The Relevance of Geriatric Impairments in Patients Starting Dialysis: A Systematic Review

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Abstract

Background and objectives With aging of the general population, patients who enter dialysis therapy will more frequently have geriatric impairments and a considerable comorbidity burden. The most vulnerable among these patients might benefit from conservative therapy. Whether assessment of geriatric impairments would contribute to the decision-making process of dialysis initiation is unknown.

Design, setting, participants, & measurements A systematic Medline and Embase search was performed on December 1, 2015 to identify studies assessing the association between risk of mortality or hospitalization and one or more geriatric impairments at the start of dialysis therapy, including impairment of cognitive function, mood, performance status or (instrumental) activities of daily living, mobility (including falls), social environment, or nutritional status.

Results Twenty-seven studies were identified that assessed one or more geriatric impairments with respect to prognosis. The quality of most studies was moderate. Only seven studies carried out an analysis of elderly patients (≥70 years old). Malnutrition and frailty were systematically assessed, and their relation with mortality was clear. In addition, cognitive impairment and functional outcomes at the initiation of dialysis were related to an increased mortality in most studies. However, not all studies applied systematic assessment tools, thereby potentially missing relevant impairment. None of the studies applied a geriatric assessment across multiple domains.

Conclusions Geriatric impairment across multiple domains at dialysis initiation is related to poor outcome. However, information in the elderly is sparse, and a systematic approach of multiple domains with respect to poor outcome has not been performed. Because a geriatric assessment has proved useful in predicting outcome in other medical fields, its potential role in the ESRD population should be the subject of future research.

Clin J Am Soc Nephrol 11: 1245–1259, 2016. doi: 10.2215/CJN.06660615

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Introduction

The ESRD population is aging rapidly. A significant percentage of patients accepted for RRT is now >75 years old, ranging from 17% to 45% (1). In addition, patients with ESRD are prone to accelerated aging (2). Underlying mechanisms, such as inflammation and microvascular damage, contribute to both decline of kidney function and development of impairment across other physiologic domains. Consequently, a high prevalence of impairment in physical and psychosocial domains, such as dependency in activities of daily living (ADLs), cognitive impairment, depression, and malnutrition, can be found in the dialysis population in both young (3) and older patients (4). There may be considerable interaction between various domains. For instance, elderly patients are at higher risk for malnutrition because of dentition loss and gastrointestinal symptoms, but mood and social circumstances may additionally compromise nutritional status (5). Accumulation and interaction of impairment of multiple domains may contribute to increased vulnerability to external stressors, also referred to as the (renal) frailty phenotype (6). This complicates treatment decisions in vulnerable and elderly patients with ESRD. Conservative care has become an accepted alternative for dialysis to discuss with selected patients with ESRD who may not benefit from dialysis (7). There is general consensus that chronologic age is not a useful selection criterion here, because ageing is a heterogeneous process (8). However, a systematic and evidence-based way to guide treatment decisions is currently lacking.

In other research fields, a systematic geriatric assessment (GA) was shown to fill this knowledge gap (8,9). A GA is defined as a multidimensional, interdisciplinary diagnostic process focusing on determining an older person's medical, psychosocial, and functional capabilities to develop a coordinated and integrated plan for treatment and long–term follow-up (10). Such a GA has been shown to successfully identify patients at risk for poor outcome in geriatric oncology (11) and improve outcomes in older patients admitted to the emergency

department (9), and it is increasingly recommended as being the standard of care in the treatment decision–making process in elderly patients (8). The aim of this review is to give an overview of all currently available evidence regarding the relation of geriatric impairments and the accumulation of impairment across these domains at initiation of dialysis with mortality and dialysis-related complications.

Materials and Methods

Search Strategy and Article Selection

We identified cohort studies investigating the relation between impairment in geriatric domains and outcome in incident patients on dialysis. Studies were included that investigated patients directly before or within 3 months of dialysis initiation. Geriatric impairment was defined as being an impairment in one or more of the following distinct domains generally considered part of a GA (6,8): cognitive function, mood, performance status or the ability to perform ADLs and instrumental ADLs, mobility (including falls), social environment, and nutritional status (12). In addition, an assessment addressing frailty was considered to be part of the assessment of geriatric impairments, because frailty may incorporate aspects of several geriatric domains (13). Studies on nutritional status were only included if a systematic assessment tool was used containing features of alimentation and physical examination. Studies only assessing body mass index, which could reflect a stable condition rather than malnutrition, or albumin, which may also reflect inflammation, were not included (12). Polypharmacy was not included, because most patients on dialysis meet the criteria for polypharmacy, and the relation with outcome would be hard to establish. Comorbidity was not included, because its relation with mortality has already been well established (14,15).

Outcome was defined as mortality or hospitalizations: duration of hospitalization, hospitalization rate, time to first hospitalization, or a combined outcome mortality and hospitalizations. A preliminary search including an age limit (≥70 years old) resulted in only a handful of publications. We, therefore, decided not to apply an age limit. In addition, we only found a few articles that included a systematic and validated assessment to determine the presence of one or more geriatric impairments. We, therefore, broadened the scope of our search and included all studies on the basis of chart review as well. We conducted a literature search in both Medline and Embase on December 1, 2015 using a combination of dialysis or renal disease with synonyms of each of the geriatric impairments or GA itself and outcomes as listed above (Supplemental Table 1). No limits in publication date were applied to the search. One investigator (I.N.v.L.) assessed the titles and abstracts of all studies retrieved by the search to determine which studies would be eligible for additional investigation. All potentially relevant articles were subsequently screened as full text by two authors (I.N.v.L. and T.W.). Studies were excluded if the primary focus was not kidney disease, patients suffered from acute kidney failure, the patient population consisted of kidney transplant recipients, or the studies focused on conservative management without dialysis. Studies with children or animals were also excluded. We distinguished between a systematic screening modality and a nonsystematic screening modality. A systematic screening modality to determine the presence of one or more geriatric impairments was defined as a validated screening tool, a validated subscale of a more elaborate screening tool, or an approximation of these screening tools on the basis of available clinical data. Only full text reports were included. Crossreferencing of the remaining articles was done to retrieve any additional relevant citations.

