Association between hemodialysis and fall risk in older adults with multiple diseases

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Research Article

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Abstract

Objectives: Falls are a major cause of morbidity and disability in older adults with multiple diseases. This study aimed to evaluate whether hemodialysis is related to fall risk in older adults with multiple diseases ,and to explore the effect of dialysis on falls was mediated through the ratio of Cr / CysC and activities of daily living (ADL).

Methods: This retrospective study included patients aged ≥60 years-old with at least two comorbid diseases admitted to the Geriatric Nephrology Department of Jiangsu Province Hospital between December 2019 and June 2021. Clinical data were extracted from the medical records. Fall risk was evaluated with a modified Thomas scale.

Results: The study included 91 patients in the non-hemodialysis group and 40 patients in the hemodialysis group. The hemodialysis group had lower activities of daily living (ADL) and higher body mass index/skeletal muscle index (SMI) ratio and modified Thomas score than the non-hemodialysis group. Linear regression revealed that older age (b= 0.07, 95% confidence interval [95%CI] = 0.06-0.09, $P < 0.001$) and hemodialysis (b= 0.67, 95%CI = 0.27-1.06, $P = 0.001$) were associated with higher fall risk. Hemodialysis exerted a significant direct effect on the modified Thomas fall risk score (b = 0.526, 95%CI = 0.432–1.433, $P = 0.015$) as well as a significant indirect effect via the Barthel index (b = 0.172, 95%CI = 0.010–0.333, $P = 0.037$)

Conclusion: Hemodialysis increases the risk of falling in older adults with comorbidities. The effects of hemodialysis on fall risk were direct and indirect. Identifying inpatients on hemodialysis who are at risk of falling would facilitate targeted intervention strategies.

Introduction

Falls are one of the major cause of morbidity and disability in the older adults[1]. Each year, about one third of the older adults over the age of 65 have one fall [2], and a substantial minority of these experience recurrent falls [3]. Older adults have a high risk of death after falling [4]. Falls are one of the most common causes of trauma in the older adults[5] and are responsible for around 55% of all injury-related deaths unexpectedly in people aged more than 65 years-old [6]. Falls are a known marker of frailty and health impairment, and the first manifestation of acute physical decline or severe disability of the older adults can be manifested as falling [7]. Falls in the older adults are an important cause of hospitalization [8] and are associated with reduction of activity function [9] and a long-period professional care is needed [10]. Even if there is no serious physical injury this time, the fall will also lead to personal psychological fear of falling again in the future [11]. For the older adults, falls can have a negative impact with this experience, such as anxiety, loss of confidence, injury-related pain, loss of independence, even death.

There are many factors affecting falls, such as old age, environmental factors, the use of multiple drugs, impaired vision, gender, gait and balance impaired, cognitive decline,the history of falls [12] and sarcopenia [13]. Sarcopenia is a syndrome characterized by progressive and systemic reduction of skeletal muscle mass and strength, which is associated with decreased individual activity, decreased quality of life, physical disability, hospitalization and risk of death [13]. Gender, age and physical activity ability are the risk factors of sarcopenia. For some people with sarcopenia, the loss in muscle mass is associated with increased body fat ("sarcopenic obesity") so there are obvious defects despite a normal or increased body weight [14]. Thus, body mass index (BMI) is not always a useful indicator of sarcopenia.

Previous studies have shown that chronic kidney disease (CKD) is one of the risk factor for serious fall injuries (such as fractures) in older adults due to renal osteodystrophy [15]. Almost all patients with end-stage renal disease need renal replacement therapy. There is some evidence that hemodialysis is associated with an increased risk of serious falls [16], and this may be due to a variety of factors such as sarcopenia, osteodystrophy, alterations in postural control, the presence of other comorbidities and polypharmacy. One reason for this is that skeletal muscle mass and strength are not commonly evaluated in the clinical setting. Serum creatinine (Cr; a byproduct of skeletal muscle metabolism) and serum cystatin C (CysC; a cysteine proteinase inhibitor expressed in all nucleated cells) are widely used in the estimation of renal function. There is evidence that CysC-based equations may be better than Cr-based equations at estimating glomerular filtration rate (GFR) in older adults with reduced muscle mass [17]. With the development of weight loss, the decrease of skeletal muscle mass, the serum Cr decrease, but the level of serum CysC will not decrease. Therefore, some researchers believe that Cr / CysC ratio may be a promising alternative index to detect muscle weight loss in patients with CKD. For example, Lin et al. found that the Cr/CysC ratio was independently associated with the skeletal muscle index (SMI, calculated as skeletal muscle mass/height^2) in patients with CKD [18]. Shiomi et al. concluded that the Cr/CysC ratio was a predictor of leg strength in patients with CKD [19]. Kusunoki et al. determined that the Cr/CysC ratio was positively correlated with both muscle mass and physical function in older adults without severe renal impairment [20]. Additionally, a decreased Cr/CysC ratio is considered a surrogate marker of sarcopenia in patients with type 2 diabetes [21]. However, there are few published studies exploring whether the Cr/CysC ratio is associated with falling in older adults.

