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Analysis of risk factors and construction of prediction model of drop out from peritoneal dialysis

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Abstract

This study is to investigate the risk factors for the drop out from peritoneal dialysis.

We retrospectively analyzed patients who underwent catheterization between January 1, 2009 and September 30, 2019. The follow-up period ended on November 30, 2019. End point events were the cessation of peritoneal dialysis, including death, conversion to hemodialysis, and kidney transplantation. Kaplan–Meier method was used to analyze peritoneal dialysis curve. Significant factors were included in the multivariate Cox proportional hazards model. Calibration curve was plotted.

A total of 377 patients were included in this study. The dropout rate of peritoneal dialysis was 41.38%. The main drop out reason was conversion to hemodialysis, accounting for 41.67% of the total number of drop out, followed by kidney transplantation (28.21%) and death (25%). According to multivariable Cox proportional hazards model analysis, the medium education level (hazard ratio (HR): 2.53, 95% confidence interval (CI): 1.08–5.91, $P = .03$), high education level (HR: 2.47, 95% CI: 1.03–5.93, $P = .04$), diabetes (HR: 1.87, 95% CI: 1.24–2.83, $P < .03$), hypertension (HR: 2.40, 95% CI: 1.64–3.51, $P < .01$), repeated peritonitis (HR: 5.18, 95% CI: 3.04–8.80, $P < .01$), and repeated chest complications (HR: 4.98, 95% CI: 2.79–8.89, $P < .01$) were independent risk factors for dropping out from peritoneal dialysis, while the number of hospitalizations after catheterization (HR: 0.94, 95% CI: 0.89–0.98, $P = .01$) was protective factor for maintenance of peritoneal dialysis. The C index of the prediction model was 0.74.

Higher education level, diabetes, hypertension, repeated peritonitis, and repeated chest complications were the risk factors of dropping out from peritoneal dialysis, while higher number of hospitalizations after catheterization was a protective factor for the maintenance of peritoneal dialysis. The nomogram could predict the probability of dropping out from peritoneal dialysis.

Abbreviations: CI = confidence interval, HR = hazard ratio.

Keywords: peritoneal dialysis, prediction model, risk factors

1. Introduction

The prevalence of end-stage renal disease is gradually increasing in China, with about 200 to 250 cases per million people,[1] which brings a huge economic burden to patients' families and society. Peritoneal dialysis is now widely used in end-stage renal disease due to the advantages such as simple operation, low cost, small impact on hemodynamics, and protection of residual renal function. Meanwhile, it has the same therapeutic effect as hemodialysis.[2] Thus, peritoneal dialysis has been the first choice for alternative treatment of renal disease in many countries and regions.[3–6] Nowadays, China has the largest number of peritoneal dialysis patients in the world. Because some patients drop out from peritoneal dialysis after a period of treatment, the annual conversion rate from peritoneal dialysis to hemodialysis is as high as 35%.[7]

Reasons for dropping out from peritoneal dialysis are varied, including factors of the patients themselves or caregivers, factors inherent to the health care monitoring system, and the peritoneal dialysis approach.[7] Death, kidney transplantation, and hemodialysis are the external manifestations that cause patients to drop out from peritoneal dialysis.[6,8,9] Herein, we aim to identify the underlying causes of these manifestations. The factors affecting the drop out from peritoneal dialysis were analyzed. A prediction model was constructed. Our findings may provide a reference for reducing the rate of peritoneal dialysis drop out.

2. Materials and methods

2.1. Patients

This is a retrospective study. Patients who underwent catheterization in Department of Nephrology, the First Affiliated Hospital

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Table 1

The clinical information of the patients.

Items	Cases	Proportion (%)
Age (yr)		
20～	41	10.88
30～	72	19.10
40～	115	30.50
50～	92	24.40
60～	57	15.12
Gender		
Male	208	55.17
Female	169	44.83
Marriage status		0.00
Unmarried	39	10.34
Married	329	87.27
Divorced	6	1.59
Widowed	3	0.80
Education level		0.00
Low level (primary education and below)	37	9.81
Middle level (secondary or technical education, etc)	207	54.91
High (college and above)	133	35.28
Ethnic		0.00
Han	308	81.70
Others	69	18.30
Combined primary disease		0.00
Diabetes	88	23.34
Glomerulus nephritis	32	8.49
Hypertension	221	58.62
Obstructive nephropathy	30	7.96
Others	6	1.59
Peritonitis		
No	307	81.43
Single infection	36	9.55
Repeated infection	34	9.02
Chest complications		
No	312	82.76
Single	37	9.81
Repeated	28	7.43
Urinary tract infection		
No	359	95.23
Yes	18	4.77
Reason for peritoneal dialysis withdrawal		
Conversion to hemodialysis	65	41.67
Kidney transplantation	44	28.21
Death	39	25.00
Lost to follow-up	8	5.12

of Xinjiang Medical University between January 1, 2009 and September 30, 2019 were enrolled in this study. The exclusion criteria were:

1) Patients with renal transplantation.
2) Patients who were transferred from hemodialysis to peritoneal dialysis.
3) Patients who were catheterized in other hospitals.

