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Nomogram Prediction Modeling of Peritoneal Dialysis-Associated Peritonitis

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Abstract: In order to find the risk factors of Peritoneal Dialysis-Associated Peritonitis (PDAP) and to construct a nomogram model for predicting the risks of PDAP, providing a basis for the prevention and treatment of PDAP. We collected the data of 181 peritoneal dialysis (PD) patients admitted to the Nephrology Department of Jiangsu Provincial Hospital of Traditional Chinese Medicine from February 2021 to October 2023. We divided them into the peritonitis group (n=62) and the non-peritonitis group (n=119) according to the hospital infection. Logistic regression analysis was used for risk factor screening, and variables with statistically significant differences in univariate analysis were included in a multifactorial Logistic regression analysis model to explore the influencing factors of Peritoneal Dialysis-Associated Peritonitis and to construct a nomogram prediction model, and by plotting the subjects' work characteristics (ROC) curve, Hosmer-Lemeshow calibration curve, and clinical decision curve (DCA) to evaluate the differentiation, calibration, and clinical applicability of the model. Resultly, based on multifactorial logistic regression analysis incorporating body mass index(BMI), age at peritoneal dialysis, neutrophil percentage/lymphocyte percentage, albumin, blood potassium, blood uric acid, blood phosphorus, and Chinese medicine concurrently were the risk factors for PDAP ($P<0.05$). Based on the constructed nomogram model, the ROC curve showed that the area under the curve (AUC) of the model was 0.959. Additionally, the calibration curve and DCA curve demonstrated good accuracy and application value. In conclusion, the nomogram prediction model constructed in this study has good predictive efficacy for PDAP, which can provide a reference for the early detection and identification of PDAP by clinicians and nurses.

1. Introduction

Chronic kidney disease (CKD) is a huge public health burden worldwide [1], and the incidence of end-stage kidney disease (ESKD) in China has been growing and accelerating year by year, with about 2% of patients entering ESKD each year. Peritoneal dialysis (PD) is one of the main renal replacement therapy modalities for patients with ESKD, because of its characteristics of slowing down the rate of decline of residual renal function, better hemodynamic stability, freer schedule, affordable, and reduced risk of infectious diseases. It accounts for approximately 11% of global patients and 14% of Chinese patients [2-6]. PDAP is the most common complication during PD and

the main cause of patients' conversion to haemodialysis or death [5-7]. Therefore, the prediction of PDAP is of great significance. Many studies at home and abroad have analysed the risk factors for the occurrence or frequency of PDAP, and some of them have established risk prediction models and column line diagrams [8-9]. And the occurrence of PDAP is also correlated with TCM evidence types, but no prediction model incorporates TCM evidence types. Therefore, this study initially established a risk assessment model for the occurrence of PDAP by incorporating TCM evidence types, which may provide a reference for clinicians to guide early treatment strategies and improve patients' prognosis.

2. Information and Methodology

2.1. Objects of Study

181 patients who were hospitalised in the Nephrology Department of Jiangsu Provincial Hospital of Traditional Chinese Medicine from February 2021 to October 2023 were selected for the study. Inclusion criteria met the following conditions: (1) Age > 18 years old. (2) Patients who underwent peritoneal dialysis placement and regular peritoneal dialysis in the hospital, and the age of peritoneal dialysis ≥ 1 month; (3) Complete and searchable clinical data; (4) All patients signed the informed consent. Exclusion criteria met the following conditions: (1) Combination of infections at other sites. (2) Those who had cardiovascular and cerebrovascular accidents during hospitalisation including acute cardiac insufficiency, acute coronary syndrome and cerebral infarction. (3) Those who have immune, blood system and liver function damage.

