Factors related to fatigue in Chinese patients with end-stage renal disease receiving maintenance hemodialysis: a multi-center cross-sectional study

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ABSTRACT

Background Fatigue is considered as a common symptom in patients with end-stage renal disease (ESRD) and can significantly decrease patients’ quality of life. This study aimed to assess fatigue in hemodialysis patients and to investigate risk factors of fatigue in Chinese patients receiving maintenance hemodialysis (MHD) in China. Methods Eligible patients completed questionnaires including demographic information, a Chinese version of the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue), the Family APGAR Index (APGAR), the medical outcomes study health status-Social Functioning subscale (SF-36, SocF), and the Pittsburgh sleep quality index (PSQI). Laboratory parameters were abstracted by medical records review. The multiple linear regression model was used to relate parameters with the FACIT-Fatigue score. Results A total of 345 MHD patients (216 men and 129 women, age 55.6 ± 12.8) were recruited in this study. The score of FACIT-Fatigue was 39 (Interquartile Range, 31-44). Fatigue was correlated with PSQI scores (p < 0.001), SocF scores (p < 0.001), comorbidity (p = 0.006), exercise time < 1 hour per day (p = 0.003), adequacy of dialysis (Kt/V) < 1.2 (p = 0.016), APGAR scores (p = 0.014), and high Scr (p = 0.043). Conclusions Fatigue is related to sleep disturbance, social and family functioning, taking physical exercise time, comorbidity condition, Kt/V and serum creatinine level in Chinese MHD patients. Future studies and interventions should focus on developing strategies and improving the quality of life in patients by addressing these significant contributing factors.

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Introduction

Chronic kidney disease (CKD) and the end-stage renal disease (ESRD) are causing severe public health burdens in both developed and developing countries. In China, the largest developing country worldwide, the overall prevalence of CKD accounted for approximately 10.8%, which affected an estimated 119.5 million adults in China. The incidence of ESRD was high and increasing rapidly, and mainland China has to face the huge burden of renal replacement therapy (RRT). RRT includes hemodialysis, peritoneal dialysis, and renal transplantation; among these, hemodialysis is the most common therapy. It can increase the survival of ESRD patients, while imposes considerable symptom burdens on patients and their families. Specifically, patients receiving maintenance hemodialysis (MHD) can suffer from various symptoms: fatigue, depression and anxiety, sleep problem, dietary and time constraints, social interaction limitation, and huge economic burden. These symptoms greatly interfere with patients’ quality of life.

Fatigue is one of the most common symptoms experienced by patients with ESRD and it can be defined as weakness, exhaustion, incapacitating, and ailment. Due to different race and the use of various fatigue measures, the prevalence of fatigue is estimated to range from 60 to 97% among the MHD patients. Previous studies showed that fatigue has a greatly negative influence on patients’ quality of life and has serious psychological, physiological, and socio-demographic implications for patients, families, and even the community; fatigue also showed significant associations with cardiovascular and suicidal risk, which substantially elevated hospitalization and mortality for the MHD patients.
Fatigue is easily neglected by patients and caregivers because this unpleasant symptom is subjective and invisible, and is difficult to be measured objectively.\textsuperscript{16,17} Despite the growing burden of fatigue on patients, unfortunately, the diagnosis and treatment of fatigue has been paid minimal attention among the MHD patients in mainland China. Wang et al.\textsuperscript{18} reported that the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-Fatigue) had acceptable psychometric properties for measurement of fatigue among these Chinese people. Fatigue in MHD patients was reported to be effectively alleviated by using traditional Chinese acupuncture.\textsuperscript{19}

At present, the relationships between fatigue, lifestyle habits, sleep habitual, and family and social functioning remain poorly understood in Chinese MHD patients. More attention was given to analyze the underlying contributing factors of fatigue among the MHD patients, so as to prevent and intervene in fatigue and thereafter improve the quality of life among this population. The present study aimed to highlight the risk factors of fatigue in Chinese MHD patients. We assessed patients’ fatigue status by the FACIT-Fatigue score and explored independent factors of fatigue in patients with MHD. To our knowledge, the risk factors of fatigue in MHD patients are not available currently from large number of participants and multiple hemodialysis centers in mainland China.

**Methods**

**Participants and procedure**

On the basis of a multicenter cross-sectional survey, this study was conducted in the hemodialysis centers of two tertiary hospitals from March 2014 to October 2014 in Tianjin, China. All participants were informed about the purpose of this study and signed informed consent before any study-related procedures were performed. This study was approved by the Research Ethics Committees of Tianjin Medical University (No. TMUhME2013040).