Data Extraction

Data regarding study design and results were independently extracted by two investigators (I.N.v.L. and T.W.) for each eligible study. Studies were subdivided into those performing the screening for geriatric impairments directly before or within 7 days after initiation of dialysis and those in which screening was performed within the first 3 months after initiation of dialysis. For each of the studies included, the following items were extracted: study design, study population (age and dialysis type), moment of inclusion (as described above), acute or planned start of dialysis, geriatric impairment of interest, assessment tools used, prevalence of geriatric impairments, length of follow-up, outcome measures examined, and the reported results on the relation between GAs and the outcome measures. In case of insufficient data in the original manuscript, an attempt was made to contact the authors for additional information.

Quality Assessment

The methodologic quality of each of the eligible studies was independently assessed by two reviewers (I.N.v.L. and T.W.) using the Newcastle–Ottawa Scale (16) for cohort studies adapted to this topic (Supplemental Table 2). Disagreement among the reviewers was discussed during a consensus meeting, and in case of persisting disagreement, the assistance of a third reviewer (M.E.H.) was enlisted.

Data Synthesis and Analyses

As a result of the heterogeneity of patient populations, the wide variety of methods of assessing the presence of geriatric impairments, and the heterogeneity in outcome measures, a meta-analysis was not considered to be feasible. Therefore, we summarized the individual study results to describe our main outcomes of interest.

Where necessary for good comparability of the effect size of the outcomes, we computed reciprocal hazard ratios (HRs) or reciprocal odds ratios (ORs). Where lacking, ORs were calculated on the basis of the presented data for optimizing comparability of the data (calculator Vassar College) (5).

Results

Characteristics of Included Studies

The literature search resulted in 19,622 citations (8121 from Medline and 11,501 from Embase), of which 6433 articles were duplicates (Figure 1). Of the remaining publications, 13,083 were excluded for reasons listed in Figure 1; 106 potentially relevant articles were subsequently screened as full text. Ultimately, 27 full-text publications were considered relevant to our search (Table 1) (17–43). Crossreferencing did not yield any additional relevant studies. The studies were published between 1991 and 2015.

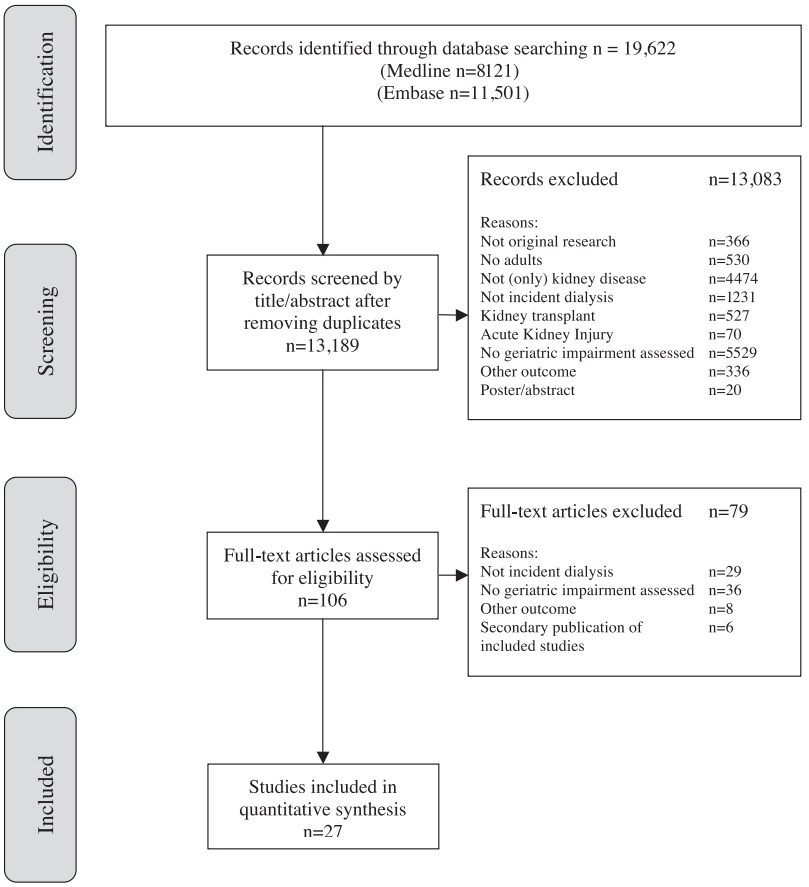

Figure 1. | Flow chart.

Eight studies focused on hemodialysis (27,28,31,33,35–38), and three studies focused on peritoneal dialysis only (24,29,43). Fifteen studies performed the screening for impairments at dialysis initiation, and 12 studies performed the screening for impairments within 3 months after initiation. The sample size ranged from 40 to 272,024 patients, and the mean age ranged from 53 to 82 years old. Seven studies focused exclusively on elderly patients (mean age ranging from 67 to 82 years old) (18,25,26,29,33,34,42), and one study performed a subgroup analysis of elderly patients (31).

Quality Assessment

Results of the quality assessment of included studies are summarized in Figure 2; details per study can be found in Supplemental Table 3. The agreement between the two reviewers in this paper was >95% for all aspects. The quality of three of 27 studies was good according to all of the established quality criteria (17,22); the remainder of studies was (somewhat) compromised. In 15 studies (56%), the representativeness of the exposed cohort was (somewhat) compromised, because the population proved to be either selected (not black or white race [41] or not ≥2 years Medicare follow-up before entering the study) or highly selected (exclusion of elderly patients [30], early deaths [43], and one study included 17% prevalent patients who were on chronic hemodialysis before peritoneal dialysis was initiated [24]). The remaining studies applied baseline assessment of geriatric impairments ≥7 days after the start of dialysis. Ascertainment of exposure was potentially compromised in seven studies (26%), because no systematic assessment was applied. In ten studies (37%), loss to follow-up was >10%, or the percentage of participants lost to follow-up was not adequately described.

