COMPARISON OF PROGNOSIS BETWEEN DIABETIC AND NONDIABETIC PERITONEAL DIALYSIS PATIENTS

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ABSTRACT

Introduction*: Diabetes mellitus (DM) nephropathy is one of the common causes of renal failure. It is unknown whether there is a difference between prognosis of DM and non-diabetes mellitus (N-DM) peritoneal dialysis (PD) patients. The aim of the study was to compare prognosis between diabetic and nondiabetic PD patients.*

Materials and methods: *We recruited patients who began PD between January 2010 and January 2018. General demographic data and biochemical indicators were collected. Patients were divided into DM and N-DM groups. All patients were followed up until death, kidney transplantation or September 1, 2019. The technical survival rate and overall survival rate between the two groups were compared. The factors influencing prognosis of PD patients were analyzed.*

Results: *A total of 246 PD patients were enrolled, including 50 DM patients(20.33%) and 196 N-DM patients (79.67%). Compared with the patients in the N-DM group, those in the DM group were older and had better residual renal function (P<0.05). Kaplan–Meier analysis showed that there was no difference in the technical survival rate between the two groups (P=0.479). The overall survival rate of the DM group was lower than that of the N-DM group (P=0.014). Cox regression analysis showed that DM was unrelated to the technical survival rate. Multivariate Cox regression showed that DM was not correlated with overall survival rate after adjusting for age and cardiovascular complications. Older age and presence of cardiovascular complications were independent mortality risk factors in PD patients.*

Conclusion: *Technical survival rate in DM patients was similar to that in N-DM patients. After adjusting for age and cardiovascular complications, DM was also not associated with overall survival rate. Patients with DM can receive PD treatment.*

Keywords: *Peritoneal dialysis, diabetes mellitus, technical survival rate, prognosis.*

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Introduction

Diabetes mellitus (DM) nephropathy is one of the common causes of renal failure. Research shows that DM is the leading cause of renal failure in Western developed countries[(1)]. In China, an epidemiological survey in 2010 showed that the incidence of DM is up to 11.6%, and pre-diabetes is estimated to be up to 50.1%[(2)]. DM nephropathy has surpassed primary glomerular disease and become the first cause of chronic kidney disease[(3)]. Renal replacement therapy is needed when diabetic nephropathy progresses to end-stage renal disease (ESRD). Peritoneal dialysis (PD) and hemodialysis (HD) are both important and effective methods of renal replacement therapy. However, there is no definite conclusion on which dialysis method is appropriate for patients with DM[(4)]. Generally, compared with N-DM patients, DM patients have higher residual renal function (RRF) when they initiate PD treatment[(5)], but DM patients suffer from higher incidence of cardiovascular complications and faster decline of RRF[(6, 7)]. It is unknown whether there is a difference between prognosis of DM and non-diabetes mellitus (N-DM) PD patients.

Methods

Study population

We conducted a retrospective analysis of patients who initiated PD therapy in the PD Center of Taixing Hospital between January 2010 and January 2018. The exclusion criteria included age<18 years, duration of PD <3 months, renal function recovery, acute renal failure, transfer from HD to PD, and renal failure after kidney transplantation.

Data collection

Demographic data of the PD patients were collected, including sex, age, height, weight, primary disease, and cardiovascular complications (including atrial fibrillation, heart failure, myocardial infarction, and cerebral hemorrhage).

Biochemical data included hemoglobin, serum creatinine, urea, uric acid, serum albumin, triglycerides, total cholesterol, parathyroid hormone, and hypersensitive C-reactive protein. The Modification of the Diet in Renal Disease (MDRD) equation was used to calculate baseline RRF of PD patients(8). Adequacy of dialysis and 4-h dialysate to plasma creatinine ratio (4h D/PCr) were recorded at 1 month after PD. Adequacy of dialysis was determined by urea clearance index (Kt/V) calculated by PD Adequest 2.0 software. Episodes of peritonitis in the first year of PD were also recorded. Patients were divided into DM and N-DM groups.

Patients were followed up until death or September 1, 2019. End-point events observed included death, kidney transplantation, and conversion to HD. This study was approved by our hospital Ethics Committee.

