

Development and validation of a novel score to predict dialysis inadequacy in continuous ambulatory peritoneal dialysis patients

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Abstract

Objective: Adequate dialysis is of great importance for continuous ambulatory peritoneal dialysis (CAPD) patients. This study aimed to develop and validate an easily applicable quantitative dialysis adequacy risk scoring system in CAPD patients based on laboratory parameters from a single blood draw.

Methods: A total of 634 CAPD patients from four study centers were enrolled in this study (345 and 289 patients in development and validation groups, respectively). A risk score model for inadequate dialysis was developed based on multivariate regression analysis, which was validated by the area under the receiver operator curve and calibrated by a calibration curve.

Results: Seven independent predictors for inadequate dialysis were identified in the development group (male sex, hypoalbuminemia, anemia, being overweight, hyperuricemia, estimated glomerular filtration rate <4.7 mL/min/1.73 m², and serum creatinine >800 μmol/L). A risk prediction score model was established and validated in the development and validation groups. Further analysis indicated that this model is suitable for CAPD patients with a wide range of clinical manifestations.

Conclusion: An easily applicable novel risk scoring system was established to detect inadequate dialysis in CAPD patients.

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Keywords

Risk prediction model, continuous ambulatory peritoneal dialysis, dialysis adequacy, inadequate dialysis, risk score, area under the receiver operator curve

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Introduction

Continuous ambulatory peritoneal dialysis (CAPD) is often chosen for end-stage renal disease (ESRD) patients, offering the advantages of low cost, simplicity, and minimal requirements for technical support. China has more than 40,000 prevalent peritoneal dialysis (PD) patients, of whom the majority have received CAPD.¹ Because inadequate dialysis is related to higher morbidity, technical failure, and mortality, the identification of patients at high risk of inadequate dialysis may be helpful in making treatment decisions and improving patient outcomes.²

Previous studies have reported conflicting results about risk factors for dialysis inadequacy in CAPD patients. Moreover, no study has established an integrated prediction model of dialysis adequacy in these patients. Currently, dialysis adequacy is usually assessed based on urea clearance (Kt/V), which is a time-consuming process requiring patients to collect 24-hour urine and 24-hour peritoneal dialysate.³ Additionally, it is difficult for older individuals and those from remote poverty-stricken areas to collect specimens correctly. Therefore, we aimed to establish an easily applicable novel model based on laboratory parameters from a single blood draw to identify CAPD patients with inadequate dialysis in this study.

Materials and methods

Design

A cross-sectional multicenter study was performed in 634 CAPD patients from four PD centers. The development group included 345 CAPD patients retrospectively collected from the PD center in West China Hospital. The validation group enrolled 289 patients from three PD centers (the Affiliated Hospital of Zunyi Medical College, the Third Hospital of Zigong City, and the People's Hospital of Mianzu City). This study was approved by the Medical Ethical Committee of West China Medical School, Sichuan University (FF-33-2019). Written informed consent was obtained from every participant.

Inclusion criteria were: 1) receiving CAPD for more than 1 month and 2) age between 18 and 70 years. Exclusion criteria were: 1) having undergone a kidney transplant, 2) missing patient data, and 3) refusal to participate in the study. All patients included in the study received glucose-based and lactate-buffered dialysis solutions (Dianeal, Baxter, Guangzhou, China) and were prescribed 2-L bags of dialysate containing 1.5% or 2.5% dextrose, sufficient for 3 to 5 exchanges per day.

Clinical variables and dialysis adequacy

Patient characteristics such as age, sex, body weight, height, primary renal disease,

diabetes mellitus, hypertensive nephrosclerosis, and duration of CAPD were collected. Laboratory data, including body mass index (BMI), albumin (Alb), prealbumin (PA), hemoglobin (Hb), uric acid (UA), serum creatinine (Cr), high-sensitivity C-reactive protein (hsCRP), interleukin-6 (IL-6), and serum phosphorus (P), were measured in all patients. Causes of ESRD were determined. The estimated glomerular filtration rate (eGFR, ml/min/1.73 m²) was calculated using the CKDEPI equation.⁴ Anemia and being overweight were defined using Chinese criteria.⁵ To examine the validity of the new method, inadequate dialysis was defined as total weekly Kt/V urea < 1.70. Total weekly Kt/V urea was calculated as the sum of peritoneal Kt/V urea and renal Kt/V urea using the formula recommended in KDOQI guidelines.⁶