Eligible participants were conveniently sampled from outpatients who were Chinese citizens, over 18 years old, and underwent routine hemodialysis more than twice per week for at least three months. Patients were excluded from this study if they had advanced and severe infection or malignancy, uncontrolled heart failure, intellectual problems, or refused to participate. Patients were selected by auditing patients’ medical records or asking patients or their medical care staffs based on the inclusion and exclusion criteria.

**Measures**

The participants were requested to complete the measures: the FACIT-Fatigue, Family APGAR Index (APGAR), the medical outcomes study health status from-Social Functioning subscale (SF-36, SocF), and Pittsburgh sleep quality index (PSQI). All participants filled out the measures at the time when they were enrolled during their hemodialysis sessions. We provided assistance for those patients who were limited by the presence of hemodialysis vascular access, or had poor visual acuity or limited literacy to complete the questionnaires. Demographic and clinical information of the participating patients were retrieved from the medical records by researchers. At the same time, patients’ laboratory parameters were also extracted from the system, including hemoglobin (HGB), albumin (ALB), triglyceride (TG), cholesterol (CHOL), high-density lipoprotein-cholesterol (HDL), low-density lipoprotein-cholesterol (LDL), serum creatinine (Scr), blood urine nitrogen (BUN), serum potassium (K), serum calcium (Ca), serum phosphorus (P), and adequacy of dialysis (Kt/V).

**Functional assessment of chronic illness therapy-fatigue**

The FACIT-Fatigue was developed to measure cancer anemia-related fatigue.\textsuperscript{20} It consists of 13 items. Patients were asked to rate each item regarding how they had felt during the past seven days by a 5-point Likert scale response. The total score ranges from 0 to 52, with a higher total score indicating less fatigue. This scale is widely used in general population and patients with various chronic illnesses. It showed excellent internal consistency and test-retest reliability, had strong association with other fatigue measurement tools, and showed great correlations with active disease characteristics.\textsuperscript{21–23} It has been previously validated in Chinese MHD patients.\textsuperscript{18,24} In this study, Cronbach’s alpha coefficient for FACIT-Fatigue was 0.930.

**Family APGAR index**

The five-item APGAR was used to measure degree of patients’ satisfaction with family function.\textsuperscript{25} It includes five items: adaptation, partnership, growth, affection, and resolution. Each item is scored by a three-point response options range from 0 (hardly ever) to 2 (almost always) and a high total score reflects good perceived family function. The total scores range from 0 to 10 with the following cut-off points: 0-3 indicates severe dysfunctional family, 4-7 indicates moderate dysfunctional family, and 8-10 indicates functional family. APGAR has
been widely used in Chinese family, with great reliability and validity. In this study, Cronbach’s alpha coefficient for family APGAR index was 0.725.

**The medical outcomes study health status-Social Functioning subscale (SF-36, SocF)**

The SocF subscale of the SF-36 was used to examine patients’ social functioning. This subscale consists of two items, which measure the injury’s influence on normal social activities. Each item is scored from 0 to 100 with a higher score indicating better social functioning. SF-36 has been widely used in previous studies among the general population and clinical patients. In this study, Cronbach’s alpha coefficient for SocF was 0.986.

**Pittsburgh sleep quality index**

The Pittsburgh sleep quality index (PSQI) was used to measure sleep problem. It consists of 18 items with seven areas regarding habitual sleep over the latest month. The seven areas include subjective sleep quality, sleep latency, sleep duration, sleep efficacy, sleep disturbance, use of sleep medication, and daytime dysfunction. The range of each area is between 0 and 3 and higher PSQI scores represent poorer sleep quality. The total score of PSQI ranges from 0 to 21, with a score ≤7 indicating better sleep quality and scores >7 reflecting worse quality of sleep. This scale is widely used in international clinical practice and research, and the Chinese version of the PSQI has been validated in mainland China as a reliable evaluating measure. In this study, Cronbach’s alpha coefficient for PSQI was 0.810.

