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Frailty assessment as part of transplant listing: yes, no or maybe?

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ABSTRACT

Frailty, characterized by a decreased physiological reserve and an increased vulnerability to stressors, is common among kidney transplant (KT) candidates and recipients. In this review, we present and summarize the key arguments for and against the assessment of frailty as part of KT evaluation. The key arguments for including frailty were: (i) sheer prevalence and far-reaching consequences of frailty on KT, and (ii) the ability to conduct a more holistic and objective evaluation of candidates, removing the inaccuracy associated with 'eye-ball' assessments of transplant fitness. The key argument against were: (i) lack of agreement on the definition of frailty and which tools should be used in renal populations, (ii) a lack of clarity on how, by whom and how often frailty assessments should be performed, and (iii) a poor understanding of how acute stressors affect frailty. However, it is the overwhelming opinion that the time has come for frailty assessments to be incorporated into KT listing. Although ongoing areas of uncertainty exist and further evidence development is needed, the well-established impact of frailty on clinical and experiential outcomes, the invaluable information obtained from frailty assessments, and the potential for intervention outweigh these limitations. Proactive and early identification of frailty allows for individualized and improved risk assessment, communication and optimization of candidates.

LAY SUMMARY

In this review, we present and summarise the key arguments for and against the assessment of frailty as part of kidney transplant evaluation.

Keywords: aging, frailty, gerontology, kidney transplantation, transplant listing

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FRAILTY OVERVIEW

Frailty, originally characterized in community-dwelling older adults, is characterized by a decreased physiological reserve and an increased vulnerability to stressors; this clinical syndrome is distinct from comorbidity and disability [1, 2]. As the number of older kidney transplant (KT) patients continues to grow [3], centres are seeking tools to help ensure that appropriate candidates gain access to this lifesaving treatment.

The most widely cited tool to measure frailty is the physical frailty phenotype (PFP), which was proposed and validated by Fried and colleagues [2, 4] and has been extensively studied in KT patients [5, 6]. This PFP is defined by having three of the five indicators: slow walk speed, low physical activity, unintentional weight loss, weakness and exhaustion [2]. It has been estimated that nationally, 16% of KT candidates and 14% of KT recipients are frail in the USA [7]. Importantly, frailty is common not only in older KT patients but also manifests at younger ages in this population. In a cohort study that calculated frailty prevalence among end-stage kidney disease (ESKD) patients, KT candidates, found that even among younger patients the burden of frailty was greater than among community dwelling older adults [8].

Frailty has been noted by transplant centres for its ability to predict adverse outcomes among ESKD and KT patients regardless of age [9–15]. Among adult KT candidates, frailty is associated with lower chance of listing, higher waitlist mortality and reduced access to KT [16–19]. Frailty was also shown to improve risk stratification for early hospital readmission [20] by improving the area under the receiver operating characteristic curve ($P = .01$) as well as the net reclassification index ($P = .04$). Furthermore, among adult KT recipients, frailty is associated with surgical complications, delayed graft function, postoperative delirium, early hospital readmission, immunosuppression intolerance and mortality [20–26]. Candidates who are older (≥65 years) are at 1.79-fold increased odds of being frail and similarly recipients who are older are at a 1.74-fold increased odds of being frail; age was the only risk factor that was significantly associated with frailty in adjusted models [8].

However, there are noted limitations to the PFP for use in transplantation [27]. Namely, the phenotype relies on the self-report of components like exhaustion, unintentional weight loss and physical activity. There have been attempts to refine the PFP for clinical use, making it specific to patients with kidney disease as has been done in liver transplantation [28]; one study sought to replace the unintentional weight loss component with a direct measure sarcopenia, via computed tomography scans, found that there was no increase in predictive validity for post-KT outcomes [29]. Other studies have sought to add aging inflammatory markers [30]. However, in each case the predictive validity of the PFP (with the minor revision to measuring dry weight for unintentional weight loss) was equal to that of any ESKD-specific measure of frailty and the validity of the PFP remained very high in this novel population of KT patients.