Assessment and Prevalence of Geriatric Impairments

Most studies focused on one or two geriatric domains only, whereas two studies assessed multiple impairments (Table 1) (29,31). The domain most frequently assessed was performance status, which was described in 12 of the 27 included studies, followed by depression (seven of 27), nutrition (five of 27), and cognition (five of 27). Table 2 shows the prevalence of the various impairments and lists the various tests and cutoff values used. Performance status was assessed with the Karnofsky Index, the World Health Organization scale, or a national performance scale (Supplemental Table 4), and two studies focused specifically on aspects of ADLs, of which one study used a systematic ADL screening test (29). Severely impaired performance status ranged from 13% to 33%. Depressive symptoms were present in 24%–55% of patients in the studies that applied a systematic assessment (20,23,27,35),

Table 1. Baseline characteristics and geriatric impairments

Baseline Characteristics				Study Setting and Design		
Authors	Year of Publication	No. of Patients	Age, yr (SD/range)	Dialysis Modality	Setting	Planned Start Only
Inclusion at initiation of dialysis						
Alfaadhel *et al.* (17)	2015	390	63 (15)	HD, PD	Monocenter	
Arai *et al.* (18)	2014	202	80 (4)	HD, PD	Monocenter	
Chandna *et al.* (22)	1999	292	61 (18–92)	HD, PD	Monocenter	
Churchill *et al.* (43)	1996	680	54 (18–82)	PD	Multicenter	x
Couchoud *et al.* (25)[d,e]	2009	2500	81 (4)	HD, PD	Database (REIN 2002–2006)	
Couchoud *et al.* (26)[d]	2015	12,500	81 (?)	HD, PD	Database (REIN 2005–2012)	
Doi *et al.* (28)	2015	688	69 (59–77)	HD	Multicenter (UMINCTR)	x
Genestier *et al.* (29)	2009	122	81 (4)	PD	Monocenter	x
Jassal *et al.* (31)	1996	99	65 (41–90)	HD	Monocenter	
Joly *et al.* (33)[f]	2003	107	82 (3)	HD	Monocenter	
Kim *et al.* (34)[g]	2014	410	72 (5)	HD, PD	Database (CRC for ESRD)	
Mauri *et al.* (38)[d]	2008	3455	65 (14)	HD	Database (RMRC)	
Rakowski *et al.* (40)	2006	272,024	63(?)	HD, PD	Database (USRDS 1995–1999)	
Soucie *et al.* (41)[d]	1996	15,245	57 (16)	HD, PD	Database (Network 6)	
Thamer *et al.* (42)	2015	52,796	77 (7)	HD, PD	Database (USRDS 2009–2010)	
Inclusion after initiation of dialysis						
Bao *et al.* (19)	2012	1576	60 (14)	HD, PD	Database USRDS 2005–2007	
Boulware *et al.* (20)	2006	917	? (19–95)	HD, PD	Database (CHOICE Study)	x
Chilcot *et al.* (23)	2011	160	57 (16)	HD, PD	Three centers	x
Chan *et al.* (21)	2012	167	65 (14)	HD, PD	Monocenter	x
Chung *et al.* (24)	2009	219	54(13)	PD	Monocenter	x
Diefenthaeler *et al.* (27)	2008	40	55 (15)	HD	Monocenter	x
Honda *et al.* (30)	2007	328	53 (12)	HD, PD	Monocenter	x
Johansen *et al.* (32)	2007	2275	58 (16)	HD, PD	Database (Dialysis Wave II Study)	
Lacson *et al.* (35)	2012	6415	62 (15)	HD	Multicenter (FMCNA)	
Lacson *et al.* (36)[h]	2013	8776	62 (15)	HD	Multicenter (FMCNA)	
Lopez Revuelta *et al.* (37)	2004	318	60 (?)	HD	Multicenter	
McClellan *et al.* (39)	1991	294	57 (15)	HD, PD	Multicenter	

whereas the prevalence of the International Statistical Classification of Diseases diagnosis depression ranged from 4% to 28% (23,29,39,41). Prevalence of cognitive impairment ranged from 6% to 13% in general (25,26,29,31,40) and was 41% in the very old (18). No studies assessed the relation between falls or social environment and poor outcome in the incident dialysis population.

Relation of Geriatric Impairments and Outcome

The relations between geriatric impairments, mortality, and hospitalization are shown in Table 3. Table 3 also shows studies that focused on elderly patients. Details and effect sizes are shown in Tables 4 and 5.

Relation of Geriatric Impairments and Mortality

Overall, 1-year mortality ranged from 12% (23) to 35% (29); the latter was in a study focusing on elderly patients (mean age =81±4 years old). Frailty was associated with mortality in all three studies assessing this domain, with HRs ranging from 1.22 (95% confidence interval [95% CI], 1.04 to 1.43) per point increase of the frailty scale (17) to 2.24 (95% CI, 1.60 to 3.15) between frail and nonfrail (32) (Tables 4 and 5). Four of five studies assessing malnutrition found it to be associated with mortality (21,24,30,43), with HRs ranging from 1.33 (95% CI, 1.18 to 1.52) (43) per point increase of the Subjective Global Assessment (SGA) to 2.01 (95% CI, 1.46 to 2.86) between two SGA categories

Table 1. (Continued)

Study Setting and Design			Geriatric Impairments Assessed					
Exclusion Criteria	P/R	Median/Mean Follow-Up, mo[a]	Cognition	Mood	ADL	Performance	Mobility	Nutrition
	P	20 (11–34)[b]						
AKI, dialysis <1 wk in own dialysis center								
None	R	6[c]					+	
AKI	P					+		
Early deaths/transplant (<6 mo), HIV, hepatitis B positive, active inflammatory disease	P	24[c]				+		+
Acute renal failure, <75 yr old	R	6[c]	+				+	
Acute renal failure, <75 yr old	R	3[c]	+				+	
No predialysis care, withdrawal within 1 yr, eGFR>10 at start of dialysis	R	12[c]				+		
≤75 yr old	R	18 (?)	+	+	+	+		
AKI	P	?	+	+	+	+		
Patients <80 yr old, AKI	P	100[c]				+		
AKI, <65 yr	R	60[c]				+		+
No minimum follow-up of 1 yr	R	12[c]				+		
None	R	24[c]	+				+	
Nonwhite or black patients	R	3[c]		+		+		
Did not have 2-yr previous Medicare claims history, <67 yr old	R	6[c]			+			
AKI	R	35 (?)						
None	R	18 (2–24)[b]		+				
No visual, physical, or cognitive (MMSE<22) impairment	P	17 (2–34)		+		+		
AKI, early transplant, early transfer other unit	R	53 (23–83)						+
None	P	23 (±10)						+
MMSE<18, blindness, illiteracy	P	11 (5–22)		+				
≥70 yr old, overt infection, acute vasculitis, liver disease	P	21 (1–72)						+
None	R	12[c]						
None	R	12[c]		+				
None	R	12[c]		+				
AKI, severe physical or psychiatric impairments	P	26 (0–42)				+		
None	P	16 (1–19)		+		+		