Statistical analysis

Continuous variables were analyzed using unpaired *t* tests. Differences between development and external validation groups were compared using univariate analysis.⁷ Logistic regression was performed to identify independent predictors of inadequate dialysis and to establish a risk prediction model. The β coefficient was divided by the model's minimum coefficient value and rounded up to the nearest integer to assign a score. In the validity analysis, discrimination and calibration were evaluated by the area under the receiver operator curve (AUC) and calibration curve as previously described.⁷ The Hosmer–Lemeshow goodness-of-fit test was used to assess model calibration. All statistical procedures were performed using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$ as two-sided.

Results

Baseline characteristics

A total of 679 patients were identified in the current study, of whom 45 were excluded: 27 patients with PD treatment of less than 1 month, three patients who had undergone kidney transplantation, and 15 patients with incomplete data. Of the remainder, 345 patients were included in the development group and 289 in the validation group. Baseline characteristics of both groups are shown in **Table 1**. Significant differences were observed between groups with respect to being overweight, anemia, hypoalbuminemia, inadequate dialysis, and hsCRP levels ($p < 0.05$). The proportion of inadequate CAPD in development and validation groups was 44.6% ($n = 154$) and 29.8% ($n = 86$), respectively.

Development of the risk prediction score

For ease of interpretation and analysis, we represented those risk factors as binary predictor variables. eGFR < 4.7 mL/min/1.73 m² and Cr > 800 μ mol/L were selected under the logistic regression model based on the optimal cut-off value of AUC for dialysis inadequacy. Univariate analysis indicated that nine variables: male sex, anemia (Hb < 120 g/L), hyperphosphatemia (P > 1.45 mmol/L), being overweight (BMI > 24 kg/m²), hyperuricemia (UA > 380 μ mol/L), hypoalbuminemia (Alb < 40 g/L), eGFR < 4.7 mL/min/1.73 m², Cr > 800 μ mol/L, and hsCRP > 3.5 mg/L were associated with a significantly higher risk of inadequate dialysis ($p < 0.05$). Further multivariate analysis revealed that male sex, hypoalbuminemia, anemia, being overweight, hyperuricemia, eGFR < 4.7 mL/min/1.73 m², and serum creatinine > 800 μ mol/L were significant independent predictors of dialysis inadequacy ($p < 0.05$, **Table 2**). The risk

Table 1. Baseline characteristics.

Variable	Development group (n=345)	Validation group (n=289)	p-value
Age (years)	48.05±15.17	47.58±13.30	0.683
Men, n (%)	203 (57.7%)	142 (50.4%)	0.077
DM, n (%)	48 (13.9%)	34 (11.8%)	0.476
HTN, n (%)	50 (14.5%)	56 (19.4%)	0.109
BMI > 24 (kg/m ²)	123 (35.7%)	80 (27.7%)	0.033*
Alb < 40 (g/L)	291 (84.3%)	181 (64.9%)	<0.001*
PA < 300 (mg/L)	84 (25.3%)	55 (19.4%)	0.082
hsCRP < 3.5 (mg/L)	189 (55.4%)	188 (65.1%)	0.015*
IL-6 > 7.0 (pg/mL)	112 (35.0%)	93 (32.3%)	0.493
Hb < 120 (g/L)	318 (92.2%)	235 (81.6%)	<0.001*
P > 1.45 (mmol/L)	164 (47.5%)	168 (58.1%)	0.008*
UA > 380 (μmol/L)	194 (56.2%)	163 (56.4%)	1.000
Cr > 800 (μmol/L)	196 (56.8%)	181 (62.6%)	0.144
eGFR < 4.7 (mL/min/1.73 m ²)	158 (45.8%)	142 (49.1%)	0.224
Inadequate dialysis, n (%)	154 (44.6%)	86 (29.8%)	<0.001*

Data shown as number (percentage). * p<0.05.

DM, Diabetes mellitus; HTN, hypertensive nephrosclerosis; BMI, body mass index; Alb, albumin; PA, prealbumin; hsCRP, high-sensitivity C-reactive protein; IL-6, interleukin-6; Hb, hemoglobin; P, serum phosphorus; UA, uric acid; Cr, serum creatinine; eGFR, estimated glomerular filtration rate.