Measures of physical function are often used as surrogates of frailty: the Short Physical Performance Battery (SPPB), functional status, Kidney Disease Quality of Life Short Form Physical Component Subscale (SF-12 PCS), gait speed, and timed up and go. These surrogates are also associated with adverse post-KT outcomes among ESKD and KT patients [31–37]. Finally, it is worth noting that an additional frailty framework is the deficit accumulation model (Frailty Index) which defines frailty as a state of accelerated deficit accumulation [38] and had been found to have similar predictive value to PFP for clinical outcomes in non-KT populations [39]. While these surrogates may capture a patient's 'vulnerability' prior to surgery they are not direct measures of a patient's underlying physiologic reserve. Physiologic reserve is an underlying, unobservable construct; this is why we must measure markers of physiologic reserve through markers of frailty [40].

In a US survey of 133 KT programs [11], 99% of KT programs felt that frailty could be helpful in assessing KT candidacy during evaluation, and 96% indicated it should be a factor in deciding whether a candidate is selected for transplantation. Strikingly, 69% of US KT programs reported conducting a standardized frailty assessment during transplant evaluation, although there was little consensus on the tool to measure frailty [11]. This survey was linked to the US national registry. Centres that performed a frailty assessment at evaluation had better waitlist outcomes and post-transplant outcomes. However, only centres that used validated tools (SPPB, functional status, SF-12 PCS, gait speed, timed up and go) had better waitlist survival [41]. For example, centres that used a validated measure of frailty had a lower waitlist mortality rate [incidence rate ratio (IRR) = 0.89, 95% confidence interval (CI) 0.83–0.96], and this benefit was also observed among older patients (IRR = 0.82, 95% CI 0.72–0.93) [41]. There are likely a number of reasons why transplant centres that use a validated frailty tool have better waitlist mortality and this should be investigated in future studies.

In this review we present the pro and con side of a debate: should frailty assessment be part of the transplant listing process? Below we first consider the pro perspective and then the con perspective (Fig. 1). We conclude this debate with a summary of the arguments and practical considerations for assessing frailty as part of the transplant listing process.

PRO: VALIDATED FRAILTY ASSESSMENT IS ESSENTIAL TO MAXIMIZE TRANSPLANTATION OUTCOMES

Nephrologists, transplant surgeons and transplant clinical nurse specialists counsel people with advanced chronic kidney disease (CKD) on the risks and benefits of transplantation. This cannot be wholly realized without an awareness of a potential candidate's frailty status, given its importance as a predictor of adverse transplantation outcomes.

When compared with validated frailty assessment methodology, the accuracy of nephrologist-perceived frailty is not much better than tossing a coin [42]. Although frailty is a state of age-associated physiological decline [43], chronological age is often a poor surrogate for physiological age; older people can be robust (non-frail) whilst younger people, particularly those living with chronic conditions, can be frail [8, 15, 44]. In these situations, individuals may be inappropriately perceived as frail or robust, respectively. Consequently, patients may decline, or worse be denied, an intervention that affords clear benefits or accept an intervention on the basis of understated associated risks [16]. Adopting an objective frailty assessment method that is not reliant on personal perceptions and that is directly measurable offers an accurate, consistent, and reliable approach to the transplantation assessment process that subjective frailty assessment, influenced by personal perceptions, does not afford. It provides justification for the risks and benefits conveyed to patients, relatives and other healthcare providers, transparency for the basis of decision-making, and ensures fair, equitable and impartial access to organ donation. Finally, it allows parity of data collection from transplant centres to compare KT candidate and recipient outcomes, with a view to standardizing