2.2. Research Method

This study is a retrospective study, a total of 181 patients were included, the general information, past history, clinical data, Chinese medicine evidence of the patients were recorded, the corresponding databa body mass index se was set up, two people double entry, and the database was locked after determining that there was no error. The following were included: age, gender, body mass index (BMI), history of hypertension, history of diabetes mellitus, age at peritoneal dialysis, ultrasensitive C-reactive protein, haemoglobin, neutrophil ratio, lymphocyte ratio, neutrophil/ lymphocyte ratio, albumin, prealbumin, alkaline phosphatase, blood urea nitrogen, blood creatinine, blood potassium, blood sodium, blood calcium, blood carbon dioxide binding capacity, blood uric acid, blood phosphorus , blood magnesium, Chinese medicine's own evidence, Chinese medicine's concurrent evidence.

2.3. Diagnostic Criteria for Peritoneal Dialysis-Associated Peritonitis

We recommend that peritonitis should be diagnosed when at least two of the following are present: (1) clinical features consistent with peritonitis, that is, abdominal pain and/or cloudy dialysis effluent; (2) dialysis effluent white cell count > 100/mLor >0.1 ×109/L (after a dwell time of at least 2 h), with > 50% polymorphonuclear leukocytes (PMN); (3) positive dialysis effluent culture.

2.4. Statistical Methods

In the description of the study population, continuous data variables were tested for conformity to normal distribution using the Shapiro-Wilk test, continuous information conforming to normal distribution was described by mean ± standard deviation, continuous information with skewed distribution was described by median and upper and lower quartiles (25th-75th), and intergroup

variability was described by t-test. Categorical data were described by frequency and percentage (n, %), and intergroup variability was tested by chi-square test. One-way logistic regression was used to analyse the relationship between different variables and TCM certificates and the occurrence of PDAP in PD patients. Variables with P<0.05 were included in multifactorial logistic regression to establish a nomogram prediction model. The area under the subject curve (ROC curve) was used to reflect the degree of discrimination in constructing the cnomogram model, the calibration curve was used to reflect the degree of calibration in constructing the model, and the clinical decision curve (DCA) was used to reflect the degree of net benefit of the model. All statistical analyses were performed using the R language (version 4.3.0), and all analyses were performed using a two-sided p-test, with P<0.05 considered statistically significant.

