RESEARCH ARTICLE

Spiritual well-being of patients with chronic renal failure: A cross-sectional study

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Abstract

Aims: The study aimed to investigate the relationship among physical symptom distress, sleep quality, depression and spiritual well-being of patients with chronic renal failure (CRF) and analyse the predictors of the spiritual well-being.

Design: A cross-sectional study.

Methods: A total of 188 patients were selected. The collection tools were the Physical Symptom Distress Scale, the Chinese version of PSQI, the Geriatric Depression Scale and the Spiritual Well-Being Scale. Hierarchical regression analysis was conducted using SPSS 20.0.

Results: Patients with different treatments exhibited significantly different physical symptom distress. Furthermore, spiritual well-being was significantly negatively correlated with physical symptom distress, poor sleep disturbances and depression. After controlling for the variables, sleep quality and haemodialysis treatment were the key predictors of spiritual well-being.

Conclusion: To achieve holistic caregiving for patients' physiological, psychological and spiritual health, Nurses should evaluate patients' symptom distress and depression when providing care for these patients to enhance their spiritual well-being.

KEYWORDS

chronic renal failure, depression, nursing, physical symptom distress, sleep quality, spiritual well-being

1 | INTRODUCTION

The population of patients with chronic renal failure (CRF) has rapidly increased with the increasing prevalence of chronic kidney diseases worldwide. According to the international rankings for uraemia reported in the 2018 Annual Report of the United States Renal Data System (Saran et al., 2019), Taiwan has the highest rate of kidney dialysis worldwide. The 2018 Annual Report on Kidney Disease in Taiwan revealed that the prevalence of dialysis in Taiwan has increased in recent years. Nephrotic syndromes and nephropathy rank

ninth among the 10 leading causes of death in Taiwan and contributed to death in 72.1% of adults aged 65 years or older. Thus, emphasis is warranted on the effects of these types of chronic health issues in everyday life (Ministry of Health & Welfare, 2019).

Patients with CRF may experience discomfort symptoms such as anaemia, decreased urine output, oedema, increased blood pressure, acidosis and pruritus (Lin et al., 2013). These symptoms are related to the patients' renal function indices (i.e. blood urea nitrogen, serum creatinine and glomerular filtration rate [GFR]). Combs et al., (2015) indicated that pruritus was the most common discomfort symptom

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in patients with Stage V CRF who had not received dialysis. Although pruritus does not directly influence disease severity or mortality, it significantly influences patients' sleep quality. Because of poor sleep quality, patients may experience reduced mobility in everyday, which may cause them to develop depression (Lin et al., 2014).

With the progress of treatment, they may experience dialysisassociated symptoms, to immense psychological distress and may cause them to develop depression (Sumanathissa et al., 2011). This may be because of the influences of physical symptoms, including diet limitations, treatment-induced fatigue, limited physical activity and muscle cramps (Lin, 2014). Thus, early assessment of depression among patients with CRF is crucial.

Patients with CRF perceive spiritual well-being as a multidimensional concept that combines physical and psychological health. Those who accept death as a natural process and are willing to abandon their fears can achieve spiritual serenity and peace, and they are able to understand the meaning of life. By contrast, patients with poor spiritual well-being often wish to die, feel helpless and have suicidal intentions. Studies on late-stage chronic diseases have stated that spiritual well-being is closely related to daily life functions, symptom distress and changes in physical conditions (e.g. sleep quality and psychological health), and emphasizing spiritual well-being as a key indicator of QoL (Pilger et al., 2017).

Physical symptom distress, sleep disturbances and depression are common among patients with CRF. However, previous studies on patients receiving dialysis have primarily discussed depression, QoL and spiritual well-being. Few studies have investigated the relationship of dialysis methods with these conditions, and few have adopted physiological values for discussion. Studies on the physical symptom distress, sleep quality and spiritual well-being of patients with CRF are limited. In particular, spiritual well-being is an effective coping mechanism that enhances patients' ability to cope with negative events, thereby enabling them to positively embrace and adapt to the haemodialysis treatment process. This indicates that spiritual well-being is a protective factor for patients with CRF; it enhances their inner strength and enables them to endure symptom distress and negative emotions. Therefore, spiritual well-being assists patients with disease adaption and prevention (Ottaviani et al., 2014). The physical health of older patients with CRF is constantly deteriorating; therefore, we must focus on patients' spirituality in order to understand their life values and enhance their spiritual well-being and comfort (Song et al., 2018).