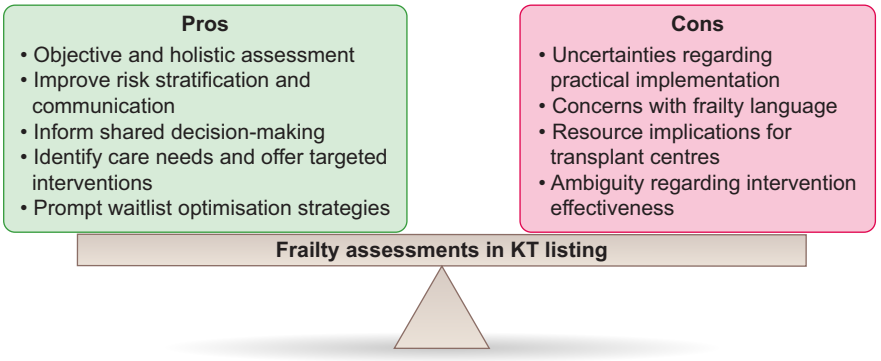

Figure 1: Weighing the pros and cons of frailty assessment in KT listing.

practice between centres and identifying where improvements are necessary.

Not all frailty assessment methods are created equal [5, 45]. The most well-studied frailty assessment in the context of kidney transplantation is the PFP [2, 15], as described above. The PFP combines objective components (walk speed and weakness) with subjective components (exhaustion and physical activity). The most commonly used frailty screening tool in the USA is simply an assessment of walking speed [11], which has good diagnostic accuracy for frailty as measured by the PFP [2, 45]. There are frailty screening tools available that do not involve objective physical assessments and take less time to perform [45, 46], but require further evaluation in the transplantation setting. In practical terms, a walking speed assessment can be introduced into clinical practice with access to only a corridor, a measuring tape and a stopwatch. The PFP assessment can be performed with the addition of a handgrip dynamometer and self-report questionnaires; this would be preferred given that the vast majority of the literature supports the use of the PFP in kidney transplantation. Considering the time and resource invested in extensive costly cardiac investigations prior to transplantation (with an arguably less convincing evidence base [47, 48]), implementation of routine PFP assessment is surely attainable.

Accurately identifying frailty during KT candidacy assessments provides an opportunity to consider a more holistic review to identify and address care needs [11, 41]. After a KT patient is identified as frail the next step can be unclear. However, from geriatric medicine literature, there are potential assessments to better understand why a patient is frail, identify associated geriatric impairments and prompt consideration of what can be done to improve their health and well-being. For example, Comprehensive Geriatric Assessment (CGA), defined as 'a multidimensional, multidisciplinary process which identifies medical, social and functional needs, and the development of an integrated/co-ordinated care plan to meet those needs' [49], improves outcomes for older adults, including those living with frailty [50, 51]. CGA, or modified versions, have been used to identify frailty and other associated geriatric impairments in advanced CKD cohorts [52–54], and provide reason to set targeted interventions [55]. CGA has not yet been evaluated in the transplantation setting, but existing evidence suggests the potential for benefit for the waitlisted transplant candidate [56].

Rather than being seen as a dichotomous state, frailty should be considered on a spectrum from mild to severe, with the risk of adverse outcomes increasing with worsening frailty status [57]. The goals of management are different for an individual living with mild frailty compared with an individual living with severe frailty [58]. In the latter, the focus shifts to supportive care, including symptom management and advance care planning. In those with less severe frailty, there is an emphasis on implementing interventions that mitigate progression of the frailty syndrome. In fact, we know that frailty is reversible for some with advanced CKD, indeed it has been shown to improve in people receiving haemodialysis and following KT [29, 59]. Precisely when frailty is more amenable to reversibility is uncertain. It may be that frailty primarily driven by advanced CKD, rather than multiple chronic conditions (multimorbidity) and ageing itself, may be more amenable to reversal with kidney replacement therapy. There may also be opportunity to improve less severe frailty states with targeted interventions. Preliminary studies suggest that exercise interventions, including transplantation prehabilitation, may maintain or improve frailty status, physical function, exercise capacity and endurance in advanced CKD populations [60–63]. There is evidence that multicomponent intervention, including exercise, dietetic and psychological components, improves exercise capacity and reduces the decline in cardiorespiratory fitness in the general CKD population [64]. Multicomponent intervention may also prove to be effective for people living with advanced CKD and frailty, and could be used in the optimization of waitlisted transplant candidates [65–67].