The aim of the present study was to evaluate whether hemodialysis is related to fall risk in people aged 60 years-old and over with multiple diseases. An additional objective was to investigate whether the effects of hemodialysis on fall risk were mediated directly or indirectly.

Methods

Study design and patients

This retrospective study included older adults with comorbid diseases who were admitted to the Geriatric Nephrology Department of Jiangsu Province Hospital, Nanjing, Jiangsu, China between December 2019 and June 2021. The inclusion criteria were: aged 60–99 years-old; and at least two comorbid diseases (e.g., CKD, hypertension, coronary heart disease and other chronic diseases). Patients meeting any of the following criteria were excluded from the analysis: incomplete data; limb deformities; metal implants; or pacemaker implants.

The patients were divided into a hemodialysis group and a non-hemodialysis group according to whether they had received maintenance hemodialysis for more than 3 months.

Data collection

The following demographic and clinical data were collected from the inpatient medical records and information system: age, gender, education level, height, weight, BMI, SMI, serum Cr level, serum CysC level, blood albumin (ALB) level, blood hemoglobin level, serum triglyceride (TG) level, serum total cholesterol (TC), serum C-reactive protein (CRP) level, white blood cell count (WBC), number of chronic diseases, Nutritional Risk Assessment Scale score (NRS-2002, which assesses the risk of malnutrition) [22], modified Thomas fall risk assessment scale score [23], and modified Barthel index [24].

SMI was determined according to body composition data measured by fully trained staff using a body composition analyzer (Inbody S10 Water Analyzer, Inbody, Seoul, South Korea). SMI was calculated as: SMI = Total mass of skeletal muscle of limbs divided by height ^{2}.

The modified Thomas fall risk assessment scale designed by Jiangsu Province Hospital [23] included the following items: fall history, consciousness disorder, activity disorder, excretion disorder, visual impairment, special symptoms (dizziness, fatigue, postural hypotension, etc.), drug therapy (hypoglycemic drugs, antihypertensive drugs, sedative and hypnotic drugs, etc.), age, and whether the patient insists on getting out of bed when weak (1 point for "yes", 0 points for "no"). A total score ≥ 2 points indicates that the patient is at high risk of falling. The modified Thomas fall risk assessment scale used in this study was shown to have high sensitivity and strong predictive power [23].

The Barthel index was used to measure activities of daily living (ADL) and includes items relating to feeding, dressing,bathing, grooming, bladder control, bowel control,toilet use, transfer between bed and chair, mobility on level surfaces and stair climbing. Each item is scored according to the patient’s ability, and a higher score indicates greater self-care ability [24].

Statistical analysis

The statistical analyses were performed using R version 4.1.1. Categorical variables are described as *n* (%) and were compared between groups with the chi-squared test. Normally distributed continuous variables are described as the mean ± standard deviation and were compared between groups using Student’s t-test. Non-normally distributed continuous variables are described as median (interquartile range [IQR]) and were compared between groups using the Mann-Whitney U test. Linear regression was explored to examine the relationship between fall risk (modified Thomas scale) and hemodialysis. Age, gender, education level and number of comorbid diseases were considered as confounders and included in the model as covariates. Regression slopes, 95% confidence intervals (95%CIs) and coefficients of determination (R2) were calculated. Then, two path models (an extension of linear regression) were used to further investigate the causal relationships between hemodialysis, Barthel index, Cr/CysC ratio and fall risk (i.e., modified Thomas scale). The crude path model included hemodialysis, Barthel index and Cr/CysC ratio, and the adjusted model also included the covariates in the linear regression model. The results of the two models were compared to test the robustness of our findings. The indirect, direct and overall effects and *P*-value were calculated. A two-sided *P*-value < 0.05 was considered statistically significant.