Therefore, we hypothesized that physical symptom distress, sleep quality and depression are each significantly correlated with and spiritual well-being, and that the spiritual well-being of patients with CRF from different sociodemographic backgrounds differs significantly.

2 | AIM

The present study aimed to investigate the relationship among physical symptom distress, sleep quality, depression and spiritual well-being of patients with chronic renal failure (CRF), and analyse the predictors of the spiritual well-being of patients with CRF.

3 | METHODS

3.1 | Study design

This study adopted a cross-sectional research design.

3.2 | Sample

The inclusion criteria were as follows: (1) aged ≥65 years; (2) had a diagnosis of CRF by a doctor and GFR <59 ml/min/1.73 m² (i.e. Stage III–V CRF); (3) had received haemodialysis or long-term outpatient follow-up at a Division of Nephrology for 3 months or longer; and currently receiving treatment; (4) had clear, conscious, and normal mental status without psychiatric diseases; (5) could communicate using Mandarin or Taiwanese; and (6) did not have severe visual and audio disabilities. The exclusion criteria are as follows: (1) diagnosis of moderate or high cognitive impairment according to the Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) and (2) intellectual disabilities. The G*Power statistical software package was used to calculate the required sample size. For an effect size of 0.15 and a 95% power, the software suggested that 204 participants were required.

3.3 | Data collection procedure

In this study, patients with Stage III–V CRF were recruited from a medical centre in Northern Taiwan. We used convenience sampling to select patients from nephrology clinics, peritoneal dialysis clinics and haemodialysis centres. When the patient was in dialysis or waiting for the outpatient clinic, the objective of study was explained to the patients. The questionnaires contained a cover letter, explaining all the ethical considerations (confidentiality, anonymity, informed written consent and the right to withdraw) and an explanation of the research procedure. The patients were invited to voluntarily participate in the study, and we also provided a quiet and comfortable place. Then, we conducted one-on-one interviews to complete all scales. Data were collected from each participant around 50–60 min.

However, during participant recruitment, we discovered that the number of older patients with peritoneal dialysis was lower than expected. Therefore, this study recruited 188 participants.

3.4 | Instruments

3.4.1 | Basic information questionnaire

The basic information included sex, age, marital status, education level, financial status, religion, residence status, leisure activities, biochemical values, GFR staging, dialysis, treatment type, chronic diseases and sedative or antipsychotic drug use.



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3.4.2 | Glomerular filtration rate (GFR)

The GFR is a renal function index used for screening early renal impairments and aids in the diagnosis of chronic kidney disease. A normal GFR is approximately $100-120 \text{ ml/min/1.73 m}^2$. GFR values decrease with age; lower GFR values indicate worse renal function (Chen et al., 2012).

3.4.3 | Physical Symptom Distress Scale (PSDS)

This scale uses a 3-point Likert scale to measure physical symptom distress experienced during the five stages of chronic kidney disease. Higher scores indicate higher levels of distress. The scale comprises 27 items, and it has satisfactory reliability and validity with a Cronbach's α of .87 (Niu, 2004). The internal consistency of this study was .93 (Cronbach's α = .93), which was favourable.

3.4.4 | Chinese version of the Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) assessed sleep quality during the month before testing (Buysse et al., 1989). The index comprises seven components, namely subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Each component is scored 0–3 points, resulting in an overall score of 0–21. Higher PSQI scores indicate less favourable sleep quality (Tsai et al., 2005). This study employed the Chinese version of the PSQI, which was translated by Tsai et al. (2005). The internal consistency (Cronbach's α) of the index was .83, and the test–retest reliability coefficient was .77–.85.

3.4.5 | Geriatric Depression Scale (GDS)

This study adopted the Geriatric Depression Scale, a yes-no questionnaire designed by Yesavage et al. (1982). The Geriatric Depression Scale–Short Form comprises 15 simplified items, which are easier to answer for older patients. The total score was 15 points; scores of 0–4, 5–9 and 10–15 points are considered to indicate normal status, mild depression and moderate or severe depression, respectively. Liao et al. (1995) verified the reliability and validity of the Geriatric Depression Scale–Short Form and revealed that the scale had an internal consistency (Cronbach's α) of .92. The split-half reliability and test–retest reliability (Pearson's r) of the scale were .94 and .84, respectively, indicating that the scale has outstanding internal consistency and concurrent validity.

