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Geriatric Assessment and the Relation with Mortality and Hospitalizations in Older Patients Starting Dialysis

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Keywords
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Abstract
Background and Objectives: A geriatric assessment (GA) is a structural method for identifying frail patients. The relation of GA findings and risk of death in end-stage kidney disease (ESKD) is not known. The objective of the GA in OLder patients starting Dialysis Study was to assess the association of GA at dialysis initiation with early mortality and hospitalization. ***Design, Setting, Participants, and Measurements:*** Patients ≥65 years old were included just prior to dialysis initiation. All participants underwent a GA, including assessment of (instrumental) activities of daily living (ADL), mobility, cognition, mood, nutrition, and comorbidity. In addition, a frailty screening (Fried Frailty Index, [FFI]) was applied. Outcome measures were 6- and 12-month mortality, and 6-month hospitalization. Associations with mortality were assessed with cox-regression adjusting for age, sex, comorbidity burden, smoking, residual kidney function and dialysis modality. Associations with hospitalization were assessed with logistic regression, adjusting for relevant confounders. ***Results:*** In all, 192 patients were included, mean age 75 ± 7 years, of whom 48% had ≥3 geriatric impairments and were

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considered frail. The FFI screening resulted in 46% frail patients. Mortality rate was 8 and 15% at 6- and 12-months after enrolment, and transplantation rate was 2 and 4% respectively. Twelve-month mortality risk was higher in patients with ≥3 impairments (hazard ratio [HR] 2.97 [95% CI 1.19–7.45]) compared to less impaired patients. FFI frail patients had a higher risk of 12-month mortality (HR 7.22 [95% CI 2.47–21.13]) and hospitalization (OR 1.93 [95% CI 1.00–3.72]) compared to fit patients. Malnutrition was associated with 12-month mortality, while impaired ADL and depressive symptoms were associated with 12-month mortality and hospitalization. ***Conclusions:*** Frailty as assessed by a GA is related to mortality in elderly patients with ESKD. Individual components of the GA are related to both mortality and hospitalization. As the GA allows for distinguishing between frail and fit patients initiating dialysis, it is potentially of added value in the decision-making process concerning dialysis initiation.

Introduction

The chronic kidney disease population is ageing and an increasing number of older patients start with dialysis [1]. Over the past decade the number of octogenarians on dialysis has almost doubled [2]. Approximately half of the octogenarians and nonagenarians starting dialysis will die within 1 year after initiating dialysis and dropout is particularly high early after initiation [2, 3]. As the burden of dialysis can be high in the elderly, nephrologists increasingly face the dilemma whether initiation of dialysis would be appropriate. Older patients with end-stage kidney disease (ESKD) often exhibit impairments across various geriatric domains, such as dependency in activities of daily living (ADLs), mobility impairment, cognitive impairment, depression and malnutrition [4]. Accumulation and interaction of impairment of multiple domains may contribute to increased vulnerability to external stressors, also referred to as the frailty phenotype [5].

Although emerging evidence exists on the relation between frailty and poor outcome, there is no consensus on the definition. While there are many operationalizations of frailty, most stem from 2 major frailty models: the phenotypic frailty model where frailty is seen as the final common pathway of ageing [6] and the cumulative deficits model [7]. In nephrology, the first model using the Fried Frailty criteria, is most often used to assess frailty; this screening tool measures physical reserves, malnutrition and exhaustion, and is associated with increased hospitalizations and mortality after dialysis initiation [6, 8–10]. A broader concept of frailty is the cumulative deficits model that includes impairment across various geriatric domains, such as somatic, functional and psychosocial impairment [11]. By systematically assessing geriatric domains, a geriatric assessment (GA) is an evidenced-based approach to assess this cumulative deficits construct of frailty. In ESKD, although a myriad of studies showed various geriatric impairments are related to poor outcome, no data is available on whether a GA at initiation of dialysis is related to outcome [4]. Whether frailty according to a GA is capable of distinguishing between fit patients and frail patients, in whom the benefits of dialysis do not offset the burden, is not known yet.

The GA in OLder patients starting Dialysis (GOLD) Study was conducted to assess the relation between frailty according to a GA and early mortality and hospitalization in older patients incident to dialysis. In addition, the relation between the individual geriatric impairments and poor outcome was assessed. Finally, we looked at other frailty instruments and poor outcome.