But what about the decision to waitlist? How do we identify those living with frailty that may be reversed and who therefore may experience greater benefits with transplantation? It is perhaps easier to identify those in whom frailty is likely irreversible and therefore have the highest risk of adverse outcomes with transplantation. Hospitalization and higher inflammatory markers are associated with worsening frailty status in people receiving haemodialysis [59]. We also know that KT candidates whose frailty status worsens prior to transplantation have a higher mortality risk post-transplantation and longer length of hospitalization suggesting that frailty is dynamic between evaluation and admission for KT [68]. Repeated frailty assessment (at each clinical encounter at the transplant centre on non-dialysis days) of those referred for KT candidacy evaluation allows for the identification of individuals with worsening frailty and higher risk of adverse transplantation outcomes. For those waitlisted, regular frailty assessment ensures timely suspension from the KT waitlist for those in whom transplantation risks have increased. It also offers the opportunity to implement targeted interventions leading to the avoidance of further unplanned hospitalizations, and may, for some, lead to improvement in physical frailty and subsequent reactivation

on the transplant waitlist. Listing decisions should weigh the totality of evidence, including frailty, when deciding whether to list a patient. Frailty should never be used as the sole reason for disqualifying a patient for KT, as is supported by patients and experts [69, 70]. Frailty is particularly useful when deciding to list an older candidate such that robust older adults should be listed regardless of their age.

In summary, the evidence that frailty is associated with adverse transplantation outcomes is compelling. Frailty assessments have been validated in advanced CKD and transplantation settings, are practical to introduce and can ensure equitable access to kidney donation. Accurate identification of frailty provides an opportunity to introduce interventions that optimize the potential transplant recipient, maximizing their opportunity to receive a KT and minimizing the risk of perioperative adverse outcomes. Finally, regular frailty assessment allows the identification of those in whom the risks of KT exceed the benefits and provides transparency for decisions not to waitlist for patients, relatives and the transplant community. If they have not already, transplant centres should introduce a validated frailty assessment within candidacy evaluation and thereafter regular assessment for those waitlisted to maximize patient outcomes.

CON: INTRODUCING FORMAL ASSESSMENT OF FRAILTY AS PART OF TRANSPLANT ASSESSMENT IS PREMATURE

Nobody doubts the use of frailty assessment in our specialty or disputes current evidence pointing towards frailty as a useful marker of prognosis after KT. What is currently not clear is whether formal assessment and scoring of frailty in KT candidates is better than the current standard of transplant assessment and whether such formal assessment would change our decisions on whom to list. We would argue that transplant assessment has always taken frailty into account although perhaps not in a formal way.

The lack of consensus regarding tools for frailty assessment remains a key concern [71] and some form of international consensus is eagerly awaited. It is worth remembering that frailty scores were originally devised for use in an elderly population and only some have been validated in renal patients including those younger than 65 years, an age bracket where many renal patients already fulfil PFP criteria [30]. A good example where this is often the case is the KT candidate with long-standing type 1 diabetes and multiple diabetic complications. It is likely that trajectories of frailty are very different in at least some of our renal patients and perhaps we should consider more specific scores for use in this population.

Secondly, the choice of terminology is worth considering. Patients themselves often reject the term 'frail' [72]. A discussion around consensus for tools should also include the terminology and take into account the views of patients and their families and caregivers.

