



## Original Article

# Effect of Social Support, Fatigue, and Depression on the Quality of Life of Patients Undergoing Peritoneal Dialysis

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**Purpose:** This study investigated the effects of social support, fatigue, and depression on the quality of life of patients undergoing peritoneal dialysis. **Methods:** This descriptive research included 130 patients undergoing peritoneal dialysis, who were treated in an artificial kidney room. Data were collected from June 2021 to August 2021, and a hierarchical multiple regression analysis was performed. **Results:** Social support, depression, and medical staff providing dialysis-related information were significant factors influencing the quality of life of patients undergoing peritoneal dialysis, and the explanatory power of the model was found to be 41%. Among the factors, social support ( $\beta=.52$ ) had the greatest impact on quality of life. **Conclusion:** The results of this study suggest the need to develop nursing interventions and educational programs that can improve the social support of patients with peritoneal dialysis and reduce depression, thereby improving their quality of life.

**Key Words:** Depression; Fatigue; Peritoneal dialysis; Quality of life; Social support

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## INTRODUCTION

As the society ages, the number of patients with diabetes and chronic kidney disease (CKD) are rapidly increasing, which often leads to end-stage renal disease (ESRD) [1]. According to the Korean Society of Nephrology's ESRD registration data, as of 2019, there were approximately 81,000 patients with end-stage renal disease, and 15,000 new patients appeared for treatment every year [2,3]. Additionally, according to the Korean Society of Nephrology criteria, if ESRD in chronic renal failure with a glomerular filtration rate (GFR) of less than 15 mL/min/1.73 m<sup>2</sup> persists for more than 2 years, lifelong renal replacement therapy (RRT) is required for survival [2,4]. RRT options include hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation, and are selected based on a comprehensive assessment of the needs and treatment of patients with CKD [2].

Among these, PD has the advantage of preserving residual kidney function for a long period of time because it offers convenience and ease of use owing to its slower solute removal rate compared to HD [2]; however, patients experience a psychological burden by managing dialysis on their own [5]. Hence, patients undergoing PD need social support to reduce their psychological burden. Social support plays an important role in buffering and relieving stress by deriving resources through interactions with others [6], and since patients with PD can only survive with lifelong treatment [2], social support and quality of life are important. Social support also increases treatment compliance through encouragement and hope in life [7].

A comprehensive analysis of psychiatric disorders in a large adult ESRD population found that 8.9% of the patients on dialysis were hospitalized with a primary or secondary psychiatric diagnosis. However, psychiatric information about patients with ESRD remains under-recognized in clinical practice [8].

PD patients experience fatigue due to the daily exchange of dialysate fluid, typically every 4~5 hours or at intervals of approximately 8-10 hours [9]. This fatigue can lead to peritonitis, a serious condition requiring antibiotic treatment and hospitalization, because neglecting the daily management of PD catheters can cause inflammation of the peritoneum, the thin membrane covering the abdominal cavity and its organs [10]. Patients with peritonitis often report physical and psychological stress, including negative thoughts, depression, anxiety, and sleep disturbances [11], impacting their quality of life.

Fatigue and depression are significant predictors, with depression particularly affecting treatment compliance,

increasing hospitalization rates due to complications, and substantially affecting both quality of life and survival rates [9-11]. Furthermore, patients with PD with catheters inserted into their abdomen may experience diminished body image and feelings of being different, leading to higher levels of depression and lower quality of life [5].

The number of PD patients in Korea is relatively small [2], and because they perform self-dialysis at home and visit the hospital once a month, there are fewer opportunities to see medical experts compared with patients of other renal replacement therapies [12]. Patients with PD perform dialysis at home, which results in limited access to healthcare and less interaction with healthcare providers [5], highlighting the need to identify factors affecting the quality of life. Therefore, this study aimed to analyze the impact of social support, fatigue, and depression on the quality of life of patients with PD and to seek ways to improve it. The results of this study can be used to develop individually tailored and systematic nursing interventions based on patient-centered care, thereby promoting the continuous participation of patients with PD in treatment.

## METHODS

### 1. Design

This descriptive study aimed to determine the levels of social support, fatigue, depression, and quality of life in patients with PD and to determine the relationship between these variables and their impact on quality of life.