Patient information was listed in Table 1. We further divided all participants into subgroups according to age, gender, marital status, education level, ethnicity, combined primary diseases, peritonitis, chest complications, urinary tract infection, and reason for peritoneal dialysis drop out. Written informed consent was obtained from every patient and the study was approved by the ethics review board of First Affiliated Hospital of Xinjiang Medical University.

2.2. Data collection

The following patient information was collected: gender, age, ethnicity, marital status, education level at the beginning of dialysis, catheterization date, primary disease, peritonitis and the number of peritonitis, chest complications (pulmonary infection and pleural effusion) and frequency, urinary system infection, and number of hospitalizations after catheter placement.

2.3. Follow-up

The follow-up started at the time of diagnosis and ended when the patients stopped peritoneal dialysis or was censored. All the patients in this study were followed up regularly. Peritoneal dialysis conditions were actively obtained every 3 months within the first year and then every 6 months thereafter. The deadline for follow-up was November 30, 2019. End point events were the cessation of peritoneal dialysis, including death, conversion to hemodialysis, and kidney transplantation.

2.4. Statistical analysis

Statistical analysis was performed using R (version 3.6.1) software with survminer, rms, and forestplot package. The peritoneal dialysis curve was analyzed by Kaplan–Meier method. Differences in cumulative peritoneal dialysis rate between groups were analyzed by univariate and multivariate Cox proportional hazards regression model. Measurement data of normal distribution are expressed as mean ± standard deviation; measurement data of skewed distribution are expressed as range; and count data are expressed as rate or proportion. A nomogram for dropping out from peritoneal dialysis was constructed. A P value $<.05$ was considered statistically significant.

3. Results

3.1. Baseline information of patients

Initially, 418 patients who underwent catheterization and peritoneal dialysis were enrolled. According to the exclusion criteria, 41 patients were excluded, including 11 patients with renal transplantation, 13 patients who were transferred from hemodialysis to peritoneal dialysis, and 17 patients who were catheterized in other hospitals. Finally, a total of 377 patients who underwent catheterization and peritoneal dialysis in our center were included in this study (Table 1). There were 208 male patients, accounting for 55.17%. Patients at the age of (40–49) years old accounted for 30.5%, which was the highest among all age groups. Married people accounted for 87.27%. The education level of patients was mainly medium level education (54.91%). The majority of patients were Han (81.70%). The most common primary disease was hypertension (58.65%), followed by diabetes and kidney disease. The incidence of peritonitis in the included patients was 18.57%. Chest complications were mainly pulmonary infection and pleural effusion, with an incidence of 17.24%. The incidence of urinary tract infection in the included patients was 4.77%. The main reason of dropping out from peritoneal dialysis was conversion to hemodialysis (41.67%), followed by kidney transplantation (28.21%) and death (25%).

Kaplan–Meier method was used to analyze the peritoneal dialysis curve. Of the 377 patients, 8 patients were lost to follow-up and 369 were followed up with a dialysis time of (0.1–141.5)

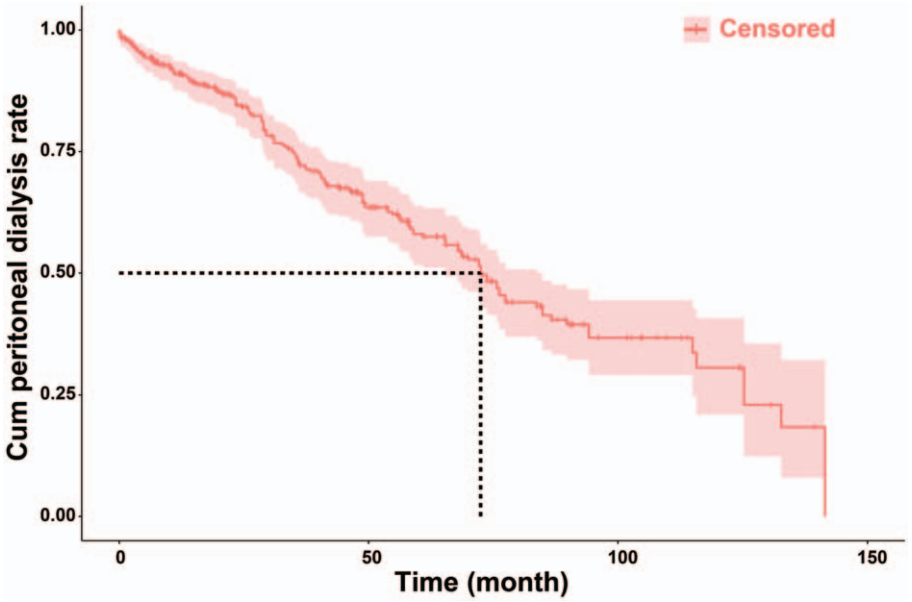

Figure 1. Overall peritoneal dialysis curve for 377 patients. Kaplan–Meier method was used to analyze peritoneal dialysis curve. The median dialysis time was 72.5 mo. The 95% confidence interval was (65.4–84.9) mo.

months and a median dialysis time of 72.5 months (Fig. 1). The 95% confidence interval was (65.4–84.9) months.