Thirdly, we need to consider the implications on workload and resources overall. There are specific feasibility concerns with frailty assessment: space to conduct the assessments, addition of an assessment that takes 10–20 minutes to complete, cultural appropriateness of the questions in the PFP. Consider a department that assesses around 200 patients annually for transplantation. Assuming that a PFP assessment and its documentation will add at least 10 minutes, then this additional element of the assessment pathway would lead to an extra workload of 33 hours annually. It is difficult to see how teams could accommodate this additional work in our assessment clinics and it is equally difficult to see how nursing colleagues, or the referring teams and nephrologists, could take this on. The issue of resources becomes more significant if we accept that we would also have to reassess frailty whilst patients are waitlisted. To do this in our 250 patients listed for kidney and 50 patients listed for combined kidney and pancreas transplantation (who are reviewed twice a year) would add another 58 hours of work annually excluding reassessments after intercurrent illness and operations. The workload generated by communication to other healthcare providers [73] is difficult to gauge but we could surely expect to spend a significant amount of time with this as well, at least initially. It is also certain that documenting and assessing frailty during KT assessment will require additional discussion time with patients and families not least to allow them to understand the concept.

Linked to the concept of frailty assessment in KT candidates is the idea that intervention is feasible and effective to improve post-transplant outcomes [74]. Early evidence shows that prehabilitation is both safe and feasible in this population [60–63]. What is much less clear is the magnitude of a positive effect, if any, on outcomes. The resource implications of such a program are also significant and it is worth noting that even studies in this regard have been suspended due to the impact of the pandemic on workforce and resources [75]. Studies to demonstrate the benefit of a prehabilitation program are under way and demonstrating the real-world effectiveness and cost-effectiveness will be an important part of this work.

In summary, current evidence is intriguing but does not justify the resources required to do this routinely and do it well. Key steps would include more research to establish that formal assessment of frailty is superior to standard of care, agreement on tools and terminology (and ideally international harmonization of both), demonstration of cost-effectiveness, and also a better understanding of the magnitude of clinical benefit of prehabilitation in patients specifically identified as frail prior to transplantation.

CONCLUSION

Having presented and summarized the key arguments it is the overwhelming opinion of the authors that the time has come for frailty assessments to be incorporated into KT listing. Although ongoing areas of uncertainty exist and further evidence development is needed, the well-established impact of frailty on clinical and experiential outcomes, the invaluable information obtained from frailty assessments and the potential for intervention outweigh these limitations. Proactive and early identification of frailty allows for individualized and improved risk assessment, communication and optimization of candidates [5]. Frailty assessments are integral to the care provided for older or vulnerable people across a variety of other specialties already, with routine assessment now part of many UK secondary-care admissions [76]. A recent guideline from the Centre for Perioperative Care and British Geriatric Society has developed an approach to addressing frailty in both emergency and elective surgery, and may provide a framework for adoption into KT assessment [77]. Nephrology, and specifically transplantation, must now respond to this proven need or risk being left behind.

Integral to achieving this is development of a balanced approach, recognizing the increased demand frailty assessments place on existing services, but in doing so, allow for improved effectiveness and outcomes for both patients and transplant units. Accordingly, we have developed Table 1 to

Table 1: Practical tips for implementing frailty assessments in existing practice.

