

Clinical Characteristics and Influencing Factors of Gastrointestinal Dysfunction Associated with Uremia and Peritoneal Dialysis (Postprint)

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Abstract

Background Gastrointestinal dysfunction is a highly prevalent complication in peritoneal dialysis patients, severely impacting appetite and mood, leading to malnutrition, dehydration, electrolyte disturbances, and systemic inflammatory responses, while also reducing peritoneal dialysis efficacy, increasing medical complexity, and diminishing patients' quality of life.

Objective To investigate the clinical characteristics and influencing factors of peritoneal dialysis-related gastrointestinal dysfunction in uremic patients, thereby providing references for clinical diagnosis and treatment.

Methods A retrospective study was conducted on 304 uremic patients undergoing maintenance peritoneal dialysis in the Department of Nephrology, First Affiliated Hospital of Tianjin University of Traditional Chinese Medicine, between September 1, 2019 and September 1, 2021. Patients were divided into gastrointestinal dysfunction and non-gastrointestinal dysfunction groups based on the presence of gastrointestinal dysfunction. General demographics, comorbidities, laboratory parameters, and dialysis adequacy indices were collected and compared between groups. SPSS 23.0 software was used for statistical analysis of clinical data to summarize the clinical characteristics of peritoneal dialysis-related gastrointestinal dysfunction, and binary Logistic regression analysis was performed to identify influencing factors.

Results Of the 304 uremic peritoneal dialysis patients, 189 (62.2%) had concurrent gastrointestinal dysfunction, with a median age of 62 (52, 67) years in this group. Statistically significant differences were observed between groups in age, proportion of diabetic nephropathy as primary disease, and rates of concurrent hypertension and coronary heart disease ($P < 0.05$). Significant differences were

also found in serum calcium, cholesterol, creatine kinase, C-reactive protein, total bilirubin, blood glucose, glycated hemoglobin, procalcitonin, and triglyceride levels ($P < 0.05$), as well as in blood urea nitrogen, residual renal urea clearance index (Kt/V), peritoneal Kt/V, total creatinine clearance rate (Ccr), residual renal Ccr, and standardized total Ccr ($P < 0.05$). Multivariate Logistic regression analysis revealed that diabetic nephropathy as primary disease (OR=7.471, 95%CI=1.161~48.061, $P=0.034$) and elevated glycated hemoglobin (OR=1.367, 95%CI=1.080~1.731, $P=0.009$) were independent risk factors, while elevated residual renal Ccr (OR=0.952, 95%CI=0.908~0.997, $P=0.038$) was an independent protective factor for peritoneal dialysis-related gastrointestinal dysfunction in uremic patients.

Conclusion The incidence of peritoneal dialysis-related gastrointestinal dysfunction is high in uremic patients, particularly among the elderly. Diabetic nephropathy as primary disease and elevated glycated hemoglobin may be independent risk factors, while elevated residual renal Ccr may be an independent protective factor for peritoneal dialysis-related gastrointestinal dysfunction in uremic patients.

Full Text

Preamble

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Analysis of Clinical Characteristics and Influencing Factors of Gastrointestinal Dysfunction Associated with Peritoneal Dialysis in Uremia

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Abstract

Background: Gastrointestinal dysfunction is a very common complication in peritoneal dialysis patients, which not only seriously affects patients' appetite and mood, but also induces malnutrition, dehydration, electrolyte disorders, or systemic inflammatory responses, and even leads to decreased peritoneal dialysis efficacy, thereby increasing medical difficulty and lowering patients' quality of life.

Objective: To observe the clinical characteristics and analyze the influencing factors of peritoneal dialysis-related gastrointestinal dysfunction in uremic patients, providing reference for clinical prevention and treatment.

Methods: A retrospective study was conducted on 304 uremic patients undergoing maintenance peritoneal dialysis in the Nephrology Department of the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine from September 1, 2019, to September 1, 2021. Patients were divided into gastrointestinal dysfunction and non-gastrointestinal dysfunction groups based on the presence of gastrointestinal dysfunction. General data, comorbidities, laboratory indicators, and dialysis adequacy-related indexes were collected and compared between groups. SPSS 23.0 software was used for statistical analysis of clinical data to summarize the clinical characteristics of peritoneal dialysis-related gastrointestinal dysfunction, and binary logistic regression was employed to explore influencing factors.