Statistical analysis

All data were analyzed by SPSS version 25.0 (SPSS, Chicago, IL, USA). Continuous normal distribution data were expressed as mean ± standard deviation; non-normal distribution data were expressed as medians (1/4,3/4); and categorical data were expressed as frequencies with percentages. Independent Student's test or Wilcoxon rank sum test was used to compare the differences of two continuous measurement data. The chi-square test was used to compare the differences between two categorical data. The Kaplan-Meier curve was used to analyze survival rate and a log-rank test was applied to compare survival differences between the two groups.

The Cox regression model was used to analysis risk factors for treatment failure or death. Covariates with P<0.1 in univariate models were selected for multivariable Cox regression models. P<0.05 was considered to be statistically significant.

Results

Patient characteristics

We recruited 246 new-onset PD patients, including 50 with DM (20.33%) and 196 without DM (79.67%). Patients in the DM group were older and had better RRF compared with patients in the N-DM group when they initiated PD therapy. The incidence of cardiovascular complications in the DM group was higher than that in the N-DM group, but the difference was not significant.

There was no difference in sex, height, weight, body mass index, hemoglobin, serum albumin, uric acid, intact parathyroid hormone, high-sensitivity C-reactive protein, triglyceride, total cholesterol, incidence of peritonitis in the first year, 4h D/PCr and Kt/V (Table 1).

	DM	N-DM	$t/\chi^2/Z$	p
Number of patients	50	196	-	-
Sex (male/female)	35/15	110/86	3.17	0.075
Ages	53.92±12.33	48.36±13.01	-2.725	0.007
Hight	164.49±8.40	164.01±8.75	-0.325	0.745
Weight	61.45±7.32	61.30±11.78	-0.078	0.938
BMI	22.72±2.30	22.68±3.27	-0.076	0.939
Cardiovascular disease (%)	90.00%	84.18%	1.079	0.299
Hemoglobin	80.39±17.73	79.67±17.64	-0.246	0.806
eGFR	6.72±2.73	5.38±1.89	-3.822	0.001
Albumin	40.54±9.69	39.48±4.88	-1.01	0.314
Uric acid	532.82±117.71	576.00±141.55	1.877	0.062
iPTH	278 (127, 459)	280 (92, 483)	-0.015	0.988
hsCRP	3.31 (1.91,13.42)	3.44 (2.30, 6.26)	-0.119	0.905
Triglycerides	1.65±1.07	1.58±0.94	-0.453	0.651
Total cholesterol	4.27±1.03	431±1.01	0.179	0.858
Peritonitis episodes in the first year	0 (0,0)	0 (0,0)	-0.041	0.967
4h D/PCr	0.54±0.15	0.56±0.14	0.758	0.449
Total Kt/V	1.90±0.61	1.81±0.49	-1.064	0.288
RRF Kt/V	0.68±0.44	0.60±0.40	-1.115	0.266
RRF Kt/V	1.23±0.48	1.21±0.35	-0.251	0.266

Table 1: Comparison of baseline characteristic between DM and N-DM groups of PD patients.

BMI = body mass index; eGFR = estimate glomerular filtration rate; iPTH = intact parathyroid hormone; hsCRP = high-sensitivity C-reactive protein; 4h D/PCr = 4-h dialysate to plasma creatinine ratio; Kt/V = urea clearance index; RRF = residual renal function; PD = peritoneal dialysis.

Follow-up time and outcome

The average follow-up time was 1133±753 days in the DM group and 1329±843 days in the N-DM group. There was no difference in the follow-up time between the two groups (P=0.135). Up to September 1, 2019, 26 patients in the DM group withdrew from PD, including 17 (65.38%) who died, eight (30.77%) who transferred to HD and one (3.84%) who underwent kidney transplantation. The causes of death included 15 (88.23%) from cardiovascular events and two (11.76%) from infections. Ninety-two patients in the N-DM group withdrew from PD, including 38 (41.30%) who died, 48 (52.17%) who transferred to HD, and six (6.52%) who underwent kidney transplantation. The causes of death included 29 (76.32%) from cardiovascular events, three each (7.89%) from severe infections or abandoning treatment, two (5.26%) from malignant tumors, and one (2.63%) from gastrointestinal bleeding.