Planning	(i)	Explore existing resources in place at your institutions: • Frailty tools already in use. • Frailty support resources (e.g. personnel/teams already conducting frailty assessments, interventions in place to support frailty management).
	(ii)	Liaise with other specialties who have frailty experience in your institutions [geriatric medicine colleagues, surgical specialties already addressing frailty in their services (e.g. orthopedics)].
	(iii)	Engage early and involve multi-disciplinary colleagues within your institutions throughout all stages (e.g. physiotherapists, pharmacists, dietitians, occupational therapists, social workers).
	(iv)	Identify a timeline for frailty to be reassessed at defined intervals (e.g. alongside existing timelines for transplant waitlist reviews or when other investigations are repeated).
	(v)	Recognize and prepare that additional frailty reassessments may be required following a change in circumstances or condition of individuals.
Implementation	(i)	Start by picking an 'easy-to-use' frailty assessment or tool that your unit already has experience of using, e.g. Clinical Frailty Scale (CFS).
	(ii)	Two potential approaches for introduction: • Apply a global, easy to perform, frailty screen for all waitlist candidates—then perform a more detailed frailty assessment for those individuals identified as pre-frail/frail from the initial screen (e.g. CFS for all then a Frailty Phenotype assessment for those at risk). Or • Initially focus on assessing frailty in at-risk groups only (e.g. older people, multi-morbid candidates, or where they are perceived to be frail).
	(iii)	Involve and utilize multidisciplinary colleagues to feedback frailty assessment results and provide targeted interventions to address the deficits identified.
	(iv)	Communicate with patients from the start to explain the rationale for introducing frailty assessments, provide assurances for patients and encourage patients to get involved with their goal setting and intervention targets.
Evaluation and review	(i)	Set defined timepoints for reviewing the implemented tool, including feedback and experiences from both patients and colleagues using the tools. This provides an opportunity to refine practice and identify areas for improvement or additional training needs.

Table 2: Recommended topics for future research.

Topics for future research
(i) Agreement and validation of the optimal frailty tool to be used for assessing renal populations.
(ii) Research on both targeted and multicomponent interventions which can be administered for managing and addressing frailty deficits, and the effectiveness of these interventions in renal populations.
(iii) Development of a frailty guideline or toolkit, to provide a framework for implementation by nephrology units and standards to be met.
(iv) Better understanding of timing of frailty assessments and reassessments, to improve comprehension around frailty dynamics and to ensure frailty assessment strategies are optimised.
(v) Involvement and engagement with renal patients directly to help address and reduce the stigma, anxiety and stress associated with the assessment and identification of frailty, to identify acceptable terms, assessments and interventions, and to improve patient acceptance of frailty considerations in clinical practice.

suggest practice points that may help facilitate incorporation. Although many approaches are possible, these suggestions are aimed at engaging transplant units to think practically about frailty and its realistic inclusion in their work-up practices.

Future considerations

Recognizing frailty and measuring its prevalence in populations served by transplant units is the first step towards addressing frailty and providing holistic approaches to management. Incorporation is possible in the presence of ongoing uncertainties. However, nephrologists must maintain an awareness of where limitations do exist, to ensure they are practicing accurately, and that future work is directed appropriately. Table 2 highlights the research areas that still need addressing.

Through presentation of the pertinent evidence and by offering practical approaches, the authors hope to have provided a convincing overview and a clear mandate for action, as well as incentivized transplant units to act in realistic ways. Through adoption of frailty assessments KT units, patients

and healthcare systems all stand to benefit by achieving better optimization of candidates, improved utilization of organs and ultimately maximization of outcomes.

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DATA AVAILABILITY STATEMENT

No new data were generated or analysed in support of this research.

CONFLICT OF INTEREST STATEMENT

A.W. is member of the CKJ editorial board. The results presented in this paper have not been published previously in whole or part, except in abstract format.