3.4.6 | Spiritual Well-Being Scale (SWBS)

The Chinese version of the Spiritual Well-Being Scale, which was translated by Su (2002), originated from the Spiritual Well-Being

Scale developed by Ellison and Paloutzian (1982) and comprises 20 items. The total score ranges from 20 to 120 points. The scale comprises the subscales of Religious Well-Being and Existential Well-Being. Items were scored using a 6-point Likert scale, with higher scores indicating higher spiritual well-being. Five nursing professors and experts were invited to verify the expert content validity of the scale. The content validity and internal consistency (Cronbach's α) of the scale were .88 and .78, respectively, indicating satisfactory reliability and validity.

3.5 | Statistical methods

The collected data were analysed using SPSS Windows 20.0. The analysis included descriptive statistics (i.e. percentages, means and standard deviations), independent samples *t* tests, variance analysis, analysis of Pearson's correlation coefficient and analysis of hierarchical regression.

3.6 | Ethical considerations

First, the data collection process received approval from an ethics committee (2016–12-001AC). Subsequently, the researchers contacted and received approval from the administration departments of nephrology, peritoneal dialysis and haemodialysis clinics. The researchers personally visited the case collection units to explain the research objectives, methods and participant inclusion criteria. Structural questionnaires were employed to collect data on the patients' basic information, physical symptom distress, sleep quality, depression and spiritual well-being, and 15–30-min one-on-one interviews were conducted for data collection.

4 | RESULTS

4.1 | Demographic characteristics and spiritual well-being

The mean age of the patients was 78.85 ± 8.86 years, and the majority of patients were men (58.5%), married (66%) and lived with other family members (91%). Most participants had Stage V CRF (70.2%). The haemodialysis, peritoneal dialysis and pharmacological treatment groups comprised 75 (39.89%), 38 (20.21%) and 75 (39.89%) patients, respectively. In addition, most patients with CRF had high blood pressure (49.4%) (Table 1)

4.2 | Analysis of variance for patient demographic characteristics and spiritual well-being

The analysis of variance revealed significant differences in the patients' clinic characteristics, including spiritual well-being among

TABLE 1 Demographic characteristics and medical condition of participants (N = 188)

Demographic analysis	Total / (Mean)	Per cent / (Standard deviation)
Gender	(* ********	
Male	110	58.50
Female	78	41.50
Age	(78.85)	(8.86)
Marital status	(70.03)	(0.00)
Single	64	34.00
Married	124	66.00
Education status	124	00.00
Elementary school or below	70	37.20
	84	44.70
High school	34	
College or above	34	18.10
Economic status	170	02.00
Enough Difficult	173	92.00
2	15	8.00
Economic sources	(1.15)	(0.43)
No	7	3.20
Private savings	61	28.20
Children provide	58	26.90
Other	21	9.70
Religion	(1.01)	(0.13)
No	49	25.90
Buddhism	95	50.30
Taoism	23	12.20
Christianity	13	6.90
Other	9	4.70
Living condition		
Live alone	17	9.00
With family	171	91.00
Leisure activities	(1.74)	(1.63)
No	9	2.70
Yes	179	95.20
Stages of glomerular filtration rate		
Third stage	35	18.60
Fourth stage	21	11.20
Fifth stages	132	70.20
Chronic disease		
No	37	19.70
One	68	36.20
Two or above	83	44.10
	(1.39)	(0.99)
Types of chronic diseases		
Types of chronic diseases Diabetes	80	30.70
•	80 129	30.70 49.40

(Continues)

TABLE 1 (Continued)

, ,		
Demographic analysis	Total / (Mean)	Per cent / (Standard deviation)
Heart disease	37	14.20
Hyperuricaemia	2	0.80
Hyperlipidaemia	5	1.90
Chronic obstructive pulmonary disease	5	1.90
Use of sedative / emotional drugs		
No	133	70.7
Yes	54	28.7
Treatment types		
Conservative treatment ¹	75	39.89
Haemodialysis ²	75	39.89
Peritoneal dialysis ³	38	20.21
Renal function index		
Glomerular filtration rate	(14.52)	(14.24)
Spiritual well-being	(3.61)	(0.30)
Religious well-being	(1.78)	(0.20)
Existential well-being	(1.84)	(0.15)

