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Editorial

Age is just a number: Is frailty being ignored in vascular access planning for dialysis?

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Abstract

Current international guidelines advocate fistula creation as first choice for vascular access in haemodialysis patients, however, there have been suggestions that in certain groups of patients, in particular the elderly, a more tailored approach is needed. The prevalence of more senior individuals receiving renal replacement therapy has increased in recent years and therefore including patient age in decision making regarding choice of vascular access for dialysis has gained more relevance. However, it seems that age is being used as a surrogate for overall clinical condition and it can be proposed that frailty may be a better basis to considering when advising and counselling patients with regard to vascular access for dialysis. Frailty is a clinical condition in which the person is in a vulnerable state with reduced functional capacity and has a higher risk of adverse health outcomes when exposed to stress inducing events. Prevalence of frailty increases with age and has been associated with an increased risk of mortality, hospitalisation, disability and falls. Chronic kidney disease is associated with premature ageing and therefore patients with kidney disease are prone to be frailer irrespective of age and the risk increases further with declining kidney function. Limited data exists on the relationship between frailty and vascular access, but it appears that frailty may have an association with poorer outcomes from vascular access. However, further research is warranted. Due to complexity in decision making in dialysis access, frailty assessment could be a key element in providing patient-centred approach in planning and maintaining vascular access for dialysis.

Keywords

Frailty, dialysis, arteriovenous fistula, aging, premature, kidney failure, chronic, renal insufficiency, chronic, risk assessment

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Introduction

Creation of vascular access is a necessary but significant milestone for patients with end-stage renal disease (ESRD) in their progression towards haemodialysis. Current international guidelines encourage the creation of arteriovenous fistulas (AVF) as a first choice for dialysis access followed by arteriovenous grafts (AVG) and as a last resort insertion of central venous catheter (CVC).[1–4]

The 'Fistula First' approach has evolved into a 'Fistula First – Catheter Last' approach[5] based on evidence showing that patients dialysing using AVFs (and AVGs) have better overall patient survival as well as decreased rates of infection, interventions and overall morbidity than those reliant on CVCs.[6–8]

Although the guidelines generally advocate fistula creation in haemodialysis patients, there have been suggestions that in certain groups of patients, in particular the elderly, a more tailored approach is needed[9,10]). As the prevalence of more senior individuals (aged >65) suffering from chronic kidney disease (CKD)[11,12] and receiving renal replacement therapy (RRT) has increased steadily in recent years and as a consequence the importance of including patient age in

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decision making regarding choice of vascular access (VA) for dialysis has been discussed.[13,14]

The distal first approach as defined in guidelines is largely to maintain future options for subsequent access although the primary failure is higher in distal fistulas.[15] A systematic review by McGrogan et al.[14] identified that in the elderly, brachiocephalic AVF have superior primary (58.5% vs 49.7%) and secondary patency rate (72.7% vs 65.1%) at 12 months post fistula creation compared to radiocephalic AVFs.

Creation of an AVF with subsequent failure represents a source of distress and anxiety which may deter further attempts. Even where a successful fistula is created it may never be used due to failure to mature or due to death of the patient before reaching the requirement for dialysis.[14,16,17]

Accordingly, some authors have supported that in older CKD patients with diabetes, peripheral vascular disease (PVD) or limited life expectancy using a proximal location for the primary AVF might be more suitable choice or even to use an early cannulation graft as a first line option.[1,10,18]

However, the use of age as a factor in deciding on vascular access is flawed. Whilst older individuals may have an increased burden of existing comorbidities per se the presentation in CKD and renal failure does not show that age alone is a risk factor of access failure. Additionally, the terms 'elderly' and 'older' are vague[19] and largely not representative of an individual's state of health or suitability for clinical decision making.

It is generally implied that age is being used as a surrogate for overall clinical condition and it can be proposed that frailty may be a better basis to considering when advising and counselling patients with regard to vascular access for dialysis.