3. Results

3.1. Baseline Description of the Study Population and One-way Logistic Analysis

Table 1: Baseline description of the study population

Clinical parameters	total (n = 181)	non-peritonitis group (n = 119)	peritonitis group (n = 62)	t/Z/χ^2 value age	P-value
age, Mean ±SD	53.45 ±12.99	50.52 ±13.40	59.08 ±10.06	t=-4.829	<.001
gender, n (%)				χ^2=0.595	0.441
women	86 (47.51)	59 (49.58)	27 (43.55)		
men	95 (52.49)	60 (50.42)	35 (56.45)		
BMI, Mean ±SD	24.39 ±3.22	23.87 ±3.43	25.39 ±2.51	t=-3.397	<.001
hypertension, n (%)				-	1.000
no	2 (1.1)	1 (0.84)	1 (1.61)		
yes	179 (98.9)	118 (99.16)	61 (98.39)		
diabetes mellitus, n (%)				χ^2=1.143	0.285
no	137 (75.69)	93 (78.15)	44 (70.97)		
yes	44 (24.31)	26 (21.85)	18 (29.03)		
age at peritoneal dialysis, M (Q_1, Q_3)	18.00 (10.00 - 39.00)	15.00 (10.00 - 29.00)	27.50 (8.25 - 68.25)	Z=2.328	0.020
CRP, M (Q_1, Q_3)	5.10 (1.03 - 34.30)	1.86 (0.52 - 5.13)	49.14 (27.90 - 105.95)	Z=5.462	<.001
Hb, Mean ±SD	93.33 ±20.13	92.28 ±19.52	95.34 ±21.29	t=-0.971	0.333
Ne%, M (Q_1, Q_3)	67.90 (62.00 - 78.30)	64.40 (59.50 - 69.50)	81.25 (74.85 - 88.18)	Z=7.734	<.001
Lm%, Mean ±SD	19.05 ±11.77	22.41 ±7.64	12.60 ±15.21	t=5.782	<.001
NLR, M (Q_1, Q_3)	3.65 (2.52 - 6.67)	2.93 (2.19 - 4.05)	7.80 (5.22 - 16.06)	Z=7.633	<.001
Alb, M (Q_1, Q_3)	30.80 (27.70 - 33.10)	32.00 (29.05 - 34.05)	28.20 (26.15 - 30.67)	Z=5.461	<.001
Pa, Mean ±SD	197.53 ±77.00	210.28 ±73.92	173.05 ±77.44	T =3.164	0.002
Alp, M (Q_1, Q_3)	76.00 (56.00 - 103.00)	75.00 (55.00 - 100.50)	78.50 (61.25 - 107.50)	Z=0.939	0.348
Bun, M (Q_1, Q_3)	20.40 (16.36 - 27.04)	20.10 (17.06 - 26.85)	21.98 (15.57 - 27.27)	Z=0.143	0.886
Scr, Mean ±SD	979.94 ±326.02	1027.10 ±334.31	889.44 ±291.18	t=2.744	0.007
K, M (Q_1, Q_3)	3.84 (3.38 - 4.27)	3.96 (3.51 - 4.37)	3.53 (3.25 - 3.88)	Z=4.293	<.001
Na, M (Q_1, Q_3)	138.40 (135.60 - 140.80)	139.60 (137.05 - 141.55)	135.80 (133.83 - 138.38)	Z=5.161	<.001
Ca, M (Q_1, Q_3)	2.24 (2.08 - 2.41)	2.27 (2.08 - 2.43)	2.20 (2.09 - 2.37)	Z=0.688	0.492
CO2CP, M (Q_1, Q_3)	25.00 (23.30 - 27.20)	24.40 (22.60 - 26.45)	26.20 (24.25 - 28.20)	Z=4.210	<.001
Ua, M (Q_1, Q_3)	387.00 (323.00 - 458.00)	421.00 (357.00 - 484.00)	347.00 (305.75 - 389.25)	Z=4.321	<.001
P, Mean ±SD	1.92 ±0.62	1.85 ±0.68	2.07 ±0.47	t=-2.539	0.012
Mg, M (Q_1, Q_3)	0.93 (0.82 - 1.03)	0.97 (0.89 - 1.08)	0.82 (0.73 - 0.93)	Z=5.423	<.001
Chinese medicine's own evidence, n (%)				χ^2=1.209	0.877
deficiency of both qi and yin	35 (19.34)	22 (18.49)	13 (20.97)		
yin deficiency of liver and kidney	32 (17.68)	20 (16.81)	12 (19.35)		
deficiency of spleen and kidney qi	31 (17.13)	19 (15.97)	12 (19.35)		
deficiency of the spleen and kidney yang	42 (23.2)	29 (24.37)	13 (20.97)		
deficiency of both Yin and Yang	41 (22.65)	29 (24.37)	12 (19.35)		
Chinese medicine's concurrent evidence, n (%)				χ^2=16.539	<.001
water and gas syndrome	48 (26.52)	35 (29.41)	13 (20.97)		
Moisture and turbidity syndrome	50 (27.62)	39 (32.77)	11 (17.74)		
dampness-heat syndrome	51 (28.18)	22 (18.49)	29 (46.77)		
Syndrome of blood stasis	32 (17.68)	23 (19.33)	9 (14.52)		

Note: BMI: body mass index; CRP: ultrasensitive C-reactive protein; Hb: haemoglobin, Ne% :neutrophil ratio; Lm%: lymphocyte ratio; NLR: neutrophil/lymphocyte ratio; Alb: albumin; Pa:

prealbumin; Alp: alkaline phosphatase; Bun: blood urea nitrogen; Scr: blood creatinine; K: blood potassium; Na: , blood sodium; Ca: , blood calcium; CO2CP: blood carbon dioxide binding capacity; Ua: blood uric acid; P: blood phosphorus; Mg: blood magnesium; Age, Bmi, Hb, Pa, Scr, P data are normally distributed and the rest are data are skewed.