Methods

Study Design and Patient Selection

The GOLD study is a multicentre, prospective, cohort study assessing the relation between a GA and poor outcome in ESKD patients. The GOLD study included both patients starting dialysis and patients choosing conservative care. For this analysis we included only the dialysis patients. Participants were enrolled from 17 different hospitals across the Netherlands (Appendix 1) in the period from August 2014 to September 2017. Consecutive patients eligible for dialysis were included between 3 weeks before and 2 weeks after the first dialysis session. Patients were excluded if informed consent was not provided, if they had insufficient understanding of the Dutch language or if they suffered from a terminal non-renal related condition. Patients were followed from start of dialysis until kidney transplantation, death or censoring (recovery kidney function or loss to follow-up). The study was conducted in accordance with the Declaration of Helsinki and approved by the medical ethics review boards of all participating hospitals. Written informed consent was obtained from all patients and participating caregivers prior to enrolment.

Data Collection and Analysis

Baseline demographic data collected from medical charts included age, sex, educational level and living situation, cause of kidney failure, residual renal function, acute start of dialysis, type of dialysis, dialysis access, blood pressure, body mass index and smoking habit.

For the GA, participants were either visited at home (on a non-dialysis day for haemodialysis [HD] patients) or in the dialysis centre, before starting the dialysis session. The assessments were per-

formed by the investigators (I.N.L. or N.A.G.) or by one of the trained research nurses. The GA consisted of validated questionnaires or structured assessments of 7 domains (Appendix 2): (ADL, Katz et al. [12]), instrumental ADL (IADL, Lawton and Brody [13]), mobility (Timed-Up-and-Go [14]), depressive symptoms (Geriatric Depression Scale [15], Appendix 4), nutrition (Mini Nutritional Assessment [16]), comorbidity burden (the Cumulative Illness Rating Scale-Geriatrics) [17, 18] and cognition (Mini-Mental State Examination, [19] Clock drawing test, [20] fluency test [21] and enhanced cued recall test) [22]. Impaired cognition was defined as one or more impaired cognitive tests. The time needed to apply a GA was approximately 1–1.5 h. The outcome of the GA was composed by the sum of impairment in the 7 geriatric domains [23]. Patients were defined as being frail when they had impairments in ≥2 impairments (GA2+) [23], all patients with <2 impairments were considered fit. Results of the structured GA were not communicated with the treating physician and therefore did not influence treatment decisions.

In addition, 4 frailty screening methods were applied: Fried Frailty Index (FFI) [6], Groningen Frailty Indicator (GFI) [24], (Appendix 3), the clinical judgment of the nephrologist by means of the "Surprise Question" and the nephrologists' estimation of the level of frailty. For the Surprise Question, clinicians were asked whether *they would be surprised if the patients would die within 6 months after dialysis initiation* [25]. For the estimation of frailty, the treating nephrologist was asked to indicate how frail the patients was in his/her opinion on a scale from 0 to 10, where 0 was fit and 10 was frail. A score of ≥5 was a priori defined as frail.

For follow-up, data on 6- and 12-month mortality and 6-month hospitalizations were collected from each centre. The patients who were alive after 6 months were contacted by telephone and asked whether the dialysis therapy was according to (or above) or below their initial expectations.

Statistical Analysis

Data is summarized using means with SD, or proportions when appropriate. All domains were dichotomized into impaired and not impaired according to the pre-defined cut-off values (Appendix 2). Differences between groups were assessed using chi-squared tests for dichotomous variables and *t* tests for normally distributed continuous variables.

The relation of the GA and frailty screening methods with mortality was assessed with log rank tests. Factors significantly associated with 12-months mortality (or with a p value ≤0.10) were analysed with a cox proportional hazards model, adjusting for age, sex and high comorbidity as defined by the Cumulative Illness Rating Scale-Geriatrics (model 1) and additionally for current smoking, residual renal function and dialysis modality (model 2). Frailty as measured with the GA was a priori defined as having impairments in ≥2 domains (GA2+) [23]. As none of the patients screened as fit by this definition died, the relation between GA2+ and mortality could not be analysed with a cox-regression model. Thus, we further used ≥3 impairments (GA3+) for the definition of frailty, and analyzed this accordingly [23]. Due to a low number of deaths, multivariate analysis for 6-month mortality was not performed. Proportional hazards assumptions were assessed using a log-minus-log plot.

A logistic regression analysis was performed for the relation of geriatric impairment with hospitalization (yes/no), adjusted for age, sex and comorbidity burden. A two-tailed $p < 0.05$ was considered statistically significant. Data analysis was performed with SPSS version 22 software [15].