P, prospective cohort study; R, retrospective cohort study; ADL, activity of daily living; HD, hemodialysis; PD, peritoneal dialysis; +, addressing this geriatric impairment; REIN, Ramipril Efficacy in Nephropathy; ?, not reported; UMINCTR, University Hospital Medical Information Network Clinical Trials Registry; CRC for ESRD, Clinical Research Center for End Stage Renal Disease; RMRC, Registre de Malalts Renals de Catalunya; USRDS, US Renal Database System; CHOICE, Choices for Healthy Outcomes in Caring for; MMSE, Mini Mental State Examination; FMCNA, Fresenius Medical Care North America.

[a]If mean is reported, SD is in parentheses; if median is reported, range is in parentheses.

[b]Interquartile range instead of range.

[c]Total study follow-up.

[d]Data of development/training cohort only.

[e]Small overlap of patients of the two cohorts in works by Couchoud *et al.* (25,26) (years 2005–2006, with a maximum potentially overlap of 20%).

[f]Data of the dialysis cohort only.

[g]Data of the ≥65 years old cohort only. Early deaths (unless otherwise described) are <3 months.

[h]Important overlap of the two cohorts in the works by Lacson *et al.* (35,36).

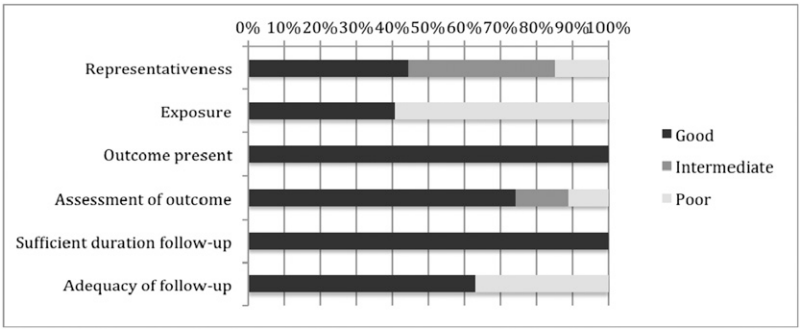

Figure 2. | Quality assessment of the included studies.

(21). Functional dependency on the basis of ADLs, performance status, or mobility was related to mortality in the majority of studies assessing these domains, despite a broad variety of assessment tools and cutoff values used. A positive association between depressive symptoms and mortality was found in three of seven studies only (23,35,41). However, when focusing on the database studies, which included the vast majority of patients, depressive symptoms were associated with mortality in two studies (OR, 1.30; 95% CI, 1.00 to 1.60 [41] and OR, 1.08; 95% CI, 1.01 to 1.14 [35]), and in one study, depression was associated with noncardiovascular mortality (HR, 1.94; 95% CI, 1.10 to 3.42 [20]).

In elderly patients, impaired mobility was associated with 1-year mortality in an univariate analysis of a single publication (OR, 4.22; 95% CI, 1.87 to 9.57) (18), and total dependence for transfers was independently associated with 3- and 6-month mortality (OR, 6.53; 95% CI, 5.38 to 7.92 and OR, 1.7; 95% CI, 1.4 to 2.0, respectively) (25,26). Dependence in ADLs was associated with mortality in two of three studies (OR, 1.41; 95% CI, 1.08 to 1.85) (31,42). Impaired cognitive function, defined as severe behavioral disorder, was associated with mortality as well (25,26), but two smaller studies did not find this relation (29,31). Depressive symptoms were not associated with mortality is this population (29,31). One study systematically assessed malnutrition in the elderly and found no relation with mortality (34). No studies focused on frailty in the elderly population specifically.

Relation of Geriatric Impairments and Hospitalization

Hospitalization days after dialysis initiation were assessed in three studies (Table 3) showing that malnutrition (43), depression (36), and performance status (37,43) were associated with more days in hospital. However, the association between performance status and hospitalization duration was lost after adjustment for potential confounders in one of the two studies (P=0.50) (37). Depressive symptoms were related to hospitalization rate (HR, 1.13; 95% CI, 1.02 to 1.25) (36). One study assessed the association of frailty and time to first hospitalization (19), and another study focused on the combined outcome time to first hospitalization or death or time to first nonvascular hospitalization and death (32). All three outcomes were individually associated with frailty at dialysis initiation.

Discussion

As shown by this review, the relation between geriatric impairment and poor outcome has not been assessed elaborately within the incident dialysis population. Only malnutrition and frailty have been well assessed using a systematic approach, and evidence on the relation with mortality is clear, although it is lacking in the elderly population specifically. Other geriatric impairments seem to be related to poor outcome, and data resulting from a systematic assessment of these impairments are sparse. None of the studies performed a GA incorporating a systematic assessment across multiple impairments. Only two small studies assessed impairment across multiple domains in a geriatric population. These studies found performance status (31) and ADLs (29) to be associated with survival of elderly patients on dialysis.

In other fields within geriatric medicine, expanding evidence on the predictive value of geriatric impairments has led to the implementation of a systematic assessment for prognostic and diagnostic purposes (8,9). A systematic assessment aids in staging the aging, thereby discriminating between fit and relatively vulnerable patients (44), and it reveals deficits that are not routinely captured in standard history and examination (8). A multidisciplinary discussion on the basis of the results of a GA can lead to adjustments of initial treatment proposals in elderly patients in the oncology department by either increasing or decreasing the treatment intensity (45,46).