A total of 181 patients with PD were included in this study, including 62 in the peritonitis group and 119 in the non-peritonitis group. Univariate analysis revealed that there was no statistically significant difference between the two groups in terms of gender, history of hypertension, history of diabetes mellitus, haemoglobin, alkaline phosphatase, blood urea nitrogen, blood calcium and blood magnesium (P>0.05). Age, BMI, age at peritoneal dialysis, CRP, Ne%, NLR, CO2CP, P, and the proportion of wet and hot evidence were higher in the peritonitis group than in the non-peritonitis group (p<0.05), whereas Lm%, Alb, Pa, Scr, K, Na, and Ua were lower than those in the non-peritonitis group (p<0.05). (Table 1)

3.2. Multifactorial logistic regression of the occurrence of PDAP

Variables with p < 0.05 in the univariate logistic regression were included in the multivariate logistic regression, and statistically significant results were found for BMI, age at peritoneal dialysis, NLR, Alb, K, Ua, P, and TCM concurrent factors (p < 0.05). (Table 2)

Table 2: The results of Multifactorial logistic regression

Variables	Beta	S.E	Z	P	OR (95%CI)
Age	0.01	0.03	0.23	0.820	1.01 (0.95 - 1.07)
Bmi	0.40	0.14	2.78	0.005	1.49 (1.13 - 1.98)
age at peritoneal dialysis	0.02	0.01	2.08	0.038	1.02 (1.01 - 1.04)
Crp	0.00	0.00	0.85	0.393	1.00 (1.00 - 1.01)
Ne.	0.02	0.05	0.45	0.655	1.02 (0.93 - 1.12)
Lm.	0.02	0.03	0.59	0.555	1.02 (0.96 - 1.08)
NLR	0.48	0.23	2.08	0.037	1.61 (1.03 - 2.52)
Alb	-0.33	0.11	-2.88	0.004	0.72 (0.58 - 0.90)
Pa	0.01	0.01	1.09	0.276	1.01 (0.99 - 1.02)
Scr	-0.00	0.00	-1.93	0.054	1.00 (0.99 - 1.00)
K	-2.15	0.76	-2.83	0.005	0.12 (0.03 - 0.52)
Na	-0.07	0.08	-0.88	0.378	0.93 (0.79 - 1.09)
Co2	0.15	0.09	1.64	0.101	1.17 (0.97 - 1.40)
Ua	-0.01	0.00	-2.01	0.044	0.99 (0.99 - 0.99)
P	2.55	0.79	3.21	0.001	12.82 (2.70 - 60.91)
Chinese medicine's concurrent evidence					
Syndrome of blood stasis					1.00 (Reference)
dampness-heat syndrome	2.80	1.34	2.10	0.036	16.46 (1.20 - 225.74)
Moisture and turbidity syndrome	-0.24	1.20	-0.20	0.839	0.78 (0.08 - 8.17)
water and gas syndrome	1.11	1.22	0.91	0.364	3.03 (0.28 - 33.11)

3.3. Construction and Evaluation of a nomogram prediction model for the Occurrence of PDAP

Based on the eight influencing factors of BMI, age at peritoneal dialysis, NLR, Alb, K, Ua, P, and Chinese medicine concurrent evidence, we constructed a nomogram model for the prediction of the risk of PDAP (Figure 1); the analysis of the ROC curve suggests that the Area under the Curve (AUC) of the model is 0. 959 (Figure 2), and the calibration curve is close to the ideal curve (Figure 3). The DCA curve showed good accuracy and application value (Figure 4).

