



Validation of risk prediction tools in elderly patients who initiate dialysis

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Abstract

Purpose The number of elderly patients with end-stage renal disease on maintenance dialysis therapy is gradually increasing. The elderly population has difficulties in making decisions regarding initiation of dialysis treatment because of their high morbidity and frailty. The purpose of this study was to determine the best prognostic tool in predicting short-term mortality in elderly patients undergoing dialysis.

Methods This study is a multicenter retrospective study. We enrolled patients, aged ≥ 75 years, who began hemodialysis at three university hospitals in Korea from January 2010 to December 2016. We applied two comorbidity-based score tools (Thamer and Wick, each consisting of seven variables) and the Clinical Frailty Scale (CFS, seven scales), which were validated for mortality prediction in elderly incident patients. Patient's information was obtained from electronic medical records in the participating center, and mortality data (up to December 2016) were obtained from the Korean National Statistical Office. Models were compared using the area under the receiver operating characteristic curve.

Results Among the 219 patients enrolled in this study, the 3- and 6-month mortality rates were 31 (14.4%) and 48 (22.4%), respectively. Receiver operating characteristic curve analysis revealed that both score systems and the CFS showed similar performance while predicting 3- and 6-month mortality. The scores from these indices correlated with survival time.

Conclusion Predicting short-term mortality and long-term survival time for elderly patients is possible using the Thamer and Wick scores and the CFS.

Keywords Elderly · Dialysis · Risk · Mortality

Introduction

The number of elderly patients with end-stage renal disease (ESRD) on maintenance dialysis therapy is gradually increasing in many countries [1, 2]. Data from the United States Renal Data System indicate that the incidence of ESRD is increasing among persons older than 65 years, especially among those older than 80 years [1]. The number of dialysis patients increased approximately by 7–10% per year in Korea, and the proportion of elderly dialysis patients also increased [3]. The proportion of elderly dialysis population (65 years and older) in Korea was 11% in 1990, 19% in 2000, 35% in 2010, and 45.2% in 2017, whereas the mean age of the population on dialysis increased from 55.2 years in 2005 to 61.7 years in 2017 [4].

The elderly population has difficulties in decision making regarding initiation of hemodialysis due to the high prevalence of comorbidities and frailty in this population [5].

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Therefore, elderly patients undergoing hemodialysis are at an increased risk of poor outcomes including death, with a mortality rate of up to 37 deaths/100 person-years within the first 6 months of initiation of dialysis therapy [6]. In general, dialysis patients aged 75 years and older have a three to sixfold increased risk of mortality as compared with their counterparts aged 45 years and younger [7]. Dialysis patients have a lower quality of life by almost 50%, compared with the rest of the population [8]. Additionally, elderly dialysis patients report a lower quality of life compared with age-matched controls [7].

Recently, clinical risk stratification tools have been developed for elderly dialysis patients [9–11]. These algorithms are designed to predict early mortality by measuring and scoring the identified risk factors in each elderly dialysis patient. These tools are composed of patient's age and comorbidities. Frailty (loss of cognitive function and health reserves, leading to increased vulnerability) in dialysis patients was suggested as a risk factor for death [12]. In addition, frailty is common in elderly patients [13]. The Clinical Frailty Scale (CFS) was validated in relatively old dialysis patients (mean age, 63 ± 15 years), and higher CFS at dialysis initiation was associated with higher mortality [14]. This finding suggests that the degree of frailty has a predictive value for short-term mortality in elderly dialysis patients. However, there is no comparative study assessing the superiority of these tools designed to assess the risk of dialysis initiation in elderly patients with ESRD. Therefore, the purpose of this study was to compare the risk stratification tools for early mortality in elderly Korean patients with ESRD to guide relevant decision making.

Methods

Study population, data, and design

This study is a multicenter retrospective study. We enrolled patients, aged ≥ 75 years, who began hemodialysis at three university hospitals in Seoul (capital), Gyeonggi-do (metropolitan area), and Chungcheongnam-do (urban and rural areas) in Korea, from January 2010 to December 2016. Patients who were initiated on hemodialysis due to acute renal failure and those who selected peritoneal dialysis as a renal replacement therapy were excluded from this study. The study was approved by the participating institutional review boards (IRB file nos. 2018–04-028, 2018–05-002, and 2018–05-028).

