

Postprint: Meta-Analysis of Frailty Prevalence and Influencing Factors in Chinese Maintenance Hemodialysis Patients

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Abstract

Background Chronic kidney disease has become a focus of global concern, with China having the highest prevalence of kidney disease worldwide. Approximately 89.5% of patients require hemodialysis. In recent years, the prevalence of frailty among maintenance hemodialysis (MHD) patients has increased significantly, severely impacting patient quality of life and prognosis.

Objective To investigate the prevalence and influencing factors of frailty among MHD patients in China through meta-analysis.

Methods A systematic search was conducted for cross-sectional and cohort studies on the prevalence and influencing factors of frailty among Chinese MHD patients in CNKI, VIP, Chinese Biomedical Literature Database, Wanfang Data, Web of Science, PubMed, Cochrane Library, Embase, and CINAHL databases from inception to July 2023. Two researchers independently performed literature screening, data extraction, and quality assessment. Meta-analysis was performed using Stata 15.0 software.

Results Thirty-two articles were included, comprising 6,746 patients, of whom 2,566 were frail, involving 37 influencing factors. Meta-analysis results showed that the prevalence of frailty among MHD patients in China was 37.4% (95%CI=30.3%~44.5%). Age (OR=1.09, 95%CI=1.06~1.13), age >60 years (OR=3.81, 95%CI=2.31~6.30), female gender (OR=2.13, 95%CI=1.47~3.08), living alone (OR=2.42, 95%CI=1.22~4.80), sleep (OR=1.28, 95%CI=1.08~1.50), depression (OR=1.97, 95%CI=1.26~3.08), dialysis vintage (OR=3.25, 95%CI=1.82~5.79), low-level social support (OR=1.99, 95%CI=1.39~2.86), comorbidities (OR=1.79, 95%CI=1.40~2.30), malnutrition (OR=1.17, 95%CI=1.07~1.28), Charlson Comorbidity Index (CCI) (OR=1.32, 95%CI=1.01~1.71), C-reactive protein (CRP) (OR=1.15,

95%CI=1.09~1.21), hemoglobin (Hb<110 g/L) (OR=2.70, 95%CI=1.67~4.36), diabetes mellitus (OR=2.16, 95%CI=1.48~3.16), cerebrovascular disease (OR=2.66, 95%CI=1.85~3.82), and coronary heart disease (OR=3.50, 95%CI=2.15~5.70) were risk factors for frailty in MHD; high economic income (OR=0.02, 95%CI=0.01~0.14), high-level social support (OR=0.86, 95%CI=0.76~0.97), good nutrition (OR=0.47, 95%CI=0.26~0.85), activities of daily living (ADL) (OR=0.80, 95%CI=0.70~0.91), serum albumin (ALB) (OR=0.84, 95%CI=0.77~0.91), Hb \geq 110 g/L (OR=0.70, 95%CI=0.54~0.90), and 25-hydroxyvitamin D [25-(OH)VD] (OR=0.69, 95%CI=0.49~0.98) were protective factors against frailty in MHD.

Conclusion The prevalence of frailty among MHD patients in China is at a relatively high level, with age, female gender, living alone, economic income, sleep, depression, dialysis vintage, social support, comorbidities, nutritional risk score, ADL, CCI, CRP, ALB, Hb, 25-(OH)VD, diabetes mellitus, cerebrovascular disease, and coronary heart disease being the main influencing factors for frailty among Chinese MHD patients. Early screening and intervention should be implemented for hemodialysis patients with frailty in the future to slow down or prevent its occurrence.

Full Text

Prevalence and Influencing Factors of Frailty in Maintenance Hemodialysis Patients in China: A Meta-analysis

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Abstract

Background: Chronic kidney disease has become a major global health concern, with China exhibiting the highest prevalence of kidney disease worldwide. Approximately 89.5% of patients require hemodialysis. In recent years, the prevalence of frailty among maintenance hemodialysis (MHD) patients has increased significantly, severely impacting patients' quality of life and prognosis.

Objective: To investigate the prevalence of frailty and its influencing factors among MHD patients in China through meta-analysis.