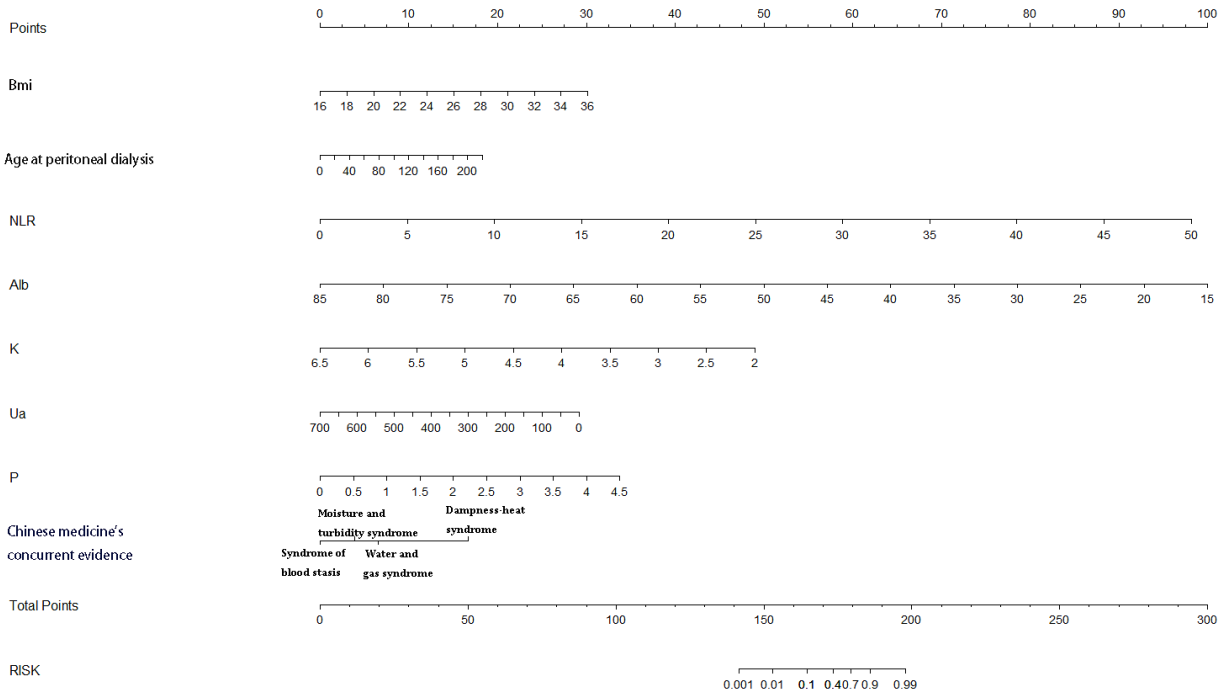

Figure 1: Nomogram for predicting the occurrence of PDAP risk

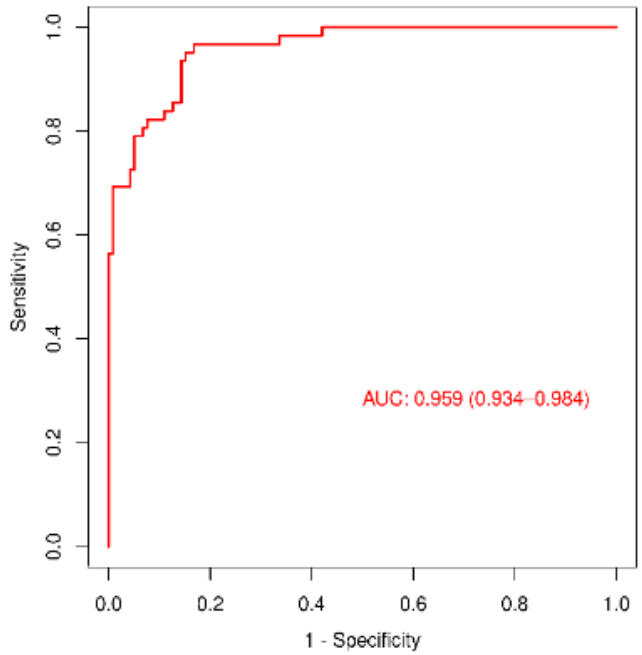

Figure 2: ROC curve of the nomogram prediction model to predict the occurrence of PDAP risk

