

## Frailty Raises as a New Target in Patients with Chronic Hemodialysis in any Country and the Problem we Should Solve

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### STUDY DESCRIPTION

The population undergoing dialysis is aging and increasing around the world. A particularly problematic issue plaguing the elderly population is the frailty. Frailty is usually defined as “a state of increased vulnerability to stressors resulting from a decrease in physiologic reserves in multiple organ systems causing limited capacity to maintain homeostasis” [1]. There are two major approaches to assess frailty: one is frailty phenotype model developed by Fried et al. and the other is accumulated deficit model by Rockwood et al. While the most widely used assessment of frailty is Fried’s phenotype model, regardless of assessment method, frailty remains highly associated with an increased risk of several deleterious outcomes including disability, falls, hospitalization, institutionalization, and death [2].

Potential pathophysiological factors of frailty present in patients with chronic kidney disease (CKD), furthermore are found in patients with end stage of renal disease (ESRD). Several reports showed that toxic factors in uremic state accelerated aging and led to a progressively impaired organ function [3]. In addition, anorexia caused by uremic toxins, dialysate and urine nutrient losses, catabolic effect, chronic low-grade inflammation, deficiency or resistance to anabolic hormone and sedentary life style have been reported to induce PEW and frailty [4]. Therefore, patients with CKD and ESRD are particularly susceptible to frailty. The prevalence of frailty ranged from 7% to 20.9% among the pre-dialysis CKD, and frailty is more prevalent among patients on hemodialysis (HD) with the range from 24% to 78% [5], moreover ESRD with frailty is reported to be associated with severe mortality and the other adverse health outcomes in several countries [2].

On the other hand, Japanese patients with HD were reported to have a much better prognosis than other developed countries in the DOPPS survey, despite of older age of patients than other countries [6]. This suggests that the situation of frailty in patients with HD may differ considerably between Japan and the other

developed countries. However, the status of frailty among Japanese patients with HD remained unknown. Thus, we investigated to identify the current status of frailty in Japanese patients with HD, using the modified Fried’s frailty phenotype model adjusted for Japanese, as known as J-CHS frailty phenotype model [7]. In total of 388 patients, 52.6% of participants were categorized as pre-frailty and 21.4% as frailty. The prevalence of frailty increased steadily with age and was more prevalent in females than in males and the subjects with frailty received polypharmacy. In addition, frailty was associated with the multimorbidity. Contrary to expectations, there was no marked difference in the frequency or efficiency of dialysis among each frailty phenotype [7]. Regarding the etiology of ESRD, diabetic nephropathy was determined as an independent risk factor for frailty [8].

The prevalence of frailty in Japanese patients with HD was relatively lower than that previously reported in other developed countries; however, it was extremely high compared to the general population. We also investigated the prognosis of frail patients with ESRD. Frailty detected by J-CHS phenotype model, was associated with risk of death (hazard ratio [HR] 2.42, 95% confidence interval [CI] 1.12–5.23 adjusted for age and gender) and independently associated with the combined outcome of death or hospitalization (HR 2.85, 95% CI 1.74–4.69, adjusted for age, gender and all comorbidities). According to the results above, patients with ESRD easily fall into frailty, and the frailty has the influence on mortality and healthy life, regardless of the prognosis of the underlying patient population. Therefore, the early detection and intervention for frail patients with ESRD are urgently required to prevent the adverse outcomes in any country.

We also examined the influence of peripheral artery disease (PAD) on patients with ESRD. The prevalence of frailty in HD patients with PAD was significantly higher than in HD patients without PAD (34% vs. 18%,  $p=0.010$ ). Non-shunt side grip strength was significantly stronger in the patients without PAD than the patients with PAD (23.6 kg vs. 17.0 kg,  $p<0.001$ ) [9].

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Furthermore, frailty complicated with PAD was independently associated with higher risk of death (HR 4.72, 95% CI 1.37–16.26) and the combined outcome of death or hospitalization (HR 5.89, 95% CI 2.94–11.77), adjusted for age, gender and all comorbidities, compared with frailty only or PAD only. We found that frailty itself significantly worsens the prognosis of patients with ESRD, moreover the presence of PAD further exacerbates the prognosis of frail patients with ESRD, while PAD is very common among ESRD patients. Patients with PAD were reported to have a higher incidence of mobility loss and becoming unable to walk [10]. Probably, poor gait ability may reduce overall locomotor activity, decrease overall muscle mass, and reduce energy consumption leading to low appetite, as a result, the cycle of frailty [11] turns faster.