### 2. Study Population and Sample Size

The study participants were patients receiving PD treatment in the artificial kidney ward of Y University Hospital, located in D Metropolitan City. The criteria for selecting the recipients were as follows: 1) Patients who had received PD for more than 3 months; 2) patients between 20 and 65 years of age; and 3) those who understood the purpose of this study and voluntarily provided written consent to participate.

The sample size in this study was based on a previous study that investigated the quality of life of patients undergoing dialysis [13]. The G\*power 3.1.9.4 program was used, with power .80, effect size .15, level of significance .05, number of predictors 10; thus the sample size was estimated to be 118 through hierarchical multiple regression analysis. Considering a 10% dropout rate, questionnaires were distributed to 132 patients, and a final analysis was

conducted on 130 people, excluding two people who dropped out.

### 3. Data Collection

Research participants were informed that the collected data would be used only for research purposes and would be stored for three years after the end of the research in accordance with the Bioethics Act, and that personal information would be destroyed in accordance with the Article 16 of the Enforcement Decree. The questionnaire was completed between June 11 and August 11, 2021. It took approximately 20~30 minutes to complete, and the participants received a small gift for their participation.

### 4. Research Tools

#### 1) Social support

This tool is used with permission from the tool developer. Social support was assessed using a tool developed by Kim for patients undergoing dialysis [6], used with the permission from the developer. This tool comprises 24 questions, divided equally between family and professional medical support. Responses are rated on a 5-point Likert scale ranging from “completely disagree” to “completely agree.” A higher score indicates a greater level of social support. The reliability of the instrument at the time of development was indicated by Cronbach’s  $\alpha = .94$  for family support and, Cronbach’s  $\alpha = .93$  for medical support. In this study, Cronbach’s  $\alpha$  for social support was .96.

#### 2) Fatigue

This tool is used with permission from the tool developer. Fatigue was measured using a fatigue measurement tool developed by Tack [14] and supplemented by Choi [15] for patients undergoing dialysis, and was used with the permission from the developer. The tool has 11 questions, including 8 questions on the effects of fatigue and 3 on the degree of fatigue. Responses are rated on a 10 points scale, with higher scores indicating greater fatigue. The reliability of the instrument at the time of development was Cronbach’s  $\alpha = .93$ . In the study by Choi [15], Cronbach’s  $\alpha = .93$ , and in this study, Cronbach’s  $\alpha = .93$ .

#### 3) Depression

This tool is used with permission from the tool developer. Depression was measured using the Korean version of the Beck Depression Inventory originally developed by Beck et al. [16], with and the Korean version adapted by

Kim et al. [17]. The tool was used with the permission from the developers. The depression scale consists of 21 questions on a 4-point scale, and the measurement score ranges from 0 to 63, with higher scores indicating a higher degree of depression. At the time of development, the Cronbach’s  $\alpha$  of the instrument was .86, indicating the reliability of the tool. According to Kim et al.’s study [17], Cronbach’s  $\alpha$  was .89, and in this study, Cronbach’s  $\alpha$  was .94.

#### 4) Quality of life

This tool is used with permission from the tool developer. Quality of life was assessed using a tool developed by Bang [18] for patients undergoing dialysis, which was later modified and supplemented by Kim [6]. This tool was used with permission from the developer. It comprises 41 questions covering various domains including emotional state, social activities, physical symptoms, family relationships, economic status, attitude toward life, and health awareness. Some questions are reversed for scoring purposes. Responses are rated on a 5-point Likert scale ranging from “never” to “always,” with higher scores indicating a better quality of life. The tool demonstrated high reliability during development, with Cronbach’s  $\alpha = .94$ . In Kim’s study [6], the reliability remained high at .94, while in this study, it was further validated with Cronbach’s  $\alpha = .96$ .

### 5. Ethical Considerations

This study was approved by the K University Institutional Review Board (IRB No.: 40525-202103-HR-002-02) before data collection to ensure the protection of research participants. The data were collected between June 11 and August 11, 2021. The research plan was submitted to and approved by the head and manager of the nursing department of a university hospital in Metropolitan City D that has more than 1,000 beds. The researcher explained the purpose, method, and data collection procedures to the participants, obtained their written consent, and collected data using a questionnaire. The participants completed the questionnaire directly, with assistance provided when necessary.