We adopted and compared three tools. Among them, two score systems, arbitrarily named Thamer score [10] and Wick score [11] in this study, were designed to predict early mortality in the elderly hemodialysis population in Korea. The Thamer score was designed on the basis of retrospective

administrative and clinical data for prediction of mortality in patients 67 years and older who were undergoing dialysis therapy between 2009 and 2010 in the United States. Seven variables were chosen (Table 1), and the total score ranged from 0 to 9, with 0 point predicting 6-month mortality of 4%; 1 point, 7%; 2 points, 12%; 3 points, 20%; 4 points, 27%; 5, points 35%; 6 points, 44%; 7, points 49%; ≥ 8 points, 55% [10]. The Wick score was designed on the basis of retrospective administrative and clinical data for predicting mortality in patients older than 65 years who initiated dialysis between May 2003 and March 2012 in Canada. The algorithm included seven variables (Table 1), and the total score ranged from 0 to 19, with a score < 5 predicting $< 25\%$ 6-month mortality, whereas a score > 12 predicting $> 50\%$ [11]. Another tool was necessary to score the subjective symptom of respiratory distress; however, this tool was excluded because of the retrospective nature of our study [9]. CFS was developed to predict death or need for institutional care for elderly people [12]. CFS is graded from 1 to 7 (Table 1). We applied the above three scales to the Korean elderly patients and used the predicted mortality for each case to compare whether they could be considered for the prediction of actual short-term mortality. The receiver operating characteristic (ROC) curve was obtained by applying mortality prediction rate. Patient information was obtained from electronic health records of the participating centers. We collected data such as age, sex, comorbidities, cause of chronic kidney disease (CKD), and laboratory data. The comorbidities of each subject were identified by screening the medical records before or at the time of hemodialysis initiation. In addition, the patients were divided into two groups according to their ages (75–84 years and 85 years and older), and their baseline characteristics according to age difference were analyzed.

Mortality data

Mortality data were obtained from the Korean National Statistical Office (Microdata Integrated Service, on-demand, 20,180,619, <https://mdis.kostat.go.kr>). It is mandatory to report the death of any Korean national to the National Statistical Office. We analyzed early mortality after dialysis initiation and restricted our analyses to deaths that had occurred until December 2016. The researchers called the patients who had initiated their dialysis after June 2016 and checked their status (6 months' mortality).

Statistical analysis

Statistical analysis was performed using the SPSS software for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). All data have been expressed as mean \pm standard

Table 1 Risk assessment variables in the two predictive scores and scale of Clinical Frailty Scales

Wick score		Thamer score		The Canadian Society of Health and Aging CFS	
Variables	Points if Yes	Variables	Points if Yes	Scale	
Age \geq 80 years	2	Age		1	Very fit: robust, active, energetic, well motivated, and fit: fittest in their age group
		70–84 years	1		
		85–89 years	2		
		\geq 90 years	3		
eGFR 10–14.9 mL/min/1.73m ² \geq 15 mL/min/1.73 m ²	1 3	Albumin level < 3.5 g/dL or unknown	1	2	Well: without active disease but not as fit as those in category 1
Atrial fibrillation	2	Needs assistance for daily living	1	3	Well: with treated comorbid disease
Congestive heart failure	2	Lives in nursing home	1	4	Apparently vulnerable: not dependent but has symptoms from comorbid disease
Lymphoma	5	Cancer	1	5	Mildly frail: limited dependence on others for instrumental activities of daily living
Metastatic cancer	3	Heart failure	1	6	Moderately frail: help is needed for instrumental activities of daily living and activities of daily living
Hospitalization in prior 6 months	2	Hospitalization > 1× or > 1 months in last year	1	7	Severely frail: completely dependent on others for instrumental activities of daily living and activities of daily living or terminally ill

eGFR estimated glomerular filtration rate

deviation or proportion (%), unless otherwise specified. *P* values < 0.05 were considered statistically significant. The baseline characteristics of the ESRD patients were compared according to age using the Pearson Chi-square test for categorical variables. A life table was used for the comparison of unadjusted survival rates. For comparison of the effectiveness of the algorithms, the area under the curve (AUC) was compared and analyzed with R version 3.3.1, pROC package. The Pearson correlation coefficient was used to compare mortality changes, with increasing scores for each model.