Methods: We systematically searched cross-sectional and cohort studies on the prevalence and influencing factors of frailty in Chinese MHD patients across nine databases: CNKI, VIP, CBM, Wanfang Data, Web of Science, PubMed, Cochrane Library, Embase, and CINAHL, from inception to July 2023. Two researchers independently conducted literature screening, data extraction, and quality assessment. Meta-analysis was performed using Stata 15.0 software.

Results: Thirty-two studies were included, comprising 6,746 patients with 2,566 frailty cases and involving 37 influencing factors. The meta-analysis revealed that the prevalence of frailty among Chinese MHD patients was 37.4% (95%CI=30.3%-44.5%). Risk factors included age (OR=1.09, 95%CI=1.06-1.13), age >60 years (OR=3.81, 95%CI=2.31-6.30), female gender (OR=2.13, 95%CI=1.47-3.08), living alone (OR=2.42, 95%CI=1.22-4.80), sleep disturbances (OR=1.28, 95%CI=1.08-1.50), depression (OR=1.97, 95%CI=1.26-3.08), dialysis vintage (OR=3.25, 95%CI=1.82-5.79), low social support (OR=1.99, 95%CI=1.39-2.86), comorbidities (OR=1.79, 95%CI=1.40-2.30), malnutrition (OR=1.17, 95%CI=1.07-1.28), Charlson Comorbidity Index (CCI) (OR=1.32, 95%CI=1.01-1.71), C-reactive protein (CRP) (OR=1.15, 95%CI=1.09-1.21), hemoglobin (Hb<110 g/L) (OR=2.70, 95%CI=1.67-4.36), diabetes mellitus (OR=2.16, 95%CI=1.48-3.16), cerebrovascular disease (OR=2.66, 95%CI=1.85-3.82), and coronary heart disease (OR=3.50, 95%CI=2.15-5.70). Protective factors comprised high economic income (OR=0.02, 95%CI=0.01-0.14), high social support (OR=0.86, 95%CI=0.76-0.97), good nutrition (OR=0.47, 95%CI=0.26-0.85), activities of daily living (ADL) (OR=0.80, 95%CI=0.70-0.91), serum albumin (ALB) (OR=0.84, 95%CI=0.77-0.91), Hb \geq 110 g/L (OR=0.70, 95%CI=0.54-0.90), and 25-hydroxyvitamin D [25-(OH)VD] (OR=0.69, 95%CI=0.49-0.98).

Conclusion: The prevalence of frailty among Chinese MHD patients is high. Key influencing factors include age, female gender, living alone, economic income, sleep, depression, dialysis vintage, social support, comorbidities, nutritional risk scores, ADL, CCI, CRP, ALB, Hb, 25-(OH)VD, diabetes mellitus, cerebrovascular disease, and coronary heart disease. Early screening and intervention for frailty in hemodialysis patients are warranted to slow or prevent its onset.

Keywords: Maintenance hemodialysis; Frailty; Influencing factors; China; Meta-analysis

Introduction

Chronic kidney disease (CKD) has emerged as a major public health issue, with a global prevalence of 10%-13% that continues to rise [1]. China has the high-

est prevalence and annual growth rate of kidney disease worldwide, and approximately 89.5% of patients with end-stage renal disease require maintenance hemodialysis (MHD) treatment [2]. MHD represents a crucial renal replacement therapy for end-stage renal disease patients [3]. Due to long-term dialysis treatment, MHD patients experience substantial loss of protein and bound amino acids, compounded by sedentary behavior that impairs muscle synthesis and reduces physical capacity, predisposing them to frailty [4]. Reported frailty prevalence among MHD patients ranges from 14% to 73% [5], substantially higher than in the general elderly population and other disease groups [6]. Frailty is defined as a medical syndrome characterized by decreased physiological reserve or multi-system dysregulation that increases vulnerability and reduces stress resistance, leading to adverse outcomes such as falls, delirium, disability, and death [7], and serves as an independent predictor of hospitalization and mortality [8]. Therefore, understanding the prevalence and influencing factors of frailty among Chinese MHD patients is essential for promoting health management. Although numerous cross-sectional studies have examined frailty prevalence and factors in MHD patients, their conclusions vary considerably due to limitations in sample size and geographic region. This study systematically reviews the occurrence and influencing factors of frailty in Chinese MHD patients to provide a reference for early identification and reduction of frailty in clinical practice.