3.2. Factors affecting the drop out from peritoneal dialysis

The univariate Cox proportional hazards regression (Figs. 2–4) showed that age, ethnicity, marital status, primary disease of obstructive nephropathy, and urinary tract infection during peritoneal dialysis had no effect on the drop out from peritoneal dialysis. However, gender (female), medium or high education level, combined primary disease (diabetes, glomerulonephritis, and hypertension), low hospitalization number after catheterization ($P = .015$), repeated peritonitis, and repeated chest complications were risk factors for drop out from dialysis.

Multivariate Cox proportional hazards regression showed that higher education level (high VS low, hazard ratio (HR) = 2.47, 95% confidence interval (CI) = (1.03–5.39); medium VS low, HR = 2.53, 95% CI = (1.08–5.91)), combined primary disease of diabetes (HR = 1.87, 95% CI = (1.24–2.83)) and hypertension (HR = 2.40, 95% CI = (1.64–3.51)), repeated peritonitis (HR = 5.18, 95% CI = (3.04–8.80)), and repeated chest complications (HR = 4.98, 95% CI = (2.79–8.89)) were risk factors for drop out from dialysis (Fig. 5). The high number of hospitalization after catheterization was a protective factor for patients to maintain peritoneal dialysis (Fig. 5).

We further constructed and predicted a nomogram for dropping out from peritoneal dialysis, with the patient's education level, combined primary disease of diabetes and hypertension, peritonitis, chest complications, and the high number of hospitalizations after catheterization as relevant factors. The C index of this model was 0.74 (Fig. 6). Based on this prediction model, we predicted and analyzed calibration curves for 3 and 6 years of peritoneal dialysis (Fig. 7).

4. Discussion

As a family-based treatment, peritoneal dialysis has many inherent advantages, including simplicity, low requirements for medical resources, and low cost, which can reduce the inconvenience and financial burden of patients traveling to and from hospitals. However, peritoneal dialysis faces higher drop out rates. Therefore, it is of great importance to reveal the reasons for dropping out from peritoneal dialysis. In this study, we found that the main reason for dropping out from peritoneal dialysis was conversion to hemodialysis (41.67%), followed by kidney transplantation (28.21%) and death (25%). The main reason for dropping out from dialysis is consistent with the report by Kawaguchi et al in Japan,[8] but different from the studies by Wang et al[9] and Ma et al[10]. This may be related to differences among different populations.

Common reasons for patients to transfer to hemodialysis are dialysis-associated peritonitis, inadequate dialysis, catheter dysfunction, and failure of ultrafiltration.[11,12] In this study, we observed that repeated peritonitis, but not single peritoneal infection, was a risk factor for dropping out from peritoneal dialysis. When the peritoneum undergoes an inflammatory response, the weakened filtration function leads to insufficient dialysis. In particular, peritoneal fibrosis caused by repeated peritoneal inflammation has a greater impact on filtering function.[13] The effect of gender on the occurrence of peritonitis and conversion to hemodialysis in patients is controversial.[14–16] Our study found that gender had an effect on the drop out from peritoneal dialysis by univariate Cox proportional hazards regression model, but not by the multivariate analysis.

However, we found that diabetes was a risk factor for dropping out from peritoneal dialysis by both univariate analysis and multivariate analysis. In addition to increasing the risk of peritoneal infection, diabetes can also damage the vascular wall, cause peritoneal fibrosis, and transparent vascular disease, which finally will lead to poor peritoneal function, affect the efficiency of lipolytic transport, and result in insufficient dialysis and ultrafiltration failure.[9] During peritoneal dialysis, some patients experience chest complications such as pleural effusion due to thoracic and abdominal leaks. The formation of thoracoabdo-