Results

Baseline characteristics

During the study period, 1,908 patients were initiated on hemodialysis at three centers. Of these, 260 patients (13.6%) were older than 75 years. A total of 219 patients were enrolled, excluding 41 patients with acute renal failure. There was no difference in the percentage of elderly (older than 75 years) patients undergoing hemodialysis and in the percentage of patients who had just initiated dialysis among the three centers. The demographic characteristics

of the population have been summarized in Table 2. The oldest patient was a 95-year-old male patient with survival of 3.9 months. The single most important etiology of ESRD was diabetes mellitus (DM). However, the definitive cause of ESRD was not identified in almost half of the cases. Underlying commodities did not differ according to age groups. There was no significant difference in laboratory results between the age groups. Only 11% of them had a prepared hemodialysis access (arteriovenous fistula or arteriovenous graft). Among them, 119 (51%) had a history of hospitalization within 1 year prior to initiation of dialysis and 22 (10%) were staying in a nursing care center before dialysis. A total of 174 (80%) patients could walk independently. A single case with severe behavioral disorder was reported. On echocardiographic examination, 22 (10%) had regional wall motion abnormality or depressed ejection fraction. Six patients had arrhythmias other than atrial fibrillation.

Outcomes and scores

During the study period, the median survival time was 15.6 [5.6–32.8] months. The 3- and 6-month mortality was 14.4% and 22.4%, respectively. The scores of the three scales were not normally distributed (Shapiro–Wilk

Table 2 Demographic and clinical characteristics of the study cohort

	Total (n=219)	75–84 years (n=189)	≥ 85 years (n=30)	P value
Age (years), mean ± SD [IQR]	79.9 ± 3.9 [77–82]	78.8 ± 2.6 [76–81]	87.2 ± 2.0 [86–88]	< 0.001
Male sex (n, (%))	106 (48.4)	96 (50.8)	10 (33.3)	0.075
CKD etiology (n, (%))				
DKD	4 (42.9)	84 (44.4)	10 (33.3)	0.232
GN	9 (4.1)	7 (3.70)	2 (6.67)	0.448
Hypertension	13 (5.9)	10 (5.3)	3 (10.0)	0.242
Others	103 (47.0)	88 (46.5)	15 (50.0)	
Comorbidity (n, (%))				
Hypertension	197 (89.9)	171 (90.4)	26 (86.6)	0.754
Diabetes mellitus	134 (61.1)	115 (60.8)	19 (63.3)	0.887
Coronary artery disease	53 (24.2)	48 (25.4)	5 (16.6)	0.3
Cerebrovascular disease	38 (17.3)	33 (17.4)	5 (16.6)	0.915
Congestive heart failure	49 (22.3)	45 (23.8)	4 (13.3)	0.201
Malignancy	15 (6.8)	11 (5.8)	4 (13.3)	0.130
Atrial fibrillation	28 (12.8)	24 (12.7)	4 (13.3)	0.923
Laboratory data				
Hb (g/dL)	12.8 ± 55.9	13.3 ± 60.2	9.6 ± 1.4	0.956
eGFR (mL/min/1.73 m ²)	8.8 ± 4.4	8.7 ± 4.4	9.1 ± 4.2	0.436
Albumin (g/dL)	3.4 ± 0.6	3.5 ± 0.6	3.3 ± 0.5	0.734
HbA1c (%)	6.2 ± 1.1	6.2 ± 1.0	6.6 ± 1.6	0.075
Total cholesterol (mg/dL)	142.5 ± 43.4	143.3 ± 44.3	137.5 ± 37.2	0.902
Triglyceride (mg/dL)	108.9 ± 59.8	108.1 ± 61.4	114.2 ± 46.8	0.642
HDL cholesterol (mg/dL)	38.3 ± 14.0	38.0 ± 13.9	40.3 ± 14.4	0.565
LDL cholesterol (mg/dL)	85.2 ± 32.1	84.6 ± 32.8	88.8 ± 27.3	0.716
Total calcium (mg/dL)	8.2 ± 1.0	8.2 ± 0.9	8.0 ± 1.0	0.284
Phosphorus (mg/dL)	4.9 ± 1.5	5.0 ± 1.5	4.7 ± 1.5	0.751
iPTH (pg/mL)	181.4 ± 159.6	183.4 ± 166.7	169.9 ± 108.7	0.224
hs-CRP (mg/dL)	3.4 ± 5.3	3.5 ± 5.4	2.5 ± 4.3	0.733

DKD diabetic kidney disease, GN glomerulonephritis, eGFR estimated glomerular filtration rate

test, all $P < 0.001$). The Thamer and Wick scores were higher in the group 85 years and older than the group 75–84 years (Table 3). However, the CFS score did not differ between the two groups. The maximum Thamer score was 7 points, and the maximum Wick score was 11 points. Figure 1 shows the short-term mortality, survival time of study cohort, and distribution of scores.