Methods

1.1 Search Strategy We systematically searched nine databases: CNKI, VIP, CBM, Wanfang Data, Web of Science, PubMed, Cochrane Library, Embase, and CINAHL, from inception to July 2023. We combined MeSH terms with free-text keywords. Chinese search terms included: “maintenance hemodialysis,” “renal dialysis,” “hemodialysis,” “blood dialysis,” “extracorporeal dialysis”; “frailty,” “frailty syndrome,” “weakness,” “fragility,” “debility”; and “risk factors,” “related factors,” “influencing factors,” “relevant factors,” “predictive factors,” “etiology.” English search terms included: “Renal Dialysis,” “*Hemodialysis*,” “maintenance hemodialysis,” “*Extracorporeal Dialyses*,” “blood dialysis,” “hemodiafiltration,” “MHD”; “Frailty,” “frail,” “*frailty syndrome*,” “*weakness*,” “*debility*,” “asthenia,” “hyposthenia,” “fragile*”; and “factor,” “risk factors,” “influence factors,” “associated factors,” “relevant factors,” “predicted factor,” “reason.” The PubMed search strategy is shown in Table 1.

1.2 Inclusion and Exclusion Criteria **Inclusion criteria:** (1) Participants: patients aged ≥ 18 years with clinically diagnosed MHD for ≥ 3 months; (2) Study design: cross-sectional or cohort studies; (3) Assessment: use of frailty-related scales; (4) Outcomes: prevalence and influencing factors of frailty in Chinese MHD patients with extractable odds ratios (OR) and 95% confidence intervals (CI); (5) Language: Chinese or English.

Exclusion criteria: (1) Severe complications; (2) Mental illness or conscious-

ness disorders; (3) Concurrent peritoneal dialysis; (4) Conference abstracts or reviews; (5) Inability to extract OR and 95%CI; (6) Duplicate publications or unavailable full text.

1.3 Literature Screening and Data Extraction Two researchers independently screened titles and abstracts, then reviewed full texts to select eligible studies and extract relevant information. Disagreements were resolved by discussion with a third researcher. Extracted data included: first author, publication year, study type, region, sample size, number of frailty cases, prevalence, assessment tool, and influencing factors.

1.4 Quality Assessment Two researchers independently assessed study quality. Cross-sectional studies were evaluated using the Agency for Healthcare Research and Quality (AHRQ) scale [9], comprising 11 items scored as “yes,” “no,” or “unclear” (total score 11: 0-3=low, 4-7=moderate, >8=high quality) [10]. Cohort studies were assessed using the Newcastle-Ottawa Scale (NOS) [11] (total score 9: 1-3=low, 4-6=moderate, 7-9=high quality).

1.5 Statistical Methods We used Stata 15.0 software for analysis. Effect sizes were expressed as pooled prevalence with 95%CI, and influencing factors as OR with 95%CI. Heterogeneity was assessed using the I^2 statistic: $I^2 < 50\%$ and $P \leq 0.1$ indicated low heterogeneity (fixed-effects model), otherwise random-effects model was used. For substantial heterogeneity, we performed subgroup analysis and meta-regression to examine the impact of study characteristics. Sensitivity analysis was conducted using one-study-removed method and by changing effect models to assess result stability. Egger’s test was used to assess publication bias for outcomes with ≥ 10 studies; $P > 0.05$ suggested low risk of publication bias. Statistical significance was set at $P < 0.05$.

Results

2.1 Literature Search Results The initial search yielded 1,149 articles. After removing 374 duplicates using Endnote X9, 715 articles were excluded following title and abstract review, and 28 were excluded after full-text reading. Finally, 32 articles [12-43] were included, comprising 24 Chinese [12-35] and 8 English studies [36-43]. The screening process is illustrated in Figure 1 [Figure 1: see original paper].

2.2 Study Characteristics and Quality Assessment The 32 included studies [12-43] involved 6,746 patients, including 2,566 frailty cases, and examined 37 influencing factors. Table 2 presents the basic characteristics and quality assessment results of the included studies.

2.3 Prevalence Analysis

2.3.1 Frailty Prevalence Meta-analysis of the 32 studies revealed significant heterogeneity ($I^2=97.9\%$, $P<0.001$). Using a random-effects model, the prevalence of frailty among Chinese MHD patients was 37.4% (95%CI=30.3%-44.5%), as shown in Figure 2 [Figure 2: see original paper].