Results

Characteristics of the patients

Table 1

Demographic characteristics of the study participants.

Characteristic	All patients (n = 131)	Non-hemodialysis (n = 91)	Hemodialysis (n = 40)	P-value
Male, n (%)	93 (71.0%)	75 (82.4%)	18 (45.0%)	0.017
Numbers of comorbidities	9 (6–10)	9 (6–10)	8 (6–10)	0.901
Education level (years)	15 (12–16)	16 (12–16)	15 (12–16)	0.183
Death, n (%)	12 (9.2%)	3 (3.3%)	9 (22.5%)	<0.001
Age (years)	81 (69–88)	80 (67–87.5)	84 (73–89)	0.200
BMI (kg/m²)	23.5 (20.9–25.7)	24.4 (21.5–26.1)	21.0 (18.8–24.2)	<0.001
SMI (kg/m²)	7 (5.7–8.0)	7.5 (6.6–8.2)	5.6 (5.2–6.3)	<0.001
BMI/SMI ratio	3.33 (3.05–3.87)	3.26 (2.98–3.61)	3.75 (3.26–4.30)	<0.001
Cr (μmol/L)	104.0 (71.3–181.2)	84.1 (66.0–116.5)	248.1 (181.2–359.6)	<0.001
CysC (mg/L)	1.69 (1.12–3.42)	1.29 (1.05–2.01)	5.67 (4.32–7.07)	<0.001
Cr/CysC ratio	63.25 (51.49–73.93)	64.30 (54.86–75.43)	53.19 (32.2–67.21)	0.001
WBC (´10^9/L)	6.53 (5.30–8.81)	6.23 (5.22–8.42)	7.06 (5.67–8.87)	0.202
ALB (g/L)	35.6 (31.6–39.5)	36.3 (32.7–40.1)	34.1 (30.1–37.2)	0.031
Hemoglobin (g/L)	119 (101–135)	125 (112–140)	96 (81–110)	<0.001
TG (mmol/L)	1.17 (0.85–1.62)	1.12 (0.84–1.56)	1.19 (0.96–1.70)	0.251
TC (mmol/L)	3.72 (3.20–4.64)	3.74 (3.22–4.78)	3.68 (2.76–4.48)	0.225
CRP (mg/L)	5.96 (2.37–21.65)	5.00 (2.20–13.20)	9.35 (5.67–29.60)	0.005
NRS-2002 score	3 (2–4)	3 (1–4)	3 (2–5)	0.009
Modified Thomas score	2 (1.25–3.33)	2 (1–3)	3 (2–4)	0.001
Barthel index	83.7 (59.0–100.0)	89.2 (72.0–100.0)	63.40 (27.40–92.00)	<0.001

Data are shown as median (interquartile range) unless otherwise stated. ALB: Albumin; BMI: body-mass index; Cr: serum creatinine; CRP: C-reactive protein; CysC: cystatin C; Hb: hemoglobin; NRS-2002: Nutritional Risk Assessment Scale 2002; SMI: skeletal muscle index; TC: total cholesterol; TG: triglyceride; WBC: white blood cell.