Table 1. Baseline characteristics

	n = 192
Demographics	
Age, years, mean ± SD	75±7
Gender, male, %	67
Medical history, %	
Hypertension	89
Diabetes mellitus	39
Myocardial infarction	33
Peripheral vascular disease	17
Cerebrovascular event	17
Clinical parameters, %	
Cause of kidney failure	
Renal vascular	50
Diabetes	16
Glomerulonephritis	7
Other	27
Dialysis modality (% PD)	23
Acute start of dialysis, %	16
Access: central venous line (% of HD)	38
BMI, kg/m^2, mean ± SD	26±5
Systolic blood pressure, mm Hg[1], mean ± SD	150±22
Diastolic blood pressure, mm Hg[1], mean ± SD	74±14
eGFR, mL/min/1.73 m^2 CKD-EPI, mean ± SD	8.0±3.0
Hemoglobin, mmol/L, mean ± SD	6.3±0.9
Albumin, g/L, mean ± SD	34±6
Smoking (current), %	14
Social setting, %	
Living alone	42
Living in a nursing home facility	5
University	22
Polypharmacy	
No of drugs, mean ± SD	11±5

[1] Pre-dialysis.

PD, peritoneal dialysis; HD haemodialysis, BMI, body mass index.

Results

Baseline Characteristics

A total of 196 incident dialysis patients were included in the GOLD Study. Another 28 patients were screened, but excluded because of terminal illness (n = 3), language barrier (n = 3) or refusal to participate (n = 22). The majority of the patients were included just after the start of dialysis (median 8 days, interquartile range 1–13). Four patients were excluded from the prospective analysis because they did not meet the inclusion criteria regarding the interval between time of inclusion and start of dialysis. No patients were lost to follow-up. The mean age was 75 (±7) years and 67% of patients were male (Table 1). Impairment across all geriatric domains was common (Table

Table 2. Geriatric impairment at baseline

Geriatric impairment	*n* = 192
Functional impairment, %	
ADL: ≥1 impairment	29
IADL: ≥1 impairment	78
Mobility: severely impaired[a]	18
Cognitive impairment, %	
MMSE[a]	13
Cognitive test battery[#, a]	72
Mood, %	
Depressive symptoms	30
Nutrition, %	
Malnutrition[$]	5
Comorbidities, %	
Severe comorbidity burden[%]	42
Frailty: GA, %	
GA ≥2 impairments	76
GA ≥3 impairments	48
Frailty: screening methods, %	
FFI[a]	46
GFI (≥4)	61
Surprise question ("not surprised")[b]	23
Clinical impression nephrologist[c]	66

[#] One or more impaired cognitive tests: MMSE, Clock drawing test, fluency test, enhanced cued recall test.
[$] As defined by the Mini Nutritional Assessment.
[%] CIRS-G score ≥2× score 3 or ≥1× score.
[a] <5% missing.
[b] 21% missing.
[c] 22% missing.
ADL, activities of daily living; IADL, instrumental ADL; MMSE, Mini Mental State Examination; GA, geriatric assessment; FFI, Fried Frailty Index; GFI, Groningen Frailty Indicator.

2). Of all patients, 76% had >2 impairments (GA2+) and 48% had ≥3 impairments (GA3+). When frailty-screening tools were applied, the prevalence of frailty ranged from 46% (FFI) to 66% (clinical impression nephrologist).

Of all patients, 77% started HD and 23% peritoneal dialysis (PD). The mean age was lower in the PD group compared to that in the HD group (73 ± 6 vs. 76 ± 7, p = 0.04) and PD patients were less likely to live alone (27 vs. 47% of the HD patients, p = 0.02). In general, the PD group was less impaired than the HD group, although this did not reach statistical significance (Appendix 5).

Follow-Up

Follow-up was complete for all patients. The 6-month mortality rate was 8% (n = 15, of whom 6 patients [40%] withdrew from dialysis prior to death) and transplantation rate was 2% (n = 3), while 12-month mortality rate was 15% (n = 29) and transplantation rate was 4% (n = 7). Patients who died within 12 months were older at baseline (mean age 79 ± 7 vs. 75 ± 6 years, p < 0.01). Other baseline characteristics did not differ significantly between patients who died and who did not.