Results: Among 304 uremic peritoneal dialysis patients, 189 (62.2%) had gastrointestinal dysfunction, with a median age of 62 (52, 67) years in this group. Statistically significant differences were observed between groups in age, proportion of primary diabetic nephropathy, and proportions of combined hypertension and coronary artery disease ($P < 0.05$). Significant differences were also found in serum calcium, cholesterol, creatine kinase, C-reactive protein, total bilirubin, blood glucose, glycated hemoglobin, procalcitonin, and triglyceride levels ($P < 0.05$). Additionally, standardized comparisons of blood urea nitrogen, residual renal urea clearance index (Kt/V), peritoneal Kt/V, total creatinine clearance (Ccr), residual kidney Ccr, and total Ccr showed statistically significant differences ($P < 0.05$). Multivariate logistic regression analysis revealed that primary diabetic nephropathy (OR=7.471, 95%CI=1.161-48.061, $P=0.034$) and elevated glycated hemoglobin (OR=1.367, 95%CI=1.080-1.731, $P=0.009$) were independent risk factors, while elevated residual kidney Ccr (OR=0.952, 95%CI=0.908-0.997, $P=0.038$) was an independent protective factor for peritoneal dialysis-related gastrointestinal dysfunction in uremic patients.

Conclusion: The incidence of peritoneal dialysis-related gastrointestinal dysfunction is relatively high in uremic patients, predominantly affecting elderly individuals. Primary diabetic nephropathy and elevated glycated hemoglobin may be independent risk factors, while elevated residual kidney Ccr may be an independent protective factor for this condition.

Keywords: Uremia; Peritoneal dialysis; Gastrointestinal dysfunction; Clinical characteristics; Root cause analysis

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Peritoneal dialysis has become a focal point of attention in nephrology as a renal replacement therapy for uremic patients. Statistics indicate that peritoneal dialysis accounts for 11% of all dialysis cases and 9% of all renal replacement therapies worldwide[1]. According to China's National Blood Purification Case Information Registration System in 2018, over 90,000 patients chose peritoneal dialysis, representing approximately 16.4% of the total dialysis population[2].

Clinical studies have demonstrated that gastrointestinal dysfunction is one of the most common complications in dialysis patients[3-4], with more than half of peritoneal dialysis patients experiencing dyspepsia, about one-third suffering from constipation and abdominal pain, and approximately 80% having at least one gastrointestinal symptom[5-6]. These symptoms can severely affect patients' appetite and mood, leading to complications such as malnutrition, dehydration, electrolyte disturbances, or systemic inflammatory responses[7-8]. They also reduce peritoneal dialysis efficacy, increase medical complexity, and decrease quality of life. Therefore, attention to peritoneal dialysis-related gastrointestinal dysfunction is crucial for maintaining catheter stability, improving quality of life, preventing malnutrition and peritonitis, and ensuring successful peritoneal dialysis[6,9].

This retrospective study analyzes clinical indicators of peritoneal dialysis patients with gastrointestinal dysfunction to explore its clinical characteristics and influencing factors, aiming to provide reference for prevention, diagnosis, and treatment.

1.1 Study Subjects

We retrospectively selected uremic patients undergoing maintenance peritoneal dialysis in the Nephrology Department of the First Teaching Hospital of Tianjin University of Traditional Chinese Medicine from September 1, 2019, to September 1, 2021. Inclusion criteria were: (1) age ≥ 18 years; (2) diagnosed with end-stage renal disease and receiving regular, stable peritoneal dialysis for ≥ 90 days; (3) meeting the Rome IV diagnostic criteria for functional gastrointestinal disorders. Exclusion criteria included: (1) concurrent hemodialysis and/or kidney transplantation; (2) peritonitis within the past 2 months; (3) primary gastrointestinal diseases; (4) hospitalization for severe infection within 2 months or use of antibiotics or gut microbiota-modulating agents (including prebiotics, probiotics, or synbiotics from medications or foods such as yogurt, lactulose, yeast) within the past 2 weeks; (5) hospitalization for severe cardiovascular or cerebrovascular diseases within 2 months (excluding scheduled admissions for examinations); (6) severe malabsorption or serious gastrointestinal diseases such as celiac disease, Crohn's disease, acute gastrointestinal bleeding, intestinal obstruction, or severe neurological disorders; (7) patients not regularly followed at our peritoneal dialysis center or with incomplete medical records. This study was approved by the Medical Ethics Committee of the First Teaching

Hospital of Tianjin University of Traditional Chinese Medicine (Approval No.: TYLL2021[K]011), and informed consent was obtained in accordance with the Helsinki Declaration.

1.2 Diagnostic Criteria

- (1) **Uremia:** Diagnosis was based on the 2012 Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines by the National Kidney Foundation[10] and the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines[11].
- (2) **Gastrointestinal dysfunction:** Diagnosis followed the Rome IV criteria for functional gastrointestinal disorders[12], with confirmation required by the attending physician.

