

Conclusions

The present study found that BMI, albumin, albumin/globulin ratio, C-reactive protein, and rapid transport are independent risk factors for CAPDP. Gram-positive bacteria are the main pathogens seen in CAPDP and are sensitive to vancomycin, teicoplanin, and linezolid.

Ethics Approval and Consent to Participate

This study was approved by the Committee of The Second Affiliated Hospital of Chongqing Medical University and was carried out in accordance with the Declaration of Helsinki.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

32. Coronel F, Cigarrán S, Herrero JA. Morbidity and mortality in diabetic patients on peritoneal dialysis. Twenty-five years of experience at a single centre. *Nefrologia*. 2010;30(6):626-32
33. Kussmann M, Schuster L, Zeitlinger M, et al. Influence of different peritoneal dialysis fluids on the in vitro activity of fosfomycin against *Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Pseudomonas aeruginosa*. *Eur J Clin Microbiol Infect Dis*. 2018;37(6):1091-98
34. Ballinger AE, Palmer SC, Wiggins KJ, et al. Treatment for peritoneal dialysis-associated peritonitis. *Cochrane Database Syst Rev*. 2014; 26(4):CD005284
35. Szeto CC, Li PK. Peritoneal dialysis-associated peritonitis. *Clin J Am Soc Nephrol*. 2019;14(7):1100-5