A GA has been proposed as a supportive instrument for treatment decision making in ESRD as well (4,26). It provides the best available evidence on the patients' physiologic reserves and consequently, a better estimation of residual life expectancy (47). Concrete information on impaired domains that could compromise dialysis treatment may facilitate shared decision making with the patient and relatives. In addition, it may reveal treatable conditions that would otherwise be overlooked (4,48), thereby forming a starting point for (preventive) interventions to optimize quality of life, such as physical and ADL impairments and social problems (45,49). Finally, the information derived from a GA may help to estimate adverse outcomes of surgical interventions (50) and other complex interventions (51). This review supports the suggestion that assessment of geriatric impairments may contribute to decision making in dialysis by showing that multiple impaired

Table 2. Prevalence of geriatric impairments

Impairment and Authors	Test	Prevalence, %	Cutoff	Scale	Test	Elderly
Mood disturbance						
Diefenthaeler *et al.* (27)	BDI	55	≥14	0–63	S	
Lacson *et al.* (35,36)	Depression score	41	>2	0–6	P	
Genestier *et al.* (29)	Depression ICD	28			R	x
Chilcot *et al.* (23)	BDI	26	≥16	0–63	S	
Chilcot *et al.* (23)	Depression ICD	15			R	
Boulware *et al.* (20)	MHI SF-36	24	≤52	0–100	P	
Soucie *et al.* (41)	Depression ICD	18			R	
Thamer *et al.* (42)	Depression ICD	10			R	x
McClellan *et al.* (39)	Depression ICD	4			R	
Cognitive impairment						
Arai *et al.* (18)	Dementia ICD	41			R	x
Jassal *et al.* (31)	Mental score	36[a]; 7[b]	<8	0–10	S	x
Genestier *et al.* (29)	Dementia ICD	13			R	x
Rakowski *et al.* (40)	Dementia ICD[c]	12			R	
Thamer *et al.* (42)	Dementia ICD	6			R	x
Couchoud *et al.* (25)	Behavioral disorders[d]	5			R	x
Couchoud *et al.* (26)	Behavioral disorders[d]	4			R	x
Immobility						
Arai *et al.* (18)	Japanese criteria	33	≥3	1–8	S	x
Couchoud *et al.* (25)	Assistance for transfers	25			R	x
Couchoud *et al.* (25)	Dependent for transfers	7			R	x
Couchoud *et al.* (26)	Assistance for transfers	22			R	x
Couchoud *et al.* (26)	Dependent for transfers	8			R	x
Rakowski *et al.* (40)	Unable to ambulate	5			R	
Rakowski *et al.* (40)	Unable to transfer	2			R	
ADLs						
Genestier *et al.* (29)	ADL scale	30	≥7	0–12	S	x
Thamer *et al.* (42)	ADL: dependent	21			R	x
Frailty						
Bao *et al.* (19)	Modified Fried score	73	≥2	0–3	P	
Johansen *et al.* (32)	Modified Fried score	68	≥3	0–5	P	
Alfaadhel *et al.* (17)	Clinical frailty score	26	≥5	1–7	P	
Malnutrition						
Churchill *et al.* (43)	SGA (mild to severe)	55	≤5	7–0	S	
Chan *et al.* (21)	SGA (idem)	52	B and C	A–C	S	
Chung *et al.* (24)	SGA (idem)	47	≤5	7–0	S	
Kim *et al.* (34)	SGA (idem)	42	≤5	7–0	S	x
Honda *et al.* (30)	SGA (idem)	32	≥2	1–4	S	

	Test	Mild to Severe Prevalence Cutoff		Severe Prevalence Cutoff		Scale	Test	Elderly
		%	No.	%	No.			
Impaired performance								
Joly *et al.* (33)	Karnofsky	69	≤70	22	≤40	10–100	S	x
Chandna *et al.* (22)	Karnofsky	54	≤70	33	≤40	10–100	C	
Churchill *et al.* (43)	Karnofsky	41	≤70	—	—	10–100	S	
Soucie *et al.* (41)	Karnofsky[e]	49	<7	18	<6	1–10	S	
Mauri *et al.* (38)	Karnofsky[e]	42	<80	13	<70	10–100	C	
McClellan *et al.* (39)	Karnofsky[e]	37	<7	20	<6	1–10	S	
Kim *et al.* (34)	Karnofsky	24	≤70	—	—	10–100	S	x
Chilcot *et al.* (23)	Karnofsky	15	<70	—	—	10–100	S	
Genestier *et al.* (29)	AGGIR	48	≤4	28	≤2	1–6	S	
Doi *et al.* (28)	WHO scale	—	—	23	≥3	0–4	C	

Prevalence of impairment. If necessary for comparison, the combined prevalence of two separate categories is shown (*e.g.*, severely dependent and dependent for ADLs). Of all of the studies that applied a systematic assessment, the scale and cutoff values are reported. BDI, Beck Depression Inventory, S, applied by staff; P, patient self-report; ICD, International Statistical Classification of Diseases; R, review of medical chart; x, analysis includes elderly patients exclusively; MHI SF-36, Mental Health Inventory Short Form 36; ADL, activity of daily living; SGA, Subjective Global Assessment; A, well nourished; B, mild-moderately malnourished; C, severely malnourished; —, not mentioned; AGGIR, Autonomie Gérontologique Groupes Iso-Ressources; WHO, World Health Organization.

[a]Age ≥65 years old.

[b]Age <65 years old.

[c]Alzheimer disease, vascular dementia, dementia not otherwise specified, or presenile dementia.

[d]Dementia, psychosis, or severe neurosis that may affect patient dependence or compliance with treatment.

[e]Modification of the Karnofsky Index (39).

Table 3. Geriatric impairments related to outcome

Geriatric Impairment	No. of Studies	Associations[a]			
		Univariate		Multivariate	
		No.	%	No.	%
Mortality					
Depressive symptoms (20,23,27,29,31,35,41)	7	5/7	71	3/7	43
Cognitive impairment (25,26,29,31,40)	5	4/5	80	3/5	60
ADL dependency (29,31,42)	3	3/3	100	2/3	67
Mobility impairment (18,25,26,40)	4	4/4	100	3/4	75
Performance (22,23,28,29,31,33,34,37–39,41,43)	12	8/12	67	7/12	55
Frailty (17,19,32)	3	3/3	100	3/3	100
Malnutrition (21,24,30,34,43)	5	4/5	80	4/5	80
Hospitalization					
Performance (37,43)	2	2/2	100	1/2	50
Malnutrition (43)	1	1/1	100	1/1	100
Depression (36)	1	1/1	100	1/1	100
Mortality in Elderly Patients					
Depressive symptoms (29,31)	2	0/2	0	0/2	0
Cognitive impairment (25,26,29,31)	4	3/4	75	2/4	50
ADL dependency (29,31,42)	3	3/3	100	2/3	67
Mobility impairment (18,25,26)	3	3/3	100	2/3	67
Performance (29,31,33,34)	4	2/4	50	2/4	50
Malnutrition (34)	1	0/1	0	0/1	0

ADL, activity of daily living.
[a]The number of studies addressing an impairment that is significantly related to adverse outcomes.

domains are related to poor outcome. However, this evidence is derived from a heterogeneous cohort of studies, of which the majority did not use a systematic approach. In addition, the predictive value of a GA itself has not been assessed so far, and this should be subject of additional research.