The two comorbidity-based scales had moderate correlation ($P < 0.001$, $r = 0.59$). The CFS score also correlated with the Thamer ($P < 0.001$, $r = 0.40$) and Wick scores ($P = 0.008$, $r = 0.17$).

Table 3 Mortality and survival time of the study cohort and distribution of scores

	Total (n = 219)	75-84 years (n = 189)	≥ 85 years (n = 30)	P value
Survival time (months)				
Median [IQR]	15.6 [5.6–32.8]	16.1 [6.6–33.8]	9.3 [4.7–26.6]	0.368
3-month mortality (n (%))	31 (14.4)	26 (14.0)	5 (17.2)	0.721
6-month mortality (n (%))	48 (22.4)	37 (20.0)	11 (37.9)	0.092
Thamer score, mean [IQR]	2.7 [2–3]	2.5 [2–3]	3.9 [3–5]	< 0.001
Wick score, mean [IQR]	2.9 [1–4]	2.8 [1–4]	3.9 [2–4.8]	0.022
CFS	4.7 [4–5]	4.68 [3–6]	5.13 [4–7]	0.148

CFS clinical frailty scale

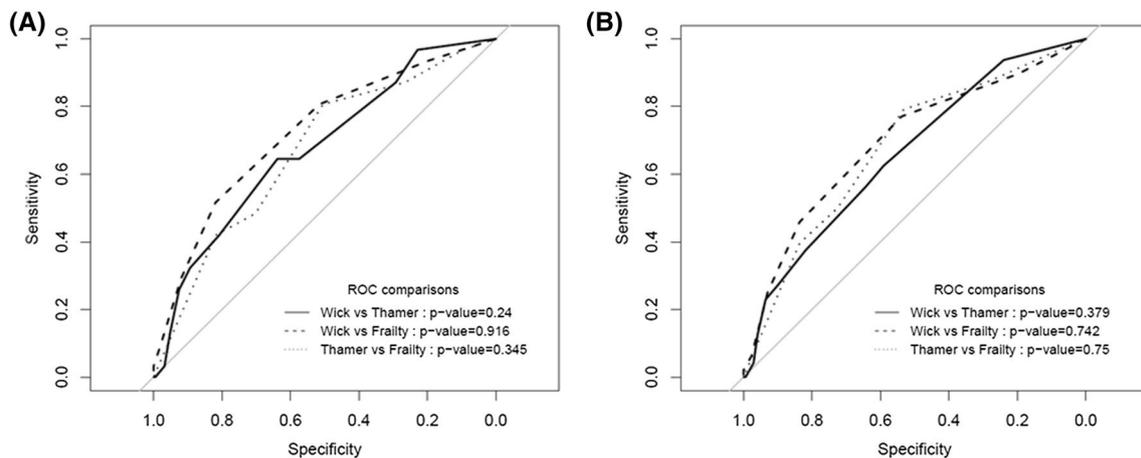


Fig. 1 Comparison of the three algorithms for predicting early mortality in elderly dialysis population using the receiver operating characteristic (ROC) curve and DeLong's test for comparison of ROC curve. **a** 3-month mortality **b** 6-month mortality

Comparison of the three scales for predicting short-term mortality

The ROC curve showed a similar performance for predicting 3- and 6-month mortality (Fig. 1). Owing to the different scales of morbidity scores, we adjusted the scores with the percentage of maximal values. Additionally, there was no difference in the ROC curve comparison. Both the scales had a significant positive correlation with mortality at 3 and 6 months during the study period (Fig. 2). Survival time also correlated in both the models (Fig. 2).