Frailty

Frailty encompasses both physical and psychological components. It is described as a clinical condition in which the person is in a vulnerable state with reduced functional capacity and has a higher risk of adverse health outcomes when exposed to stress inducing events.[20]

Prevalence of frailty increases with age and has been associated with an increased risk of mortality, hospitalisation, disability and falls. Frailty is also associated with increased overall health care costs.[20–22]

A frailty phenotype has been described as a syndrome consisting of unintentional weight loss, reduced activity, slow gait, exhaustion and weakness[21] and whilst frailty has mainly been described in association with elderly population in recent years the importance of frailty as part of chronic diseases and in younger age groups has been acknowledged.[22–24]

The prevalence of frailty in the general population does increase with age and is more seen in women compared to men. Gale et al.[25] examined the prevalence of frailty in 5450 people aged >60 years and above as part of the English Longitudinal Study of Ageing. The overall prevalence of frailty was 14% (men vs women 12% and 16%, respectively). Among those aged 60–69 years the prevalence was 6.5%, increasing to 65% among those aged 90 and over. In a large prevalence study of almost half a million UK Biobank participants aged 37–73 years the prevalence of frailty was 3% overall with 38% deemed pre-frail and 59% not frail. Only a slight increase in prevalence was noted in the 65–73 age groups with only 5% deemed frail. When frail patients were assessed for co-morbidity almost three quarters (72%) had at least one long-term condition. When multiple co-morbidities were assessed frailty was seen in 18% of people with four chronic conditions.[24]

Two main concepts of frailty measurement are used: Fried Phenotype (FP) and Frailty Index (FI). Detailed description of both methods provided in Table 1.

Several other screening tools for frailty have been developed largely based on similar concepts.[20,26,33] Table 2 summarises some of the frailty assessment tools used in CKD (including ESKD) population. No consensus exists on which measurement tool to use to assess the frailty among people with CKD, nevertheless, the focus must remain on using all effort to assess the frailty and use the outcome as part of holistic patient care.[28,34,35]

Frailty and kidney disease

Kidney disease is considered an independent risk-factor for patients' functional decline and frailty, and frailty has been acknowledged as an important factor in CKD management.[34,35]

Roshanravan et al.[39] measured the prevalence of frailty among adults with pre-dialysis CKD from the Seattle Kidney Study (SKS) cohort and compared these to a group of patients from Cardiovascular Health Study (CHS). The prevalence of frailty among CKD pre-dialysis patients was 14% compared to 7% in Cardiovascular Health Study group despite the mean age in SKS and CHS group being 59 and 76 years, respectively. In both patient cohorts half of the participants were classified as intermediately frail (52% in SKS group vs 47% in CHS group). Intermediate frailty (or pre-frailty) was defined by authors as having one or two conditions based on frailty phenotype which in itself is considered to be predictive of becoming frail in next 3–4 years.[35] The study also showed higher prevalence of frailty among participants with eGFR <45 ml/min/1.73 m^2.[39] A systematic review by Chowdhury et al.[40] demonstrated increased frailty among pre-dialysis population from 7% in community CKD cohorts (median eGFR 49 ml/min/1.73 m^2) to 42.6% in more severe CKD cohort (mean eGFR 27 ml/min/1.73 m^2). In the haemodialysis population the frailty prevalence varied from 14% to 73%.

In a separate study in a dialysis cohort a high proportion of frailty in younger age groups was seen with 44% of

Table 1. Concepts of frailty measurement.