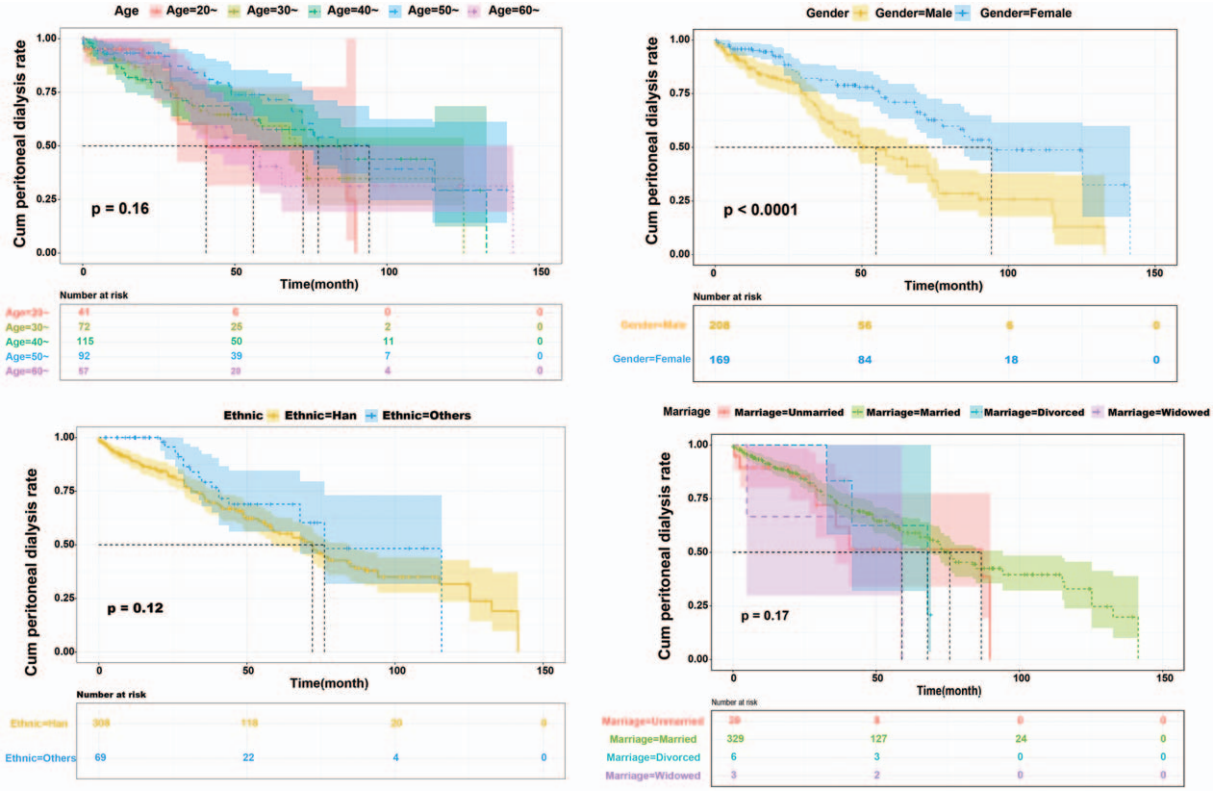

Figure 2. Kaplan–Meier curve of peritoneal dialysis rate of patients with different age, gender, ethnicity, and marriage. Age, ethnicity, and marriage had no effect on the drop out from peritoneal dialysis. Gender (female) was risk factors for drop out from dialysis.