Discussion

In this study, we analyzed the survival time and short-term mortality of the elderly (75 years and older) Korean dialysis population and suggested that the two comorbidity scores and the CFS, which were originally devised for predicting early mortality in Western countries, could be useful for predicting early death after dialysis. The performance of these scores was similar for predicting early death in elderly dialysis patients. In addition, modalities designed to predict short-term mortality showed a statistically significant correlation with survival time in this study. This implies that these modalities are suitable for planning for elderly patients with renal failure.

The high early mortality rate in our cohort is consistent with that in previous studies [1, 6, 15]. Surprisingly, there was no difference in overall mortality, survival time, and 3- and 6-month mortality rates when elderly patients were divided into two groups of 75–84 years and 85 years and older. In the population older than 75 years, it may be considered that any further increase in age does not have any additional effect on mortality. This may be due to the fact

that there was no significant difference in the percentage of comorbidities between the two groups (Table 1). This is different from the results of various studies that have reported that mortality increased with age even after 75 years [15, 16]. In addition, only 30 patients 85 years and older were included in our cohort. The number of patients older than 85 years was small, and the interquartile range of patients older than 85 years was 86–88 years. Our cohort did not include an adequate number of very old patients, such as nonagenarians or centenarians. Therefore, this may be caused by the small number of patients older than 85 years, and it is unlikely to be explained by *P* value alone.

A comorbidity-based score must be objective. Any health care giver could assess the patients, and the scores should be very well correlated. Although the CFS is easy to understand, the results could differ depending on clinicians. This scale includes items such as comorbidity, cognitive impairment, and disability and requires the judgment of physicians. However, the CFS showed good reliability between inter-raters [17], which strengthens the utility of this measure.

Both comorbidity scoring systems had seven categories and included common factors such as age, history of cancer, history of recent hospitalization, and congestive heart failure. The inclusion of these common factors in both scoring systems could have led to the moderate correlation observed between the two scoring systems. Although lymphoma had a high score (5 points) in the Wick score, no patient in our cohort had lymphoma. Therefore, the range of scores in the Wick model is up to 19, and the score in our cohort was low. Lymphoma is a heterogeneous group of diseases. Moreover, lymphoma incidence is influenced by regional and racial differences. Lymphoma comprised 3% of all cancers reported in Korea [18]. Therefore, lymphoma is considered to have a relatively low incidence in elderly Korean patients. Enrolling lymphoma patients would have altered the mortality rates in