The final analysis included 131 patients (93 males, 71.0%) with a median age of 81 (IQR, 69–88) years. The non-hemodialysis group included 91 patients (75 males, 82.4%) with a median age of 80 (67–87.5) years, and the hemodialysis group included 40 patients (18 males, 45.0%) with a median age of 84 (73–89) years. The demographic and clinical characteristics of the patients are presented in Table 1. There were no significant differences between the two groups in age, education level, number of comorbid diseases, serum TC level, serum TG level or WBC (Table 1). However, the hemodialysis group contained a higher proportion of female patients than the non-hemodialysis group ($P < 0.05$; Table 1). The hemodialysis group also had a significantly lower BMI and SMI and a significantly higher BMI/SMI ratio than the non-hemodialysis group (all $P < 0.05$; Table 1), suggesting that the hemodialysis group had lower muscle mass and strength. In agreement with this finding, the hemodialysis group had significantly higher serum levels of Cr and CysC but a significantly lower Cr/CysC ratio than the non-hemodialysis group (all $P < 0.05$; Table 1). Additionally, when compared with the non-hemodialysis group, the hemodialysis group had significantly lower blood levels of ALB and hemoglobin and a significantly higher serum CRP level (all $P < 0.05$; Table 1). The hemodialysis group also had a significantly higher NRS-2002 score (indicating a higher risk of malnutrition), a significantly higher modified Thomas fall risk score (indicating a higher risk of falling) and a significantly lower Barthel index score (indicating lower performance in ADL) than the non-hemodialysis group (all $P < 0.05$; Table 1). Mortality rate was significantly higher in the hemodialysis group than in the non-hemodialysis group (22.5% vs. 3.3%, $P < 0.001$).

Multivariate linear regression analysis of factors associated with risk of falling

The multivariate linear regression analysis revealed that older age (b = 0.07, 95%CI = 0.06–0.09, $P < 0.001$) and hemodialysis (b = 0.67, 95%CI = 0.27–1.06, $P = 0.001$) were associated with a higher modified Thomas fall risk score. Gender, education level and number of comorbidities were not related to fall risk (Table 2).

Table 2

Linear regression analyses of factors associated with fall risk (modified Thomas scale score).

Characteristic	*b* (95% confidence interval)	*P*-value
Hemodialysis	0.67 (0.27, 1.06)	0.001
Age	0.07 (0.06, 0.09)	<0.001
Gender (male vs. female)	-0.26 (-0.63, 0.12)	0.174
Education level (years)	0.04 (-0.08, 0.16)	0.521
Number of comorbid diseases	0.05 (-0.02, 0.12)	0.130

Path analysis was used to explore the direct effects of hemodialysis on fall risk (modified Thomas scale score) as well as the indirect effects of hemodialysis on fall risk mediated through the Barthel index and Cr/CysC ratio. Modified Thomas fall risk score was used as the dependent variable, spasticity and strength were used as exogenous independent variables, and the Barthel index and Cr/CysC ratio were used as the endogenous independent (mediating) variables. The proposed path models (a crude model and a model adjusted for age, gender, education level and number of comorbid diseases) are shown in Figure 1.

In the crude model, hemodialysis had no significant direct effect on the modified Thomas fall risk score and no significant indirect effect on the modified Thomas fall risk score via the Cr/CysC ratio. However, hemodialysis exerted a significant indirect effect on the modified Thomas fall risk score via the Barthel index (b = 0.402, 95%CI = 0.149–0.655, $P = 0.002$). Furthermore, there was a significant overall indirect effect (b = 0.554, 95%CI = 0.257–0.851, $P < 0.001$) and total effect (b = 0.993, 95%CI = 0.432–1.433, $P < 0.001$) of hemodialysis on the modified Thomas fall risk score (Table 3).

Table 3

Path analysis of the direct and indirect effects of hemodialysis on fall risk.

Effect	Crude model			Adjusted model		
	β	95%CI	*P*	β	95%CI	*P*
Effect of hemodialysis on Cr/CysC ratio (a1)	-12.679	-19.033, -6.324	<0.001	-12.679	-19.033, -6.324	<0.001
Effect of Cr/CysC ratio on Thomas score (b1)	-0.012	-0.024, 0	0.056	-0.004	-0.014, 0.007	0.510
Indirect effect of hemodialysis on Thomas score via Cr/CysC ratio (a1*b1)	0.152	-0.021, 0.325	0.086	0.045	-0.091, 0.181	0.516
Effect of hemodialysis on Barthel index (a2)	-22.006	-32.723, -11.29	<0.001	-22.006	-32.723, -11.29	<0.001
Effect of Barthel index on Thomas score (b2)	-0.018	-0.026, -0.011	<0.001	-0.008	-0.014, -0.002	0.015
Indirect effect of hemodialysis on Thomas score via Barthel index (a2*b2)	0.402	0.149, 0.655	0.002	0.172	0.010, 0.333	0.037
Indirect effect of hemodialysis on Thomas score via Cr/CysC ratio and Barthel index (a1*b1+a2*b2)	0.554	0.257, 0.851	<0.001	0.217	0.029, 0.404	0.023
Direct effect of hemodialysis on Thomas score (c)	0.379	-0.105, 0.862	0.125	0.526	0.101, 0.952	0.015
Total effect of hemodialysis on Thomas score (c+a1*b1+a2*b2)	0.933	0.432, 1.433	<0.001	0.743	0.339, 1.147	<0.001

The adjusted model was adjusted for age, gender, education level and number of comorbid diseases. Cr/CysC ratio: ratio of serum creatinine level to serum cystatin C level; 95%CI: 95% confidence interval.