Geriatric Impairment and Mortality

Geriatric impairments were associated with 6- and 12-month mortality (Table 3). Six-month mortality was higher among patients with impairment in IADL (10 vs. 0%, p = 0.03), cognitive impairment, as measured with the Mini-Mental State Examination, (20 vs. 6%, p = 0.01), depressive symptoms (14 vs. 5%, p = 0.04) and malnutrition (30 vs. 7%, p < 0.01). Twelve-month mortality was higher among patients with (functional) impairment compared to patients without impairment. In the multivariate analysis, ADL (hazard ratio [HR] 3.20 [95% CI 1.45–7.06]), depressive symptoms (HR 2.30 [95% CI 1.06–5.02]) and malnutrition (HR 4.52 [95% CI 1.40–14.61]) were associated with 12-month mortality (Table 4, model 2). For IADL no events occurred in the fit group, and therefore, a log rank test was applied instead of a cox regression. IADL was significantly associated with 12-month mortality, when stratified for age (<80 and ≥80 years) p < 0.01.

Relation between Frailty and Mortality

GA. Twelve-month mortality rate was 21% among patients with ≥3 impairments (GA3+) and 8% among patients with less impairment (p = 0.02). After correcting for potential confounders GA3+ was associated with mortality, HR 2.97 (95% CI 1.19–7.45; Table 4, Model 2). In this model, age was not significantly associated with mortality (HR 1.06 [95% CI 1.00–1.12], p = 0.055).

Frailty screening methods. Frail patients as measured with the FFI had a higher mortality risk compared to fit patients, with an adjusted HR 4.10 (95% CI 2.47–21.13; Table 4). In addition, the clinical impression of the nephrologist concerning frailty was related to mortality (adjusted HR 7.22 [95% CI 2.47–21.33]). The GFI and the Surprise Question were not related to mortality.

Hospitalization in the First 6 Months after Dialysis Initiation

During the first 6 months of follow-up, approximately half of the patients (49%) were hospitalized. Patients with impairments in the following geriatric domains were more likely to be hospitalized compared to non-impaired patients when adjusted for potential confounders: ADL (OR 2.88 [95% CI 1.46–5.70]), IADL (OR 2.25 [95% CI 1.07–4.76]), and depressive symptoms (OR 2.29 [95% CI

Table 3. Geriatric domains and association with 6- and 12-month mortality

Geriatric impairment	6-Month mortality					12-Month mortality				
	impaired		not impaired		*p* value	impaired		not impaired		*p* value
	n	%	*n*	%		*n*	%	*n*	%	
Functional impairment										
ADL: ≥1 impairment	7/57	12	8/135	6	0.13	16/57	28	13/135	10	*<0.01*
IADL: ≥1 impairment	15/150	10	0/42	0	*0.03*	*29/150*	*19*	*0/42*	*0*	*<0.01*
Mobility: severely impaired[a]	3/35	8	10/148	7	0.71	9/35	26	18/148	12	0.04
Cognitive impairment										
MMSE[a]	5/24	20	10/163	6	*0.01*	*6/24*	*25*	*22/136*	*14*	*0.14*
Cognitive test battery[a]	12/135	9	3/53	6	0.46	21/135	16	7/53	13	0.68
Mood										
Depressive symptoms	8/57	14	7/135	5	*0.04*	*23/99*	*23*	*6/93*	*7*	*<0.01*
Nutrition										
Malnutrition	3/10	30	12/182	7	*<0.01*	*4/10*	*40*	*25/182*	*14*	*0.02*
Comorbidities										
Severe comorbidity burden	7/81	9	8/111	7	*0.71*	*15/81*	*19*	*14/111*	*13*	*0.26*
Frailty: GA	frail		fit		*p* value	frail		fit		*p* value
GA ≥2 impairments	15/150	10	0/42	0	*0.03*	*29/150*	*19*	*0/42*	*0*	*<0.01*
GA ≥3 impairments	11/107	10	4/85	6	0.15	*22/107*	*21*	*7/85*	*8*	*0.02*
Frailty: screening modalities										
Fried frailty[a]	12/84	14	3/99	3	*<0.01*	*24/84*	*29*	*4/99*	*4*	*<0.01*
GFI (≥4)	10/117	9	5/75	7	0.64	21/117	18	8/75	11	0.17
Surprise question nephrologist[b]	3/35	9	8/117	7	0.73	5/35	14	19/117	16	0.78
Frailty according to nephrologist[c]	8/98	8	3/51	6	0.61	21/98	21	3/51	6	0.01

[a] 5% missing.
[b] 21% missing.
[c] 22% missing.
ADL, activities of daily livin; iADL, instrumental activities of daily living; MMSE, Mini-Mental State Examination; GFI, Groningen Frailty Indicator.