GFR stages (F = 9.57, p < .001) and therapeutic treatment (F = 11.99, p < .001). Scheffe post hoc analysis revealed that the total spiritual well-being scores of patients with Stage III CRF were higher than those of patients with Stage V CRF. Furthermore, the total spiritual well-being scores of the haemodialysis group was lower than those of the pharmacological treatment group (Table 2).

4.3 | Correlation of spiritual well-being with physical symptom distress, sleep quality, depression and biochemical values

Correlation analysis revealed that participants' spiritual well-being scores were negatively correlated with their physical symptom distress (r = -.220, p < .01), poor sleep quality (r = -.222, p < .001) and depression (r = -.242, p < .01). Analysis of blood biochemical parameters indicated that the GFR (r = -.295, p < .01) was positively correlated with spiritual well-being (Table 3).

4.4 | Predictors of spiritual well-being

Hierarchical regression analysis was adopted in this study. After controlling for the renal function index, physical symptom distress and depression variables, the analysis results revealed a significant relationships of spiritual well-being with poor sleep quality ($\beta = -.15$, p < .05) and haemodialysis ($\beta = -0.23$, p < .01). These two predictors explained 15% of the variance in spiritual well-being (Table 4).

TABLE 2 Comparison of spiritual well-being of CRF patients with different characteristics (N = 188)

				Ореписсезя		
Variable	Number	Mean	Standard deviation	t/F	р	Scheffe's
Gender						
Male	110	3.62	.34	.25	.804	
Female	78	3.61	.22			
Marital status						
Single	64	3.57	.25	-1.50	.135	
Married	124	3.64	.31			
Education status						
Elementary school or below	70	3.61	.19	2.59	.078	
High school	84	3.58	.30			
College or above	34	3.71	.41			
Economic status						
Enough	173	3.61	.29	10	.921	
Difficult	15	3.62	.32			
Living condition						
Live alone	17	3.51	.21	-1.44	.151	
With family	171	3.62	.30			
Stages of glomerular filtration rate						
Third stage ¹	35	3.77	.40	9.57***	.000	1 > 3
Fourth stage ²	21	3.70	.30			
Fifth stages ³	132	3.56	.24			
Dialysis or not						
No	75	3.73	.35	4.29***	.000	
Yes	113	3.53	.22			
Treatment types						
Conservative treatment ¹	75	3.73	.35	11.99***	.000	1 > 2 1 > 3
Haemodialysis ²	75	3.51	.21			
Peritoneal dialysis ³	38	3.58	.23			
Chronic diseases						
No	37	3.65	.47	0.45	.638	
One	68	3.61	.26			
Two or above	83	3.60	.21			
Use of sedative / emotional drugs						
No	133	3.62	.33	0.09	.928	
Yes	54	3.61	.21			

^{*}p<.05; **p<.01; ***p<.001

TABLE 3 Correlation analysis of Physical Symptom Distress, Sleep quality, Depression, Renal function index and Spiritual well-being (N = 188)

Variable	Spiritual well-being	Religious well- being	Existential well- being
Physical Symptom Distress	220**	136	244**
Sleep quality	222**	085	316**
Depression	242**	079	362**
Renal function index			
Glomerular filtration rate	.295***	.036	.499***

^{*}p < .05; **p < .01; ***p < .001

TABLE 4 Independent variables in hierarchical regression analysis of spiritual well-being influencing factors (N = 188)

Model 1 β	11 t	Model 2 β	+	Model 3	÷	Model 4 β	¥	Collinearity Statistics (VIF)
	1.21	.07	89.	06	09:	.05	.45	2.47
	-2.46*	31	-2.84**	30	-2.74**	23	-2.66**	2.56
	-1.32	15	-1.50	15	-1.45	14	-1.35	2.23
		16	-2.32*	10	-1.38	06	79	1.33
				16	-2.14*	15	-1.98*	1.20
						14	-1.80	1.22
		.38		.41		.42		
		.14		.16		.18		
		.03		.02		.02		
		.12		.14		.15		
- 1	8.07***	7.54***		7.07***		6.51***		

