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Retrospective Cohort Study

Risk factors for mortality within 6 mo in patients with diabetes undergoing urgent-start peritoneal dialysis: a multicenter retrospective cohort study

Mortality in USPD patients with diabetes

Si-Yu Cheng, Li-Ming Yang, Zhan-Shan Sun, Xiao-Xuan Zhang, Xue-Yan Zhu, Ling-Fei Meng, Shi-Zheng Guo, Xiao-Hua Zhuang, Ping Luo, Wen-Peng Cui

Abstract

BACKGROUND

The risk of early mortality of patients who start dialysis urgently is high; however, in patients with diabetes undergoing urgent-start peritoneal dialysis (USPD), the risk of, and risk factors for, early mortality are unknown.

AIM

To identify risk factors for mortality during high-risk periods in patients with diabetes undergoing USPD

METHODS

This retrospective cohort study enrolled 568 patients with diabetes, aged ≥18 years, who underwent USPD at one of five Chinese centers between 2013 and 2019. We divided the follow-up period into two survival phases: the first 6 mo of USPD therapy and the months thereafter. We compared demographic and baseline clinical data of living and deceased patients during each period. Kaplan–Meier survival curves were generated for all-cause mortality according to the New York Heart Association (NYHA) classification. A multivariate Cox proportional hazard regression model was used to identify risk factors for mortality within the first 6 mo and after 6 mo of USPD.

RESULTS

Forty-one patients died within the first 6 mo, accounting for the highest proportion of mortalities (26.62%) during the entire follow-up period. Cardiovascular disease was the leading cause of mortality within 6 mo (26.83%) and after 6 mo (35.43%). The risk of mortality not only within the first 6 mo but also after the first 6 mo was higher for patients with obvious baseline heart failure symptoms than for those with mild or no heart failure symptoms. Independent risk factors for mortality within the first 6 mo were advanced age (hazard ratio [*HR*], 1.908; 95% confidence interval [*CI*], 1.400–2.600; *P*<0.001), lower baseline serum creatinine level (*HR*, 0.727; 95% *CI*, 0.614–0.860;

P<0.001), higher baseline serum phosphorus level (*HR*, 3.162; 95% *CI*, 1.848–5.409; *P*<0.001), and baseline NYHA class III–IV (*HR*, 2.148; 95% *CI*, 1.063–4.340; *P*=0.033). Independent risk factors for mortality after 6 mo were advanced age (*HR*, 1.246; 95% *CI*, 1.033–1.504; *P*=0.022) and baseline NYHA class III–IV (*HR*, 2.015; 95% *CI*, 1.298–3.130; *P*=0.002).

CONCLUSION

To reduce the risk of mortality within the first 6 mo of USPD in patients with diabetes, controlling the serum phosphorus level and improving cardiac function are recommended.

Key Words: Peritoneal dialysis; Urgent start; Diabetes mellitus, Mortality within the first 6 mo; Risk factor; End-stage renal disease

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Core Tip: The first 6 mo after the initiation of urgent-start peritoneal dialysis is a high-risk period. We identified the following as risk factors for mortality within the first 6 mo in urgent-start peritoneal dialysis recipients with diabetes: advanced age, lower baseline serum creatinine level, higher baseline phosphorus level, and baseline New York Heart Association class III–IV.

INTRODUCTION

End-stage renal disease (ESRD) requiring dialysis is a global health problem[1, 2]. Patients with late-stage chronic kidney disease—who often delay visiting a doctor owing to economic difficulties or other reasons—often need to start dialysis urgently

without any preparation[3]. Several studies have documented the safety and feasibility of urgent-start peritoneal dialysis (USPD)[4-7]. USPD has several benefits over urgent-start hemodialysis (USHD), including better quality of life, better preservation of residual kidney function, and cost savings[4, 8-11].

Studies on patients undergoing peritoneal dialysis have shown that those with diabetes mellitus (DM) have a poorer prognosis than do those without DM, in addition to a poorer survival rate owing to the high prevalence of cardiovascular diseases[12, 13]. Currently, there is only a small, single-center study published on USPD in ESRD patients with diabetes[14]; it mainly compares the characteristics and complications between patients with diabetes treated with USPD and USHD. However, it does not identify the risk factors for mortality in patients with diabetes undergoing USPD.

