Associations of Body Composition, Muscle Function, and Physical Activity with Mortality in Peritoneal Dialysis Patients

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Original Paper

Introduction. Loss of skeletal muscle mass and muscle strength is common in dialysis patients. Therefore, this investigation was designed to determine the association between body composition, muscle function, and physical activity with mortality in peritoneal dialysis (PD) patients.

Methods. This was a multicenter cohort study on all eligible PD patients (n = 79) in Tehran PD centers. At baseline, skeletal muscle mass and muscle strength were determined using bioelectrical impedance analysis and handgrip strength, respectively. Physical performance was assessed by a 4-meter walk gait speed test. Physical activity level was estimated by using the long-form International Physical Activity Questionnaire at baseline. The mortality of PD patients was evaluated two years after the start of this study.

Results. The total dialysis adequacy was significantly lower in dead patients in comparison with live patients ($P < .05$). In contrast, serum hs-CRP ($P < .05$), and the total amount of glucose absorbed daily from PD solutions ($P < .05$) were significantly higher in dead patients in comparison with live patients. There were no significant associations between body fat mass, skeletal muscle mass, skeletal muscle mass index, muscle strength and physical performance with mortality in PD patients. However, in PD patients with physical activity ≤ median, odds of mortality was 7.4 times higher than those with physical activity > median (OR = 7.4, 95% CI: 1.3 to 43.3; $P < .05$).

Conclusion. This study indicates that low physical activity; low dialysis adequacy, high serum hs-CRP, and high amount of glucose absorbed from PD solutions are related with high mortality in PD patients.

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INTRODUCTION

Loss of skeletal muscle mass and muscle strength are common complications in chronic kidney disease (CKD) patients including dialysis patients,[1,2] and result from amino acid and protein losses during dialysis, hormonal changes, metabolic acidosis, a high production of inflammatory cytokines, dietary restrictions, physical inactivity, and aging.[1,3,4] These complications associated with low quality of life, physical disability, high risk of falls and fractures, and increased morbidity.[1,3,5,6]

Some studies indicated that low lean body mass[6-14] and low fat mass[7,8,10] are associated with high mortality in hemodialysis (HD) patients and nondialysis-CKD patients. In contrast, some investigations showed that lean body mass[14,15] and fat mass[9] are not related with the risk of death. Some investigations in HD patients showed

that low muscle strength[15-17] and low physical performance[5] are associated with mortality. Also, some studies showed that low physical activity was related to mortality in nondialysis-CKD and HD patients.[18-21] According to the literature, only few studies in these fields have been done yet in peritoneal dialysis (PD) patients. Huang *et al.* showed that PD patients with low lean body mass had shorter survival.[22] Kang *et al.* and Jin *et al.* indicated that low appendicular muscle mass is related to mortality in PD patients.[23,24] In addition, Kim *et al.* showed that excessive fat accumulation during the early period of PD was related to a higher mortality.[25]

Considering that few studies have been done on the association of body composition with mortality in PD patients, and no study has been conducted on the relationship between muscle function including muscle strength and physical performance,[26] and physical activity with mortality in these patients; therefore, the present study was designed to determine the associations of body composition, muscle function, and physical activity with mortality in PD patients.

MATERIALS AND METHODS

This was a multicenter prospective cohort study. All eligible PD patients (n = 79) between November and December 2015 in Tehran peritoneal dialysis centers were recruited in this cohort study. Inclusion criteria were age ≥ 18 years and being on continuous ambulatory PD for at least 6 months. End points were all-cause mortality by the end of December 2017. The Ethics Committee of the National Nutrition and Food Technology Research Institute of Iran approved the study protocol. Written informed consent was obtained from all patients.