**Statistical analysis**

All of the statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL). Continuous data were checked for normality of distributions (the Kolmogorov-Smirnov test), and expressed as mean (standard deviation), or median (IQR, Q1-Q3). Categorical variables were expressed as frequency (percentage). Since data appeared highly skewed, a reflection, and square-root transformation was applied for the dependent variable. Parameters between two groups were compared using the Student’s t-test, otherwise one-way analysis of variance (ANOVA) was used. The correlation analyses between the FACIT-Fatigue score and the continuous independent variables were conducted using Spearman’s correlation coefficient. Significant levels were set at a \( p < 0.05 \). With significant variables in the univariate analysis, we explored the independent factors by applying multiple linear regression with a stepwise procedure. The model was adjusted for age and gender.

**Results**

Eventually, 345 MHD patients were enrolled into this study. The mean age of patients was 55.6 ± 12.8. More than one half of participants were male (62.6%). The most frequent etiologies of MHD were chronic nephritis (20.0%), diabetes (19.4%) and hypertension (15.7%). The median score of fatigue in this study was 39 (IQR 31-44). Demographic and clinical variables and MHD patients’ scores of FACIT-Fatigue, APGAR, SocF, and PSQI are presented in Table 1.

Univariate analysis revealed that fatigue was significantly associated with age, exercise time per day, family economic status, patients’ employment status, comorbidity, hemodialysis vascular access, Scr, \( Kt/V \) (all \( p < 0.05 \), Table 2). Linear correlation between FACIT-Fatigue and PAGAR, SocF, PSQI in MHD patients are shown in Table 3. In the bivariate correlation analysis, FACIT-Fatigue scores were positively associated with APGAR and SocF scores \( r_s = 0.313, p < 0.001 \) and \( r_s = 0.507, p < 0.001 \), respectively.

| Variable | Median (IQR) or n (%) | Mean (SD) | Range |
|----------|-----------------------|------------|-------|
| Age      | 55.6 (12.8)           | 18–82      |
| Gendera  |                       |            |       |
| Male     | 216 (62.6)            |            |       |
| Female   | 129 (37.4)            |            |       |
| Primary cause of kidney diseasea | | | |
| Chronic nephritis | 69 (20.0) | | |
| Hypertension | 54 (15.7) | | |
| Diabetes | 67 (19.4)             |            |       |
| Polycystic | 28 (8.1)             |            |       |
| Lupus nephritis | 5 (1.4)   | | |
| Others   | 31 (9.0)              |            |       |
| Not clear | 91 (26.4)            |            |       |
| Type of residencea | | | |
| Urban    | 267 (77.4)            |            |       |
| Countryside | 78 (22.6) | | |
| Diagnosis with viral hepatita | | | |
| Yes      | 85 (24.6)             |            |       |
| No       | 260 (75.4)            |            |       |
| FACIT-Fatigueb | 39 (31–44) | | 14–52 |
| APGARc   | 8 (6–9)               |            | 0–10  |
| Dysfunctional familyc | 19 (5.5) | | |
| Moderate dysfunctional familyc | 139 (40.3) | | |
| Functional familyc | 187 (54.2) | | |
| SFd      | 50 (25–75)            | 0–100      |
| PSQIb    | 8 (4–13)              | 0–20       |
| <7a      | 161 (46.7)            |            |       |
| ≥7b      | 184 (53.3)            |            |       |

Notes: FACIT-Fatigue: Functional Assessment of Chronic Illness Therapy-Fatigue; APGAR: Family APGAR Index; SF: SF-36 Social Functioning subscale; PSQI: Pittsburgh sleep quality index; IQR: Interquartile Range.

aFrequency (%).
bMedian (IQR).

respectively), and negatively associated with the PSQI scores ($r_S = -0.559, p < 0.001$).

When multiple linear regression analysis was performed in MHD patients, the individuals with better social functioning ($\beta = -0.298, p < 0.001$) and family functioning ($\beta = -0.103, p = 0.014$) reported less fatigue. Higher scores of PSQI ($\beta = 0.379, p < 0.001$) were positively related to fatigue. Participants with comorbidity...
Table 4. Predictors of fatigue using multiple linear regression (n = 345).

| Variable | Standardized β | β | 95% CI | p-Value |
|----------|----------------|---|--------|---------|
| PSQI     | 0.303          | 0.379 | 0.069~0.108 | <0.001 |
| SF       | 0.135          | -0.298 | -0.016~0.009 | <0.001 |
| with comorbidity | 0.017          | 0.116 | 0.082~0.480 | 0.006 |
| Exercise time <1 hour/day | 0.016         | -0.122 | -0.502~0.106 | 0.003 |
| Kt/V <1.2 | 0.010        | -0.095 | -0.409~0.042 | 0.016 |
| APGAR    | 0.008          | -0.103 | -0.190~0.012 | 0.014 |
| High Scr | 0.006          | 0.079 | 0.003~0.222 | 0.043 |

Notes: Adjusted $R^2$ = 0.484. CI: confidence interval; PSQI: Pittsburgh sleep quality index; SF: SF-36 social functioning subscale; Kt/V: adequacy of dialysis; APGAR: Family APGAR Index; Scr: serum creatinine.