REFERENCES

1. Fried LP, Ferrucci L, Darer J *et al*. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;**59**:M255–63.
2. Fried LP, Tangen CM, Walston J *et al*. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci* 2001;**56**:M146–57.
3. McAdams-DeMarco MA, James N, Salter ML *et al*. Trends in kidney transplant outcomes in older adults. *J Am Geriatr Soc* 2014;**62**:2235–42.
4. Buta BJ, Walston JD, Godino JG *et al*. Frailty assessment instruments: systematic characterization of the uses and contexts of highly-cited instruments. *Ageing Res Rev* 2016;**26**:53–61.
5. Harhay MN, Rao MK, Woodside KJ *et al*. An overview of frailty in kidney transplantation: measurement, management and future considerations. *Nephrol Dial Transplant* 2020;**35**:1099–112.
6. Alsaad R, Chen X, McAdams-DeMarco M. The clinical application of frailty in nephrology and transplantation. *Curr Opin Nephrol Hypertens* 2021;**30**:593–9.
7. Haugen CE, Thomas AG, Chu NM *et al*. Prevalence of frailty among kidney transplant candidates and recipients in the United States: estimates from a National Registry and Multicenter Cohort Study. *Am J Transplant* 2020;**20**:1170–80.
8. Chu NM, Chen X, Norman SP *et al*. Frailty prevalence in younger end-stage kidney disease patients undergoing dialysis and transplantation. *Am J Nephrol* 2020;**51**:501–10.
9. Brown EA, Johansson L. Old age and frailty in the dialysis population. *J Nephrol* 2010;**23**:502–7.
10. Kallenberg MH, Kleinveld HA, Dekker FW *et al*. Functional and cognitive impairment, frailty, and adverse health outcomes in older patients reaching ESRD-a systematic review. *Clin J Am Soc Nephrol* 2016;**11**:1624–39.
11. McAdams-DeMarco MA, Van Pilsum Rasmussen SE, Chu NM *et al*. Perceptions and practices regarding frailty in kidney transplantation: results of a national survey. *Transplantation* 2020;**104**:349–56.
12. Kobashigawa J, Dadhania D, Bhorade S *et al*. Report from the American Society of Transplantation on frailty in solid organ transplantation. *Am J Transplant* 2019;**19**:984–94.
13. Cheng XS, Lentine KL, Koraishy FM *et al*. Implications of frailty for peritransplant outcomes in kidney transplant recipients. *Curr Transplant Rep* 2019;**6**:16–25.
14. Exterkate L, Slegtenhorst BR, Kelm M *et al*. Frailty and transplantation. *Transplantation* 2016;**100**:727–33.
15. Quint EE, Zogaj D, Banning LBD *et al*. Frailty and kidney transplantation: a systematic review and meta-analysis. *Transplant Direct* 2021;**7**:e701.
16. Haugen CE, Chu NM, Ying H *et al*. Frailty and access to kidney transplantation. *Clin J Am Soc Nephrol* 2019;**14**:576–82.
17. McAdams-DeMarco MA, Ying H, Thomas AG *et al*. Frailty, inflammatory markers, and waitlist mortality among patients with end-stage renal disease in a prospective cohort study. *Transplantation* 2018;**102**:1740–6.
18. Lorenz EC, Cosio FG, Bernard SL *et al*. The relationship between frailty and decreased physical performance with death on the kidney transplant waiting list. *Prog Transplant* 2019;**29**:108–14.
19. Pérez Fernández M, Martínez Miguel P, Ying H *et al*. Comorbidity, frailty, and waitlist mortality among kidney transplant candidates of all ages. *Am J Nephrol* 2019;**49**:103–10.
20. McAdams-DeMarco MA, Law A, Salter ML *et al*. Frailty and early hospital readmission after kidney transplantation. *Am J Transplant* 2013;**13**:2091–5.
21. Garonzik-Wang JM, Govindan P, Grinnan JW *et al*. Frailty and delayed graft function in kidney transplant recipients. *Arch Surg* 2012;**147**:190–3.
22. Haugen CE, Mountford A, Warsame F *et al*. Incidence, risk factors, and sequelae of post-kidney transplant delirium. *J Am Soc Nephrol* 2018;**29**:1752–9.
23. McAdams-DeMarco MA, Law A, Tan J *et al*. Frailty, mycophenolate reduction, and graft loss in kidney transplant recipients. *Transplantation* 2015;**99**:805–10.
24. McAdams-DeMarco MA, Law A, King E *et al*. Frailty and mortality in kidney transplant recipients. *Am J Transplant* 2015;**15**:149–54.
25. Dos Santos Mantovani M, Coelho de Carvalho N, Archangelo TE *et al*. Frailty predicts surgical complications after kidney transplantation. A propensity score matched study. *PloS One* 2020;**15**:e0229531.
26. McAdams-DeMarco MA, King EA, Luo X *et al*. Frailty, length of stay, and mortality in kidney transplant recipients: a national registry and prospective cohort study. *Ann Surg* 2017;**266**:1084–90.
27. Van Pilsum Rasmussen S, Konel J, Warsame F *et al*. Engaging clinicians and patients to assess and improve frailty measurement in adults with end stage renal disease. *BMC Nephrol* 2018;**19**:8.
28. Lai JC, Shui AM, Duarte-Rojo A *et al*. Frailty, mortality, and health care utilization after liver transplantation: from the Multicenter Functional Assessment in Liver Transplantation (FrAILT) Study. *Hepatology* 2022;**75**:1471–9.
29. Chen X, Shafaat O, Liu Y *et al*. Revision of frailty assessment in kidney transplant recipients: replacing unintentional weight loss with CT-assessed sarcopenia in the physical frailty phenotype. *Am J Transplant* 2022;**22**:1145–57.
30. Haugen CE, Gross A, Chu NM *et al*. Development and validation of an inflammatory-frailty index for kidney transplantation. *J Gerontol A Biol Sci Med Sci* 2021;**76**:470–7.
31. Chang SF, Yang RS, Lin TC *et al*. The discrimination of using the short physical performance battery to screen frailty