### 6. Data Analysis

The collected data were analyzed using SPSS software (version 27.0; IBM Corp.). Participants’ general and treatment-related characteristics, social support, fatigue, depression, and quality of life were analyzed using descriptive statistics. Differences in quality of life according to the

participants' general characteristics were analyzed using the t-test and analysis of variance (ANOVA), and the Scheffé test was used as a post-hoc test. The correlation between the participants' social support, fatigue, depression, and quality of life was analyzed using the Pearson correlation coefficient. Hierarchical multiple regression analysis was used to determine the impact of social support, fatigue, and depression on quality of life.

## RESULTS

### 1. Participants' General Characteristics

The participants' characteristics are shown in Table 1. There were 71 men (54.6%) and 59 women (45.4%), and the age group of 50~59 years was the largest at 55 years (42.3%). The highest level of education was college gradu-

ation or higher (n=58; 44.6%), 103 participants (79.2%) were religious, 103 (79.2%) were unemployed, and 58 (44.6%) had an average monthly family income of less than one million won. There were a lot.

Treatment-related characteristics included 67 patients (51.5%) who had been on dialysis for more than 3 years, 54 patients (41.5%) who had been hospitalized 3~4 times due to dialysis with infection of the catheter used during dialysis in 50 patients (38.5%). The number of nurses providing services was the largest, at 66 (50.8%).

### 2. Participants' Level of Social Support, Fatigue, Depression and Quality of Life

The participants' social support, fatigue, depression, and quality of life are shown in Table 2. Out of 5 points, participants' social support was  $2.87 \pm 0.86$ , and the sub-

**Table 1.** Participants' General Characteristics

(N=130)

Variables	Characteristics	Categories	n (%)
General characteristics	Gender	Men	71 (54.6)
		Women	59 (45.4)
	Age (year)	< 50	54 (41.5)
		50~59	55 (42.3)
		≥ 60	21 (16.2)
	Education	Middle school graduate	30 (23.1)
		High school graduate	42 (32.3)
		University graduate	58 (44.6)
	Religion	Yes	103 (79.2)
		No	27 (20.8)
Economic activity	Yes	27 (20.8)	
	No	103 (79.2)	
Monthly family income (10,000 won)	< 100	58 (44.6)	
	100~200	32 (24.6)	
	> 200	40 (30.8)	
Treatment characteristics	Peritoneal dialysis duration (year)	< 3	63 (48.5)
		≥ 3	67 (51.5)
	Dialysis related hospitalization (no. of times)	1~2	40 (30.8)
		3~4	54 (41.5)
		≥ 5	36 (27.7)
	Reason for hospitalization	Dialysis catheter infection	50 (38.5)
		Dyspnea of pulmonary edema	30 (23.1)
		Cardiovascular disease	25 (19.2)
		Hyperkalemia	13 (10.0)
		Hypertension and hypotonia	12 (9.2)
Dialysis information provider	Nurse	66 (50.8)	
	Doctor	46 (35.4)	
	Others <sup>†</sup>	18 (13.8)	

<sup>†</sup>Self-help organizations, internet, books.

**Table 2.** Participants' Level of Social Support, Fatigue, Depression, and Quality of Life

(N=130)

Variables	M±SD	Minimum	Maximum	Range
<b>Social support</b>				
Family support	2.83±0.91	1.00	5.00	
Medical personnel support	2.92±0.86	1.00	5.00	
Total	2.87±0.86	1.00	5.00	1~5
<b>Fatigue</b>				
Fatigue effects	4.34±1.73	2.00	8.00	
Fatigue level	4.53±1.72	2.00	8.00	
Total	4.48±1.68	2.00	8.00	1~10
<b>Depression</b>				
Normal	4.64±4.13	0	40	
Mild depression	16.25±1.60	0	40	
Severe depression	22.57±2.10	0	40	
Highly depression	33.46±3.28	0	40	
Total	13.41±12.26	0	40	0~63
<b>QOL</b>				
Emotional state	2.56±0.85	1	4	
Social activity	2.68±0.85	1	4	
Physical symptoms	2.68±0.66	1	4	
Family relations and economic conditions	2.61±0.81	1	4	
Attitude of life	2.60±0.77	1	4	
Health awareness	2.55±0.71	1	4	
Total	2.61±0.70	1	4	1~5

M=mean; SD=standard deviation; QOL=quality of life.