($\beta = 0.116, p = 0.006$) and high Scr ($\beta = 0.079, p = 0.043$) reported higher fatigue score. Participants with exercise time <1 hour every day ($\beta = -0.122, p = 0.003$) reported higher fatigue. Patients with $Kt/V <1.2$ ($\beta = -0.095, p = 0.016$) were also associated with fatigue. The multiple linear regression model of the contributing factors for fatigue is depicted in Table 4.

Discussion

In this study, we found that fatigue correlated with bad social and family functioning, $Kt/V <1.2$, and high Scr. MHD patients with comorbidity and sleep problems were particularly prone to fatigue. Exercise time of less than an hour a day was positively associated with fatigue.

Fatigue is a common and distressful symptom for patients receiving MHD. The average fatigue level among these patients of 39 (31-44) was worse than in the general population ($t=6.89, p <0.001$) and better than the non-dialysis-dependent CKD ($t=5.07, p <0.001$) and ESRD ($t=4.09, p <0.001$) patients in US. As in other chronic diseases, fatigue is associated with poor quality of life in patients with hemodialysis$^{2,31}$; it is also a vital predictor of cardiovascular disease. Despite the high prevalence of fatigue and its impact on healthcare outcomes, little attention has been paid to it, let alone to developing widely useful treatment of it for MHD patients in mainland China. Therefore, adequate management of fatigue would have a positive impact on MHD patients’ healthcare outcomes and even survival.$^{14,32}$

With the prevalence ranged from 50 to 80%, sleep disorder is an extremely common problem among long-term renal replacement therapy patients.$^{33}$ These patients suffer from sleep abnormalities, such as insomnia, restless legs syndrome (RLS), obstructive sleep apnea syndrome (OSAS), and periodic limb movement disorder.$^{34}$ In this study, more than 50% of MHD patients had sleep problem, based on the PSQI cut-off score $>$7. Sleep habitual showed a significant and positive correlation with fatigue and was the primary predictor of fatigue with 30.3% variance explained. The sleep disorder cause to fatigue has been hypothesized through two mechanisms: excessive daytime sleepiness and increased level of certain inflammatory cytokines.$^{35}$

Our finding suggests that fatigue significantly related to the self-reported sleep quality. Measures to relieve sleep disorder may decrease fatigue and perhaps improve these people’s quality of life, functional health status, and outcome.$^{36}$ Until now, the mechanism of the relationships between fatigue, RLS, and sleep disorders is still under recognized. Therefore, further studies are warranted to reveal these.

With regard to the social factors dimension, higher level of fatigue was reported by the MHD patients with current unemployment, lower family income, and less social functioning. In our study, only 15% patients had current employment, and 33.6% patients received government or enterprise subsidies. Fatigue has been described as leading to high economic costs to society because of its significant influence on patients’ career and family caring time.$^{37}$ Sajadi et al.$^{38}$ reported that hemodialysis patients who had lower income or were unemployed suffered from higher level of fatigue. This finding indicated that policy adjustment should provide benefit or suitable candidate opportunities to relieve financial burden of MHD patients. In this study, poor social and functioning was found to be a predictor of fatigue. The explanation could be that MHD patients may lack social activities and experience early retirement, low self-esteem, and family/social role alteration, thereby leading to more psychosocial distress, such as anxiety, depression, loneliness, isolation, hopelessness, and further exacerbating patients’ fatigue.$^{39,40}$ Anxiety and depression, common psychiatric disorder, influenced patients’ quality of life and contributed to emotional upset, social relationship, and poor compliance.$^{41-44}$ It was believed that social support, as a buffer system against depression, may indirectly improve fatigue.$^{45}$

As one of the primary caregivers and givers of social support for MHD patients, family members offer love and approval to the patients. The better the perceived support from patients’ families, the lower the level of fatigue patients may experience.$^{46}$ Our study found that more than half of MHD patients reported functional families and only 5.5% of participants reported their family type as dysfunctional family. Good family function was significantly associated with lower levels of fatigue. A previous study investigated the family structure in African American ESRD patients. Female patients who lived in complex households were at risk for shortened survival when compared to those who lived alone or
only with their partner. Interestingly, the current study found no significant difference between fatigue and family structure or marital status. These differing results may be related to experiences of different race and gender. In China today, family members always provide the care for patients, which is consistent with China traditional culture. Relatives tend to take responsibility for patient care, housekeeping, finical support, and transportation even if they do not live together. This contributes to developing close family relationship and functional families. Good perceived social support was a predictor of positive response to health-related quality of life.