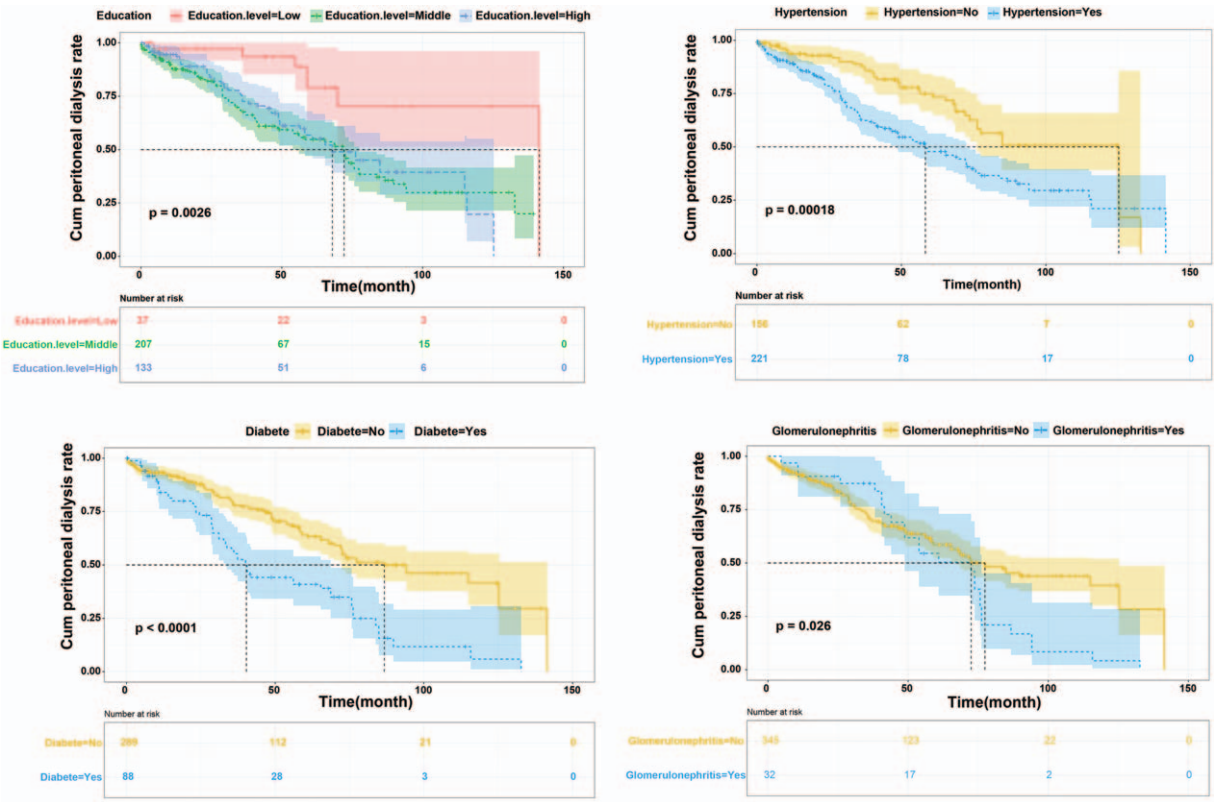

Figure 3. Kaplan–Meier curve of peritoneal dialysis rate of patients with different education level, hypertension, diabetes, and glomerulonephritis. Medium or high education level, diabetes, glomerulonephritis, and hypertension were risk factors for drop out from dialysis.