Currently, there is no consensus on which domains a GA should comprise (6,52). In addition to the items discussed in this review, comorbidity burden and social status may be of added value when focusing on risk assessment, because both are associated with mortality. However, for social status, this was assessed in the prevalent population only (53). A GA focusing on rehabilitation may additionally include geriatric syndromes, such as delirium, incontinence, constipation, osteoporosis, and sensory deficits, because these issues may be amenable to interventions that could potentially improve quality of life (52).

For many domains, the superiority of one tool over another has not been proven. An overview of the applied tests in this review and appraisal of their use in ESRD can be found in Supplemental Table 4. Some disease–specific issues might be missed by tests not specifically developed for the dialysis population. For instance, the mental test (54) was not developed to detect cognitive impairment caused by vascular damage and may consequently lack sensitivity to detect mild disturbances in the dialysis population (55). Other tests (*e.g.*, Beck Depression Inventory for depression and Barthel test for ADLs) are successfully adapted from geriatric research, because populations are comparable at this point (8). Multiple strategies exist for the assessment of functional dependency, including performance status, ADLs and instrumental ADLs, and mobility, and a considerable overlap may occur when tests are not well adjusted to each other. Cross-study comparison would benefit from agreement on uniformity of a certain subset of tests and cutoff values.

The GA should target those most likely to benefit, such as potentially frail and elderly patients. Selection of patients who would benefit from a multidisciplinary assessment in the decision-making process concerning dialysis might be facilitated by a frailty screening test (56) or a prediction rule (26). Implementation of such an approach will greatly depend on the capacity and the targets of the dialysis center. More liberal acceptance criteria for dialysis may be partly influenced by financial and capacity considerations in addition to expected patient benefit, and critical assessment of geriatric impairments may be more difficult to implement here.

The interpretation of the results retrieved by this review was limited by several factors. Not all included studies performed an assessment before the start of dialysis therapy. Consequently, confounding might have occurred here, because the influence of dialysis may have led to under- or overestimation of the prevalence of geriatric impairments at the start. However, the trajectory of these impairments shortly after dialysis initiation is not yet known. In addition, the heterogeneity of the various tests being used, the different cutoff points, and the wide variety in the factors adjusted for in multivariate analyses (Tables 4 and 5) all limit the conclusions that may be drawn regarding the relation of most geriatric domains and poor outcome after dialysis initiation, and a meta-analysis of geriatric impairments was not feasible.

Table 4. The relation of geriatric impairment with mortality

Geriatric Impairments and Authors	Relation with Mortality				Adjusted for in Multivariate Analysis (if Applicable)
	Univariate		Multivariate		
	HR/OR (95% CI)	*P* Value	HR/OR (95% CI)	*P* Value	
Mood					
Boulware *et al.* (20)	1.19 (0.88 to 1.61)	>0.05	1.24 (0.81 to 1.89)	>0.05	Age, sex, race, marital status, education, coexistent illness, dialysis modality, use of antidepressant therapy, history of CVD risk factors, systolic and diastolic BP, CRP, IL-6, WBC count, hematocrit, creatinine, albumin, calcium, phosphorus
Chilcot *et al.* (23)	2.58 (1.19 to 5.63)	0.02	2.70 (1.06 to 6.80)	0.04	Albumin, hemoglobin, dialysis vintage, Davies comorbidity score, CRP, KPS<70
Diefenthaeler *et al.* (27)	4.50 (1.10 to 17.7)	0.03	6.50 (0.80 to 55.0)	0.09	Age, hypertension, DM
Genestier *et al.* (29)	—	>0.05	—	—	—
Jassal *et al.* (31)	—	>0.05	—	—	—
Lacson *et al.* (35)	1.09 (1.03 to 1.15)	<0.01	1.08 (1.01 to 1.14)	<0.05	Age, sex, SF-36 MCS (without mental health subscale), SF-36 PCS, unknown insurance, albumin, creatinine, hemoglobin
Soucie *et al.* (41)	—	—	1.30 (1.00 to 1.60)	<0.05	Age, sex, race, dialysis vintage, dialysis modality, activity level, albumin, education, student status, housing, employment, alcoholism, smoking, substance abuse
Cognition					
Jassal *et al.* (31)	—	<0.001	—	—	—
Couchoud *et al.* (25)	3.00 (2.00 to 4.40)	<0.001	1.50 (1.20 to 1.80)	<0.05	Age, sex, DM, CHF, peripheral vascular disease, cerebrovascular disease, dysrhythmia, chronic respiratory disease, active malignancy, severe behavioral disorders, severe disabilities, unplanned dialysis
Couchoud *et al.* (26)	2.60 (2.07 to 3.26)	<0.001	1.44 (1.12 to 1.85)	<0.001	Age, sex, DM, CHF, peripheral vascular disease, ischemic heart disease, cerebral vascular disease, dysrhythmia, chronic respiratory disease, cancer, cirrhosis, mobility, albuminemia, BMI
Rakowski *et al.* (40)	—	<0.10	1.91 (1.77 to 1.98)	<0.001	Age, sex, race, DM, hematocrit, erythropoietin, creatinine, Medicaid, BMI, albumin, DM as cause of ESRD, inability to transfer, inability to walk, stroke, heart failure, ischemic heart disease, peripheral vascular disease, COPD, hypertension, alcohol use, drugs use
Genestier *et al.* (29)	—	—	—	—	

Table 4. (Continued)