The first 6 mo after the initiation of urgent dialysis is a high-risk period[5]. Patients with diabetes undergoing USPD are critically ill; hence, we speculated that the risk of mortality within the first 6 mo in these patients is high. Additionally, as the patient's peritoneal dialysis treatment progresses, the overall patient condition tends to be stable; therefore, we deliberated that the risk factors for mortality within the first 6 mo may be different from those for mortality after 6 mo in patients with diabetes undergoing USPD. However, the distribution of mortalities over time in patients with diabetes undergoing USPD has not been reported, and the risk factors for mortality within the first 6 mo in these patients are not clear. This study examines both the occurrence of and the risk factors for mortality within the first 6 mo of USPD initiation in patients with diabetes.

MATERIALS AND METHODS

Patients and study design

We screened patients with ESRD who underwent USPD between January 1, 2013, and December 31, 2019, at the following five hospitals: The Second Hospital of Jilin University, Second Part of the First Hospital of Jilin University, Jilin Central Hospital, Jilin First Automobile Work General Hospital, and Xing'anmeng People's Hospital.

Patients with incomplete data, those aged <18 years, and those without diabetes were excluded. All patients were followed up until mortality, kidney transplantation, technical failure, or the follow-up cutoff date (June 30, 2020). All patients were informed about renal replacement therapy modalities. Although experienced nephrologists guided the choice of modality, the final choice was made by the patient.

This retrospective study was approved by the Ethics Committee of the Second Hospital of Jilin University (design number, 2020031). To identify risk factors for mortality within the first 6 mo of USPD in patients with diabetes, we divided the follow-up time into two survival periods: the first 6 mo and the months thereafter. We compared demographic and baseline clinical data of patients who were living or deceased during each period. To highlight the characteristics of the patients deceased within the first 6 mo, we compared the causes of, and risk factors for, mortality after 6 mo to those of mortality within the first 6 mo.

Dialysis prescription

In the present study, automated peritoneal dialysis (APD) and continuous ambulatory peritoneal dialysis (CAPD) were the two modes of peritoneal dialysis. Peritoneal dialysis for each patient was prescribed based on fluid overload, uremia, hyperkalemia, and acid-base imbalance. A low-volume abdominal cavity (0.5–1.0 L) was initially obtained with the patient in the supine position to avoid dialysate leakage, and the volume was progressively increased to 2 L per cycle within 2 wk. The number of cycles per day was 3–4 for CAPD and 6–9 for APD. The dialysis procedure was performed by a peritoneal dialysis nurse until the patient and/or caregiver could independently perform the process. The patients were followed up every 3–6 mo and peritoneal dialysis dose was adjusted to keep the total Kt/V urea above 1.70 or creatinine clearance above 50 L/week/1.73 m^2.

Data collection and definitions

We collected the following data: (1) basic information, including sex, age, cardiac function classification, and comorbidities such as diabetes, cerebrovascular disease, hypertension, and tumors; (2) baseline (before peritoneal dialysis within 2 days) laboratory indicators, including hemoglobin, blood albumin, blood white cells, blood phosphorus, blood calcium, blood potassium, blood creatinine, and blood sodium; and (3) clinical outcomes, including mortality, technical failure, kidney transplantation, and continued dialysis. USPD was commenced within 2 wk of catheter insertion[15]. Technical failure was considered a transition to hemodialysis and its administration to the patient for at least 1 mo[16]. Cardiovascular events included myocardial infarction, stroke, heart failure, unstable angina, peripheral vascular events, fatty pulmonary embolism, sudden mortality, and unknown mortality caused by cardiovascular disease[17]. In accordance with the New York Heart Association (NYHA) categorization[18], patients without symptoms of heart failure were classified as class 0, whereas those with occasional, effort dyspnea were classified as class I; consistent with the traditional classification of cardiac function class, class II was characterized with mildly limited physical activity and general activity that can cause symptoms of heart failure, class III with obviously limited heart function and mild physical lower-than-general activities that can cause symptoms of heart failure, and class IV with symptoms of heart failure that can occur in a resting state.

Statistical analyses

Baseline characteristics are expressed as median (interquartile range) for continuous data and frequency and percentage for categorical data. For comparisons between groups, the rank-sum test was used for continuous variables, and the chi-square test or exact probability test was used for categorical variables. Kaplan–Meier curves were used to compare the survival rates of patients with different cardiac function classes. A Cox proportional hazard regression model was used to identify the risk factors for mortality during different periods of follow-up. The censored data included switching to HD, renal transplantation, technical failure, loss to follow-up, or still at our PD centers during each period. Additionally, for each selected period, mortalities after the

period were censored. Factors with P<0.1 in a univariate analysis were included in the multivariate analysis. Statistical significance was set at *P*<0.05. SPSS 24.0 software (IBM Corp., Armonk, NY, USA) was used for data analysis, and GraphPad 8.0 software (GraphPad Software, San Diego, CA, USA) was used for plotting.