2.3.2 Subgroup Analysis We conducted subgroup analyses by study year, region, study type, and frailty assessment tool: - **Region:** North China 36.0% (95%CI=27.6%-44.5%) vs. South China 38.3% (95%CI=27.6%-49.0%) - **Assessment tool:** Fried 41.5% (95%CI=31.7%-51.2%), Tilburg 48.7% (95%CI=29.4%-67.9%), FRAIL 30.7% (95%CI=21.5%-39.9%), Frailty Index (FI) 48.3% (95%CI=35.2%-61.6%) - **Study year:** Before 2020 41.0% (95%CI=23.1%-58.9%) vs. After 2020 35.9% (95%CI=28.7%-43.2%) - **Study type:** Cross-sectional 36.6% (95%CI=29.5%-43.8%) vs. Cohort 47.9% (95%CI=43.6%-52.1%)

These results are summarized in Table 3 .

2.3.3 Meta-regression and Sensitivity Analysis Meta-regression analysis using study year, region, type, and assessment tool as covariates for outcomes with \$ 10 studies did not identify sources of heterogeneity (Table 4). Sensitivity analysis using one-study – removed method for studies with $I^2 > 50\%$ and > 2 articles showed no substantial changes, indicating robust results. The sensitivity analysis for overall prevalence is presented in Figure 3 [Figure 3: see original paper].

2.3.4 Publication Bias Analysis Egger’s test for outcomes with \$ 10 studies revealed publication bias in overall prevalence, South region, post-2020 studies, cross-sectional studies, and FRAIL tool ($P<0.05$). Trim-and-fill analysis showed stable pooled results before and after adjustment, as shown in Table 5 .

2.4 Influencing Factors

2.4.1 Meta-analysis of Frailty Influencing Factors We extracted influencing factors from the 32 studies and pooled those reported in \$ 2 studies. Meta – analysis identified the following as main influencing factors of frailty in Chinese MHD patients ($P < 0.05$) : age, female gender, living alone, economic income, sleep, depression, dialysis vintage, social support, comorbid (OH)VD, diabetes mellitus, cerebrovascular disease, and coronary heart disease. High economic income, high social support, and 25-(OH)VD were protective factors (Table 6).

2.4.2 Meta-regression Meta-regression was performed for factors with \$ 10 studies (age: 17 studies; ALB: 15 studies) using study year, region, type, and tool as covariates. No heterogeneity sources were identified (Table 7).

2.4.3 Sensitivity Analysis Sensitivity analysis was conducted by (1) changing effect models and (2) using one-study-removed method. Results remained

largely stable, except for exercise, psychological resilience, and CCI scores of 3-4 and \$ \$5, indicating robust findings (Table 8).

2.4.4 Publication Bias Analysis Egger' s test for factors with \$ \$10 studies showed $P=0.109$ for age and $P=0.322$ for ALB, suggesting low risk of publication bias.

2.4.5 Descriptive Analysis We descriptively analyzed factors that could not be pooled across studies. These included BMI, SARC-F, grip strength, Kt/V, dialysis adequacy, uric acid, CCI score, HDL-C, and SMI. Some studies found protective effects (BMI, SARC-F, grip strength, Kt/V, dialysis adequacy, HDL-C, SMI), while others identified risk factors.

Discussion

3.1 Prevalence The meta-analysis revealed a frailty prevalence of 37.4% (95%CI=30.3%-44.5%) among Chinese MHD patients, which aligns with the reported range of 14%-73% [5]. Subgroup analyses showed significant variations by assessment tool, study year, and region. First, regional differences showed higher prevalence in South China (38.3%) than North China (36.0%), possibly reflecting lifestyle and dietary differences. Second, assessment tool heterogeneity was notable, with Tilburg showing the highest prevalence (48.7%) and FRAIL the lowest (30.7%). This discrepancy likely stems from instrument differences, as no gold standard exists for frailty assessment, though the Fried scale is the most widely used clinically [44]. Third, studies published before 2020 reported higher prevalence (41.0%) than those after 2020 (35.9%), possibly due to differences in the number and quality of included studies.