Assessment method	Description/scoring	Strengths	Limitations
Fried Phenotype (*aka* Fried criteria).[21,26–28]	Five domains: weight loss, reduced activity, slow gait, exhaustion, weakness. Individuals with ⩾3 positive domains considered frail. Individuals with 1–2 positive domains considered pre-frail	Validated in different population groups (including CKD). Easy to apply.	Focus on physical aspects of frailty (excludes psychosocial and cognitive function and co-morbidities). Includes measurements not used in routine care (grip strength, walking test).
Frailty Index (*aka* Frailty Index of Accumulative Deficits).[26–32]	Pre-defined 30 or more health related deficits (co-morbidities, symptoms, disabilities etc.) relevant to population of interest. Individual assessed to determine which pre-defined deficits exist. Higher number of existing deficits indicate higher risk of frailty. Existing number of deficits is divided with total number of pre-defined deficits and the result is reported as frailty index (range 0–1) indicating frailty status: FI ⩽ 0.08 non-frail. FI 0.09–0.24 pre-frail. FI ⩾ 0.25 frail	Validated in different population groups (including CKD). Includes cognitive and social aspects of frailty. Deemed more accurate in predicting adverse outcomes compared to other frailty assessment methods.	Time consuming to calculate.

Table 2. Summary of frailty measurement tools.

Assessment tool	Domains/Items	Score/Cut-off values	Validated in CKD population	Comments
Clinical Frailty Scale (CFS).[26–28,36]	1–8 categories with increasing state of frailty.	1 = very fit. 8 = very severely frail. 9 = terminally ill. ⩾5 frail	Yes	Proven to have high accuracy in identifying frailty in CKD population. Highly subjective.
Short Physical Performance Battery (SPPB).[27,28]	Three physical assessments: Standing balance. Gait speed. A chair stand test	0 – worst performance. 12 best performance. <10 frail	Yes	Rapid assessment tool. Poor correlation with Fried criteria.
Groningen Frailty Indicator (GFI).[26,28,37]	15 questions, eight domains: mobility, vision, hearing, nutrition, co-morbidity, cognition, psychosocial and physical fitness	0 = normal activity without restriction. 15 = completely disabled. ⩾4 frail	Yes	Mainly used in Netherlands.
Multidisciplinary Prognostic Index (MPI).[26,28]	Eight individual assessments: function, polypharmacy, mental status, nutrition, risk of pressure sores, co-morbidity and social circumstances.	<0.34 robust. 0.34–0.66 pre-frail. >0.66 frail	Yes	Aimed at hospitalised patients.
Edmonton Frailty Scale (EFS).[23,26]	Nine domains: cognition, health, hospitalisation, social support, nutrition, mood, function and continence.	0–5 not frail. 6–7 apparently vulnerable. 8–9 mildly frail. 10–11 moderately frail. 12–17 severely frail	No	Used among patients with CKD stages 1–5
FRAIL scale.[23,26,38]	Five items: fatigue, resistance, ambulation, illness and loss of weight	0 = robust. 1–2 pre-frail. ⩾3 frail	No	Used among patients with CKD stage 5

participants aged <40 year classed as frail and 61% between age 40 and 50 were frail. The overall frailty among study participants was 67.7% with highest prevalence among patients aged >80 years (78.8%).[41]

The prevalence studies (as summarised in Table 3) suggest that CKD patients in general are prone to be frailer irrespective of age and the risk increases further with declining kidney function. To support that statement further, chronic kidney disease is described as a state of accelerated metabolic – ageing.[12] CKD is associated with physiological and biochemical changes including chronic low-grade inflammation and oxidative stress, malnutrition, sarcopenia, protein-energy wasting syndrome, chronic anaemia, vascular disease including vascular calcification and changes in calcium metabolism. Some of these changes are considered as part of normal ageing, however, the presence of CKD and

Table 3. Summary of prevalence studies.