CT: Conservative treatment $^*p<.05; ^{**}p<.01; ^{***}p<.001$



5 | DISCUSSION

Studies have indicated that patients with severe chronic illnesses perceive spiritual well-being as a multidimensional concept that combines physical and psychological health. Patients who acknowledge death as a natural process are willing to abandon their fears and can achieve spiritual serenity and peace, thereby enabling them to understand the meaning of life (Liu & Xiao, 2019). Participants in this study exhibited a satisfactory level of spiritual well-being, and they had the highest scores for existential well-being, signifying that most participants recognized the value of their existence and accepted their current disease conditions. This is consistent with the results in a previous study (Chow & Nelson-Becker, 2010), who stated that spiritual health could ameliorate patient despair and distress and enhance self-care concepts. Spiritual experiences can induce hope in life, promote positive thinking and assist patients in taking control of the disease, thereby enabling them to reconstruct the meaning and values of their lives. Ghahfarokhi et al., (2020) recently reported that haemodialysis patients who have higher hope levels may maintain better spiritual well-being. Raising the level of hope is an effective way to improve the spiritual well-being of patients with chronic renal failure.

The changes in patients' daily lives caused by dialysis can easily cause them to lose hope, and this may be because patients in dialysis must endure the pain of needle injection. Furthermore, dialysis treatment lasts approximately 4 hr, requires 2-3 hospital visits weekly and causes patients to experience uncomfortable symptoms such as low blood pressure or cramps due to acute dehydration during dialysis (Huang et al., 2011;Li & Hung, 2014). Another recent study showed that patients with higher disease acceptance had better spiritual health (Zhang et al., 2020), in this study showed that disease acceptance in haemodialysis patients can predict better health and higher the subjective well-being and life satisfaction. At present, there are few intervention studies on the spiritual well-being of patients with chronic renal failure, so medical staff should adopt targeted intervention measures according to the influencing factor of disease condition to improve patients' physical symptom distress and thereby their spiritual health.

The results supported the hypothesis that physical symptom distress is significantly negatively correlated with spiritual well-being. It has been reported that the patients with end-stage renal disease received chronic haemodialysis generally had heavy symptom distress, which could contribute to the disturbed sleep and impaired quality of life of these patients, and which negatively affected their physical and mental health (Wang et al., 2016). The study indicated that a higher severity of physical symptom distress was related to lower spiritual well-being scores. Kao and Lin (2018) posited that caregivers must practice high-quality care and provide comfort to patients for spiritual growth. Caregivers who cannot provide comfort to alleviate patients' disease-related physical distress are incapable of providing spiritual care. Similar to social support, improvements in spiritual health aid individuals in facing pressure and coping with

risks; moreover, spiritual health incites emotions, relaxes muscles, reduces sympathetic nervous system activity and reduces stress-related hormone. Therefore, spiritual well-being can mitigate the pressures caused by physical illness.

The results supported the hypothesis that poor sleep quality is significantly negatively correlated with spiritual well-being. Lin et al., (2014) compared sleep disturbances in patients who received dialysis and those who did not receive dialysis, and they revealed that 57.3% of patients who received dialysis experienced poor sleep quality. These results are similar to those of the present study, in which patients who received haemodialysis or peritoneal dialysis experienced higher levels of sleep disturbances than did those who did not receive dialysis. A previous study showed that sleep disturbances were the most severe physical symptom of patients receiving haemodialysis, which further reduced their spiritual wellbeing (Eslami et al., 2014), our result in line with this study. Mirghaed et al., (2019) conducted a systematic review of 21 studies on sleep disturbances in patients receiving haemodialysis. The study revealed that sleep disturbance is a common health issue among patients receiving haemodialysis and that 75.3% of patients receiving dialysis had poor sleep quality. Therefore, timely evaluation of sleep quality among patients receiving dialysis is crucial for improving the sleep quality of older patients with kidney diseases.