A previous population-based cohort study indicated that hemodialysis patients with higher Deyo-Charlson comorbidity index (CCI) scores had longer hospitalization, more cost and decreased survival rate. In this study, comorbidity was found to be a predictor for fatigue in the MHD patients, which was also consistent with the study from Bossola et al. It was likely that those patients faced worse comorbidities, which need more time spent in hospital waiting for diagnostic procedures. In this situation, patients could experience stress and emotion fluctuation, all of which resulted in tiredness, exhaustion, and an increase in patients’ fatigue level.

In our present study, less than one-third of MHD patients exercised more than one hour per day. A physical exercise program was found to be one of the positive factors in managing fatigue. Previous studies have found that exercise was an effectiveness intervention to minimize fatigue. Activities such as cycling, home walking, yoga, and strength training have been highlighted in previous studies, yet some of these studies showed non-significant results and suggested that further randomized controlled trials (RCTs) are needed with a bigger sample size. When compared with those with active physical exercise, sedentary dialysis patients have been identified as having a higher risk of death within 1 year. Hence, our study indicated that it is important to alleviate or prevent fatigue in patients who take exercise for less than one hour every day. Delgado and Johansen reported that the most common barriers to physical activity by dialysis patients were lack of motivation and shortness of breath; therefore, the dialysis staff and healthcare professionals should identify and assist patients in overcoming the barriers to exercises. The staff can be incorporated into the exercise intervention program with MHD patients, to develop a truly individualized physical activity program.

In the present study, laboratory parameters were explored as predictors of fatigue. We found that fatigue was negatively correlated with Scr concentrations and positively correlated with Kt/V level rather than with other laboratory variables. Previous studies have indicated that the association between biochemical markers (i.e., HGB, p, Ca, Scr, Kt/V) and fatigue are inconsistent. In this study, Kt/V was used to evaluate the adequacy of the dialysis dose, with a target minimum level of 1.2. More than 60% of patients had a higher Kt/V level of over 1.2, which was significantly correlated with lower level of fatigue. Approximately, 77.4% patients had high Scr, which was a risk factor to fatigue. This was in agreement with the previous study by Karakan et al., who reported that creatinine concentration was correlated with Piper’s fatigue scale (PFS) affective score. However, further studies are warranted to clarify these mechanisms.

Researches indicated that, in general, older patients may have higher level of fatigue; nevertheless, inconsistent results were reported in other studies. In our study, 38% of the MHD patients were above 60 and age was positively correlated with fatigue level. It is not difficult to understand that older patients generally have poor resistance, more comorbidities, and limited ability to cope with stressors, all of which can lead to more fatigue. Unruh et al. also reported that older patients could be influenced by a lack of knowledge about coping mechanisms for fatigue.

Vascular access complications are the most important causes of high morbidity and mortality in dialysis population. Hemodialysis patients are hospitalized once or twice a year because of vascular access complications. Autogenous arteriovenous fistula carries less morbidity and mortality compared to other vascular accesses. Zhang et al. reported that the use of arteriovenous access was associated with lower mortality among older patients on hemodialysis, even for the aged elders. In the present study, 91% of patients underwent hemodialysis through arteriovenous fistula, which was associated with a low level of fatigue. Patients starting with arteriovenous fistula were reported to have lower complications and mortality when compared with those with catheter assess in the study of El Minshawy et al.

Several limitations in this study have to be addressed. First, it was a cross-sectional study, so that we can only show the associations between the variables under study and causal inference cannot be made among these variables. Second, only a small number of predictors of fatigue were explored among MHD patients in our study. We cannot exclude the contributions of other potential variables to fatigue, such as coping style, inflammatory markers, medications, nutritional assessments, etc. The results in our study may be closely related to Chinese culture and socioeconomic
factors in the population. It is unclear whether the results reported in our study could apply in other countries. Further studies in other countries are needed to clarify the findings. Despite these limitations, to our knowledge, this was the first multicenter study to explore the predictors of fatigue in Chinese MHD patients.