1.21–4.36]). FFI (OR 2.35 [95% CI 1.28–4.30]) and the clinical judgement of frailty by the nephrologist (OR 2.21 [95% CI 1.09–4.46]) were both associated with hospitalization. GA2+, GA3+ and GFI were not. One out of 6 patients reported that the dialysis treatment in the first 6 months after dialysis turned out to be worse than initially expected, while the others reported it to be according to or above expectations. The difference in coping was more pronounced among frail patients: 23% of the FFI-based frail patients reported the treatment to be worse than expected versus 10% among fit patients, $p = 0.03$.

Discussion

In the GOLD Study, we assessed geriatric impairment and frailty in older patients incident to dialysis and their relation with poor outcome. Impairment of the individual geriatric domains ADL, depressive symptoms and malnutrition at the start of dialysis were associated with 1-year mortality. In addition, the cumulative deficits model using the GA was associated with poor outcome. Frail elderly incident dialysis patients with an accumulation of deficits (≥3 geriatric impairments on a GA) were almost 3 times as likely to die within the first year compared to patients with less impairment. In addition, frail patients according to the FFI were >7 times as likely to die within the first year compared to fit patients, and >2 times as likely to be hospitalized.

A GA is recognized as the best clinical practice standard test for the identification of frailty and has been widely adopted in routine elderly care [23]. As far as we know, the relation between frailty according to a GA and mortality has not been established before in elderly dialysis patients. This prognostic information further emphasizes the benefits of using a comprehensive GA (CGA) in

Table 4. Geriatric domains and association with 12-month mortality and hospitalizations

Mortality (12 months)	Crude			Adjusted					
				model 1[1]			model 2[2]		
	HR	95% CI	*p* value	HR	95% CI	*p* value	HR	95% CI	*p* value
Functional impairment									
ADL: ≥1 impairment	3.00	1.44–6.23	<0.01	3.10	1.43–6.71	<0.01	3.20	1.45–7.06	0.04
IADL: ≥1 impairment	n/a*								
Mobility: severely impaired	2.16	0.97–4.81	0.06	2.04	0.87–4.77	0.10	1.97	0.80–4.85	0.14
Cognitive impairment									
Test battery	1.26	0.53–2.96	0.60						
MMSE	2.13	0.86–5.25	0.10	2.09	0.83–5.24	0.11	2.18	0.85–5.57	0.10
Depressive symptoms	2.39	1.15–4.94	0.02	2.30	1.09–4.84	0.03	2.30	1.06–5.02	0.04
Malnutrition	3.45	1.20–9.91	0.02	4.51	1.45–14.04	0.01	4.52	1.40–14.61	0.01
Severe comorbidity burden	1.05	0.78–1.40	0.77						
Frailty									
GA ≥3 impairments[%]	2.63	1.13–6.17	0.03	2.36	1.12–6.21	0.04	2.97	1.19–7.45	0.02
Fried frailty	8.03	2.78–23.16	<0.01	7.49	2.57–21.83	<0.01	7.22	2.47–21.13	<0.01
GFI (≥4)	1.71	0.76–3.86	0.20						
Surprise question	0.89	0.33–2.39	0.82						
Frailty according nephrologist	3.97	1.18–13.32	0.03	3.88	1.15–13.11	0.03	4.10	1.19–14.14	0.03

Hospitalizations (6 months)	Crude			Adjusted[3]		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Functional impairment						
ADL: ≥1 impairment	2.61	1.37–4.96	<0.01	2.63	1.31–5.34	<0.01
IADL: ≥1 impairment	2.23	1.09–4.56	0.03	2.10	0.99–4.45	0.05
Mobility: severely impaired	1.90	0.89–4.08	0.10	1.97	0.86–4.50	0.11
Cognitive impairment						
Test battery	0.65	0.34–1.23	0.19			
MMSE	1.86	0.77–4.50	0.17			
Depressive symptoms	2.35	1.24–4.44	<0.01	2.01	1.05–3.85	0.04
Malnutrition	1.52	0.41–5.56	0.53			
Severe comorbidity burden	1.24	1.00–1.59	0.09	1.23	0.95–1.59	0.12
Frailty						
GA ≥3 impairments[%]	1.50	0.84–2.65	0.17			
Fried frailty	2.26	1.15–4.10	<0.01	2.31	1.24–4.32	<0.01
GFI (≥4)	1.27	0.71–2.67	0.43			
Frailty according nephrologist	2.25	1.12–4.53	0.02	2.35	1.14–4.86	0.02

[1] Adjusted for age, sex, CIRS-G comorbidity burden.
[2] Adjusted for age, sex, CIRS-G comorbidity burden, smoking, residual renal function and dialysis modality.
[3] Adjusted for age, sex, CIRS-G comorbidity burden.
[%] For the relation with the GA comorbidity was not included in the model, as comorbidity was already captured in the GA.
* Analysis not applicable, as no events occurred in the non-impaired group.
ADL, activities of daily living; iADL, instrumental activities of daily living; MMSE, Mini Mental State Examination; GFI, Groningen Frailty Indicator; GA, geriatric assessment.

