Int J Clin Exp Med 2019;12(9):11825-11830
www.ijcem.com /ISSN:1940-5901/IJCEM0095896

Original Article

Higher serum cholesterol and neutrophil-to-lymphocyte ratio at dialysis initiation are risk factors for technique failure among patients undergoing peritoneal dialysis

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Received April 23, 2019; Accepted July 4, 2019; Epub September 15, 2019; Published September 30, 2019

Abstract: Background: Technique failure is the main factor responsible for delaying the advancement of peritoneal dialysis (PD). Therefore, this retrospective study was conducted to evaluate the relationship between technique failure and patient characteristics at the initiation of PD. Methods: Seventy-six patients with end stage renal disease in whom PD was initiated at the Wujin Hospital affiliated with Jiangsu University were consecutively enrolled. Participants were followed up for at least 2 years after receiving PD catheter insertion. These participants were monitored for development of technique failure or death during the period of follow-up. Results: The number of patients who died within 2 years of PD initiation was 13 patients (17.11%), while 56.58% of patients survived for more than 2 years without technique failure. In univariate Cox regression analysis, male sex, positive diabetes mellitus status, and high body mass index, serum total cholesterol (TC), and neutrophil-to-lymphocyte ratio (NLR) at the initiation of PD were significantly associated with a higher risk of developing technique failure (all $P < 0.05$). Multivariate Cox regression analysis showed that a high TC level (> 200 mg/dL) and NLR at PD initiation were independent predictors of technique failure during the follow up period. Conclusions: In conclusion, high serum TC level and NLR at PD initiation predicts a significantly higher risk of developing technique failure among patients undergoing PD.

Keywords: Peritoneal dialysis, technique failure, technique survival

Introduction

Peritoneal dialysis (PD) is one of the renal replacement therapy (RRT) modalities for patients with end-stage renal disease (ESRD). This therapy is renowned for its economic advantage compared to the cost of other RRT options. In many countries, the "PD first" policy has become increasingly popular [1, 2]. Technique failure remains an important factor that delays the advancement of PD. Consequently, improving technique survival is an important approach for the advancement of PD care among patients under chronic PD.

Previous studies have attempted to identify early predictors of technique failure after PD initiation with the hopes of addressing these risk factors through treatment [3-6]. Findings from these studies suggest that clinical characteristics including a younger age, a female sex, a negative diabetes status, a lower body mass index (BMI), a lower incidence of peritonitis, and normal serum uric acid and albumin levels are predictors of a longer survival time following PD initiation [3-6]. However, these factors have been assessed after the initiation of PD, and factors that influence the risk before the initiation of PD have been less well addressed.

Not all patients with ESRD are suitable candidates for PD, except those with contraindications to PD. Early technique failure is often encountered within one year after PD initiation and modality transfer to hemodialysis (HD) in patients that do not have contraindications to PD. This may be related to peritoneal membrane failure. If risk factors for technique failure could be identified in these patients prior to the initiation of PD, then unnecessary PD catheterization could be avoided. It was hypothesized that risk factors for technique failure existed prior to the initiation of PD. Therefore, a retrospective study was conducted to evaluate

Table 1. Demographic data and clinical outcomes

Characteristics	Data
Number	76
Sex (men:women)	42:34
Age (years)	54.84±14.20
Origin of ESRD [n (%)]	
Glomerulonephritis	45 (59.21)
Diabetic nephropathy	17 (22.37)
Hypertension	11 (14.47)
Other causes	3 (3.95)
Death within 2 years [n (%)]	13 (17.11)
Technique survival over 2 years [n (%)]	43 (56.58)

the relationship between patient characteristics before the initiation of PD and their subsequent risk of developing technique failure.

Materials and methods

Inclusion and exclusion criteria for patient enrollment

Patients with ESRD in whom PD was initiated between July 2011 and February 2017 at the Wujin Hospital affiliated with Jiangsu University were retrospectively and consecutively identified, after excluding those who subsequently received renal transplantation. The current study was approved by the Ethics Review Board of the Wujin Hospital affiliated with Jiangsu University.