Measurements

Dry weight was assessed to the nearest 0.1 kg, and height; to the nearest 0.5 cm. Assessment of body composition was carried out using bioelectrical impedance analysis by body composition analyzer X-contact 356 (Jawon medical Co., Seoul, South Korea). All anthropometric and body composition measurements were done in the fasting state, with an empty urinary bladder and gastrointestinal tract, and without dialysate in the peritoneal cavity. Skeletal muscle mass index was calculated as the ratio of skeletal muscle mass in kilograms to square of body height in meters.[3,27,28] Muscle strength was assessed based on handgrip strength by means of a hydraulic hand dynamometer Exacta™ (North Coast Medical, Giliory, USA). HGS was measured 3 times in the dominant hand with a 30-second rest interval between trials and maximum value was considered as the measure of the patient's muscle strength.[29] Physical performance was determined by a 4-meter walk gait speed test and each patient was asked to walk at his/her usual speed on a 4-meter course.[3] Time was recorded by a chronometer in seconds. Physical activity level was estimated by using long-form International Physical Activity Questionnaire.[30]

A 5 mL blood sample was taken from each patient after a 12- to 14- hour fast, and the sera were obtained by centrifugation of blood samples at 2500 rpm for 15 min. The serum high sensitive C-reactive protein (hs-CRP) was measured using enzyme-linked immunosorbent assay kits (Zellbio GmbH, Ulm, Germany). The intra-assay coefficient of variation (CV) for serum hs-CRP was 4%. Serum creatinine and urea were determined using various colorimetry methods by commercial kits (Pars-Azmoon, Tehran, Iran) with the aid of a Selectra 2 Autoanalyzer (Vital Scientific, Spankeren, The Netherlands). Intra-assay CVs for both parameter was < 3%.

Total dialysis adequacy (as total Kt/V per week) was assessed by a Kt/V calculator, using information recorded in patient files, including 24-hour dialysate drain volume, dialysate urea concentration, blood urea concentration, urine urea concentration, 24-hours urine volume, age, height, and weight .[31] In this study, from among 79 PD patients, information regarding Kt/V index was available only for 65 PD patients. In addition, the ratio of dialysate to serum creatinine and urea was determined.[32] The peritoneal equilibration test for glucose was done based on a 2 Litters 4.25% dextrose dwell with dialysate samples at 0 and 4 hours during the dwell period. The ratio of dialysate glucose level at time 4 to dialysate glucose concentration at time zero (D4/D0) was determined and then the percent of glucose absorbed from the dialysate was calculated by the 1-D4/D0 formula.[33,34] The total amount of glucose absorbed daily from PD solutions was equal to the total infused anhydrous glucose multiplied by the percent of glucose absorbed.[33]

Outcome Variable and Statistical Analysis

The outcome was all-cause mortality, and 2 years after the start of this study, the mortality of patients was evaluated. Statistical analysis of the data was done by SPPS (IBM SPSS, Chicago, IL, USA) for windows version 21. Quantitative variables are displayed as the mean ± standard error (SE) and categorical variables as frequencies or percentages. All quantitative parameters had normal distribution based on the Kolmogorov-Smirnov test. Baseline differences between live and dead patients were determined using t-test for quantitative variables and chi-square test for categorical variables. Logistic regression analysis was used to determine associations between various variables with mortality and to calculate the odds ratio and 95% confidence interval [OR, (95% CI)]. In this study, the exact date of death of patients was not known, so it is not possible to calculate the incidence rate and relative risk (or relative rate). *P* value ≤ .05 was considered statistically significant.

RESULTS

Baseline characteristics of dead and live PD patients are compared in Table 1. No significant differences were found between dead and live PD patients with regards to age, gender, dialysis vintage, the ratio of dialysate to serum creatinine and urea, serum concentrations of creatinine and urea, BMI, and the presence of diabetes. The total dialysis adequacy was significantly lower in dead patients in comparison with live patients (Table 1, $P < .05$). In contrast, serum hs-CRP ($P < .05$), and the total amount of glucose absorbed daily from PD solutions ($P < .05$) were significantly higher in dead patients in comparison with live patients (Table 1).