areas of family support was  $2.83 \pm 0.91$  and medical staff support was  $2.92 \pm 0.86$ . Participants' fatigue score was  $4.48 \pm 1.68$  points out of 10, the fatigue effect was  $4.34 \pm 1.73$ , and fatigue level was  $4.53 \pm 1.72$ . Participants' depression score was  $13.41 \pm 12.26$  out of 63 points, while quality of life was  $2.61 \pm 0.70$  points out of 5. The scores for the sub-domains of quality of life included: emotional state= $2.56 \pm 0.85$  points, social activities= $2.68 \pm 0.85$  points, physical symptoms= $2.68 \pm 0.66$  points, family relationships and economic status= $2.61 \pm 0.81$  points, attitude toward life= $2.60 \pm 0.77$  points, and awareness of health was  $2.55 \pm 0.71$  points.

### 3. Differences in Quality of Life by Participants' General Characteristics

Table 3 shows the differences in the quality of life according to the participants' general characteristics. There was a difference in quality of life in terms of age ( $F=3.60$ ,  $p=.030$ ), highest education level ( $F=3.40$ ,  $p=.037$ ), religion ( $t=4.26$ ,  $p<.001$ ), and average monthly household income ( $F=3.32$ ,  $p=.039$ ). In terms of treatment-related characteristics, there appeared to be differences in quality of life depending on the number of hospitalizations due to dialysis ( $F=11.46$ ,  $p<.001$ ) and the source of dialysis information

( $F=10.12$ ,  $p<.001$ ). According to the Scheffé test, quality of life was higher for those over 50 years than for those between 50~59 years and over 60 years. Those with education levels of college graduate or higher had a higher quality of life compared to high school graduates or middle school graduate or lower. Those with an average monthly household income of 2 million won or more had a higher quality of life than those with less than 1 million to 2 million won or less than 1 million won. Among treatment-related characteristics, the quality of life was higher in the those hospitalized due to dialysis one to two times than those hospitalized three to four times or five or more times. Those with nurses as their source of dialysis information showed a higher quality of life than those whose source were doctors and others (Internet, books, self-help groups).

### 4. Correlation between Participants' Social Support, fatigue, Depression, and Quality of Life

Table 4 shows the correlations among participants' social support, fatigue, depression, and quality of life. Quality of life was significantly correlated with social support ( $r=.82$ ,  $p<.001$ ), fatigue ( $r=-.74$ ,  $p<.001$ ), and depression ( $r=-.72$ ,  $p<.001$ ).

**Table 3.** Differences in Quality of Life According to Participants' General Characteristics

(N=130)

Variables	Characteristics	Categories	QOL		
			n (%)	M±SD	t or F (p) Scheffé
General characteristics	Gender	Men	71 (54.6)	2.58±0.73	-0.47 (.640)
		Women	59 (45.4)	2.64±0.67	
	Age (year)	< 50 <sup>a</sup>	54 (41.5)	2.76±0.71	3.60
		50~59 <sup>b</sup>	55 (42.3)	2.42±0.70	(.030)
		≥ 60 <sup>c</sup>	21 (16.2)	2.72±0.63	a, c > b
	Education	University graduate <sup>a</sup>	58 (44.6)	2.77±0.66	3.40
		High school graduate <sup>b</sup>	42 (32.3)	2.53±0.67	(.037)
		Middle school graduate <sup>c</sup>	30 (23.1)	2.39±0.77	a > c
	Religion	Yes	103 (79.2)	2.73±0.68	4.26
		No	27 (20.8)	2.13±0.60	(< .001)
Economic activity	Yes	27 (20.8)	2.36±0.66	-2.04	
	No	103 (79.2)	2.67±0.71	(.430)	
Family income (10,000 won/month)	< 100 <sup>a</sup>	58 (44.6)	2.45±0.70	3.32	
	100~200 <sup>b</sup>	32 (24.6)	2.63±0.74	(.039)	
	> 200 <sup>c</sup>	40 (30.8)	2.82±0.63	a < c	
Treatment characteristics	Peritoneal dialysis duration (year)	< 3	63 (48.5)	2.59±0.69	-0.29
		≥ 3	67 (51.5)	2.63±0.72	(.773)
	Dialysis related hospitalization (no. of times)	1~2 <sup>a</sup>	40 (30.8)	2.88±0.64	11.46
		3~4 <sup>b</sup>	54 (41.5)	2.69±0.66	(< .001)
		≥ 5 <sup>c</sup>	36 (27.7)	2.18±0.66	a > c
	Reason for hospitalization	Dialysis catheter infection	50 (38.5)	2.70±0.65	1.69
		Dyspnea of pulmonary edema	30 (23.1)	2.49±0.71	(.157)
		Cardiovascular disease	25 (19.2)	2.79±0.69	
		Hyperkalemia	13 (10.0)	2.51±0.90	
		Hypertension and hypotonia	12 (9.2)	2.25±0.59	
Dialysis information provider	Nurse <sup>a</sup>	66 (50.8)	2.82±0.67	10.12	
	Doctor <sup>b</sup>	46 (35.4)	2.51±0.68	(< .001)	
	Others <sup>c†</sup>	18 (13.8)	2.06±0.54	a > c	