PD catheter implantations were uniformly performed by one of the authors of this study (Li-feng GONG). Participants underwent straight Tenckhoff catheters implantation under spinal anesthesia using an open approach. The PD dialysates used in this hospital included 1.5% or 2.5% glucose-containing formulae (PD-4, Baxter, America).

PD training program before and after PD initiation

All participants that received PD were trained by a nursing team at the Wujin Hospital affiliated with Jiangsu University. The training program was started before catheter implantation and included preoperative simulation of the PD operation, preparation of the utilities and environment, education wound care, including how to bathe the site and details of an appropriate diet and lifestyle, as well as management of emergent situations. Each participant practiced dialysate exchange under the guidance of the nursing team, beginning 5 to 7 days after the PD catheter implantation. Participants were discharged after completing the PD technical examination.

Data collection

Clinical parameters were recorded, including all laboratory examination results and image findings from the emergency and in-patient medical records using the hospital electronic medical record system. Each patient was followed up for at least 2 years after catheterization. Participants were monitored for development of technique failure or death during the follow-up period. All variables were recorded at the initiation of PD, including age, sex, the origin of ESRD, BMI, serum total cholesterol (TC), neutrophil-to-lymphocyte ratio (NLR), white blood cell (WBC) count, neutrophil count, lymphocyte count, as well as uric acid (UA), hemoglobin (Hb), albumin (Alb), and total calcium (Ca) levels.

Technique failure was defined as the transition from PD to HD due to failed peritoneal membrane function, the development of death, catheter dysfunction or peritonitis. Failed peritoneal membrane function was defined as an ultrafiltration volume less than 100 mL using a 2.5% glucose dialysate or an ultrafiltration volume less than -400 mL using a 1.5% glucose dialysate after 4 hours of indwelling.

Statistical analysis

SPSS version 19.0 was used to analyze the collected data. Continuous data are described as mean ± standard deviation. Cox regression analyses were used to examine the relationship between the clinical features of the patients at PD initiation and the risk of developing technique failure, and between the complications arising during PD and the risk of technique failure. A P value < 0.05 was considered to be statistically significant.

Results

Demographic profile of participants

Seventy-eight patients that underwent PD initiation at our hospital were identified for inclu-

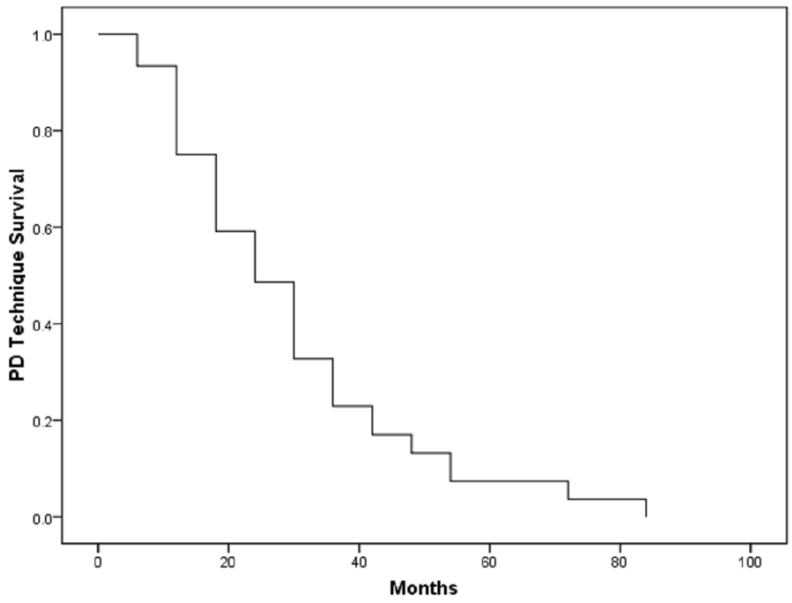

Figure 1. Technique failure-free survival curves.

sion in this study. Among these patients, two were subsequently excluded due to transfer to renal transplantation. Finally, the data from 76 patients were analyzed in the current study, including 42 men and 34 women, with an average age of 54.84±14.20 years (**Table 1**). The origin of ESRD in these participants is shown in **Table 1**.