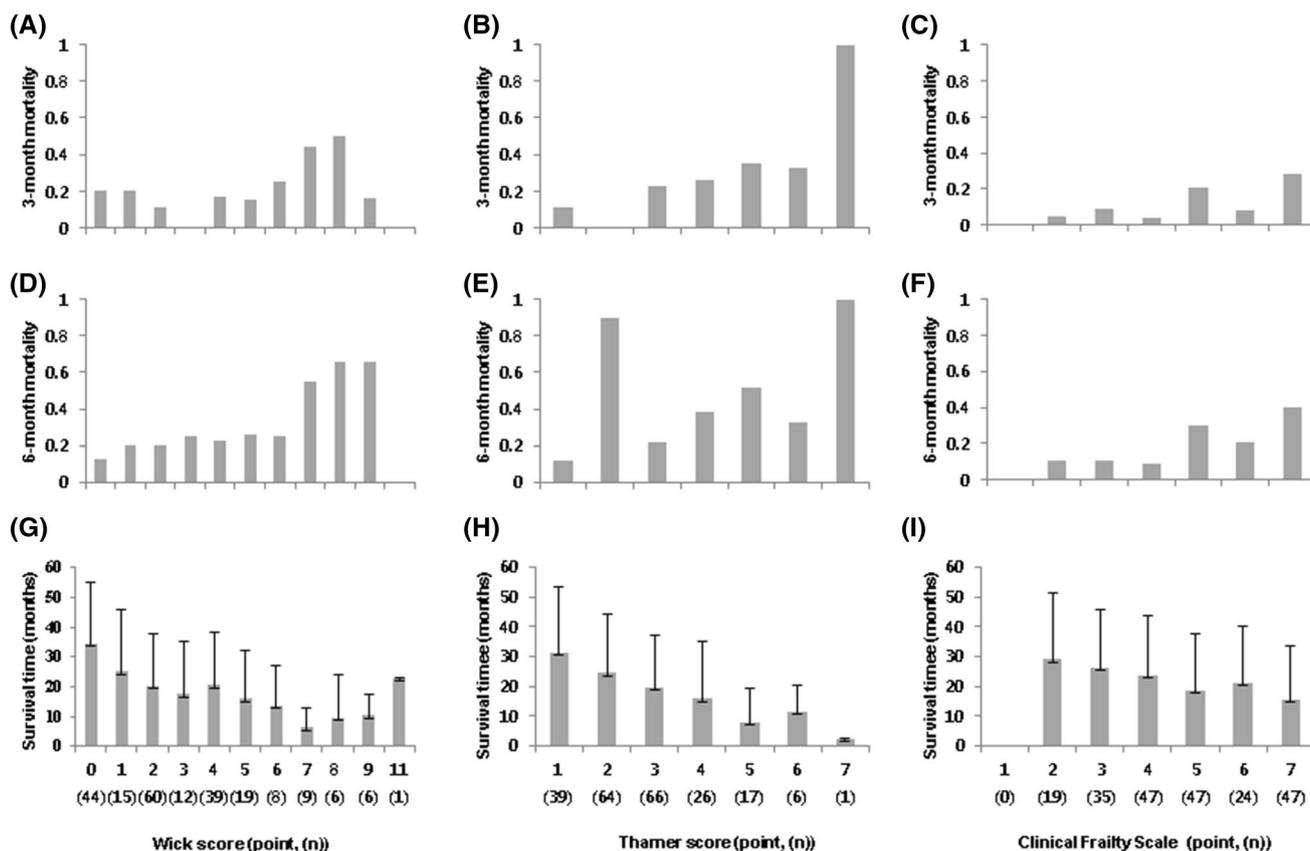


Fig. 2 Mortality and survival time according to the three scales

our cohort. It is unclear if lymphoma should be included in models for predicting death in the Korean population.

None of the scales in this study included dementia, when in fact, the number of people affected by dementia is estimated to double every 20 years, reaching up to 81.1 million by 2040 [19]. Dementia in advanced age is associated with higher mortality rates and shortened life span [20, 21]. In addition, dementia is considered to be an independent risk factor for death in dialysis patients [22]. Therefore, the decision regarding whether and when to initiate dialysis in patients with dementia can be difficult and imprecise [23].

The significance of this study is that it includes the most recent published data comparing the elderly population and the older population [10, 11, 15]. The results are thought to be even more valuable now, as aging, life span, and the number of elderly dialysis patients are progressively increasing [1, 6].

Our study had a few limitations. First, the total number of patients participating in the study was small. It would not be correct to assume that our cohort represented the entire Korean population. However, our cohort comprised of patients from three different cities and therefore had the advantage of including patients from various geographical regions. Second, the study did not include patients

undergoing peritoneal dialysis. In studies analyzing mortality due to different modalities in the elderly dialysis population, there is a high chance that elderly patients have initiated peritoneal dialysis [24, 25]. In those studies, exclusion of peritoneal dialysis patients may have led to poor mortality prediction rates in elderly patients with ESRD. However, the number of peritoneal dialysis patients in Korea is gradually decreasing, and out of the total number of renal replacement therapy patients, they accounted for 4.5% in 2017, which is a very small proportion [6]. Third, this was a retrospective study, and it is possible that we may have missed obtaining the clinical characteristics of some patients. Additionally, patients with poor baseline condition along with CKD were more likely to not have started hemodialysis, and we may have only selected relatively healthy patients for participation in our study, thus leading to bias.

Whether dialysis should be initiated in elderly patients with underlying diseases is a question that is of concern to many physicians. Our study would be helpful as a guide to appropriate decision making. However, further validated algorithms will be needed for very elderly dialysis patients.

When starting dialysis treatment in elderly patients with ESRD, it is reasonable to adopt a risk assessment scale to predict early mortality. It is also useful for predicting

long-term mortality as well as early mortality. We also found that short-term mortality of the oldest person (≥ 85 years) who had similar comorbidities did not differ from that of other elderly persons (younger than 85 years). When caring for elderly patients with CKD, a thoughtful approach should be adopted by health-care providers, the family of patients, and the patients themselves. In addition, a new predictive risk score, including cognitive function of elderly patients, should be developed.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This study was approved by the participating institutional review boards (IRB file nos. 2018–04–028, 2018–05–002, and 2018–05–028) and has been performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Because this study was retrospective and many participants were not alive informed consent was waived by IRB.

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