M=mean; QOL= Quality of life; SD=standard deviation; †Self-help organizations, internet, books.

**Table 4.** Correlations between Participants' Social Support, Fatigue, Depression, and Quality of Life

(N=130)

Variables	Social support	Fatigue	Depression	QOL
	r (p)	r (p)	r (p)	r (p)
Social support	1			
Fatigue	-.74 (< .001)	1		
Depression	-.72 (< .001)	.76 (< .001)	1	
QOL	.82 (< .001)	-.75 (< .001)	-.71 (< .001)	1

QOL= Quality of life.

## 5. Impact on Participants' Quality of Life

This study used hierarchical multiple regression analysis to identify the factors influencing quality of life in pa-

tients with PD (Table 5). Age, highest education level, religion, average monthly household income, frequency of hospitalization for dialysis, and source of dialysis information were treated as categorical variables. Age, educa-

**Table 5.** Impact on Participants' Quality of Life

(N=130)

Variables	Categories	Model I					Model II				
		B	SE	$\beta$	t	p	B	SE	$\beta$	t	p
Age (year)	< 50	0.10	0.17	.07	0.61	.545	0.15	0.10	.11	1.45	.149
	50~59	-0.27	0.16	-.19	-1.77	.080	-0.10	0.10	-.07	-1.01	.314
	≥ 60 (ref.)										
Education	Middle school graduate	0.12	0.18	.07	0.63	.530	-0.09	0.11	-.05	-0.80	.427
	High school graduate	0.14	0.13	.09	1.01	.313	0.06	0.08	.04	0.72	.471
	University graduate (ref.)										
Religion	Yes	0.54	0.14	.31	3.90	< .001	0.04	0.09	.02	0.44	.657
	No (ref.)										
Family income (10,000 won/month)	< 100	-0.18	0.15	-.13	-1.21	.228	0.04	0.09	.03	0.49	.627
	≥ 100~200	-0.20	0.15	-.12	-1.35	.180	-0.05	0.09	-.03	-0.50	.620
	> 200 (ref.)										
Dialysis related hospitalization (no. of times)	1~2	0.40	0.16	.26	2.44	.016	0.01	0.11	.01	0.13	.895
	3~4	0.29	0.14	.20	2.04	.043	0.01	0.09	.01	0.09	.931
	≥ 5 (ref.)										
Dialysis information provider	Nurse	0.71	0.17	.51	4.27	< .001	0.32	0.11	.23	2.83	.005
	Doctor	0.51	0.17	.35	2.97	.004	0.24	0.11	.16	2.13	.035
	Others (ref.)										
Social support						0.42	0.06	.52	6.81	< .001	
Fatigue							-0.05	0.04	-.11	-1.33	.187
Depression							-0.01	< .001	-.23	-2.90	.004
		Adj. R <sup>2</sup> =.33 F=6.65, p < .001					Adj. R <sup>2</sup> =.74, ΔAdj. R <sup>2</sup> =.41 F=27.66, p < .001				

SE=Standard error.

tion level, religion, income, frequency of hospitalization, and dialysis information sources had a significant impact on the quality of life of patients undergoing dialysis and were entered into Model I. In Model II, the independent variables were introduced to determine their impact on the research results.