Geriatric Impairments and Authors	Relation with Mortality				Adjusted for in Multivariate Analysis (if Applicable)
	Univariate		Multivariate		
	HR/OR (95% CI)	*P* Value	HR/OR (95% CI)	*P* Value	
ADL					
Genestier *et al.* (29)	—	<0.001	—	—	—
Jassal *et al.* (31)	—	<0.001	0.71 (0.54 to 0.93)[a]	0.01	Age, phosphate, albumin, comorbidity, KPS, alcohol intake, dyskinesia
Jassal *et al.* (31) (>65 yr old)	—	<0.001	0.53 (0.37 to 0.75)[a]	<0.001	
Thamer *et al.* (42)	—	<0.05	1.47 (1.38 to 1.57)	—	Age, sex, race, catheter use, no or late nephrology care, albumin, creatinine, living in a nursing home, cancer peripheral vascular disease, alcoholism, CHF, hospitalization in 6 mo before dialysis
Mobility					
Arai *et al.* (18)[b]	4.22 (1.87 to 9.57)	<0.05	—	—	
Couchoud *et al.* (25)	1.10 (0.90 to 1.30)[c]; 2.30 (1.90 to 2.80)[d]	0.35; <0.001	−1.70 (1.40 to 2.00)	<0.05	Age, sex, DM, CHF, peripheral vascular disease, cerebrovascular disease, dysrhythmia, chronic respiratory disease, active malignancy, severe behavioral disorders, severe disabilities, unplanned dialysis
Couchoud *et al.* (25)	2.80 (2.40 to 3.30)[c]; 9.40 (7.90 to 11.3)[d]	<0.001; <0.001	2.47 (2.10 to 2.91); 6.53 (5.38 to 7.92)	<0.05; <0.05	Age, sex, DM, CHF, peripheral vascular disease, ischemic heart disease, cerebral vascular disease, dysrhythmia, chronic respiratory disease, cancer, cirrhosis, severe behavioral disorder, albuminemia, BMI
Rakowski *et al.* (40)	—	<0.100	1.47 (1.43 to 1.52)[d]; 1.36 (1.30 to 1.43)[e]	<0.001; <0.001	Age, sex, race, DM, hematocrit, erythropoietin, creatinine, Medicaid, BMI, albumin, DM as cause of ESRD, inability to transfer, inability to walk, stroke, heart failure, ischemic heart disease, peripheral vascular disease, COPD, hypertension, alcohol use, drugs use

Table 4. (Continued)

Geriatric Impairments and Authors	Relation with Mortality				Adjusted for in Multivariate Analysis (if Applicable)
	Univariate		Multivariate		
	HR/OR (95% CI)	*P* Value	HR/OR (95% CI)	*P* Value	
Performance					
Chandna *et al.* (22)	—	<0.001	1.02 (1.02 to 1.03)[f]	0.01	Age, comorbidity score, myeloma
Chilcot *et al.* (23)	—	<0.01	—	>0.05	—
Doi *et al.* (28) (≥3 versus 0)		<0.16	6.75 (1.51 to 0.10)	<0.05	Age, sex, BMI, renal disease, eGFR, urea nitrogen, hemoglobin, albumin, potassium, calcium, phosphorus, CRP, comorbidities, fatigue, edema, pulmonary edema, nausea, dysorexia, diarrhea, constipation, CNS manifestations, peripheral nerve abnormalities, itch, hemorrhagic diathesis, hypertension, diabetic retinopathy, ESA use
Genestier *et al.* (29)	—	<0.001	1.14 (0.98 to 1.32)[f]	0.08	Early referral, CCI, AGGIR group, institution, polypharmacy
Jassal *et al.* (31)	—	<0.001	1.85 (1.20 to 2.85)[a]	0.01	Alcohol intake, dyskinesia, age, phosphate, albumin, comorbidity, Barthel score
Jassal *et al.* (31) (>65 yr old)	—	<0.001	2.16 (1.25 to 3.72)[a]	0.01	
Joly *et al.* (33) (≤40 versus >40)	2.96 (1.05 to 8.33)	<0.05	2.34 (1.00 to 5.50)	<0.05	Age, sex, catheter use, late referral, BMI, peripheral vascular disease, heavy comorbidity
Lopez Revuelta *et al.* (37)	1.69 (1.44 to 1.97)	0.18	1.13 (0.86 to 1.48)[a]	0.40	Age, sex, DM, CCI, smoking, systolic and diastolic BPs, hemoglobin, creatinine, albumin, urea reduction ratio, first dialysis modality, center
Mauri *et al.* (38) (<70 versus ≥70)			1.88 (1.45 to 2.43); 3.83 (2.84 to 5.16)	<0.05	Age, sex, primary renal disease, CVD, COPD, malignant process, chronic liver disease, BMI<20
McClellan *et al.* (39)	—	<0.001	1.28 (0.61 to 2.01)[f]	>0.05	—
Soucie *et al.* (41) (<6 versus ≥6)			2.30 (1.40 to 3.60)	<0.05	Age, race, sex, time on dialysis, dialysis modality, albumin, education, student status, housing, employment, alcoholism, clinical depression, smoking, substance abuse
Frailty					

Table 4. (Continued)

Geriatric Impairments and Authors	Relation with Mortality				Adjusted for in Multivariate Analysis (if Applicable)
	Univariate		Multivariate		
	HR/OR (95% CI)	*P* Value	HR/OR (95% CI)	*P* Value	
Alfaadhel *et al.* (17)	—	—	1.22 (1.04 to 1.43)[f]	0.002	Age, sex, race, CCI, diabetic ESRD, GFR, albumin, dialysis modality, location of start dialysis
Bao *et al.* (19)	1.79 (1.44 to 2.24)	<0.001	1.57 (1.25 to 1.97)	<0.001	Age, sex, race, smoking, comorbidities, Medicaid versus other payer, eGFR, albumin, hemoglobin, dialysis modality, erythropoietin use, early nephrology referral
Johansen *et al.* (32)	3.42 (2.45 to 4.76)	—	2.24 (1.60 to 3.15)	<0.05	Age, sex, race, BMI, albumin, dialysis modality, comorbidities, employment status, marital status, smoking
Malnutrition[g]					
Chan *et al.* (21)	—	<0.001	1.74 (1.11 to 2.72)	0.02	Age, sex, dialysis modality, albumin, BMI, smoking, comorbidities
Chung *et al.* (24)	2.34 (1.72 to 3.30)	<0.001	2.01 (1.46 to 2.86)	<0.001	Age, sex, albumin, residual renal function, dialysate/plasma creatinine concentration ratio at 4 h dwell creatinine
Churchill *et al.* (43)	—	—	1.33 (1.18 to 1.52)[f]	—	Age, DM, CVD, country, albumin, Kt/V
Honda *et al.* (30)	—	<0.05	1.89 (1.09 to 3.28)	0.02	Age, DM, CVD, CRP
Kim *et al.* (34)	1.52 (0.85 to 2.63)	0.16	—	—	