Table 2. Univariate and multivariate analysis of risk factors associated with dialysis inadequacy for patients in the development group.

Variable	Univariate analysis			Multivariate analysis			Score
	β	OR (95% CI)	p-value	β	OR (95% CI)	p-value	
eGFR < 4.7 (mL/min/1.73 m ²)	2.19	8.97 (5.41–14.86)	<0.001*	2.97	19.52 (8.51–44.81)	<0.001*	4
Men	1.24	3.45 (2.18–5.48)	<0.001*	2.08	8.03 (3.82–16.84)	<0.001*	2
Hb < 120 (g/L)	1.22	3.377 (1.34–8.16)	0.010*	1.33	3.79 (1.07–13.47)	0.040*	2
Cr > 800 (μmol/L)	1.99	7.29 (4.42–12.00)	<0.001*	1.36	3.90 (1.97–7.75)	<0.001*	2
Alb < 40 (g/L)	0.66	1.94 (1.04–3.60)	0.036*	1.10	3.02 (1.20–7.57)	0.019*	1
UA > 380 (μmol/L)	0.60	1.82 (1.18–2.81)	0.007*	0.962	2.62 (1.30–5.26)	0.007*	1
BMI > 24 (kg/m ²)	0.52	1.68 (1.08–2.61)	0.022*	0.845	2.33 (1.18–4.60)	0.015*	1
P > 1.45 (mmol/L)	1.46	4.30 (2.74–6.77)	<0.001*	–	–	–	–
hsCRP > 3.5 (mg/L)	0.42	1.53 (1.00–2.35)	0.053	–	–	–	–

*p<0.05.

CI, confidence interval; eGFR, estimated glomerular filtration rate; Hb, hemoglobin; Cr, serum creatinine; Alb, albumin; UA, uric acid; BMI, body mass index; P, serum phosphorus; hsCRP, high-sensitivity C-reactive protein.

prediction model was then converted into a risk prediction score, ranging from 0 to 13, by a simplified integer scoring system using the sum of each score. The probability of inadequate dialysis = 1/

[1 + EXP(7.716 – 0.845 * total score)]. R² was 0.590 in this prediction model. The probability of inadequate dialysis and a comparison figure of the total score are shown in Figure 1a.

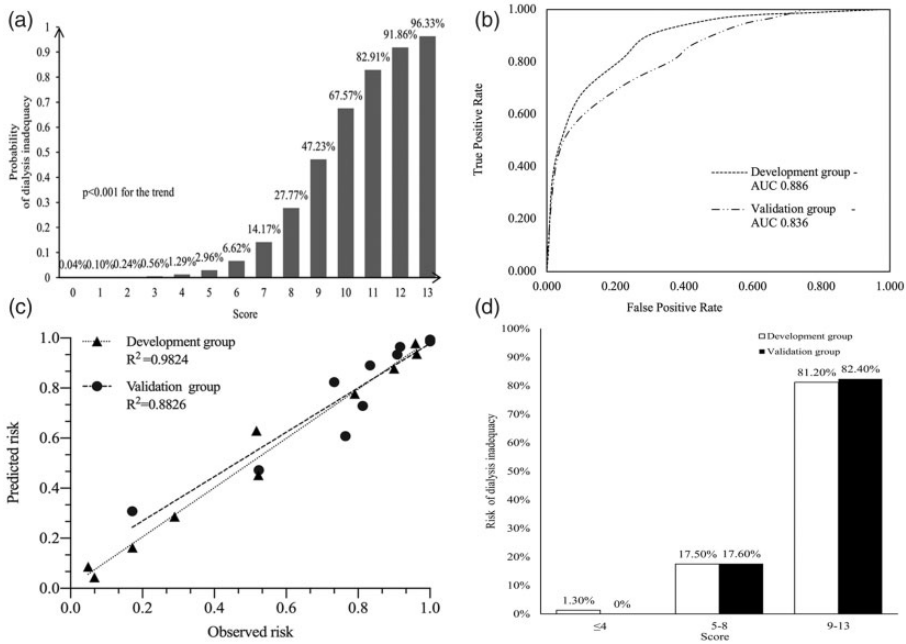


Figure 1 (a) Comparison of the total score and probability of dialysis inadequacy. (b) Receiver operator characteristic curves of the risk model for prediction of inadequate dialysis in the two groups. (c) Calibration curves of the risk model for prediction of inadequate dialysis in the two groups. (d) Risk stratification of inadequate dialysis according to the risk score model.

