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Frailty and Survival in Patients with End-Stage Renal Disease

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Abstract

Frailty is highly prevalent in patients with end-stage renal disease who require hemodialysis therapy. Frailty has been proposed by Fried and colleagues, and predicts poor outcomes in hemodialysis patients. Muscle weakness is a major component of frailty. We previously performed a single-center, prospective, observational, cohort study among 190 Japanese patients undergoing hemodialysis and examined the association of muscle weakness in lower extremity with survival. As a result, muscle weakness in the lower extremities had a significant negative effect on survival in these patients. Muscle weakness is reversibly activated by exercise training or physical therapy in patients undergoing hemodialysis. Therefore, exercise training for patients with end-stage renal disease could improve their prognosis via correction of muscle weakness. In this paper, we reviewed muscle weakness, which is one of the components of frailty, in hemodialysis patients based on our previous study.

Keywords: Dialysis; Kidney; Renal; CKD; Frailty; Muscle weakness; Physical therapy; Rehabilitation; Exercise

Introduction

Frailty is highly prevalent in patients with end-stage renal disease who require hemodialysis therapy. Frailty predicts poor outcomes in community-dwelling elderly populations, patients with chronic kidney disease, and patients undergoing hemodialysis [1-7]. Frailty has been proposed by Fried and colleagues, and the gold standard for identifying frailty is based on the following five criteria: shrinking, weakness, poor endurance and energy, slowness, and a low physical activity level [8].

Weakness is one of the five components in frailty and is determined by handgrip strength. However, handgrip strength of patients undergoing hemodialysis is decreased by the presence of a hemodialysis shunt in the arm. In some patients, handgrip strength is reduced because of carpal tunnel syndrome, cubital tunnel syndrome, or destructive cervical spondylosis. Therefore, handgrip strength potentially fails to predict generalized muscle weakness in hemodialysis patients. However, lower extremity muscle strength is not directly influenced by a hemodialysis shunt or these comorbidities in the upper extremities. Furthermore, lower extremity muscle strength directly affects walking ability, standing balance function, activity of daily living, and quality of life, and is a target of intervention for physical therapists.

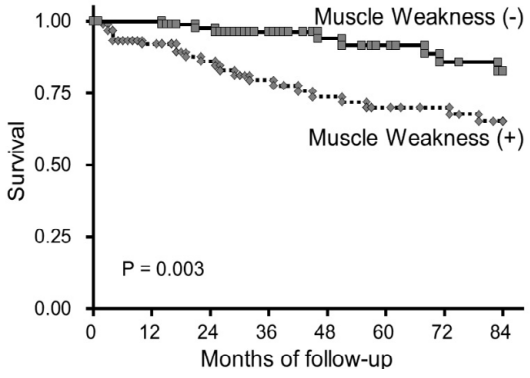

Figure 1: Muscle weakness and survival in hemodialysis patients (Modified from reference 9). Muscle weakness: Isokinetic knee extensor muscle strength (kg) was divided by dry weight and expressed as percentage (%). A cut-off point of muscle weakness was 40% in Japan. People with values under this cut-off point may need assistance with walking.

We review muscle strength, which is one of the components of frailty, in hemodialysis patients based on our previous study [9].

Lower extremity muscle strength and survival

We previously performed a single-center, prospective, observational, cohort study among 190 Japanese patients undergoing hemodialysis and examined the association of muscle weakness in lower extremity with survival [9]. Although all of the patients in our study population walked unassisted, approximately half of them had muscle strength lower than the cut-off value predicting whether people need assistance with walking. Over 7 years of follow-up, a total of 30 deaths occurred, with 17 attributed to cardio-cerebrovascular disease. The estimated cumulative survival was markedly different between the two groups, with 92.0% in the non-weakness group versus 75.6% in the weakness group (Figure 1). After adjustment for patients' characteristics and severity of comorbidity, muscle weakness in the lower extremities had a significant negative effect on survival. The hazard ratio in the weakness group was 2.73 (95% confidence interval = 1.14–6.52, P = 0.02) compared with the non-weakness group. Several possibilities can be considered regarding our results. Lower extremity muscle strength and physical activity level appear to interact. A sedentary lifestyle increases the risk of mortality in patients undergoing hemodialysis [10]. However, the underlying mechanisms remain to be determined.

Strength exercises in hemodialysis patients

Resistance training successfully enhances skeletal muscle and improves muscle strength in frail elderly populations and in those with chronic diseases. Cheema et al. investigated the effectiveness of resistance training on skeletal muscle quantity and strength in patients

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who received maintenance hemodialysis [11]. They found that resistance training improved muscle strength, but not muscle quantity. A meta-analysis showed the effect of exercise training on muscle strength in hemodialysis patients in 2014 [12]. In this meta-analysis, analysis was performed using 10 previously reported randomized, controlled trials, and exercise training was associated with improved muscle strength in these patients.

However, because almost all hemodialysis patients participated in these randomized, controlled trials of exercise training were younger than those in the clinical setting, future clinical trials for frail elderly patients undergoing hemodialysis are required to apply the evidence of exercise training in a clinical setting. Furthermore, we must encourage an active participate of frail elderly patients in exercise training program by not only physical therapist but also care manager [13].

Summary and Conclusion

Frailty is associated with poor outcomes in patients undergoing hemodialysis. Muscle weakness is a major component of frailty and is reversibly activated by exercise training or physical therapy in patients undergoing hemodialysis. Therefore, exercise training for patients with end-stage renal disease could improve their prognosis via correction of muscle weakness.

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