

**Table 1** Sensitivity and specificity of five times chair stand time as a surrogate for gait speed (cut-off point ≤ 0.8 m/s) for selected cut-off values

Chair stand time (s)	Total (n = 629)		Age ≥ 65 years (n = 357)	
	Sensitivity	Specificity	Sensitivity	Specificity
15	0.607	0.985	0.607	0.975
14	0.679	0.963	0.679	0.939
13	0.750	0.940	0.750	0.908
12	0.786	0.900	0.786	0.847

Office to correct this typo. In addition, the eligibility criteria and methods for participant selection of men were the same as those for women.

To the final comment, a standard chair means "A standard chair (with a seat height of 40 cm) with a backrest, but without armrests." There was backrest for

the participants' safety, but we asked them to stand without touching the backrest. We thank the authors for their comment for reproducibility.

Disclosure statement

The authors declare no conflict of interest.

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Chronic kidney disease, physical frailty and cognitive impairment

Dear Editor,

Shen *et al.* assessed chronic kidney disease (CKD)-related frailty and cognitive impairment, and CKD was a potential cause of frailty and cognitive impairment.¹ The authors recommended multidimensional interventions in patients with early-stage CKD. Does this mean that preventive actions for frailty and cognitive impairment in patients with end-stage CKD are too late to maintain their quality of life?

First, Costa *et al.* carried out a study with repeated measures to determine the risks for cognitive fluctuations in hemodialysis patients.² They clarified that the level of cognition fluctuated during the treatment process of hemodialysis. In contrast, Post *et al.* reported that well-dialyzed hemodialysis patients with optimized hemoglobin levels and with no history of stroke presented deterioration in the level of cognition.³ More studies on cognitive impairment in patients with CKD should be carried out, stratified by the progression of CKD.

Second, physical frailty and cognitive impairment would be modified by several factors during the progress of kidney dysfunction. Anand *et al.* speculated that small vessel disease would be a shared risk factor for

CKD and cognitive decline, as well as physical function decline.⁴ In addition, the association between CKD and neurological complications in patients with early, moderate or end-stage CKD should be separately checked.⁵

Finally, I greatly appreciate Shen *et al.* recommending therapeutic intervention in patients with early-stage CKD. To maintain a desirable lifestyle and treatment for CKD, an educational system for patients and their family should be established.

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The author declares no conflict of interest.

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Response to the letter of Dr Tomoyuki Kawada, “Chronic kidney disease, physical frailty and cognitive impairment”

Dear Editor,

The points raised by Dr Kuwada related to our study are important.¹ During the early stage of chronic kidney disease (CKD), the renal function compensation could be obtained by physiological reserve. The same is to the brain and other organs during the early stage of CKD-related physical frailty and cognitive impairment. CKD-induced physical frailty with subtle cognitive decline is a reversible cognitive frailty, and physical frailty with mild cognitive impairment is a potentially reversible cognitive frailty.² Thus, early detection and preventive intervention to asymptomatic patients is important to maintain their quality of life. Patients with moderate-stage CKD or rapid renal function decline showed a significantly high risk of developing irreversibly functional impairment, such as physical frailty, difficulty with activities of daily living and instrumental activities of daily living, mobility limitation, falls, cognitive impairment, vascular dementia, and morbidity.^{1,3} Patients with end-stage CKD undergoing ambulatory peritoneal or hemodialysis usually have more serious functional impairment or a higher risk of cerebrovascular diseases and cognitive impairment than those with moderate-stage CKD.⁴ Hemodialysis patients with slow gait speed after starting dialysis had an increased risk of short-term mortality and hospitalization.⁵ Multidimensional interventions in patients with moderate- or end-stage CKD might be a double-edged sword for their health. Anti-anemia agents decrease the risk of cognitive disorders, but result in an increased frequency of stroke. Blood or peritoneal dialysis results in a decrease in the levels of uremic toxins and inflammatory cytokines, but cause the loss of nutrients, rapid blood pressure alteration, gas embolisms and cerebral edema. Furthermore, the use of an anticoagulant increases the risk of hemorrhagic stroke in hemodialysis patients. Therefore, it is too late to maintain a patient's quality of life in the end stage of

CKD. However, after comprehensive geriatric assessment, necessary interventions will save the life and slow the decline of quality of life of patients with moderate- or end-stage CKD.

Several early studies reported that cognition performance of patients with end-stage CKD showed obvious temporal variations during hemodialysis.^{6–8} Cognitive performance was down during and immediately after hemodialysis, up 24 h postdialysis during the dialysis cycle, and then down again.^{7,8} Patients of continuous ambulatory peritoneal dialysis did not show such fluctuations.^{6,7} Costa *et al* further reported that cognitive fluctuations of minor patients during the hemodialysis cycle might result from intradialytic hypotensive episodes and the use of psychoactive medication.⁹ Dialysis did not improve patients' cognition. Post *et al.* reported that well-dialyzed patients without stroke and anemia showed more prevalent non-memory-related cognition deterioration than controls with normal kidney function independent of vascular and cognitive impairment risk factors.¹⁰ Furthermore, hemodialysis even deteriorated patients' cognitive function. As reviewed by the present authors, compared with patients with CKD, hemodialysis patients showed more severe cognitive dysfunction; and dialyzed patients had a greater 1-year Mini-Mental State Examination score reduction than control elderly patients.¹ We fully appreciate the suggestion of Dr Kuwada that more studies of hemodialysis on cognitive impairment in patients with CKD are needed, stratified by the progression of CKD, including the effects of dialysis cycle on cognitive performance.

Epidemiological evidence and mechanism studies reviewed by the present authors and other investigators have shown that traditional cardiovascular factors, such as hypertension, diabetes, hypercholesterolemia and hyperhomocysteinemia-induced small vessel disease, are common risk factors for early-stage CKD, cognitive decline and physical frailty (Fig. 1).^{1–3} At the moderate stage of CKD, non-traditional cardiovascular factors and