There were no significant associations between body composition indicators including body fat mass, skeletal muscle mass, skeletal muscle mass index, and muscle function indicators including muscle strength and walk gait speed with mortality in PD patients (Table 2). However, a significant negative association was found between physical activity and mortality in PD patients (Table 2). In PD patients with physical activity ≤ median, odds of mortality was 5.2 times higher than those with physical activity > median (OR = 5.2, 95% CI: 1.5 to 17.7, $P < .05$; Table 2). After adjusting the effect of total dialysis adequacy, as a confounding factor, odds of mortality in PD patients with physical activity ≤ median increased (OR = 7.4, 95% CI: 1.3 to 43.3, $P < .05$; Table 2).

DISCUSSION

Our study showed that no significant associations existed between body composition indicators including body fat mass, skeletal muscle mass and skeletal muscle mass index with mortality in PD patients. In agreement with this investigation, some studies indicated that lean body mass[14,15] in HD patients, and fat mass[9] in nondialysis-CKD patients are not associated with mortality. In contrast, most investigations showed that low lean body mass[6-14] and low fat mass[7,8,10] are related to

Table 1. Baseline Characteristics of Dead and Live PD Patients

Parameters	Dead Patients (n = 19)	Live Patients (n = 60)	*P*
Age, y†	57.5 ± 3.5	52.0 ± 2.0	> .05
Gender (Male / Female)	11 / 8	24 / 36	> .05
Dialysis Vintage, mo†	3.4 ± 0.5	3.0 ± 0.3	> .05
Total Dialysis Adequacy (Kt/V)†	1.5 ± 0.06	2.1 ± 0.09	< .05
Dialysate to Serum Cr Ratio, %†	74 ± 4	73 ± 2	> .05
Dialysate to Serum Urea Ratio, %†	87 ± 3	87 ± 1	> .05
Absorbed Glucose from Dialysis Solution, %†	67 ± 0.01	69 ± 0.01	> .05
Amount of Absorbed Glucose from Dialysis Solutions, g/d†	103 ± 9	82 ± 5	< .05
Serum hs-CRP, mg/L	6.9 ± 0.6	4.7 ± 0.3	< .05
Serum Cr, mg/dL†	5.6 ± 0.5	5.5 ± 0.3	> .05
Serum Urea, mg/dL†	90 ± 6.0	96 ± 3.0	> .05
BMI, kg/m^2†	26 ± 1.0	25 ± 0.5	> .05
Presence of Diabetes, %	47	35	> .05

†Mean ± SE

Table 2. Associations of body composition, muscle strength, physical performance, and physical activity with mortality in PD patients

Variable	Death Patients (n = 19)	Live Patients (n = 60)	Crude OR (95% CI)	*P*	Adjusted OR† (95% CI)	*P*
Body Fat Mass, kg						
≤ Median	10	30	1.1 (0.4 to 3.1)	> .05	1.2 (0.3 to 4.9)	> .05
> Median	9	30	1		1	
Body Fat Percentage						
≤ Median	9	30	0.9 (0.3 to 2.5)	> .05	1.0 (0.2 to 4.3)	> .05
> Median	10	30	1		1	
Skeletal Muscle Mass, kg						
≤ Median	7	33	0.5 (0.2 to 1.4)	> .05	0.9 (0.2 to 4.2)	> .05
> Median	12	27	1		1	
Skeletal Muscle Mass Percentage						
≤ Median	10	30	1.1 (0.4 to 3.1)	> .05	0.9 (0.2 to 4.1)	> .05
> Median	9	30	1		1	
Skeletal Muscle Mass Index, kg/m^2						
≤ Median	6	33	0.3 (0.1 to 1.1)	> .05	0.6 (0.1 to 3.1)	> .05
> Median	13	27	1		1	
Muscle Strength, kg						
≤ Median	12	26	2.2 (0.8 to 6.5)	> .05	3.4 (0.7 to 16.5)	> .05
> Median	7	34	1		1	
4-meter Walk Gait Speed, m/s						
≤ Median	6	34	0.3 (0.1 to 1.1)	> .05	0.5 (0.1 to 2.2)	> .05
> Median	13	26	1		1	
Physical Activity (MET), min/d						
≤ Median	15	25	5.2 (1.5 to 17.7)	< .05	7.4 (1.3 to 43.3)	< .05
> Median	4	35	1		1	