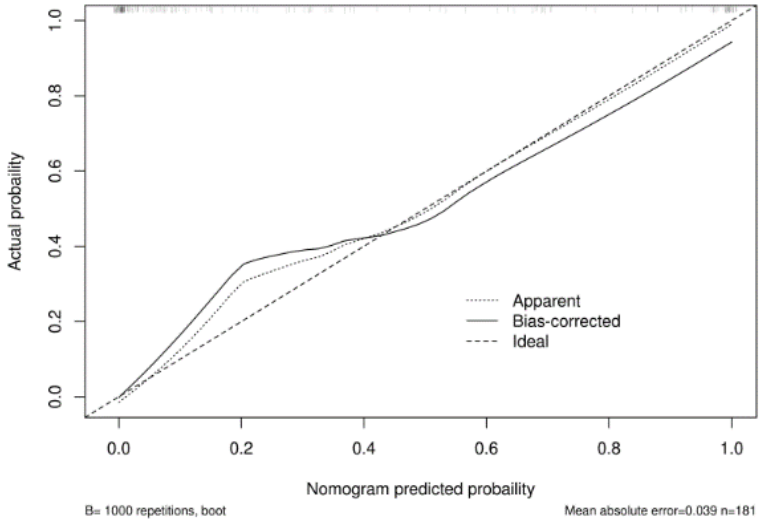

Figure 3: Hosmer-Lemeshow calibration curve of the nomogram prediction model

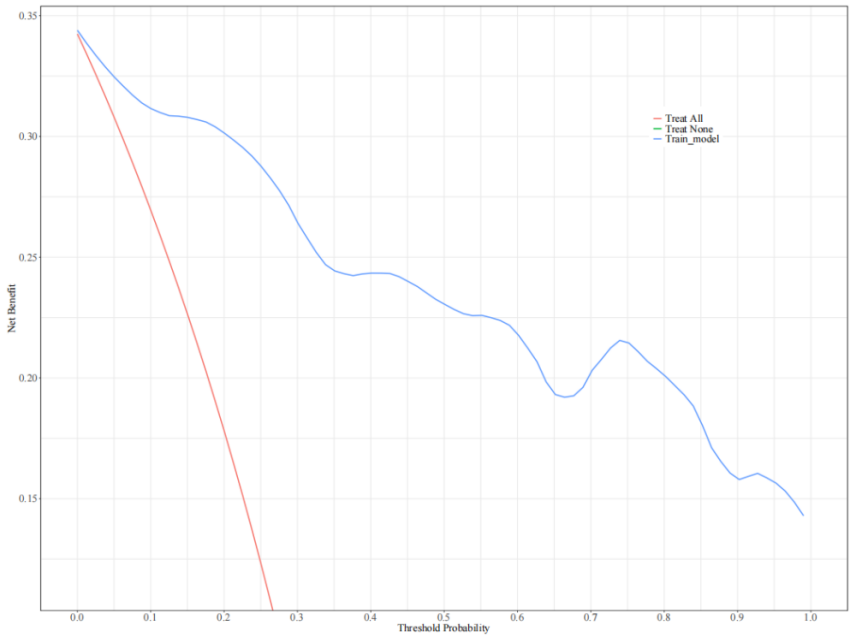

Figure 4: DCA analysis of the nomogram prediction model

4. Discussion

PDAP is the most common infectious complication of PD, which can cause structural and functional changes in the peritoneum, increase the number of hospitalisations and healthcare costs, and reduce the quality of life of patients [8]. Therefore, early detection of peritonitis and effective prevention and treatment strategies are key to the success of PD. Previous studies have identified old age, low educational level, comorbid diabetes mellitus, hypoproteinaemia, and disorders of calcium and phosphorus metabolism as risk factors for the development of PDAP, and the risk factors found varied from study to study [10]. In this study, BMI, age at peritoneal dialysis, NLR, Alb, K, Ua, P, and Chinese medicine concurrent evidence were found to be independent influences on the occurrence of PDAP by multifactorial logistic regression analysis, and based on these eight influences, a predictive model for the occurrence of PDAP risk. It has been found that overweight patients with

higher BMI have more total body water, making the calculated Kt/V value smaller, and this miscalculation leads to premature or even volume overload changes in PD prescription [5], and there are patients with higher BMI who have higher peritoneal protein clearance [11]. High BMI is associated with PDAP poor prognosis.