nephrology care. Besides identifying geriatric problems that may inform us on mortality risk, a CGA focuses on a multidisciplinary approach and creating an overall plan for treatment and follow-up [26–28]. In other fields of medicine, a GA contributes to tailor-made care in the elderly. A recent systematic review in geriatric oncology showed that after geriatric evaluation, the initial oncologic treatment plan was altered in 28% of patients, mainly towards less invasive treatment, and additional non-oncologic interventions were recommended in the ma-

jority of patients. A positive effect was found on treatment completion and less treatment-related toxicity [29]. Although a CGA has proven beneficial in non-ESKD patients, we do not know yet what effect the CGA has on outcome in patients initiating dialysis [30].

The main disadvantage of a GA is that it is time consuming. Besides, the experience with a GA in nephrology care is sparse so far and it is unclear how, when in the illness trajectory, and how frequently it should be used. Furthermore, several combinations of tools and various models are available for implementation of a GA [23, 31]. As an example, an expert panel of the European Renal Association-European Dialysis Transplant Association and the European Union Geriatric Medicine Society could not endorse one physical functioning test over another [32]. For the assessment of functional status of older patients, the guideline recommended using a simple score to assess functional status, including a self-reported scale and a field test (i.e., sit to stand, gait speed, 6 min walk test). Clinical practice and cross-study comparison would benefit from agreement on uniformity of a certain subset of tests and cut-off values in the nephrology population. The next step would be to assess how to identify patients that would benefit from a GA as a guide for treatment decision-making, or for identifying targets to improve overall quality of life. Whether implementation of a GA in the (pre-) dialysis phase could be (cost-) effective in ESKD patients has to be established as well.

Compared to the cumulative deficits model of frailty, the FFI screening for frailty had a stronger relation with mortality and was associated with hospitalization risk and worse coping. In addition, the FFI is an easy-to-apply screening instrument in clinical practice. The most elaborate aspects are measuring handgrip strength and walking speed, which can be performed within a few minutes if the right tools are available. However, the physical frailty phenotype is not static but may fluctuate over time [33]. Therefore, it should be used with care and conclusions on poor risk should not be made on a single frailty measurement. It may be useful to perform repeated measurements as kidney function declines. While very specific to physical frailty, the sensitivity of FFI to other geriatric impairments that may be relevant to decision making, such as the psychosocial and cognitive domains is poor [34]. Thus, in the context of optimizing personalized care, the FFI provides very limited additional information on the overall health status. Consequently, the role of FFI in the process of decision-making appears limited to screening patients with poor prognosis.

Several clinical scores have been developed to predict short-term mortality, with a moderate to good predictive value [25, 35–37]. Some of these models included geriatric impairment, such as immobility and dementia [25, 35], and assistance with daily living [36], but these impairments were collected registry data and International Statistical Classification of Diseases and Related Health Problems codes. Geriatric impairments usually falls outside traditional disease-oriented care, and as a result are frequently overlooked and not well documented [38, 26, 28]. For example, in a cohort of HD patients, a cognitive test battery revealed severe cognitive impairment in 31% of patients and moderate impairment in 36%, while in <3% the diagnosis cognitive impairment was actually documented in the medical chart [38]. In our study, we found that prospectively assessed impairment in ADL, depressive symptoms and malnutrition at the start of dialysis were associated with 1-year mortality. This is in line with the outcome of previous studies assessing the association between specific geriatric impairments and poor outcome in this population [4]. Interestingly, impairments in these domains can potentially improve with applying interventions [30, 39]. In our study, cognitive impairment was not related to mortality after correction for confounders. This may be explained by the low number of patients and by the fact that we have included mild cognitive impairment instead of (severe) dementia. As our study shows there is a strong relation between geriatric impairments and poor outcome, we advocate expanding the prospective assessment of geriatric impairments in a larger population and assessing the predictive value of geriatric impairment. These factors may be adopted into a more accurate prediction model.