Comparison of technical survival between the two groups

The 1-year, 2-year, 3-year and 5-year technical survival rates were 90.39%, 65.52%, 41.76% and 34.30%in the DM group and 85.41%, 71.05%, 60.54% and 42.31% in the N-DM group, respectively. There was no significant difference in technical survival rates between the two groups (P=0.479, Figure 1).

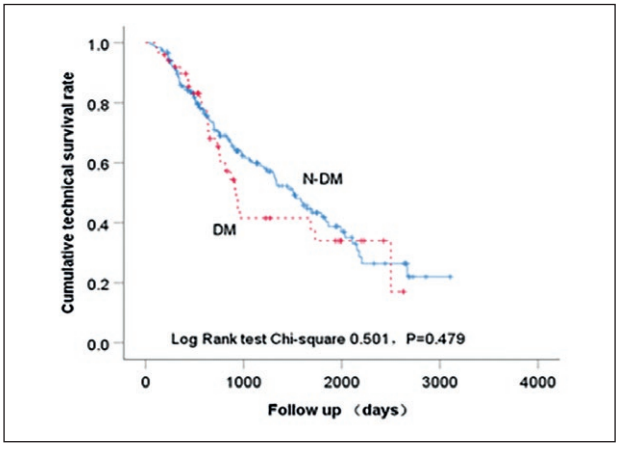

Figure 1: Comparison of cumulative technical survival rates between DM and N-DM patients on peritoneal dialysis. DM, diabetes mellitus; N-DM, non-diabetes mellitus.

Comparison of overall survival between the two groups

The 1-year, 2-year, 3-year and 5-year overall survival rates were 94.81%, 81.27%, 61.93% and 58.06% in the DM group and 95.91%, 88.46%, 82.93% and 73.54% in the N-DM group, respectively. The overall survival rate of DM group was lower than that of the N-DM group (P=0.014, Figure 2).

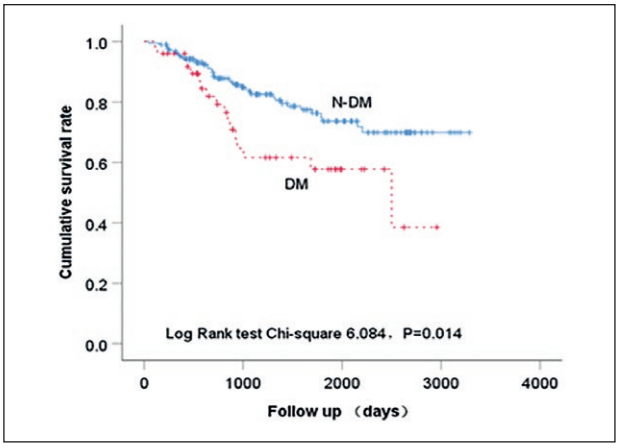

Figure 2: Comparison of cumulative survival rates between DM and N-DM patients on peritoneal dialysis. DM, diabetes mellitus; N-DM, non-diabetes mellitus.

COX regression analysis of technical survival rate of PD patients

Univariate Cox regression analysis showed that male sex, presence of cardiovascular complications, peritonitis episodes in the first year, and high 4h D/PCr were risk factors for PD withdrawal, and high total Kt/V and RRF Kt/V were protective factors for PD maintenance (Table 2).