The statistical methods of this study were reviewed by Li-Na Jin from School of Public Health, Jilin University, Changchun, Jilin, China.

RESULTS

Mortalities within the first 6 mo vs. after 6 mo

In this study, we screened 1751 patients undergoing USPD in the aforementioned five centers between 2013 and 2019, of which, we ultimately included 568 patients with diabetes undergoing USPD (Figure 1). Figure 2 shows the mortality proportions of patients with diabetes for the entire follow-up period calculated at 6-month intervals after the initiation of USPD. As shown, the highest proportion (26.62%) of mortalities occurred between 0 and 6 mo. In the first 6 mo, 41 people died, with a mortality rate of 7.2%. A total of 113 people died after 6 mo of USPD, with a mortality rate of 22.38%.

Demographic and clinical characteristics of included patients

Patient age and blood glucose level were significantly higher in patients who died within the first 6 mo than in those who survived the first 6 mo (*P*<0.001, *P*=0.011, respectively). The patients who died within the first 6 mo had a lower proportion of those with NYHA class 0–II and a much higher proportion of those with NYHA class III–IV than did patients who survived the first 6 mo (*P*=0.009) (Table 1).

Among the patients who were still followed at our PD centers after the first 6 mo, those who died after 6 mo had more advanced age (*P*=0.001) and lower levels of baseline serum creatinine and serum phosphorus (*P*=0.009, *P*=0.001, respectively) than did those who survived throughout follow-up. Compared with the patients who died after 6 mo of USPD, those who survived throughout the follow-up period included a

higher proportion of patients with NYHA class III–IV and a lower proportion of patients with NYHA class 0–II (*P*=0.026) (Table 1).

Causes of mortality within the first 6 mo vs. after 6 mo

The top three known causes of mortality in the 41 patients who died within the first 6 mo were cardiovascular diseases (26.83%), respiratory failure (19.51%), and infectious diseases (9.76%) (Table 2). Furthermore, the top three causes of mortality after 6 mo were the same as those for mortality within the first 6 mo (Table 2).

Survival analysis for all-cause mortality according to NYHA classification

Considering that cardiovascular disease was the main reason for mortality within the first 6 mo and also after 6 mo, we further analyzed the survival of patients with different classes of cardiac function. As shown in Figure 3A, in the first 6 mo, the mortality rate for patients with baseline cardiac function of NYHA III–IV was much higher than that of patients without cardiac function limitation (*P*=0.003). Similar results were found for these comparisons after 6 mo (Figure 3B).

Risk factors for mortality within the first 6 mo vs. after 6 mo

After correcting for confounding factors (serum calcium levels and blood glucose levels), multivariate Cox modeling analysis identified the following as independent risk factors for mortality within the first 6 mo in patients with diabetes receiving USPD: increased age (hazard ratio [*HR*], 1.908; 95% confidence interval [*CI*], 1.400–2.600; *P*<0.001); lower levels of baseline serum creatinine (*HR*, 0.727; 95% *CI*, 0.614–0.860; *P*<0.001); higher levels of baseline serum phosphorus (*HR*, 3.162; 95% *CI*, 1.848–5.409; *P*<0.001); and NYHA class III–IV at baseline (*HR*, 2.148; 95% *CI*, 1.063–4.340; *P*=0.033) (Figure 4A). Additionally, after adjusted serum creatinine calcium, phosphorus, and blood glucose levels, we found that advanced age (*HR*, 1.246; 95% *CI*, 1.033–1.504; *P*=0.022) and baseline NYHA class III–IV (*HR*, 2.015; 95% *CI*, 1.298–3.130; *P*=0.002) were risk factors for mortality after 6 mo (Figure 4B).

DISCUSSION

To the best of our knowledge, our study provides the first multicenter evaluation of the risk factors for mortality within the first 6 mo in patients with diabetes undergoing USPD. Advanced age and NYHA class III–IV at baseline were risk factors for mortality within the first 6 mo and after 6 mo; however, higher serum phosphorus levels and lower serum creatinine levels before dialysis were the only independent risk factors for mortality within the first 6 mo. The strength of the study was that it included data from five hospitals, making it representative and comprehensive.