In the adjusted model, hemodialysis exerted a significant direct effect on the modified Thomas fall risk score (b = 0.526, 95%CI = 0.432–1.433, $P = 0.015$) as well as a significant indirect effect via the Barthel index (b = 0.172, 95%CI = 0.010–0.333, $P = 0.037$), but there was no significant indirect effect via the Cr/CysC ratio. The overall indirect effect (b = 0.217, 95%CI = 0.029–0.404, $P = 0.023$) and total effect (b = 0.743, 95%CI = 0.339–1.147, $P < 0.001$) of hemodialysis on the modified Thomas fall risk score were significant (Table 3).

Discussion

A notable finding of this study of hospitalized older adults with multiple comorbid diseases is that hemodialysis and older age were associated with a higher modified Thomas fall risk score. Additionally, after adjustment for age, gender, education level and number of comorbid diseases, path analysis indicated that hemodialysis had both direct and indirect effects on fall risk. Our findings provide further support that hemodialysis increases the risk of falling in hospitalized older adults with comorbidities.

Previous clinical investigations have suggested that CKD increases the risk of serious fall injuries in older adults [15]. Furthermore, it has been reported that hemodialysis exerts negative effects on postural balance [25] and that the incidence of falls is increased after the initiation of hemodialysis in older patients [26]. Hence, our results are consistent with those of the above studies. When CKD progresses to renal failure and requires renal replacement therapy, it may mark the decline of functional status and the deterioration of health [27], which is a known predisposing factor for falls [28]. Indeed, we found that the hemodialysis group had a significantly lower Barthel index score (indicating lower functional status) than the non-hemodialysis group. Furthermore, the path analysis indicated that hemodialysis had an indirect effect on fall risk via functional status, supporting the proposal that the influence of hemodialysis on fall risk may be mediated in part by a deterioration in general health condition that is reflected by a reduction in functional status.

It has been suggested that the progression of CKD can directly lead to falls in the older adults through protein energy consumption, resulting in weakness and loss of muscle mass [29–31]. Cooper et al. found that lower physical capability was associated with a higher risk of negative outcomes [32]. There is an important correlation between muscle mass, strength loss and lack of exercise, so physical activity is an effective measure to prevent and manage sarcopenia [33]. The decrease of muscle mass can directly lead to the impairment of muscle function, including the loss of strength, the loss of self-care ability and the increase of the incidence of falls [34]. Acute and chronic comorbidities will also contribute to the development of sarcopenia in older adults on hemodialysis. Comorbidities may lead to reduced physical activity and periods of bed rest as well as the generation of proinflammatory cytokines that promote proteolysis [33]. In terms of etiology, age-related muscle mass loss is an important cause of weakness [35] At the same time, it can cause disability and increase the risk of all-cause mortality, and increase medical-related expenditure [36, 37]. Furthermore, muscle function is more reliable than muscle mass in predicting disability and mortality [36, 37]. The present study found that the hemodialysis group had significantly higher values for the BMI/SMI ratio and Cr/CysC ratio than the non-hemodialysis group, both of which are markers of muscle sarcopenia [18–21]. This would support the idea that loss of muscle mass contributes to fall risk in older adults on hemodialysis.

We also observed that the hemoglobin level was significantly lower in the hemodialysis group than in the non-hemodialysis group. Renal anemia is a common complication of advanced CKD and thus occurs in some patients on hemodialysis. Anemia may underly some of the detrimental effects of CKD [38] including the decreases of cognitive function, motor function, immune response and nutritional status, at the same time, the incidence rate and mortality of heart failure and depression..