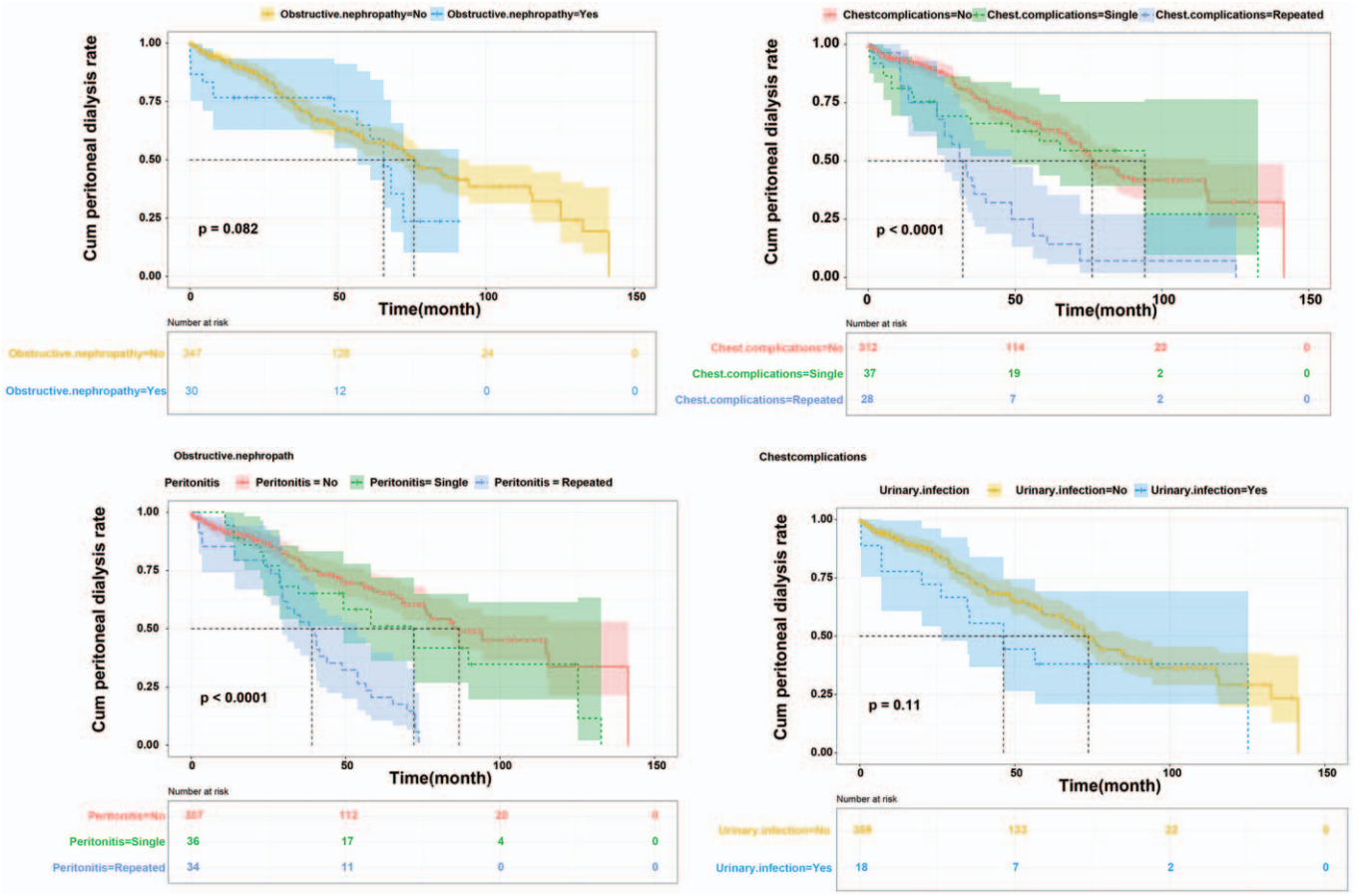

Figure 4. Kaplan–Meier curve of peritoneal dialysis rate of patients with obstructive nephropathy, chest complication, peritonitis, and urinary infection. Primary disease combined with obstructive nephropathy urinary tract infection during peritoneal dialysis had no effect on the drop out from peritoneal dialysis. Repeated chest complications and repeated peritonitis were risk factors for the drop out from dialysis.

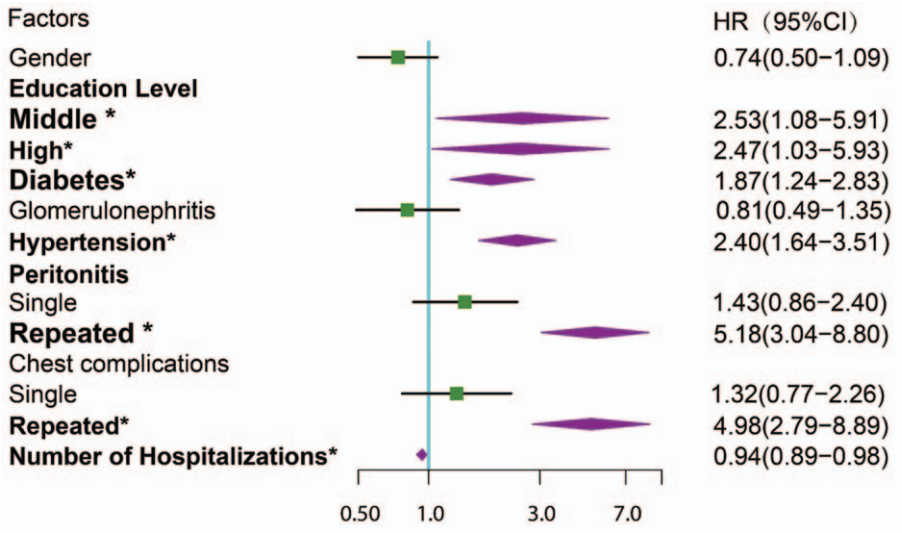

Figure 5. Multivariate Cox proportional hazard analysis of the drop out from peritoneal dialysis. Higher education level (high VS low, HR = 2.47, 95% CI = (1.03–5.39), medium VS low, HR = 2.53, 95% CI = (1.08–5.91)), combined primary disease of diabetes (HR = 1.87, 95% CI = (1.24–2.83)) and hypertension (HR = 2.40, 95% CI = (1.64–3.51)), repeated peritonitis (HR = 5.18, 95% CI = (3.04–8.80)), as well as repeated chest complications (HR = 4.98, 95% CI = (2.79–8.89)) were all risk factors for drop out from dialysis. The high number of hospitalization after catheterization was a protective factor for patients to maintain peritoneal dialysis.