In conclusion, findings of this study indicated that fatigue is a common problem that bothers MHD patients and is associated with patients’ physical and psychosocial factors. Multiple linear regression analyses suggested that sleep disorder, poor social and family functioning, comorbidity, exercise less than one hour every day, \( Kt/V < 1.2 \) and high Scr contribute were significant predictors of fatigue. These findings can help dialysis staff and healthcare professionals to identify risk factors of fatigue and develop strategies to handle the burdens of fatigue on patients. Longitudinal studies are still needed to describe the trajectory of fatigue and the risk factors of fatigue among the MHD patients. It is desirable to reduce complaints of fatigue and enhance quality of life and survival rate for MHD patients by further interventions.

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Disclosure statement

The authors declare that they have no conflict of interest.

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References

1. Intiso D. The rehabilitation role in chronic kidney and end stage renal disease. *Kidney Blood Press Res*. 2014;39(2–3):180–188.
2. Kazancıoğlu R. Risk factors for chronic kidney disease: An update. *Kidney Int Suppl*. 2013;3(4):368–371.
3. Zhang L, Wang F, Wang L, et al. Prevalence of chronic kidney disease in China: A cross-sectional survey. *Lancet*. 2012;379(9818):815–822.
4. Zuo L, Wang M. Current burden and probable increasing incidence of ESRD in China. *Clin Nephrol*. 2000;74 Suppl 1:S20–S22.
5. United States Renal Data System. *United States Renal Data System 2012 Annual Data Report. Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States*. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2013.
6. Cukor D, Cohen SD, Peterson RA, Kimmel PL. Psychosocial aspects of chronic disease: ESRD as a paradigmatic illness. *J Am Soc Nephrol*. 2007;18(12):3042–3255.
7. Jhamb M, Weisbord SD, Steel JL, Unruh M. Fatigue in patients receiving maintenance dialysis: A review of definitions, measures and contributing factors. *Am J Kidney Dis*. 2008;52(2):353–365.
8. Abdel-Kader K, Unruh ML, Weisbord SD. Symptom burden, depression, and quality of life in chronic and end-stage kidney disease. *Clin J Am Soc Nephrol*. 2009;4(6):1057–1064.
9. Jahromi SR, Hosseini S, Razeghi E, Meysamie AP, Sadrazadeh H. Malnutrition predicting factors in hemodialysis patients. *Saudi J Kidney Dis Transpl*. 2010;21(5):846–851.
10. Evans EJ, Wickstrom B. Subjective fatigue and self-care in individuals with chronic illness. *Med surg Nurs*. 1999;8(6):363–369.
11. Egленe R, Karataş N, Taşci S. The effect of acupressure on the level of fatigue in hemodialysis patients. *Altern Ther Health Med*. 2013;19(6):23–31.
12. Talas MS, Bayraktar N. Kidney transplantation: Determination of the problems encountered by Turkish patients and their knowledge and practices on healthy living. *J Clin Nurs*. 2004;13(5):580–588.
13. Davison SN, Jhangri GS. Impact of pain and symptom burden on the health-related quality of life of hemodialysis patients. *J Pain Symptom Manage*. 2010;39(3):477–485.
14. Koyama H, Fukuda S, Shoji T, et al. Fatigue is a predictor for cardiovascular outcomes in patients undergoing hemodialysis. *Clin J Am Soc Nephrol*. 2010;5(4):659–666.
15. Chen CK, Tsai YC, Hsu HJ, et al. Depression and suicide risk in hemodialysis patients with chronic renal failure. *Psychosomatics*. 2010;51:528.e6.
16. McCann K, Boore JR. Fatigue in persons with renal failure who require maintenance hemodialysis. *J Adv Nurs*. 2000;32(5):1132–1142.
17. O’Sullivan D, McCarthy G. An exploration of the relationship between fatigue and physical functioning in patients with end stage renal disease receiving hemodialysis. *J Clin Nurs*. 2007;16(11C):276–284.
18. Wang SY, Zang XY, Liu JD, Gao M, Cheng M, Zhao Y. Psychometric properties of the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) in Chinese patients receiving maintenance dialysis. *J Pain Symptom Manage*. 2015;49(1):135–143.
19. Cho YC, Tsay SL. The effect of acupuncture with massage on fatigue and depression in patients with end-stage renal disease. *J Nurs Res*. 2004;12(1):51–59.
20. Yellen SB, Cella DF, Webster K, Blendowski C, Kaplan E. Measuring fatigue and other anemia-related symptoms with the Functional Assessment of Cancer Therapy (FACT) measurement system. *J Pain Symptom Manage*. 1997;13(2):63–74.
21. Cella DF, Lai J, Chang C, Peterman A, Slavin M. Fatigue in cancer patients compared with fatigue in the general United States population. *Cancer*. 2002;94(2):528–538.
22. Cella D, Yount S, Sorensen M, Chartash E, Sengupta N, Grober J. Validation of the Functional Assessment of
Chronic Illness Therapy Fatigue Scale relative to other instrumentation in patients with rheumatoid arthritis. J Rheumatol. 2005;32(5):811–819.