3.2 Influencing Factors

3.2.1 Sociodemographic Factors **Age** demonstrated a positive correlation with frailty, with age >60 years identified as a significant risk factor. Advanced age inevitably leads to physiological decline in multiple systems and organs, reducing physiological reserve and daily activity capacity while impairing stress resistance, thereby increasing frailty risk [43]. **Female gender** was associated with higher frailty rates, potentially due to weaker constitution and muscle strength compared to males [45]. **Living alone** emerged as a risk factor, likely reflecting how demographic aging and changing family structures reduce emotional support and exacerbate frailty [46]. **Economic income** was a protective factor, as higher income provides better medical security, enabling timely treatment and reducing complications, consistent with CHAKURKAR et al. [47]. **Sleep disturbances** correlated positively with frailty, as poor sleep inhibits secretion of growth hormone, insulin-like growth factor-1, and testosterone, increasing muscle protein catabolism and frailty risk [48]. **Depression** and **dial-**

ysis vintage also showed positive correlations, with longer dialysis duration reducing quality of life and physical function [49]. Clinicians should prioritize frailty screening in elderly, female, solitary, low-income, and sleep-disordered MHD patients.

3.2.2 Disease-related Factors **Malnutrition** increased frailty risk, as reduced protein intake impairs muscle mass and function [50]. **ADL score** was protective, with higher scores associated with lower frailty risk; ADL and frailty have a reciprocal relationship where decreased activity increases dependency and dysfunction. **CCI score**, used to assess survival and multi-morbidity, effectively predicts readmission and mortality in end-stage renal disease patients [51]; those with multiple comorbidities have higher frailty risk [52]. **C-reactive protein**, a sensitive inflammatory marker, activates the neuromuscular system, causing progressive skeletal muscle consumption and accelerating frailty [54]. **Serum albumin** was protective, serving as a key nutritional indicator; strict dietary restrictions in MHD patients often lead to hypoalbuminemia, increasing muscle wasting and frailty [55]. **Hemoglobin level** was another influential factor, with anemia reducing oxygen-carrying capacity, impairing tissue oxygenation, and affecting daily activities and cognitive function [56]. **25-(OH)VD deficiency** was linked to frailty syndrome in elderly CHD patients, consistent with VAN DEN BERG et al. [57], likely due to associations between vitamin D deficiency and reduced muscle mass, grip strength, and mobility [58]. **Comorbidities** including coronary heart disease, diabetes, and cerebrovascular disease increased frailty severity, as complications and chronic diseases accelerate organ depletion, disrupt homeostasis, and create chronic catabolic states [59].

3.2.3 Psychosocial Factors **Depression** shares pathological mechanisms with frailty, creating a bidirectional relationship where depression activates inflammatory markers to increase frailty risk, while frailty also precipitates depressive symptoms [60]. **Social support**, defined as material and emotional assistance from family, friends, and society [61], was protective against frailty. Higher social support levels correlate with lower frailty risk, likely because strong support networks improve quality of life, promote physical and mental health, and delay frailty onset. Healthcare providers should address negative emotions and help patients develop positive mindsets to reduce frailty risk.

3.3 Limitations This study is the first to examine frailty prevalence and influencing factors in Chinese MHD patients with a relatively large sample from diverse regions, providing valuable insights for future research. However, several limitations exist: (1) High heterogeneity remained unexplained despite subgroup and meta-regression analyses; (2) Most included studies were cross-sectional (30/32), with only two cohort studies, making results susceptible to confounding bias; (3) Non-uniform frailty assessment tools may introduce measurement bias; (4) Some influencing factors were reported in fewer than two studies, precluding heterogeneity analysis. Future large-sample, high-quality longitudinal studies

are needed to validate these findings.

Conclusion

This study demonstrates a high prevalence of frailty (37.4%) among Chinese MHD patients. Key influencing factors include age, female gender, living alone, economic income, sleep, depression, dialysis vintage, social support, comorbidities, nutritional risk scores, ADL, CCI, CRP, ALB, Hb, 25-(OH)VD, diabetes mellitus, cerebrovascular disease, and coronary heart disease. Healthcare professionals should strengthen health education for MHD patients, encourage lifestyle modifications, and promote positive psychological states to reduce frailty incidence.

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