This study has some limitations. First, this was a retrospective analysis, so some degree of selection bias or information bias cannot be ruled out. Second, this was a single-center study, so it remains unknown whether the findings are generalizable. Third, the sample size was quite small, so it is possible that the analysis was underpowered to detect some real differences between groups. Fourth, we only considered fall risk calculated from the modified Thomas scale score, and we did not perform a prospective study to determine the actual incidence of falls. Additional prospective studies will be needed to extend our findings are further characterize the influence of hemodialysis on fall risk in older adults with comorbidities.

Conclusion

Hemodialysis has both direct and indirect effects to increase fall risk in hospitalized older adults with comorbidities. Further research is merited to establish whether interventions to improve nutritional status, promote exercise and optimize drug therapy would help to improve skeletal muscle mass and function and thereby reduce the risk of falling in older adults undergoing hemodialysis.

Declarations

Ethics approval and consent to participate

Our study was conducted in accordance with the Declaration of Helsinki and was approved by the ethical review committee at the First Affiliated Hospital of Nanjing Medical University, ethical review No. 2021-SR-546. This was a retrospective study, and only medical records were analyzed. This study was approved with a waiver of informed consent as the research involves no more than minimal tangible or intangible risk to the subjects. Therefore the ethical review committee at the First Affiliated Hospital of Nanjing Medical University has waived need for informed consent.

Authors' contributions

Rumei Yang and Lihong Wan conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Jin Liu carried out the statistical analysis and reviewed the manuscript. Weihong Zhao and Xiaohua Pei, critically reviewed the manuscript for important intellectual content. Ting Li and Wenting Qin coordinated and supervised the data collection. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

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Competing interests

All authors have contributed significantly to the manuscript and declare that the work is original and has not been submitted or published elsewhere. None of the authors have any conflict of interest.

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Figures

Direct and indirect effects of hemodialysis on fall risk

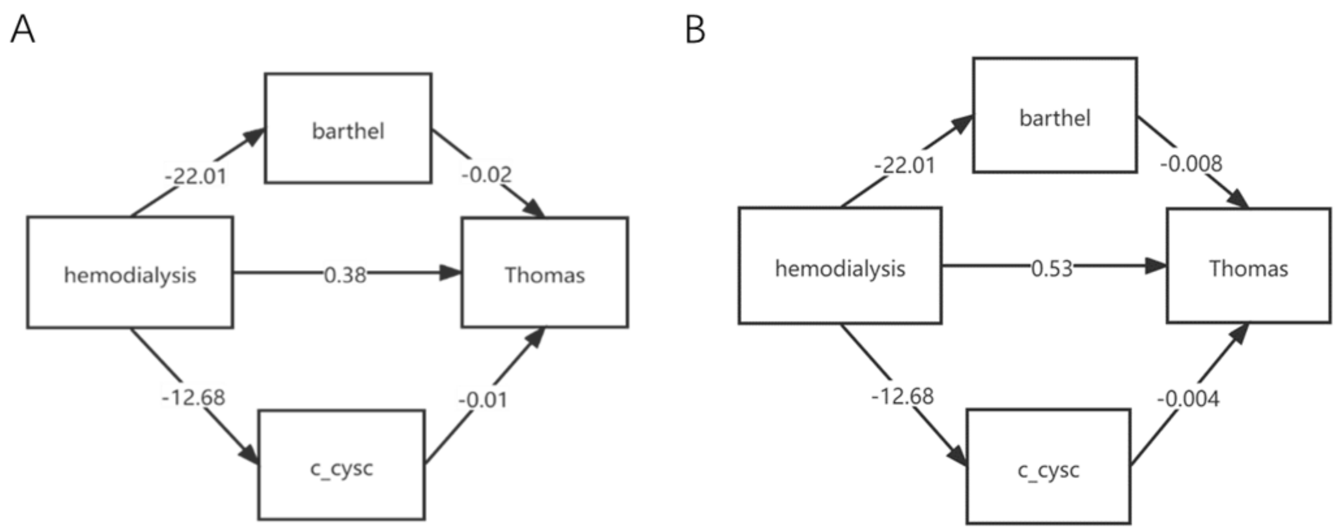

Figure 1

Path analysis models of the effects of hemodialysis on fall risk (Thomas scale score). (A) Crude model. (B) Adjusted model.