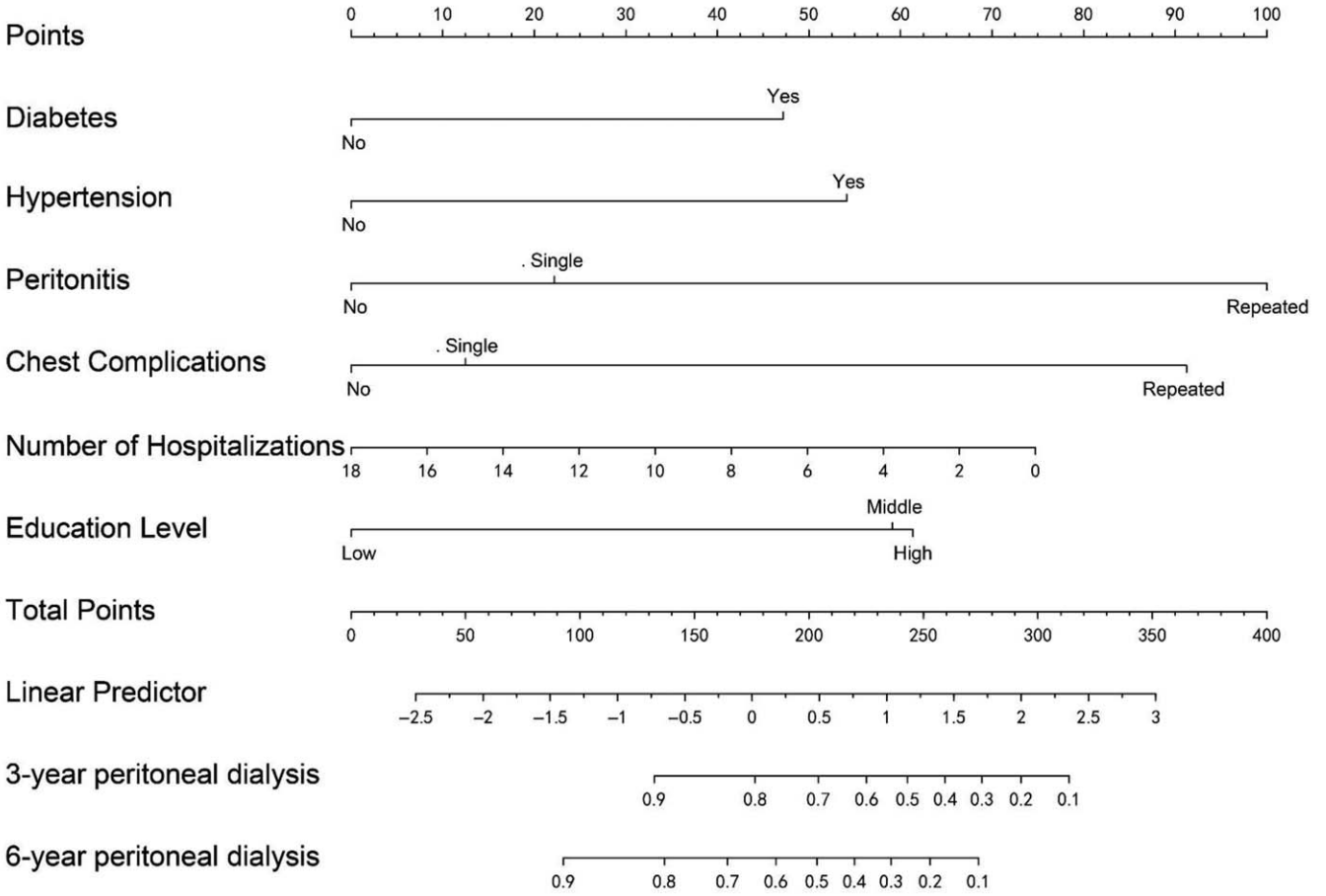

Figure 6. Nomogram of the risk of the drop out from peritoneal dialysis. The nomogram was constructed with the patient's education level, combined primary disease of diabetes and hypertension, peritonitis, chest complications, and the high number of hospitalizations after catheterization to predict the probability of dropping out from peritoneal dialysis.

minal fistula not only affects the dialysis effect, but also affects the patient's respiratory and circulation function, and is even life threatening. Thus, it is necessary to terminate the peritoneal dialysis when the treatment is not effective.[17–19] In addition, we found that patients with combined primary disease of hypertension were more likely to drop out from the peritoneal dialysis, which may be related to the excessive volume load and intolerance.

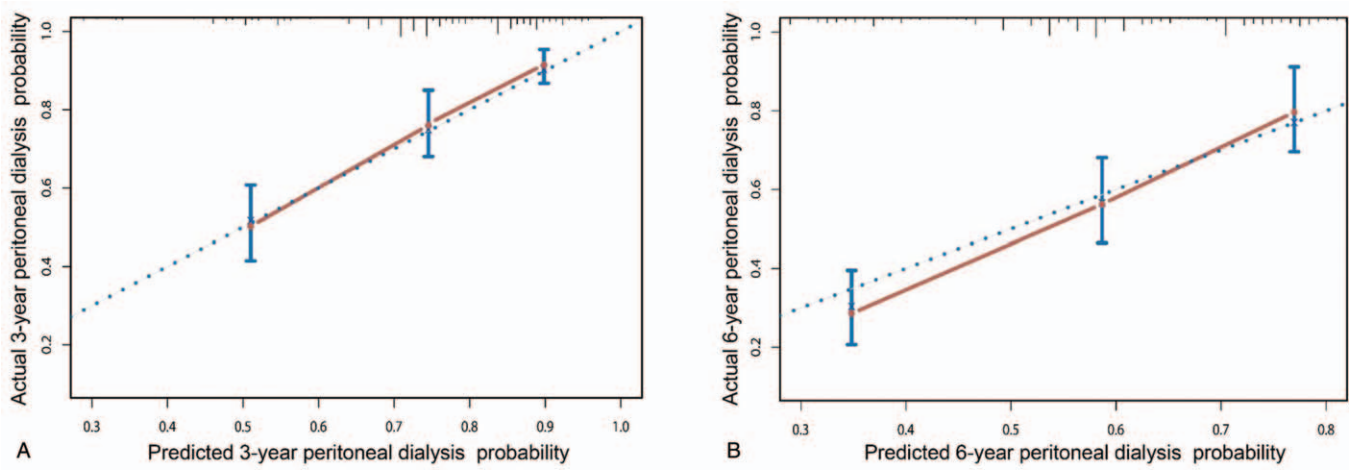

Figure 7. Calibration curves of 3- and 6-yr peritoneal dialysis drop out. The *x*-axis is the predicted probability and the *y*-axis is the actual probability. Based on the prediction model, we predicted and analyzed calibration curves for 3 and 6 yr of peritoneal dialysis.