1.3 Data Collection

Two licensed Chinese medicine practitioners collected clinical data from electronic medical records and regularly reviewed and verified the entered information. (1) **General data:** age, sex, height, weight, BMI, peritoneal dialysis duration, and primary diabetic nephropathy. (2) **Comorbidities:** anemia, diabetes, hypertension, coronary atherosclerotic heart disease (coronary heart disease), and chronic heart failure. (3) **Laboratory indicators:** albumin (ALB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum calcium (Ca), total cholesterol (TC), creatine kinase isoenzyme (CK-MB), carbon dioxide combining power (CO₂CP), serum cystatin C (CysC), estimated glomerular filtration rate (eGFR), erythrocyte sedimentation rate (ESR), glycated hemoglobin (HbA_{1c}), serum homocysteine (HCY), hemoglobin (Hb), intact parathyroid hormone (iPTH), serum iron concentration (IRON), potassium (K), lactate dehydrogenase (LDH), lymphocyte count (LYM), neutrophil count (NEUT), neutrophil-to-lymphocyte ratio (NLR), phosphorus (P), platelet-to-lymphocyte ratio (PLR), platelet count (PLT), ferritin (SF), triglycerides (TG), total iron binding capacity (TIBC), total protein (TP), transferrin (TRF), serum uric acid (SUA), unsaturated iron binding capacity (UIBC), white blood cell count (WBC), blood urea nitrogen (BUN), C-reactive protein (CRP), blood glucose (GLU), creatine kinase (CK), total bilirubin (TBIL), direct bilirubin (DBIL), and procalcitonin (PCT).

1.5 Statistical Methods

This study used SPSS 23.0 software for statistical analysis. Normally distributed or homoscedastic continuous variables were expressed as ($\bar{x} \pm s$) and compared between groups using independent samples t-test; non-normally distributed or heteroscedastic variables were expressed as M(P₂₅, P₇₅) and compared using rank-sum test. Categorical data were expressed as relative frequencies and compared using χ^2 test. Univariate and multivariate logistic regression analyses were performed to explore influencing factors of peritoneal dialysis-related gastrointestinal dysfunction in uremic patients. Two-sided tests were used with $P < 0.05$ considered statistically significant.

2.1 Comparison of General Data and Comorbidities

A total of 304 peritoneal dialysis patients were included and divided into two groups: 189 (62.2%) in the gastrointestinal dysfunction group and 115 in the non-gastrointestinal dysfunction group. Statistically significant differences were found between groups in age, primary diabetic nephropathy, and proportions of combined hypertension and coronary artery disease ($P < 0.05$). The median age in the gastrointestinal dysfunction group was 62 (52, 67) years. No significant differences were observed in sex, BMI, peritoneal dialysis duration, or proportions of anemia, diabetes, or chronic heart failure ($P > 0.05$).

2.2 Comparison of Laboratory Indicators

Significant differences were found between groups in serum calcium, total cholesterol, creatine kinase, C-reactive protein, direct bilirubin, blood glucose, glycosylated hemoglobin, procalcitonin, and triglyceride levels ($P < 0.05$). No significant differences were observed in other laboratory indicators ($P > 0.05$).

2.3 Comparison of Dialysis Adequacy Indicators

Statistically significant differences were observed between groups in blood urea nitrogen, residual renal Kt/V, peritoneal Kt/V, total Ccr, residual kidney Ccr, and standardized total Ccr ($P < 0.05$). No significant differences were found in other dialysis adequacy indicators ($P > 0.05$).

2.4 Univariate Logistic Regression Analysis of Influencing Factors

Using the occurrence of peritoneal dialysis-related gastrointestinal dysfunction in uremic patients (assignment: yes=1, no=0) as the dependent variable and indicators from Tables 1-3 as independent variables, univariate logistic regression analysis showed that age, male sex, primary diabetic nephropathy, combined hypertension, combined coronary artery disease, serum calcium, glycosylated hemoglobin, blood urea nitrogen, residual renal Kt/V, peritoneal Kt/V, total Ccr, residual kidney Ccr, and standardized total Ccr were potential influencing factors ($P < 0.05$).

2.5 Multivariate Logistic Regression Analysis of Influencing Factors

Variables with statistical significance in univariate analysis were included in multivariate logistic regression. Results showed that primary diabetic nephropathy (OR=7.471, 95%CI=1.161-48.061, $P=0.034$) and elevated glycosylated hemoglobin (OR=1.367, 95%CI=1.080-1.731, $P=0.009$) were independent risk factors, while elevated residual kidney Ccr (OR=0.952, 95%CI=0.908-0.997, $P=0.038$) was an independent protective factor for peritoneal dialysis-related gastrointestinal dysfunction in uremic patients.