	Outcomes			
	Time to treatment failure		Time to death	
	HR (95%CI)	P	HR (95%CI)	P
Diabetes (present vs absent)	0.854 (0.552,1.322)	0.479	0.493 (0.278, 0.875)	0.016
Sex (female vs male)	1.392 (1.143,1.695)	0.001	1.027 (0.599, 1.762)	0.922
Ages	0.992 (0.978, 1.007)	0.301	1.053 (1.031, 1.076)	0.001
BMI				
Cardiovascular comorbidity (present vs absent)	0.432 (0.284,0.659)	0.001	0.383 (0.214, 0.687)	0.001
Peritonitis episodes in the first year	1.497 (1.095, 2.046)	0.011	1.258 (0.778, 2.033)	0.349
RRF	0.984 (0.894, 1.083)	0.742	1.029 (0.895, 1.183)	0.690
Albumin	0.977 (0.936, 1.019)	0.255	0.953 (0.899, 1.010)	0.107
Hemoglobin	1.004 (0.992, 1.015)	0.538	1.001 (0.984, 1.018)	0.944
Uric acid	1.001 (0.999,1.002)	0.293	0.999 (0.996, 1.001)	0.226
iPTH	1.000 (0.988,1.001)	0.843	1.000 (1.000,1.001)	0.301
hsCRP	1.002 (0.996, 1.008)	0.447	0.986 (0.947,1.026)	0.488
Triglycerides	1.037 (0.831, 1.294)	0.750	0.800 (0.527, 1.215)	0.295
Total cholesterol	0.941 (0.807, 1.097)	0.436	1.123 (0.920, 1.372)	0.255
4h D/P_{Cr}	1.497 (1.095, 2.046)	0.011	1.721 (0.329, 9.007)	0.520
Total Kt/V	0.350 (0.223, 0.549)	0.001	0.720 (0.391, 1.325)	0.720
RRF Kt/V	0.341 (0.187, 0.620)	0.001	1.078 (0.412, 2.823)	0.878
PD Kt/V	0.801 (0.690, 1.265)	0.320	0.653 (0.297, 1.436)	0.289

Table 2: Univariate analysis of parameters associated with primary outcomes.

BMI = body mass index; CI = confidence interval; eGFR = estimate glomerular filtration rate; HR = hazard ratio; hsCRP = high-sensitivity C-reactive protein; iPTH = intact parathyroid hormone; 4h D/PCr = 4-h dialysate to plasma creatinine ratio; Kt/V, = urea clearance index; PD = peritoneal dialysis; RRF = residual renal function.

Multivariate Cox regression analysis showed that after adjusting for the above factors, there was still no correlation between DM and PD technical survival rate. Male sex, peritonitis episodes in the first year, higher 4h D/PCr and lower RRF Kt/V were independent risk factors for PD withdrawal (Table 3).

	Time to treatment failure	
	HR (95%CI)	P
Diabetes (present vs absent)	1.019 (0.611, 1.701)	0.943
Gender (female VS male)	1.684 (1.059, 2.676)	0.028
Cardiovascular comorbidity (present vs absent)	0.746 (0.420, 1.325)	0.371
Peritonitis episodes in the first year	1.526 (1.083, 2.148)	0.016
4h D/P_{Cr}	3.623 (1.008, 13.020)	0.049
RRF Kt/V	0.389 (0.210, 0.719)	0.003

Table 3: Multivariable analysis of parameters associated with treatment failure.
4h D/PCr = 4-h dialysate to plasma creatinine ratio; CI = confidence interval; HR = hazard ratio; Kt/V = urea clearance index; RRF = residual renal function.

COX regression analysis of overall survival rate of PD patients

Univariate Cox regression analysis showed that presence of diabetes, older age and presence of cardiovascular complications were risk factors for mortality in PD patients (Table 2).

Multivariate Cox regression analysis showed that after adjusting for age and presence of cardiovascular complications, DM was not related to survival rate, while advanced age and combination of cardiovascular complications were independent risk factors affecting survival rate (Table 4).

	Time to death	
	HR (95%CI)	P
Diabetes (present vs absent)	1.631(0.903, 2.947)	0.105
Ages (years)	1.051 (1.028, 1.074)	0.001
Cardiovascular comorbidity (present vs absent)	0.339 (0.189, 0.609)	0.001

Table 4: Multivariable analysis of parameters associated with mortality.
CI = confidence interval; HR = hazard ratio.