The Hosmer–Lemeshow goodness-of-fit test p -value was 0.78. The AUC of the development group was 0.886 (95% confidence interval [CI] 0.851–0.921) (**Figure 1b**), and the cut-off value that maximizes both sensitivity and specificity of the risk score for the prediction of dialysis inadequacy was 7.5 (sensitivity 67.5%, specificity 81.2%, Youden’s index 0.49) in the development group. Increasing risk scores were significantly correlated with increasing dialysis inadequacy incidence. Patients with a total score of 9 to 13 have a high risk of developing inadequate dialysis

External validation of the risk prediction model

External validation was performed to confirm the accuracy of the risk prediction

model. The AUC of the validation group was 0.836 (95% CI 0.782–0.891). Further calibration curves of the development and verification groups (**Figure 1c**) showed that the predicted scores were well calibrated. The Hosmer–Lemeshow statistic was Chi-square = 4.79 ($p = 0.78$) in the development group and Chi-square = 12.05 ($p = 0.15$) in the validation group. CAPD patients were then divided into three risk groups based on their score as follows: low risk (score 0–4; $n = 49$, 14.2%), moderate risk (score 5–8; $n = 129$, 37.4%), and high risk (score 9–13; $n = 167$, 48.4%). The incidence of dialysis inadequacy in the three risk groups was 1.3, 17.5, and 81.2% in the development group, respectively, in accord with the incidence of dialysis inadequacy in the validation group, which was 0.0, 17.6, and 82.4%, respectively (**Figure 1d**).

Discussion

Adequate dialysis is crucial for CAPD patients to avoid technical failure, high morbidity, and high mortality. Several studies have reported anemia, malnutrition, high inflammatory indexes, and an imbalance of electrolytes as risk factors of dialysis inadequacy in CAPD.^{3,8} In the current study, we found that sex, Cr, Alb, eGFR, BMI, Hb, and UA were risk predictors of inadequate dialysis for CAPD, similar to previous studies. However, we did not confirm hsCRP and P as risk factors.⁸ To make the prediction model more suitable for clinical practice, we integrated all identified risk factors into an easily applicable risk prediction model. Although several studies previously reported prediction models for all-cause and cardiovascular mortality in PD patients,^{9,10} ours appears to be the first to report a risk score model to evaluate inadequate dialysis in CAPD patients.

We developed an easily applicable score system based on routine clinical indexes of CAPD patients to detect inadequate dialysis risk based on logistic regression analysis. Seven variables (Cr > 800 $\mu\text{mol/L}$, Alb < 40 g/L, UA > 380 $\mu\text{mol/L}$, Hb < 120 g/L, eGFR < 4.7 mL/min/1.73 m², BMI > 24.0 kg/m², and male sex) were included. Patients scoring 9 to 13 were identified as having a high risk of developing inadequate dialysis, and external validation found that our prediction model had adequate discriminative ability to distinguish those patients likely to develop inadequate dialysis. Because the AUROC of the validation group (0.836; **Figure 1b**) exceeded 0.8, this indicated a good prediction performance. Moreover, the incidence of dialysis inadequacy in the development and validation groups suggested that the prediction model is suitable for CAPD patients with a wide range of clinical manifestations. Additionally, compared with the conventional Kt/V assessment method, our new

model has the advantages of simplicity, low cost, and being based on laboratory parameters from a single blood draw. Its application could help clinicians identify patients at risk of inadequate dialysis, enabling them to make interventions to avoid clinical deterioration.

There are some limitations in the present study. First, the incidence of inadequate dialysis was not matched in this study (44.6% vs 29.8%, $p < 0.001$), which may have led to an overestimation of prediction performance because of the limited number of patients. Second, most variables were represented as binary variables for statistical convenience, so their severity was not taken into account. Additionally, eGFR and Cr are high correlation variables, which may have caused a collinearity problem. Future work should include more variables and patients, and perform a more accurate verification of the model.

Conclusion

We developed and validated a convenient, cost effective, and easy-to-perform functional scoring system for the detection of inadequate dialysis risk in CAPD patients.

Author contributions

AQ, MA, SW, and XL collected and analyzed the data. AQ and XL also wrote the main manuscript. YT reviewed and edited the manuscript. WQ supervised the work and revised the manuscript.


Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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