Another reason of dropping out from dialysis is death.[20] Diabetes is not only one of the main causes of end-stage renal disease, but also the leading cause of end-stage renal disease in many countries and regions.[21] It is also an independent risk factor for death in patients with peritoneal dialysis. There are high levels of advanced glycation end products in the blood of diabetic patients. These products are likely to be associated with cardiovascular impairment, which may result in an increased incidence of cardiovascular and cerebrovascular diseases, and, an increased risk of death.[21,22] However, there are also opinions that diabetes per se is not an independent risk factor for death in patients with peritoneal dialysis.[14,23] The impact of diabetes on patients is comprehensive. Diabetes also increases the risk of peritoneal peritonitis associated with dialysis.[24] In addition, infection is also one of the important causes of peritoneal extubation and patient death.[25] Peritoneal dialysis rate in patients with repeated peritonitis is significantly shortened.[12,25,26] With repeated peritonitis, antibiotics increase the risk of fungal peritonitis and increase the risk of death for patients. Another common infection that causes patient death is lung infection. Patients with peritoneal dialysis have a higher incidence of lung infection, which can cause death by inducing other system diseases such as cardiovascular and cerebrovascular diseases or exacerbating the primary disease.[27,28] Cardiac and cerebrovascular events can occur in patients with underlying diseases such as hypertension, ventricular hypertrophy, myocardial hypoxia, and cardio-cerebral vascular sclerosis.[7] Studies have found that hypertensive patients with peritoneal dialysis have a higher risk of death than non-hypertensive patients.[9,29] Consistently, our study also found that patients with hypertension were more likely to drop out from dialysis.

Older age is another risk factor for patients with peritoneal dialysis.[30] However, older age had no significant effect on the drop out from peritoneal dialysis in this study. This may be because some elderly patients have poor cardiopulmonary function and cannot tolerate kidney transplantation and hemodialysis. In addition, this may also be related to the lower proportion of elderly patients included in this study. In this study, we also found that higher levels of education increased the risk of the drop out from dialysis. This may be because less educated people prefer to use simple and low-cost peritoneal dialysis. Meanwhile, we found that the number of hospitalizations was a protective factor for patients to maintain peritoneal dialysis. Increasing the number of hospitalizations may reduce the probability of complications such as peritoneal infections and lung infections, and thus reduce mortality. This also reflects from another perspective that patients with peritoneal dialysis maintain a high number of hospitalizations.

Another reason for dropping out from peritoneal dialysis is kidney transplantation.[20] In this study, 44 patients received kidney transplantation. However, due to high cost of kidney transplantation, lack of kidney source, and immunological rejection, most patients still choose dialysis treatment.

The nomogram is a statistical method that integrates various predictors to facilitate the statistical prediction of prognostic survival models. In the nomogram, each prediction is calculated in the form of a score, and the probability of a patient event occurring is calculated by a transfer function between the number of each predictor and the probability of the event outcome. It can be used to analyze the survival probability of patients, and has high application value in clinical statistics.[31] By using nomograms, doctors can clearly understand complex statistical predictions to improve patient compliance and treatment outcomes.[31] In this study, by quantifying different classifications of possible factors that affect peritoneal dialysis, we constructed a relatively accurate and reliable nomogram to predict and assess the prognosis of patients undergoing peritoneal dialysis. We found that the C-index of the nomogram was 0.74, which had high reliability and was very close to the theoretical calibration curve.

However, there are still some limitations in this study. First, the study is a single-center study. Second, the sample size is relatively small. Finally, the included factors are limited. The prediction model cannot include all possible predictors and cannot make an absolutely accurate prediction. Further studies are warranted.

5. Conclusions

In summary, our study suggested that higher education levels, diabetes, hypertension, repeated peritonitis, and repeated chest complications were all risk factors for the drop out from peritoneal dialysis. However, the number of hospitalizations after catheterization was a protective factor for patients to maintain peritoneal dialysis. These results indicate that preventing and managing peritoneal dialysis-associated peritonitis and chest complications, actively controlling blood glucose and blood pressure, and educating patients may help the maintenance of peritoneal dialysis in patients.

Author contributions

Conceptualization: Li Li, Jingjing Zhang.
Data curation: Hualian Pei, Zhenhui Liu.
Supervision: Jingjing Zhang.
Writing – original draft: Li Li.
Writing – review & editing: Jingjing Zhang.

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