†Adjusted by Total Dialysis Adequacy

high mortality in HD patients and nondialysis-CKD patients. Some studies in PD patients showed that low lean body mass,[22] and low appendicular muscle mass[23,24] are associated with mortality. In addition, Kim *et al.* showed that excessive fat accumulation during the early period of PD was associated with a higher mortality.[25]

The reasons for the associations between low muscle mass and low fat mass with high mortality in dialysis patients may be the presence of poor nutritional status and/ or high level of inflammation in these patients.[14] It has been shown that poor nutritional status and inflammation are related to high mortality in dialysis patients.[35,36] In our study, the lack of a significant association between body composition and mortality may be due to small sample size.

This study indicated that no significant associations existed between muscle function indicators including muscle strength and physical performance with mortality in PD patients. In contrast to our study, some studies showed that low muscle strength[6,15-17,37,38] and low physical performance[15,39] were related to mortality in dialysis patients and nondialysis-CKD patients. Because all factors that affect loss of skeletal muscle mass may cause low muscle function,[4] therefore, the mechanisms by which low muscle function indicators affect mortality in dialysis patients are similar to mentioned mechanisms for low muscle mass. In the present study, the lack of significant associations between muscle strength and physical performance with mortality may be due to small sample size.

In our study, in PD patients with physical activity ≤ median, mortality was considerably higher than those with physical activity > median. To our knowledge, only one study in this field has been done yet in PD patients. Shi *et al.* showed that PD patients who could not walk a 6-min distance had less survival than PD patients who could walk a 6-min distance.[40] In addition, some investigations showed that low physical activity was associated with mortality in nondialysis-CKD[18-20] and HD patients.[21] Physical activity reduces mortality in dialysis patients by improving insulin sensitivity

and endothelial function and lowering inflammation in uremic patients.[14,18,41] In our study, serum hs-CRP was significantly higher in dead patients compared to live patients.

Our study indicated that the total dialysis adequacy was significantly lower in dead patients in comparison with live patients. In agreement with our study, some investigations showed that higher dialysis adequacy is associated with better survival in PD patients.[42,43] The beneficial effect of dialysis adequacy on patient survival may be due to removing toxins more effectively.

In the present study, serum hs-CRP was significantly higher in dead patients compared to live patients. Some studies indicated that CRP is an indicator of all cause and cardiovascular death in dialysis patients.[44,45] In PD patients, inflammation is caused by low clearance of inflammatory cytokines due to kidney failure, and high synthesis of inflammatory cytokines because of the accumulation of various compounds and the bioincompatibility of PD solutions.[46]

Our study showed that the total amount of glucose absorbed daily from PD solutions was significantly higher in dead patients in comparison with live patients. In agreement with our study, some investigations showed that higher glucose concentration of PD solutions is related to higher all-cause and cardiovascular mortality in PD patients.[47,48] Evidence shows that continuous exposure to hyperosmotic and hyperglycemic dialysis solutions may cause chronic inflammation [(49)] and inflammatory markers are one of the most important risk factors for cardiovascular diseases.[50]

A limitation of our study was small sample size; therefore, the power of our study was low compared with other studies in this field.

CONCLUSION

This study indicates that low physical activity; low dialysis adequacy, high serum hs-CRP, and high amount of glucose absorbed from PD solutions are associated with high mortality in PD patients.

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DISCLOSURE

The authors declare that they have no conflicts of interest.

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