The results supported the hypothesis that depression is significantly negatively correlated with spiritual well-being. Tsai et al., (2015) indicated that enhancements in spirituality reduced and mitigated depression, which was in agreement with the findings of the present study. Emotions dictate the living functions and QoL of patients with depression, and they influence patients' thoughts about the meaning and value of life; therefore, depression has a strong influence on spiritual well-being. Most of the suffering caused by diseases is attributed to psychological and spiritual problems. Individuals who lack motivation to pursue the purpose and meaning of life often develop negative emotions, such as depression and fear. In turn, depression affects patients' rehabilitation behaviour, delays recovery of physical functions and increases the burden on family caregivers. Thus, satisfying the spiritual needs of patients is crucial. Patients with high spiritual well-being have relatively low sickness, mortality, depression and suicide rates, and they have a higher QoL, self-reported health status and well-being (Song & Oh, 2016).

After controlling for the renal function index, physical symptom distress and depression variables, the regression coefficient between sleep quality and haemodialysis treatment was significant, thereby indicating the importance of sleep quality for patients with CRF. Maung et al., (2017) claimed that although sleeping problems are not immediately life-threatening, they severely affect physiological and psychological health and QoL. Severe sleep problems cause depression, which may result in suicidal thoughts. Because of sleeping problems among older patients, high doses of medication should not be administered to older patients with CRF to avoid potential comorbidities and excessive kidney burden. Accordingly, studies have proposed nonpharmacological treatment for sleep problems. Sariati et al., (2019) conducted a systematic review of 15 studies that

employed music therapy to improve the sleep quality of patients receiving haemodialysis and revealed that music therapy increased their endorphin and serotonin levels, altered their respiratory rate and blood oxygen saturation levels, and improved their sleep quality. Bouya et al., (2018) conducted a systematic review of 22 studies that employed aromatherapy to improve complications in patients receiving haemodialysis. The study indicated that aromatherapy reduced complications related haemodialysis, such as pruritus, sleep quality and depression. Therefore, nonpharmacological treatments are indispensable for improving the psychological and spiritual wellbeing of patients receiving haemodialysis.

6 | CONCLUSION

In conclusion, the spiritual well-being was significantly negatively correlated with physical symptom distress, poor sleep disturbances and depression for the patients with chronic renal failure (CRF). After controlling for the key variables, sleep quality and haemodialysis treatment were revealed to be key predictors of spiritual well-being. Patients who have better sleep quality and accept haemodialysis treatment, may maintain better spiritual health. These findings can help nurses identify influencing factors and improve the spiritual health of CRF. Finally, approaches should be considered to increase sleep quality and spiritual well-being in these patients.

6.1 | Relevance to clinical practice

The research results revealed the following: (1) The pharmacological treatment group had more severe symptoms of foot oedema and low attention span than did the two other groups did; the peritoneal dialysis group had more severe symptoms of pruritus and vision deterioration than the two other groups did. (2) The total depression score of the peritoneal dialysis group was higher than that of the pharmacological treatment group. (3) The pharmacological treatment group and the peritoneal dialysis group had the most satisfactory and unsatisfactory sleep quality, respectively. (4) The total spiritual well-being scores of the pharmacological treatment group were higher than those of the other two groups. (5) Patients with the earlier stages of chronic kidney disease, those who had not received dialysis, and those are receiving pharmacological treatment exhibited higher spiritual well-being scores. (6) Sleep quality and haemodialysis treatment are key predictors of spiritual well-being.

6.2 | Limitations

Because this study was a cross-sectional study, the results only reflected the short-term conditions of the participants during the recruitment period. Therefore, the results cannot serve as a reference to infer the influence of factors on the spiritual well-being of patients at different stages of their disease and period, thus limiting

the potential inference of our findings. Future studies should adopt a longitudinal research design to conduct long-term and continuous follow-up on physical symptom distress, depression, sleep quality and spiritual well-being among patients with all stages of CRF. Such studies would improve the explanatory power of the results.

6.3 | IRB approved

This research application was reviewed by the Ethics Review Committee of Taipei Veterans General Hospital, IRB number: 2016–12-001AC.

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CONFLICT OF INTEREST STATEMENT

The author(s) declare that they have no conflict of interests.

AUTHOR CONTRIBUTIONS

CJ and CY made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; CJ involved in drafting the manuscript or revising it critically for important intellectual content; CJ, CY, YL and YT gave final approval of the version to be published. Each author should have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DATA AVAILABILITY STATEMENT

The data set generated during the current study is available from the corresponding author on reasonable request.

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