3.1 High Incidence of Peritoneal Dialysis-Related Gastrointestinal Dysfunction in Uremic Patients

Among 304 included uremic patients, 189 (62.2%) had gastrointestinal dysfunction, indicating a high incidence. YI et al.[14] conducted a cross-sectional study of 471 peritoneal dialysis patients and found 82.2% had varying degrees of gastrointestinal symptoms. Another study of 50 dialysis patients reported that 90% experienced at least one gastrointestinal symptom[15]. Although sample sizes differed, these studies collectively suggest that gastrointestinal dysfunction is common in uremic patients undergoing peritoneal dialysis, warranting further attention.

3.2 Predominance of Elderly Patients

According to China's Law on the Protection of the Rights and Interests of the Elderly, individuals aged 60 and above are defined as elderly[16]. The median age in the gastrointestinal dysfunction group was 62 (52, 67) years, significantly higher than 54 (42, 65) years in the non-gastrointestinal dysfunction group ($P < 0.05$), indicating a higher proportion of elderly patients. Univariate analysis also showed age was a positive influencing factor ($P < 0.05$), corroborating the higher incidence in elderly populations. Age affects physical function in dialysis patients, and previous studies have identified advanced age as an independent risk factor for mortality in peritoneal dialysis patients[17]. WU et al.[18] also reported higher peritonitis prevalence and peritonitis-related mortality in elderly peritoneal dialysis patients compared to younger patients.

3.3.1 Microinflammatory State

This study found that CRP levels were lower while PCT levels were higher in the gastrointestinal dysfunction group ($P < 0.05$). Intestinal inflammation is a source of chronic inflammation in chronic kidney disease, and reduced intestinal alkaline phosphatase activity may increase gastrointestinal disease risk by altering microbiota composition, intestinal inflammation, and permeability[19], ultimately triggering gastrointestinal symptoms. WANG et al.[20] compared 120 peritoneal dialysis patients without infection signs with healthy controls, finding significantly higher PCT levels in peritoneal dialysis patients even under non-infectious conditions, suggesting PCT as an indicator of microinflammatory status and indirect evaluation of nutritional status and dialysis adequacy.

3.3.3 Cardiovascular Disease

The gastrointestinal dysfunction group included 175 patients with hypertension, 116 with coronary artery disease, and 70 with chronic heart failure. The proportion with hypertension was lower while coronary artery disease was higher compared to the non-gastrointestinal dysfunction group ($P < 0.05$). Univariate analysis showed both combined hypertension and coronary artery disease were

influencing factors. Clinically, cardiovascular disease frequently causes gastrointestinal symptoms, with studies showing esophageal reflux and constipation are common in coronary artery disease patients[26-27]. Furthermore, end-stage chronic kidney disease promotes atherosclerosis development, and peritoneal dialysis patients often have comorbid hypertension and coronary artery disease with generalized vascular stiffening. This leads to gastrointestinal vascular sclerosis, causing mucosal ischemia and reduced barrier function[28]. This study provides reference for future research on cardiovascular factors affecting peritoneal dialysis patients with gastrointestinal dysfunction.

3.3.4 Dialysis Adequacy

For long-term maintenance dialysis patients, dialysis adequacy is a crucial indicator measuring dialysis quality and necessary for maintaining internal environment stability and quality of life. Ensuring adequate dialysis improves systemic symptoms and long-term survival. This study found significant differences between groups in BUN, residual renal Kt/V, peritoneal Kt/V, total Ccr, residual kidney Ccr, and standardized total Ccr ($P < 0.05$). Univariate analysis identified these as potential influencing factors. Multivariate analysis revealed that elevated residual kidney Ccr was an independent protective factor, with each 1-unit increase reducing gastrointestinal dysfunction risk by 4.9%. DONG et al.[29] also reported that residual renal Kt/V was negatively correlated with gastrointestinal symptoms, consistent with our findings. Thus, dialysis adequacy plays a critical role in peritoneal dialysis-related gastrointestinal dysfunction, and residual renal function may be an important factor directly related to proper toxin clearance.

In summary, peritoneal dialysis-related gastrointestinal dysfunction is common in uremic patients, predominantly affecting the elderly. Primary diabetic nephropathy and elevated glycated hemoglobin may be independent risk factors, while elevated residual kidney Ccr may be an independent protective factor. As a single-center retrospective study with limited sample size, there may be regional and selection biases. Only inpatients from the nephrology department over two years were included, limiting sample size and data collection. Additionally, the cross-sectional design precludes causal inference. Future multicenter, large-sample, prospective studies are needed to provide stronger evidence for prevention and treatment.

Author Contributions: LI Jing was responsible for data collection and analysis, chart preparation, and manuscript drafting. MA Leilei participated in conceptualization and design. WANG Guanran assisted with data verification and entry. JIANG Chen and XING Haitao were responsible for quality control. YANG Hongtao revised and approved the manuscript and takes overall responsibility.

Conflict of Interest: None declared.

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