Currently, the only report published on patients with diabetes undergoing USPD included 50 participants and reported an early mortality rate of 4.1%[14], similar to that of the present study. Moreover, we have demonstrated for the first time that the mortality in patients with diabetes undergoing USPD is highest in the first 6 mo. Thus, special attention should be paid to these patients during this time period. As in previous studies[19, 20], the leading cause of mortality within the first 6 mo for the USPD recipients with diabetes in our study was cardiovascular disease. Active treatment is therefore required at an early stage to reduce the risk of mortality due to cardiovascular events in these patients.

In agreement with previous reports[4, 5, 21], we identified advanced age as an independent risk factor not only for mortality within the first 6 mo but also after 6 mo of USPD in patients with diabetes. A reasonable explanation is that advanced age increases the incidence of cardiovascular events and consequently mortality in patients with diabetes[22]. Immune dysfunction and microinflammation in patients with renal failure can easily lead to sepsis, which increases the risk of mortality. The more advanced the age, the worse the immune function and, consequently, the greater the risk of mortality[23].

We found that the baseline serum creatinine level inversely correlated with mortality within the first 6 mo of USPD in patients with diabetes. We believe that the condition of the patient mainly accounts for this linkage. Patients with diabetes who start dialysis

urgently often present with severe symptoms rather than biochemical indicators of severe renal failure. A lower serum creatinine level in patients with diabetes before USPD is reflective of an earlier initiation of emergency peritoneal dialysis, which contrarily reflects more severe symptoms in the patient at initial presentation. However, the baseline serum creatinine level was not an independent risk factor for mortality after 6 mo. A possible reason was that as the course of USPD progressed, the patient's condition improved, and the baseline serum creatinine level did not reflect the disease severity on follow-up; therefore, the results indicated that USPD alleviated the patient's condition.

For patients with diabetes undergoing USPD, a link between the serum phosphorus level and mortality has not been reported. For these patients, we found that the risk of mortality within the first 6 mo increased by 16.7% for each 1 mmol/L increase in the baseline serum phosphorus level. Other studies have shown that a high level of serum phosphate correlates with vascular calcification in uremic patients[24-26], and that vascular calcification increases the risk of myocardial infarction[27], coronary artery disease[28], and mortality[29]. Serum phosphate level has also been found to be a powerful independent predictor of coronary heart disease in patients with diabetes[28]. Baseline serum phosphorus level was not a risk factor for mortality after 6 mo, which is similar to findings in other studies[30, 31]. In our study, we focused on the risk factors for mortality within the first 6 mo; therefore, we only collected the baseline serum phosphorus levels. We speculated that with the progress of dialysis and the use of phosphorus-reducing drugs during dialysis, serum phosphorus levels would gradually be corrected; therefore, the baseline serum phosphorus level is not reflective of the overall level after 6 mo of treatment. This suggests that it is crucial and beneficial to control the serum phosphorus level of patients in the initial stage of dialysis to reduce early mortality.

Patients with ESRD and diabetes are more likely to develop cardiovascular diseases than are non-diabetic patients with ESRD[32]. Additionally, it was proved that patients on dialysis with poor cardiac function have a very poor prognosis[33]. Therefore,

exploration of the relationship between mortality and cardiac function in patients with diabetes undergoing USPD is critical and significant. We found that among patients with diabetes undergoing USPD, those with obvious heart failure symptoms have a higher risk of mortality within the first 6 mo and after 6 mo than do those with mild or no heart failure symptoms. We found that NYHA class III–IV was a risk factor for mortality both within and after the first 6 mo; however, the risk of mortality after 6 mo was lower than that within the first 6 mo for patients with poorer baseline cardiac function. As a possible cause, we speculated that patients with poorer baseline cardiac function are more likely to suffer from complications of heart disease, and after a series of treatments such as dialysis, although their cardiac function improves, it cannot be completely corrected; therefore, the risk of mortality is merely reduced. Thus, routine monitoring of the patient's cardiac function in the early stages of dialysis is advised. Moreover, when the patient's cardiac function is not ideal, appropriate measures should be taken to promptly improve it.

Our study had several limitations. First, because it was retrospective, information bias could not be avoided. For example, the laboratory indicators such as cardiac function and serum phosphorus levels at different time points had not been determined, and the cause of mortality could not always be precisely established. Second, our sample size was small, and larger studies are needed to accurately predict mortality within the first 6 mo in diabetic patients undergoing USPD to provide further guidance for clinical applications.

CONCLUSION

The risk of mortality within the first 6 mo in patients with diabetes was the highest after USPD initiation. We suggest that controlling serum phosphorus levels and improving cardiac function will decrease the risk of mortality within the first 6 mo in these patients.

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