Regression analysis examining the relationship between technique failure and patient characteristics

The patients were then observed for a follow-up period of 2 years. Within this period, 13 patients (17.11%) died and technique survival was observed in 43 patients (56.58%; **Table 1**). The technique failure-free survival curves are shown in **Figure 1**. Univariate analyses showed that, at the initiation of PD, being male, being positive for diabetes, having a high BMI, TC level, or NLR were significantly associated with a higher risk of technique failure ($P < 0.05$; **Table 2**). Conversely, age, WBC, neutrophil and lymphocyte counts, and UA, Hb, Alb, and Ca levels were not found to be significant risk factors for the development of technique failure (**Table 2**). Multivariate Cox regression analyses showed that, at PD initiation, a high TC level (> 200 mg/dL) or NLR were both independent predictors of the development of technique failure during the follow-up period (**Table 2**).

Regression analysis examining the relationship between technique failure and PD complications

Additionally, the relationship between PD complications and the risk of technique failure was examined (**Table 3**). The overall incidence of peritonitis was 0.036 episodes per patient-month during the follow-up period (**Table 3**). Univariate Cox regression analyses showed that the presence or absence of peritonitis, the number of prior incidences of peritonitis, tunnel infection, and catheter tip migration failed to exhibit an association with technique failure (**Table 3**).

Discussion

In this study, it was found that at PD initiation, a high TC level was an independent predictor of developing technique failure during the follow-up period, with an increased risk more than 2-fold higher than observed in participants with TC levels within the normal range (150-200 mg/dL; **Table 2**). The cholesterol hypothesis suggests that elevated levels of serum TC can lead to atherosclerosis and increase the risk of the development of stroke, heart disease, and peripheral vascular disease [7, 8]. Prior studies have also examined the relationship between the level of TC, mortality and cardiovascular disease (CVD) in ESRD patients. However, few studies have focused on the relationship between the level of TC and technique survival in patients receiving PD. Lin et al. reported that TC levels > 285 mg/dL and < 120 mg/dL were both associated with an increased risk of mortality among PD patients [9]. However, Lim et al. observed that high levels of TC might have a protective effect against CVD in patients receiving HD or PD [10]. In this study, a high level of TC (> 200 mg/dL) at PD initiation was an independent predictor of the development of technique failure. This association may result from the damage to peritoneal transport function that originates from injured peritoneal arterioles in relation to high cholesterol levels. Cu-

Table 2. Cox Regression Analysis of the Relationship between Technique Failure and Patient Characteristics at the initiation of PD

Characteristic		Value	Univariate			Multivariate		
			HR	95% CI	*P*	HR	95% CI	*P*
Sex	Male [n (%)]	42 (55.26)	1.789	1.085-2.948	0.023	1.342	0.778-2.317	0.291
	Female [n (%)]	34 (44.74)	Reference			Reference		
Age (years)		54.84±14.20	0.999	0.982-1.015	0.878			
BMI (kg/m^2)		23.45±3.55	1.112	1.034-1.196	0.004	1.085	0.983-1.197	0.105
Disease	Diabetes [n (%)]	24 (31.58)	1.749	1.042-2.936	0.035	1.043	0.519-2.098	0.905
	Non-diabetes [n (%)]	52 (68.42)	Reference			Reference		
TC (mg/dl)	> 200 [n (%)]	20 (26.32)	2.041	1.091-3.818	0.026	2.526	1.293-4.933	0.007
	< 150 [n (%)]	19 (25.00)	1.430	0.752-2.717	0.275	1.223	0.615-2.431	0.565
	150-200 [n (%)]	37 (48.68)	Reference			Reference		
NLR		5.27±3.95	1.129	1.042-1.224	0.003	1.107	1.019-1.202	0.016
WBC (10^9/L)		6.82±2.73	1.066	0.985-1.155	0.113			
N (10^9/L)		5.05±2.24	1.090	0.990-1.200	0.078			
L (10^9/L)		1.13±0.48	1.120	0.621-2.022	0.706			
UA (mg/dL)	> 10 [n (%)]	38 (50.00)	1.160	0.648-2.078	0.617			
	< 7 [n (%)]	5 (6.58)	0.535	0.125-2.290	0.399			
	7-10 [n (%)]	33 (43.32)	Reference					
Hb (g/dL)		7.91±1.70	1.006	0.993-1.020	0.369			
Alb (g/L)		34.95±4.66	1.003	0.950-1.060	0.902			
Ca (mmol/L)		2.10±0.30	0.710	0.303-1.661	0.430			
P (mmol/L)		2.19±0.60	0.997	0.679-1.465	0.989			
Alp (mmol/L)		106.09±89.71	1.003	0.999-1.008	0.121			