23. Hagell P, Höglund A, Reimer J, et al. Measuring fatigue in Parkinson’s disease: A psychometric study of two brief generic fatigue questionnaires. J Pain Symptom Manage. 2006;32(5):420–432.

24. Leng CX. Study on effects of aerobic exercise intervention in patients receiving maintenance hemodialysis. Dissertatian, Tianjin Medical University; 2012.

25. Smilkstein G. The family APGAR: A proposal for a family function test and its use by physicians. J Fam Pract. 1978;6:1231–1239.

26. Lv F, Zeng G, Liu SN, Zhong TL, Zhan ZQ. A study on validity and reliability of the family APGAR. Chin J Public Health. 1999;15(11):987–988.

27. Ware Jr, Snow KK, Kosinski M, Gandek B. SF-36 Health Survey: Manual and Interpretation Guide. Boston, MA: The Health Institute, New England Medical Center; 1993.

28. Buyse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: A new instrument for psychiartic practice and research. Psychiatry Res. 1989;28:193–213.

29. Liu XC, Tang MQ, Hu L, et al. Reliability and validity of the Pittsburgh Sleep Quality Index. Chin J Public Health. 1996;29:103–107.

30. Nierenberg AA, Adler LA, Peselow E, Zornberg G, Rosenthal M. Trazodone for antidepressant associated insomnia. Am J Psychiatry. 1994;151(7):1069–1072.

31. Okpechi IG, Nthite T, Swanepoel CR. Health-related quality of life in patients on hemodialysis and peritoneal dialysis. Saudi J Kidney Dis Transpl. 2013;24(3):519–526.

32. Jhamb M, Pike F, Ramer S, et al. Impact of fatigue on outcomes in the hemodialysis (HEMO) study. Am J Nephrol. 2011;33(6):515–523.

33. Joshwa B, Khakha DC, Mahajan S. Fatigue and depression and sleep problems among hemodialysis patients in a tertiary care center. Saudi J Kidney Dis Transpl. 2012;23(4):729–735.

34. Baglioni C, Spiegelhalder K, Lombardo C, Riemann D. Sleep and emotions: A focus on insomnia. Sleep Med Rev. 2010;14(4):227–238.

35. Kopple JD, Cheung AK, Christiansen JS, et al. OPPORTUNITY: A randomized clinical trial of growth hormone on outcome in hemodialysis patients. Clin J Am Soc Nephrol. 2008;3:1741–1751.

36. Parker KP. Sleep disturbances in dialysis patients. Sleep Med. 2003;7:131–143.

37. Chisholm D, Godfrey E, Ridsdale L, et al. Chronic fatigue in general practice: Economic evaluation of counselling versus cognitive behaviour therapy. Br J Gen Pract. 2001;51(462):15–18.

38. Sajadi A, Farmahini Farahani B, Esmaeilpoor Zanjan S et al. Determine of factors relation to fatigue in patients suffering from ESRD undergoing Hemodialysis treatment. Iran J Crit Care Nurs. 2010;3:38–43.

39. Tell GS, Mittelmark MB, Hylander B, Shumaker SA, Russell G, Burkart JM. Social support and health related quality of life in black and white dialysis patients. ANNA J. 1995;22(3):301–308.

40. Levy NB. Psychiatric considerations in the primary medical care of the patient with renal failure. Adv Ren Replace Ther. 2000;7(3):231–238.

41. Rosenthal Asher D, Ver Halen N, Cukor D. Depression and nonadherence predict mortality in hemodialysis treated end-stage renal disease patients. Hemodial Int. 2012;16(3):387–393.