Previous studies have demonstrated that long PD age is a risk factor for PDAP [13-14]. Moreover, the longer the age of PD the more likely patients are to neglect correct technical practice, whereas studies have shown that patient technique retraining and even technique assessment are associated with a lower incidence of Peritonitis [14-17].

NLR is a widely available, inexpensive, and easily accessible inflammatory marker that reflects the inflammatory state of end-stage renal disease and is a new predictor of the occurrence and poor prognosis of PDAP. Inflammatory state is very common in patients with end-stage renal disease and chronic dialysis, and may be related to the uremic microenvironment, reduced clearance of pro-inflammatory cytokines, volume overload, and oxidative stress. The results of the present study showed that elevated NLR is an independent risk factor for the development of PDAP, which is in keeping with the findings of previous studies [9,18,19].

In this study, low Alb was found to be an independent risk factor for the development of PDAP in PD patients, which is in line with previous studies [9,12,13,19,20]. PD increases peritoneal protein loss in CKD patients [11]. Hypoalbinaemia reduces peritoneal defences and increases the risk of infection. In inflammatory state, Alb synthesis is further reduced and it is possible that the combination of both together leads to peritonitis. Studies have shown that a mean ALB value of <35 g/L is an independent risk factor for new-onset peritonitis in PD patients; and the risk of new-onset peritonitis in PD patients is significantly higher as the duration of hypoalbuminaemia increases [21]. Given that malnutrition is reversible in nature, early identification of patients at risk of malnutrition and appropriate nutritional interventions are important for alleviating and preventing the development of peritonitis.

International data from seven countries according to PDOPPS suggests that persistent hypokalaemia leads to a substantially increased risk of death and peritonitis [22]. This is consistent with the study. And in the observational and mechanistic studies of hypokalaemia in Thai PD studies, the main contributing factor to hypokalaemia was low dietary potassium intake rather than increased potassium excretion or intracellular transfer [23]. Dietary interventions are recommended to reduce hypokalaemia [24].

Hyperphosphatemia is a common complication in PD patients, which facilitates the development of endothelial dysfunction and vascular calcification, and is an independent specific risk factor for cardiovascular disease in CKD patients [25]. Data from various PD centres in China showed that the control rate of CKD-MBD was about 55.1%, and the control rates of blood calcium, blood phosphorus, iPTH and vitamin D were 70.6%, 57.4%, 59.8% and 60.1%, respectively. The lowest rate of blood phosphorus compliance was found [22]. Hyperphosphatemia was associated with the incidence of PDAP.

Blood uric acid is the most abundant antioxidant in plasma, and hypouricaemia is thought to increase the risk of reduced renal function by reducing antioxidant capacity [26]. Previous studies have not been consistent about the effect of blood uric acid levels on PDAP [26-27], but the lower the uric acid the greater the likelihood of PDAP [29], which reminds us that that we should keep blood uric acid levels relatively stable.

The results of several studies have been shown that there is a potential association between dampness-heat syndrome in TCM evidence and PDAP [28,30]. In this study, we constructed a longitudinal study based on real-world data to confirm the value of the dampness-heat syndrome in TCM concurrent evidence in predicting the risk of PDAP.

5. Summary

In summary, this study finally constructed a risk prediction model for the occurrence of PDAP based on the eight influencing factors of BMI, age at peritoneal dialysis, NLR, Alb, K, Ua, P, and Chinese medicine concurrent evidence, and the model has good differentiation and calibration. The indicators included in the column chart model are commonly and easily available in clinical practice, and the visualisation of the column chart model avoids cumbersome formula calculations, which is more convenient for clinical application.

The shortcomings of this study are: (1) this study analysed common patients' own conditions and commonly used laboratory indicators, which did not completely cover all factors; (2) this study is a single-centre, retrospective study with a small sample size, which may affect the reliability of the results to a certain extent, and we look forward to multi-centre and prospective cohort studies with larger samples, to further improve the model, and provide reference bases for the early identification of clinical PDAP high-risk group.

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