HR, hazard ratio; OR, odds ratio; 95% CI, 95% confidence interval; CVD, cardiovascular disease; CRP, C-reactive protein; WBC, white blood count; KPS, Karnofsky performance score; DM, diabetes mellitus; —, not mentioned; SF-36 MCS, Short–Form (36) Health Survey Mental Component Score; SF-36 PCS, Short–Form (36) Health Survey Physical Component Score; CHF, chronic heart failure; BMI, body mass index; COPD, chronic obstructive pulmonary disease; ADL, activity of daily living; CNS, central nervous system; ESA, erythropoietin stimulating agent; CCI, Charlson Comorbidity Index; AGGIR, Autonomie Gérontologique Groupes Iso-Ressources.

[a]Risk per increase in score of 10.

[b]The OR was calculated by comparing group 1 (independent mobility at start) and group 2 (independent mobility at start but decline in mobility after start) with group 3 (impaired mobility at start). Multivariate analysis was, therefore, not possible.

[c]Need assistance for transfers.

[d]Totally dependent for transfers.

[e]Unable to ambulate.

[f]Risk per point increase.

[g]Reference group is similar to that in Table 2.

Table 5. The relation of geriatric impairment with hospitalization

Geriatric Impairment and Authors	Relation with Hospitalization				Outcome	Adjusted for in Multivariate Analysis (if Applicable)
	Univariate		Multivariate			
	HR/RR/OR (95% CI)	*P* Value	HR/RR/OR (95% CI)	*P* Value		
Depression						
Lacson *et al.* (36)	—	<0.001	1.13 (1.02 to 1.25)	0.02	Hospitalization rate	Age, sex, race, DM, albumin, creatinine, hemoglobin, calcium, phosphorus, transferrin saturation, SF-36 PCS, SF-36 MCS (two mental health items of interest removed), dialysis vintage
Lacson *et al.* (36)	—	<0.001	1.20 (1.07 to 1.35)	0.002	Duration of hospitalization	Age, sex, race, DM, albumin, creatinine, hemoglobin, calcium, phosphorus, transferrin saturation, SF-36 PCS, SF-36 MCS (two mental health items of interest removed), dialysis vintage
Performance						
Churchill *et al.* (43) (≤80 versus >80)	—	—	1.63 (—)	<0.05	Duration of hospitalization	Age, sex, KPS, CVD, DM, albumin, malnutrition, CCr, Kt/V, β2M, country
Lopez Revuelta *et al.* (37)	1.25 (1.05 to 1.48)[a]	0.01	1.12 (0.92 to 1.36)[a]	0.51	Duration of hospitalization	KPS, CCI, logarithmic time, hospital, SF-36 PCS, SF-36 MCS
Malnutrition						
Churchill *et al.* (43)	—	—	0.82 (—)[b]	<0.05	Duration of hospitalization	Age, sex, KPS, CVD, DM, albumin, CCr, Kt/V, β2M, country
Frailty						
Bao *et al.* (19)	1.44 (1.26 to 1.66)	<0.001	1.26 (1.09 to 1.45)	<0.001	Time to first hospitalization	Age, sex, race, smoking, comorbidities, Medicaid versus other payer, eGFR, albumin, hemoglobin, dialysis modality, erythropoietin use, early nephrology referral
Johansen *et al.* (32)	1.90 (1.67 to 2.17)	<0.05	1.56 (1.36 to 1.79)	<0.05	Time to first hospitalization or death	Age, sex, race, BMI, albumin, dialysis modality, comorbidities, employment status, marital status, smoking
Johansen *et al.* (32)	—	—	1.98 (1.41 to 1.87)	<0.05	Time to first nonvascular–related hospitalization or death	Age, sex, race, BMI, albumin, dialysis modality, comorbidities, employment status, marital status, smoking

HR, hazard ratio; RR, relative risk; OR, odds ratio; 95% CI, 95% confidence interval; —, not mentioned; DM, diabetes mellitus; SF-36 PCS, Short–Form (36) Health Survey Physical Component Score; SF-36 MCS, Short–Form (36) Health Survey Mental Component Score; KPS, Karnofsky performance score; CVD, cardiovascular disease; CCr, creatinine clearance; β2M, β2-microglobulin; CCI, Charlson Comorbidity Index.

[a]Risk per increase in score of 10.

[b]Risk per point increase.

Matching nephrology care to the needs of vulnerable patients with ESRD is becoming increasingly relevant with aging of the population. As was shown in other fields of research, a GA may be successful in identifying vulnerable patients at risk of poor outcome and contribute to early interventions improving quality of life. In nephrology, a systematic approach to frail patients is currently lacking. This review shows that geriatric impairment across multiple physical and mental domains at dialysis initiation is related to poor outcome. However, systematic assessment of impairment in relation to outcome is sparse, especially in the elderly. Whether systematic assessment of geriatric impairments could discriminate between fit and vulnerable patients in the context of treatment decisions concerning dialysis initiation should be assessed in more detail before the implementation in clinical practice. In addition, research should focus on standardization of assessment tools specifically for the CKD population, thereby enhancing the comparability of clinical and research results.

Acknowledgments

This study was supported by the Cornelis de Visser Stichting.

The study sponsor had no role in study design, collection, analysis, and interpretation of data; writing the report; or the decision to submit the report for publication.

Disclosures

None.

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Received: June 19, 2015 **Accepted:** March 22, 2016

Published online ahead of print. Publication date available at www.cjasn.org.

This article contains supplemental material online at http://cjasn.asnjournals.org/lookup/suppl/doi:10.2215/CJN.06660615/-/DCSupplemental.