HR: Hazard ratio; CI: Confidence interval; TC: Serum total cholesterol; NLR: neutrophil-to-lymphocyte ratio; WBC: Leukocyte count; N: Neutrophil count; L: Lymphocyte count; UA: Serum uric acid; Hb: Hemoglobin; Alb: Serum albumin; Ca: Serum total calcium; P: Serum phosphorus; Alp: Serum alkaline phosphatase.

Table 3. Cox regression analysis of the relationship between technique failure and PD complications

Complications		Data	Univariate		
			HR	95% CI	*P*
Peritonitis [n (%)]		40 (52.63)	1.505	0.920-1.401	0.103
Number of peritonitis episodes	4 [n (%)]	4 (5.26)	2.292	0.797-6.593	0.124
	3 [n (%)]	5 (6.58)	1.223	0.471-3.171	0.679
	2 [n (%)]	5 (6.58)	1.119	0.431-2.904	0.817
	1 [n (%)]	26 (34.21)	1.625	0.929-2.843	0.089
	0 [n (%)]	36 (47.37)	Reference		
Tunnel infection [n (%)]		8 (10.53)	1.027	0.467-2.260	0.947
Catheter tip migration [n (%)]		8 (10.53)	1.817	0.819-4.028	0.142

The overall rate of peritonitis was 0.036 episodes per patient-month. HR: Hazard ratio; CI: Confidence interval.

rrent studies are exploring the mechanisms underlying this relationship.

In this study, a high NLR was another independent predictor of technique failure at PD initiation. NLR is widely regarded as a marker of subclinical inflammation, and a high NLR has been found to be an independent predictor of mortality in patients undergoing angiography or cardiac revascularization [11]. An increased NLR is also a poor prognostic factor in patients with various cancers [12]. This is also the case for PD patients; Lu et al. found that a high NLR predicted greater cardiovascular and all-cause mortality among patients receiving PD [13]. Turkmen et al. showed that a high NLR could predict a higher risk of vascular calcification among patients receiving PD or HD [14]. Pineault et al. discovered that the NLR could be a good marker for inflammation among patients

receiving PD or HD [15]. However, few existing studies have focused on the relationship between the NLR and technique survival. In this study, a high NLR was found to be independently associated with a higher risk of technique failure. However, a threshold NLR that correlated with this observed increased risk could not be determined. Further studies are needed to confirm the clinical significance of NLR in patients receiving PD.

In this study, clinical characteristics at PD initiation, such as a male sex, diabetes, and a high BMI, were found to correlate with technique failure. Similar findings have been reported previously with regard to the relationship between these characteristics and mortality in patients with PD [3, 6]. In addition, the presence of peritonitis and the number of peritonitis episodes failed to correlate with the risk of technique failure. This is likely to be due to the fact that the frequency of peritonitis in the effected patients was low and that the sample size was relatively modest.

Based on these findings, the benefit of PD should be weighed against the higher risk of technique failure for ESRD patients with a high TC level (> 200 mg/dL) or a high NLR at the initiation of dialysis. The option of HD may prevent unnecessary PD catheterization for these patients, although further studies are still needed to determine whether HD is a better option than PD for these patients.

There are several limitations to this study. First, the relatively small number of participants may limit the generalizability of our findings, requiring larger scale studies for the confirmation of our findings. Second, the retrospective nature of this study also decreases the applicability of our results. There is thus an urgent need for studies comparing the outcomes of ESRD patients with these risk factors that receive HD to those that receive PD.

In conclusion, a higher serum TC level (> 200 mg/dL) and NLR at the initiation of PD are independent predictors of the development of technique failure during the follow up period in patients that receive PD.

Acknowledgements

This study was supported by Jiangsu University Medical Clinical Science and Technology Development Fund of China (JLY20160035) and Changzhou Wujin Science and Technology Bureau Fund of China (WS201610).

Disclosure of conflict of interest

None.

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