Discussion

With the rapid development of China's economy, aging of the population is increasing along with the incidence of DM. A recent survey found that in Northern China, the overall prevalence of DM in 1992 was lower than that in 2011. The prevalence of DM in the male population in 2011 was 5.2 times higher than that in 1992 (10.5 vs. 1.7%), and that in the female population was nearly 4.3 times higher than that in 1992 (11.2 vs. 2.1%)[9]. Another survey showed that from 2009 to 2016, the overall prevalence of pre-diabetes and DM increased from 8.4% and 7.7% to 19.0% and 9.5%, respectively in Southwest China(10). In recent decades, with the increasing incidence of DM, the incidence of DM-related nephropathy in the general and hospitalized populations has also increased[3]. After deterioration to ESRD, the choice of dialysis method is particularly important for DM patients. In this study, we found that there was no difference in technical survival rate between patients with DM and those without DM. After adjusting for age and presence of cardiovascular complications, DM was not associated with overall survival rate, suggesting that PD is also effective renal replacement therapy for DM patients.

We investigated 246 PD patients, including 50 (20.33%) with DM. The incidence of DM in the general population ranges from 9.5% to 11.6%(2,10). The incidence of DM in the PD patients in our study was higher than that in the general population. In our study, DM patients were older than N-DM patients, which may have been because of the higher incidence of DM in older patients[11]. Udo et al. found that with the same RRF, DM patients are more prone to hypoalbuminemia and hypervolemic load[12], which may be why DM patients are recommended to receive renal replacement therapy earlier than D-DM patients are. In our study, DM patients had better baseline RRF than N-DM patients, which was consistent with the European practice guidelines(5). Previous reports show that, compared to N-DM PD patients, DM PD patients have higher incidence of cardiovascular complications[6, 13, 14].

The incidence of cardiovascular complications in our DM group was higher, but not significantly. This may be because patients began PD treatment with poor RRF in our study and both groups of patients had high incidence of cardiovascular complications. At the end of follow-up, 15 patients in the DM group (88.23%) and 29 in the N-DM group (76.32%) died of cardiovascular and cerebrovascular events. The main causes of death in the two groups were cardiovascular and cerebrovascular events, consistent with previous studies[15]. Kaplan-Meier analysis showed that DM patients had similar survival rate to N-DM patients, although DM patients were older. Cox regression analysis showed that male sex, episodes of peritonitis in the first year, high 4h D/PCr and low RRF Kt/V were independent risk factors affecting technical survival rate of PD patients, and DM was not related to technical survival rate.

Kitterer et al. found that the technical survival rate of female PD patients is significantly higher than that of male patients, which is consistent with the results of ourstudy[16]. The reason may be that female patients are smaller in size and eat less, so it is easier for them to maintain PD sufficiency[17, 18]. See et al. found that patients with early-onset peritonitis had a high PD withdrawal rate[19]. Prevention and appropriate treatment of peritonitis are key to long-term success of PD[20]. Hong et al. concluded that peritoneal transport function affects the technical survival rate of PD patients, and patients with high transport function are often prone to ultrafiltration failure, leading to withdrawal from PD[21, 22]. In addition, RRF Kt/V represents the RRF of PD patients, and better RRF can maintain better PD sufficiency[23]. According to the American database of kidney diseases (2011), the 1-year, 3-year and 5-year survival rates of PD patients with DM were 87.4%, 54.9% and 34.8% respectively[1]. In this study, the survival rate of PD patients with DM was higher than that in the USA 10 years ago, which may be related to the improvement of PD technology[24]. Kaplan–Meier analysis showed that the survival rate of the DM group was lower than that of the N-DM group. Univariate Cox regression analysis showed that DM, older age and cardiovascular complications were risk factors for mortality in PD patients. However, multivariable Cox regression analysis found that after adjusting for age and cardiovascular complications, DM was not correlated with prognosis of PD patients, and age and cardiovascular complications were independent risk factors for mortality in PD patients. The lower survival rate in DM patients may be caused by advanced age and higher incidence of cardiovascular complications[25, 26].

This study had some limitations. First, this was a single-center study, which may have had sample selection errors. The numeric gap between DM patients and N-DM patients is too large and the sample size needs to be expanded. Second, the use of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers and diuretic drugs was not recorded during follow-up.

Conclusion

We found that there was no difference in technical survival rate between DM and N-DMPD patients. After adjusting for age and cardiovascular complications, DM was not associated with mortality. PD may be an effective alternative therapy for DM patients with ESRD.

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