ORIGINAL RESEARCH

Combined Contribution of Reduced Functional Mobility, Muscle Weakness, and Low Serum Albumin in Prediction of All-Cause Mortality in Hemodialysis Patients: A Retrospective Cohort Study

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Objectives: The combined effects of reduced functional mobility, muscle weakness, and low serum albumin on mortality in hemodialysis patients have not been clarified. Here, we examined the associations of reduced functional mobility, muscle weakness, and low serum albumin—both alone and in combination—with all-cause mortality in hemodialysis patients.

Methods: A total of 490 patients treated between July 2010 and October 2016 were enrolled retrospectively in this study. The independent prognostic effect of the combination of reduced functional mobility, muscle weakness, and low serum albumin on survival was estimated by Cox proportional hazard regression analysis. We calculated the increases in predictive capacity by combining the associations of reduced functional mobility, muscle weakness, and low serum albumin in comparison to each component alone based on the receiver-operating characteristic curves, continuous net reclassification improvement (NRI), and integrated discrimination improvement (IDI).

Results: The final study population consisted of 314 hemodialysis patients, and 56 patients died during the 6.5-year follow-up period. The high Combined score group showed a significantly lower cumulative survival rate than the low Combined score group (hazard ratio, 3.30; 95% confidence interval, 1.59-6.87; $P = .001$). Both NRI and IDI suggested that the addition of Combined score to patient characteristics improved discrimination of patients at high risk of mortality (NRI, 0.038 95% CI: 0.096 - 0.064, $P < .001$ IDI, 0.029 95% CI: 0.004 - 0.055, P = .025).

Conclusions: The combined assessment of reduced functional mobility, muscle weakness, and low serum albumin was associated with poorer prognosis in patients on hemodialysis. The results presented here indicated that the combination of reduced functional mobility, muscle weakness, and low serum albumin is useful for accurate prediction of prognosis in hemodialysis patients.

Introduction

THE PREVALENCE OF physical frailty characterized by reduced functional mobility and muscle weakness is high in patients with end-stage renal disease.[1] A previous study indicated that the proportion of older adults with physical frailty on hemodialysis is at least 70%. Poor physical status is strongly associated with elevated risks of adverse events[2,3] and mortality[4,5] in hemodialysis patients.

Patients with chronic kidney disease, especially those undergoing dialysis, show a high prevalence of a syndrome of adverse metabolic and nutritional derangements designated as protein energy wasting (PEW). PEW was suggested to indicate concurrent depletion of protein and energy stores, and the International Society of Renal Nutrition and Metabolism proposed the following causes of PEW in dialysis patients: (1) nutrient loss into dialysate; (2)

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dialysis-related inflammation; (3) dialysis-related hypermetabolism; and (4) loss of residual renal function.[6] PEW is closely associated with elevated mortality risk in hemodialysis patients,[7-12] serum albumin is readily utilizable criteria for the clinical diagnosis of PEW.[13]

As reduced functional mobility, muscle weakness, and low serum albumin are prognostic indicators of survival, the effectiveness of their combined contribution to mortality in hemodialysis patients is a matter of clinical interest. Green et al.[14] developed the Green score, which consists of a composite of handgrip strength, gait speed, activities of daily living status, and serum albumin, as a prognostic predictor in older adults with heart failure. However, there have been no studies regarding its prognosis predictive capacity. The present study was performed to determine the isolated and combined associations of reduced functional mobility, muscle weakness, and low serum albumin with all-cause mortality in patients undergoing hemodialysis.

Methods

Study Population

A total of 490 patients from the Hemodialysis Center, were retrospectively enrolled in this study between July 2010 and October 2016. All patients were undergoing maintenance hemodialysis therapy 3 times a week, which is the most common schedule in Japan according to the Japanese Society for Dialysis Therapy. The exclusion criteria were as follows: hospitalization within 3 months before the study; recent myocardial infarction or angina pectoris; uncontrolled cardiac arrhythmia, hemodynamic instability, uncontrolled hypertension, or renal osteodystrophy with severe arthralgia; or requirement for assistance in walking. The study was approved by the Research Ethics Committee. In this study, all data were obtained in standard clinical practice of our hemodialysis center.

Patients Characteristics

Data on demographic factors (age, sex, and time on hemodialysis), physical constitution (body mass index [BMI]), primary cause of end-stage renal disease, and comorbidities (atherosclerotic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, peripheral artery disease, dysrhythmia, and other cardiac diseases, chronic obstructive pulmonary disease, gastrointestinal bleeding, liver disease, cancer, and diabetes) were collected at the time of entry into the study. Laboratory values (hemoglobin) were obtained from hospital charts. Comorbidities were quantified using a comorbidity index developed for dialysis populations composed of the primary cause of end-stage renal disease, and 11 comorbidities were calculated using the method described previously to analyze survival in hemodialysis patients.[15]

Exposure Measurement

As the Combined score, we used the Green score based on the frailty score consisting of 4 components: slowness, weakness, malnutrition, and inactivity. Slowness was evaluated by measuring the usual gait speed. Briefly, patients were asked to walk at their usual pace using any necessary assistive devices and were timed over the middle 10 m of a 12-m walkway. Weakness was evaluated by measuring handgrip strength in the sitting position using a digital dynamometer (Grip-D; Takei, Tokyo, Japan). Two maximal isometric voluntary contractions of the hands for 3-s each were performed for both hands, with the elbow joint at 90° flexion. The greatest strength, expressed as absolute value (kg), was used in the analyses. Malnutrition was assessed by measuring serum albumin level. Inactivity was detected based on the dependence of following 5 activities related to lower-extremity function in the Functional Independence Measure[16]: transfer to bed, chair, or wheelchair; transfer to toilet; transfer to tub or shower; and walking and stair climbing. The Green score was then obtained by combining these four assessments, as described previously.[14] Gait speed and serum albumin were divided into quartiles. Handgrip strength was divided into quartiles stratified by sex. Inactivity was dichotomized into a group with dependence in any ADL versus those with no ADL dependence. The Green score was calculated as follows: (1) quartiles of albumin, gait speed, and handgrip strength were assigned values of 0-3 in descending order; (2) functional dependence was given a score of 0 for ADL independence; and (3) for any ADL dependence. These components were then summed to derive the Green score for each patient (0 = low risk to 12 = high risk; Supplemental Table 1).

Outcome

All-cause mortality was assessed by death registry at the clinic. Recruitment started on July 2010, and date of death was determined on February 2017. We truncated the data for the follow-up to 6.5 years.

Statistical Methods

Demographic and clinical factors are presented as means ± standard deviation or number (percentage) and were examined for significance by unpaired t test and χ^2 test. For Kaplan–Meier estimates of survival curves, the data for the 6.5-year follow-up period were truncated to avoid insufficient numbers of patients at risk. The participants were divided into two groups by a Combined score cutoff value of 5, which was defined according to the best cutoff from the quartile distribution for mortality.[17] Differences between groups were examined for using the log-rank test. The independent prognostic effect of Combined score on survival was estimated by Cox proportional hazard regression analysis after adjustment for confounders, including age, sex, time on hemodialysis, BMI, primary