To date, frailty is very common among patients with ESRD and important as a prognostic indicator in any country. Timely and regular assessment of frailty, and effective intervention are very important to prevent poor patients' outcome. Since simple evaluation and intervention methods for frailty have been steadily established, it is desirable to practice them at each facility. Patients must come to dialysis unit three times per week. Taking advantage of the situation, recently intradialytic exercise such as cycle ergometer and rubber tube training during dialysis are prescribed. Nutritional intervention is also important. Intradialytic oral nutrition had reported to improve protein homeostasis [12]. Dual intervention (nutritional and exercise intervention) reported to improve nutritional or physical factors and quality of life [13,14], in addition, it is expected to improve mortality and adverse health outcomes. However, many of reports are small size and there have been few trials evaluating the impact of exercise on frailty in detail, and few reports using prospective, randomized, and controlled trials. Thus, many of effectiveness regarding interventions for population of ESRD still remain unclear. Furthermore, several reports revealed many rates of participants' withdrawal from interventions. Therefore, in addition to further investigation and continuing verifications, the development of an effective strategy for promoting adherence rates to interventions are required. We should solve these difficult problems.

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#### REFERENCES

- Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. *Lancet* (London, England). 2013;381(9868):752-762.
- Sy J, Johansen KL. The impact of frailty on outcomes in dialysis. *Curr Opin Nephrol Hypertens*. 2017;26(6):537-542.
- Kooman JP, Broers NJ, Usvyat L, Thijssen S, van der Sande FM, Cornelis T, et al. Out of control: accelerated aging in uremia. *Nephrology, dialysis, transplantation: Official publication of the European Dialysis and Transplant Association-European Renal Association*. 2013;28(1):48-54.
- Kim JC, Kalantar-Zadeh K, Kopple JD. Frailty and protein-energy wasting in elderly patients with end stage kidney disease. *J Am Soc Nephrol*. 2013;24(3):337-351.
- Carrero JJ, Johansen KL, Lindholm B, Stenvinkel P, Cuppari L, Avesani CM. Screening for muscle wasting and dysfunction in patients with chronic kidney disease. *Kidney Int*. 2016;90(1):53-66.
- Goodkin DA, Bragg-Gresham JL, Koenig KG, Wolfe RA, Akiba T, Andreucci VE, et al. Association of comorbid conditions and mortality in hemodialysis patients in Europe, Japan, and the United States: The Dialysis Outcomes and Practice Patterns Study (DOPPS). *J Am Soc Nephrol*. 2003;14(12):3270-3277.
- Takeuchi H, Uchida HA, Kakio Y, Okuyama Y, Okuyama M, Umabayashi R, et al. The Prevalence of Frailty and its Associated Factors in Japanese Hemodialysis Patients. *Aging and Dis*. 2018;9(2):192-207.
- Kakio Y, Uchida HA, Takeuchi H, Okuyama Y, Okuyama M, Umabayashi R, et al. Diabetic nephropathy is associated with frailty in patients with chronic hemodialysis. *J Geriatrgerontolo Int*. 2018;18(12):1597-602.
- Okuyama M, Takeuchi H, Uchida HA, Kakio Y, Okuyama Y, Umabayashi R, et al. Peripheral artery disease is associated with frailty in chronic hemodialysis patients. *Vascular*. 2018;26(4):425-431.
- McDermott MM, Guralnik JM, Tian L, Liu K, Ferrucci L, Liao Y, et al. Associations of borderline and low normal ankle-brachial index values with functional decline at 5-year follow-up: The WALCS (Walking and Leg Circulation Study). *J Am Coll Cardiol*. 2009;53(12):1056-1062.
- Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, et al. Frailty in older adults: Evidence for a phenotype. *J Gerontol A BiolSci Med Sci*. 2001;56(3):146-156.
- Lacson E, Wang W, Zebrowski B, Wingard R, Hakim RM. Outcomes associated with intradialytic oral nutritional supplements in patients undergoing maintenance hemodialysis: A quality improvement report. *Am J Kidney Dis*. 2012;60(4):591-600.
- Hristea D, Deschamps T, Paris A, Lefrancois G, Collet V, Savoie C, et al. Combining intra-dialytic exercise and nutritional supplementation in malnourished older haemodialysis patients: Towards better quality of life and autonomy. *Nephrol*. 2016;21(9):785-790.
- Martin-Aleman G, Valdez-Ortiz R, Olvera-Soto G, Gomez-Guerrero I, Aguire-Esquivel G, Cantu-Quintanilla G, et al. The effects of resistance exercise and oral nutritional supplementation during hemodialysis on indicators of nutritional status and quality of life. *Nephrology, dialysis, transplantation: Official publication of the European Dialysis and Transplant Association-European Renal Association*. 2016;31(10):1712-1720.