This is the first longitudinal study that focuses on the prognostic value of the cumulative deficits model by means of a GA in incident older dialysis patients. However, some limitations exist. The number of patients was not sufficient to apply a standard multivariate analysis on 6-month mortality, and for 12-month mortality, the model could be adjusted for only a few variables leaving a potential risk of residual confounding. This was due to the fact that overall mortality was lower than expected based on mortality rates reported in other cohorts [35, 37]. Furthermore, this is a selected cohort in which the decision to start dialysis has already been made. Thus, the results cannot directly be extrapolated to the predialysis phase. In addition, as we included mainly Caucasian patients with a relatively low rate of diabetes, our findings may not be fully generalizable to all elderly incident di-

alysis patients. Although it is likely that the GA is related to mortality at the moment of decision-making as well, data are currently lacking. In addition, the cut-off values of the GA for the definition frailty are arbitrary, although patients with ≥2 or ≥3 geriatric impairments are generally considered impaired [23].

Conclusion

This prospective analysis of the GOLD study shows that frailty at the time of dialysis initiation demonstrates a good prognostic value for poor outcome in the elderly, both the cumulative deficits model of frailty, measured with a GA, and the physical frailty model, measured with the FFI, are related to mortality. A GA is capable to distinguish between frail and fit patients initiating dialysis but can also identify potential targets for intervention. Consequently, a GA may be of added value in decision-making in ESKD. Whether the findings of our study can be extrapolated to the predialysis population and whether the actions derived from a GA may improve outcome should be topics of the research agenda in the developing field of geriatric nephrology.

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Statement of Ethics

This study complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest. This manuscript had not been published and is not under consideration for publication elsewhere.

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Author Contributions

F.T.J.B., E.K.H., L.G., E.F.H.B., P.J.G.V., C.E.D., P.J.G.V., Y.C.S., J.L., M.A.S., A.C.A., and M.C.V. participated in the GOLD study, including data collection. I.N.L., N.A.G., M.L.B., and M.E.H. carried out the present analyses and wrote the draft of the manuscript. F.T.J.B., E.K.H., L.G., E.F.H.B., P.J.G.V., C.E.D., P.J.G.V., Y.C.S., J.L., M.A.S., A.C.A., and M.C.V. critically revised the draft and contributed with comment to improve the manuscript. All authors read and approved the final manuscript.

Appendix 1

List of participating centres across The Netherlands

Albert Schweitzer Hospital, Dordrecht; Amsterdam University Hospital, Amsterdam; Bernhoven Hospital, Uden, Diakonessenhuis, Utrecht; Groene Hart Hospital, Gouda; Jeroen Bosch Hospital's Hertogenbosch; Spaarne Gasthuis, Hoofddorp, Haarlem; Maasstad Hospital, Rotterdam, St. Antonius Hospital, Nieuwegein; St. Elisabeth Hospital, Tilburg; Franciscus Gasthuis & Vlietland hospital, Rotterdam, Schiedam; Ter Gooi Hospital, Hilversum; University Medical Center Utrecht, Utrecht; Zaans Medical Center, Zaandam; Gelderse Vallei Hospital, Ede

Appendix 2

Geriatric assessment

Domain	Test	Category	Range	Cut-off	Source
ADL	Katz-scale		1–6	≥1	Patient
iADL	Lawton and Brody		1–7	≥1	Patient
Mobility	Timed up and go[&]	Severe		>20 s	Patient
Cognitive impairment	MMSE		0–30	<25	Patient
	Clock		0–14	≤10	
	ECR		0–16	<14	
	Fluency		0–40	<5th percentile[^]	
Depressive symptoms	GDS	*No impairment*	0–15	<5	Patient
		Mild symptoms		5–10	
		Severe symptoms		>10	
Malnutrition	MNA	*Malnutrition*	0–30	0–17	Patient
Comorbidities	CIRS-G	Severe[#]			Chart
Frailty					
GA[%]	GA2+	≥2 geriatric impairments	0–7[%]	(≥2)	
	GA3+	≥3 geriatric impairments	0–7[%]	(≥3)	

[%] Sum of impairment in (i)ADL, severe mobility impairment, impairment in ≥ cognitive domain, severe depressive symptoms, malnutrition, severe comorbidity score.

[&] The average of 3 measurements was recorded; immobility was scored as severely impaired.

[^] Corrected for age and education level.

[#] CIRS-G ≥ 2× score 3 or ≥ 1× score 4; renal comorbidity excluded.

GA, Geriatric Assessment; ADL, activities of daily living; (i)ADL, (instrumental) activities of daily living; MMSE, Mini Mental State Examination l; GDS, Geriatric Depression Scale; ECR, Enhanced cued recall; MNA, Mini Nutritional Assessment; CIRS-G, Cumulative Illness Rating Scale Geriatrics.