Study	Population (n = No. of patients)	Age or mean age (*SD) in years	Assessment method	Prevalence of frailty
Gale et al.[25]	General population (n = 5450)	>60	Fried criteria	Overall 14%
Hanlon et al.[24]	General population (n = 493,737)	37–73	Fried criteria	Overall 3%
Roshanravan et al.[39]	Pre-dialysis CKD. (n = 336)	Mean 59 (±13)	Fried criteria	CKD cohort 14%
	Community-dwelling population (number of patients not provided)	Mean 76 (no SD provided)		Community-dwelling population 7%
Chowdhury et al. 2017 (systematic review)[40]	Pre-dialysis and dialysis patients	–	Majority (72%) tools used were based on Fried criteria	Pre-dialysis 7–42.6% Dialysis 14–73%
Johansen et al.[41]	Dialysis population (n = 2275)	Mean 58.2 (±15.5)	Fried criteria	Overall 67.7%

*SD = standard deviation.

progressively declining kidney function accelerates the process leading to premature ageing and earlier clinical manifestation of aspects of frailty syndrome.[11,12,23,35,42,43]

Frailty and dialysis access

Despite the multiple studies concentrating on age and vascular access, as summarised previously, there has been negligible work on the association of frailty and vascular access.

Chao et al.[44] conducted a study of frailty in dialysis patients using the FRAIL scale. Using this self-reported measure demonstrated that around one fifth of the patients were deemed frail. Vascular access failure was 37.3% overall in the study and in those classified as frail the risk of failure increased by a hazard ratio of 2.63. The underlying mechanisms of access failure are not defined although endothelial dysfunction has been associated with frailty in CKD patients. Mansur et al.[45] studied the association in pre-dialysis population (eGFR between 16 and 39 mL/min/1.73²), the study sample included 61 participants with mean age of 64.9 years (±10.3 years) of which 42.6% were deemed frail (measured with Short Form-36 questionnaire) and 46% of frail participants were classified as non-elderly (<60 years of age). Frailty was associated with endothelial dysfunction (OR 3.86 (95% CI 1.00–14.88)) together with older age, female gender and obesity. The hypothesised reasons behind endothelial dysfunction based around hyper-activation of the sympathetic system and oxidative stress, both features of CKD progression.

Johansen et al.[41] assessed frailty in >3000 incident dialysis patients and determined that individuals with a permanent vascular access (AVF or AVG) were less likely to be frail with hazard ratio 0.72 (95% CI 0.51–0.98) and it was independent of the time of nephrology referral. However, reasons behind it are unclear. Nevertheless, it seems to associate with findings by Garcia-Canton et al.[46] who observed non-frail dialysis patients to be more frequently hospitalised due to issues with dialysis access and need for surgical intervention. Frail counterparts had tendency to be hospitalised due to infection or cardiovascular issues.

Although the data is limited it appears that frailty may have an association with poorer outcomes from vascular access. As this is seen in younger patients and is not limited to an arbitrary cut off such as has been previously suggested using age, it would appear that frailty scoring may have a role in studying vascular access outcomes.

In addition, it may be a suitable measure to include in the individualised ESRD Life-Plan proposed in the 2019 KDOQI guidelines. Frailty scoring could easily be performed as part of the plan and this could be started in the pre-dialysis period and reviewed regularly.[1] The possible advantages of using functional assessments such as frailty scores allows a patient centric approach to be applied which may address previously described disparities in priorities in VA decision-making between patients and clinicians.[47,48] The inter-relation between frailty and comorbidities may act as an overarching measure for burden of disease in CKD population and since frailty assessment includes physical, cognitive and social aspects of patient's health and wellbeing, irrespective of age[39] it may serve as a much better tool with which to consider an access option.

Summary

Decisions regarding dialysis access are becoming more complex with recent guidelines advocating a more individualised approach in collaboration between patient/carer and renal team members. The basis of this approach is stated to consider the patient's 'medical condition, current and future life goals and preferences, social support, functional status, logistics and other relevant aspects of the disease management together with enhanced dialysis access strategy'.[1]

As part of that assessment and attempting to incorporate a universal reproducible approach, which can be subsequently audited and studied, it would appear that frailty scoring would be a key component of ongoing future access care.

Further studies will be required to better understand which approach to frailty scoring is best suited to dialysis access, although the validated methods described may be applicable in different settings.

Author's contribution

NI: Research idea and study design; NI and KK: Literature search; NI and KK Drafting of the manuscript; NI and KK: Review and approval of the final draft.

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