42. Peng T, Hu Z, Guo L, Xia Q, Li D, Yang X. Relationship between psychiatric disorders and quality of life in nondialysis patients with chronic kidney disease. Am J Medical Sci. 2013;345(3):218–221.

43. Jadoulle V, Hoyois P, Jadoul M. Anxiety and depression in chronic hemodialysis: Some somatopsychic determinants. Clin Nephrol. 2005;63(2):113–118.

44. Feroze U, Martin D, Kalantar-Zadeh K, Kim JC, Reina-Patton A, Kopple JD. Anxiety and depression in maintenance dialysis patients: preliminary data of a cross-sectional study and brief literature review. J Ren Nutr. 2012;22(1):207–210.

45. Williams AG, Crane PB, Kring D. Fatigue in African American women on hemodialysis. Nephrol Nurs J. 2007;34(6):610–617.

46. Karadag E, Kilic SP, Metin O. Relationship between fatigue and social support in hemodialysis patients. Nurs Health Sci. 2013;15(2):164–171.

47. Turner-Musa J, Leidner D, Simmens S, Reiss D, Kimmel PL, Holder B. Family structure and patient survival in an African-American end-stage renal disease population: A preliminary investigation. Soc Sci Med. 1999;48(10):1333–1340.

48. Lin YT, Wu PH, Kuo MC, et al. High cost and low survival rate in high comorbidity incident elderly hemodialysis patients. PLoS One. 2013;8(9):e75318.

49. Bossola M, Luciani G, Tazza L. Fatigue and its correlates in chronic hemodialysis patients. Blood Purif. 2009;28(3):245–252.

50. Bossola M, Luciani G, Giungi S, Tazza L. Anorexia, fatigue, and plasma interleukin-6 levels in chronic hemodialysis patients. Ren Fail. 2010;32(9):1049–1054.

51. Astroth KS, Russell CL, Welch JL. Non-pharmaceutical fatigue interventions in adults receiving hemodialysis: A systematic review. Nephrol Nurs J. 2013;40(5):407–427.

52. O’Hare AM, Tawney K, Bacchetti P, Johansen KL. Decreased survival among sedentary patients undergoing dialysis: Results from the dialysis morbidity and mortality study wave 2. Am J Kidney Dis. 2003;41(2):447–454.

53. Delgado C, Johansen KL. Barriers to exercise participation among dialysis patients. Nephrol Dial Transplant. 2012;27(3):1152–1157.

54. Bennett PN, Breugelmans L, Barnard R, et al. Sustaining a hemodialysis exercise program: A review. Semin Dial. 2010;23(1):62–73.

55. IV. NKF-K/DOQI Clinical Practice Guidelines for Anemia of Chronic Kidney Disease: Update 2000. Am J Kidney Dis. 2001;37(Suppl 1):182–238.

56. Karakan S, Sezer S, Ozdemir FN. Factors related to fatigue and subgroups of fatigue in patients with Parkinson’s disease: A psychometric study of two brief instruments in patients with rheumatoid arthritis. J Rheumatol. 2005;32(5):811–819.

57. Horigan AE. Fatigue in hemodialysis patients: A review of current knowledge. J Pain Symptom Manage. 2012;44(5):715–724.

58. Unruh M, Miskulin D, Yan G. Racial differences in health-related quality of life among hemodialysis patients. Kidney Int. 2004;65(4):1482–1491.
59. El Minshawy O, Abd El Aziz T, Abd El Ghani H. Evaluation of vascular access complications in acute and chronic hemodialysis. *J Vasc Access*. 2004;5(2):76–82.
60. Vazquez MA. Vascular access for dialysis: Recent lessons and new insights. *Curr Opin Nephrol Hypertens*. 2009;18(2):116–121.
61. Lafrance JP, Rahme E, Lelorier J, Iqbal S. Vascular access-related infections: Definitions, incidence rates, and risk factors. *Am J Kidney Dis*. 2008;52(5):982–993.
62. Mendelssohn DC, Ethier J, Elder SJ, Saran R, Port FK, Pisoni RL. Hemodialysis vascular access problems in Canada: Results from Dialysis Outcomes and Practice Patterns Study (DOPPS II). *Nephrol Dial Transplant*. 2006;21:721–728.
63. Zhang JC, Al-Jaishi AA, Na Y, de Sa E, Moist LM. Association between vascular access type and patient mortality among elderly patients on hemodialysis in Canada. *Hemodial Int*. 2014;18(3):616–624.