Appendix 3

Frailty screening measurements as used in the study

FFI Components	Measurements	Description/cut-off	Score
Malnutrition	Unintentional weight loss	4,5 kg or ≥5%	Yes = 1
Physical performance	Slowness[5]	≥6 seconds/4 meters	Yes = 1
	Low level of physical activity	Last 3 months ≥4 h sedative lifestyle, no activities like cycling or running	Yes = 1
	Grip strength (kg)[#]	Male: <70 year: <28.2; ≥70 year: <21.3 Female: <70 year: <15.4; ≥70 year: <14.7	Yes = 1
General health	Exhaustion	Exhaustion (self-report)	Yes = 1
Frailty: ≥3 points			

GFI Components	Description/cut-off	Score
Physical performance	*Are you able to carry out these tasks single-handedly and without any help?* (The use of help resources, such as a walking stick, walking frame, or wheelchair, is considered to be independent) 1. Shopping 2. Walking around outside (around the house or to the neighbours) 3. Dressing and undressing 4. Going to the toilet	Yes = 0, No = 1
General health	5. *What mark do you give yourself for physical fitness? (scale 010)*	0–6 = 1, 7–10 = 0
Neurosensory deficits	6. *Do you experience problems in daily life because of poor vision?* 7. *Do you experience problems in daily life because of being hard of hearing?*	Yes = 1, No = 0
Malnutrition	8. *During the past 6 months have you lost a lot of weight unwillingly?* *(3 kg in 1 month or 6 kg in 2 months)*	Yes = 1, No = 0
Polypharmacy	9. *Do you take 4 or more different types of medicine?*	Yes = 1, No = 0
Cognition	10. *Do you have any complaints about your memory?*	No = 0 Sometimes = 0 Yes = 1
Mood, psychosocial	11. *Do you sometimes experience emptiness around you?* 12. *Do you sometimes miss people around you?* 13. *Do you sometimes feel abandoned?* 14. *In the past 4 weeks did you feel downhearted or sad?* 15. *In the past 4 weeks did you feel nervous or anxious?*	No = 0 Sometimes = 1 Yes = 1
Frailty: ≥4 points		

[#] Grip strength of the dominant hand; best out of three measurements; using electronic hand dynamometer (Model EH101).
[%] Fastest time of two measurements.
FFI, Fried Frailty Index; GFI, Groningen Frailty Indicator.

Appendix 4

Comorbidity burden assessment. CIRS-G [23]. The CIRS-G measures the chronic medical illness burden in the following organ-system categories with a score from 0 to 4. A severe comorbidity burden is defined as a CIRS-G score ≥2× score 3 or ≥1× score 4

Organ systems		
Cardiac	Vascular	Haematological
Respiratory	Ophthalmological and otorhinolaryngology	Upper gastrointestinal
Lower gastrointestinal	Hepatic and pancreatic	Renal[#]
Genitourinary	Musculoskeletal	Neurological
Endocrine	Metabolic and breast	Psychiatric

Score	
0	No problem affecting that system
1	Current mild problem or past significant problem
2	Moderate disability or morbidity and/or requires first line therapy
3	Severe problem and/or constant and significant disability and/or hard to control chronic problems
4	Extremely severe problem and/or immediate treatment required and/or organ failure and/or severe functional impairment

[#] Category renal was excluded in this population with end-stage kidney failure.
CIRS-G, Cumulative Illness Rating Scale – Geriatrics.

Appendix 5

Differences baseline between HD and PD

	HD	PD	*p* value
n (%)	148 (77)	44 (23)	
Demographics			
Age, years, mean ± SD	76±7	73±6	0.04
Male, %	62	84	<0.01
BMI, mean ± SD	27±6	26±7	0.70
University, %	22	21	0.80
Smoking (former, now), %	76	81	0.50
Social setting, %			
Living alone	47	27	0.02
Living in a nursing home facility	6	2	0.32
Drugs, mean ± SD			
No. of drugs	11±4	13±5	0.11
Impairment in geriatric domains, %			
ADL	33	18	0.06
iADL	81	68	0.07
Mobility	21	12	0.15
Cognition	13	11	0.74
Mood	32	23	0.25
Nutrition	54	43	0.21
Comorbidity	43	39	0.59
Frailty, %			
GA ≥2 impairments	79	66	0.07
GA ≥3 impairments	52	36	0.07
Fried	48	38	0.23
GFI	46	27	0.03
Nephrologist frailty	65	70	0.59

HD, haemodialysis; PD, peritoneal dialysis; BMI, body mass index; ADL, activities of daily living; iADL, instrumental ADL; GA, geriatric assessment; GFI, Groningen Frailty Indicator.

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