As a result of the regression analysis assumption test, the autocorrelation of the errors tested using the Durbin-Watson test was 1.93, which was larger than the test statistic, indicating that there was no autocorrelation. As a result of multicollinearity verification, the tolerance limit for Model I was .37-.81, and for Model II, it was .28-.68, which is over 0.1. The variance inflation factor (VIF) values were 1.24~2.67 for Model I and 1.47~3.54 for Model II, which did not exceed 10, indicating no problem with multicollinearity. In the second step (Model II), social support, fatigue, and depression, which correlated with quality of life, were added, and the sources of dialysis information were nurses (B=0.32, p=.005) and doctors (B=0.24, p=.035), while social support (B=0.42, p<.001) and depres-

sion (B=-0.01, p=.004) had a significant effect on quality of life. Therefore, factors affecting quality of life were social support ( $\beta=.52$ ,  $p<.001$ ), depression ( $\beta=-.23$ ,  $p=.004$ ), and nurses as dialysis information source ( $\beta=.23$ ,  $p=.005$ ) followed by doctors ( $\beta=.16$ ,  $p=.035$ ). The adjusted coefficient of determination (adjusted R<sup>2</sup>), which indicates the explanatory power of the model, was 33% in Model I and 74% in Model II, and the explanatory power increased significantly with the change in adjusted R<sup>2</sup>.

## DISCUSSION

In this study, we attempted to determine the impact on the quality of life of patients with peritoneal dialysis and provide basic data for the development and implementation of nursing intervention programs to strengthen the factors affecting their quality of life.

Among the sub-domains of quality of life, social support scored the highest, with treatment time and daily life restrictions being less severe compared to in other renal

replacement therapies [10,19,20]. Social support significantly influences quality of life through satisfaction with relationships, confidence, and adaptation to environmental changes [6,7]. Strengthening social support, including emotional and material support from family and medical staff [21], can have a positive impact on quality of life of patients. However, relying solely on family support can be insufficient and burdensome. Therefore, a holistic approach that integrates medical, psychological, and emotional support is required. Collaboration between health-care facilities, human services agencies, and the community is essential to establish self-help groups and community networks and ensure effective strategies to maintain a high quality of life for patients with PD.

This study also found that depression affected patients' quality of life, which is similar to the results of previous studies [22]. Depression is a negative emotion experienced by patients with PD who require lifelong dialysis. It interferes with role performance, exposes them to various complications due to non-compliance with dialysis treatment, and even threatens life [21,23]. Therefore, medical professionals must understand patients' depression, identify ways to relieve negative emotions and stress, and intervene accordingly. In addition, we suggest that medical staff working in PD wards conduct systematic research, such as analyzing depression in patients with PD.

This study showed that patients with PD obtain their dialysis-related information primarily from nurses or doctors, which significantly affects their quality of life. This showed the importance of medical professionals continuously providing dialysis-related information and forming trusting relationships with their patients [6,7,24]. Meanwhile, this study did not analyze fatigue as a factor affecting quality of life. Although there are no studies directly comparing the relationship between fatigue and quality of life, Table 4 shows a negative correlation between higher levels of fatigue and quality of life. To identify factors affecting quality of life, variables that showed significant results were included in the analysis. It was found that general characteristics influenced fatigue, resulting in fatigue not being significant in affecting quality of life. Therefore, follow-up research is needed to better understand the relationship between fatigue and quality of life.

Healthcare providers need to discuss treatment processes, support decision-making, and explore ways to ease treatment burdens and enhance quality of life. However, the study recognizes limitations, such as the need for better measurement tools to assess quality of life and broader generalization of the findings. Future research should con-

sider various diseases and treatment characteristics to better understand the factors affecting the quality of life of patients with PD.

## CONCLUSION

This descriptive study aimed to determine the impact of social support, fatigue, and depression on quality of life in 130 patients with PD. Social support, depression, and medical staff providing dialysis-related information were significant influencing factors affecting the quality of life of patients with PD. The study findings suggest that it is important for medical professionals to specifically understand the social support resources and depression levels of patients with PD and provide treatment assistance tailored to the patient's characteristics. It is also necessary to understand the treatment characteristics and living environments of patients with PD, establish a customized system for each individual, and ensure continuous treatment intervention efforts. Thus, quality of life of patients with PD must be focused on through factor analysis and program development and application to provide a positive quality of life.

## CONFLICTS OF INTEREST

The authors declared no conflict of interest.

## AUTHORSHIP

Study conception and design acquisition -

## DATA AVAILABILITY

Please contact the corresponding author for data availability.

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