for community-dwelling elderly people. *J Nurs Scholarsh* 2014;**46**:207–15.
32. Chu NM, Chen X, Bae S *et al*. Changes in functional status among kidney transplant recipients: data from the scientific registry of transplant recipients. *Transplantation* 2021;**105**:2104–11.
33. Harhay MN, Hill AS, Wang W *et al*. Measures of global health status on dialysis signal early rehospitalization risk after kidney transplantation. *PLoS One* 2016;**11**:e0156532.
34. Nastasi AJ, Bryant TS, Le JT *et al*. Pre-kidney transplant lower extremity impairment and transplant length of stay: a time-to-discharge analysis of a prospective cohort study. *BMC Geriatr* 2018;**18**:246.
35. Nastasi AJ, McAdams-DeMarco MA, Schrack J *et al*. Pre-kidney transplant lower extremity impairment and post-kidney transplant mortality. *Am J Transplant* 2018;**18**:189–96.
36. Michelson AT, Tsapepas DS, Husain SA *et al*. Association between the "Timed Up and Go Test" at transplant evaluation and outcomes after kidney transplantation. *Clin Transplant* 2018;**32**:e13410.
37. Kutner NG, Zhang R, Huang Y *et al*. Gait speed and mortality, hospitalization, and functional status change among hemodialysis patients: a US Renal Data System Special Study. *Am J Kidney Dis* 2015;**66**:297–304.
38. Mitnitski AB, Mogilner AJ, Rockwood K. Accumulation of deficits as a proxy measure of aging. *ScientificWorldJournal* 2001;**1**:323–36.
39. Guaraldi G, Malagoli A, Theou O *et al*. Correlates of frailty phenotype and frailty index and their associations with clinical outcomes. *HIV Med* 2017;**18**:764–71.
40. Bandeen-Roche K, Gross AL, Varadhan R *et al*. Principles and issues for physical frailty measurement and its clinical application. *J Gerontol A Biol Sci Med Sci* 2019;
41. Chen X, Liu Y, Thompson V *et al*. Transplant centers that assess frailty as part of clinical practice have better outcomes. *BMC Geriatr* 2022;**22**:1–12.
42. Salter ML, Gupta N, Massie AB *et al*. Perceived frailty and measured frailty among adults undergoing hemodialysis: a cross-sectional analysis. *BMC Geriatr* 2015;**15**:52.
43. Clegg A, Young J, Iliffe S *et al*. Frailty in elderly people. *Lancet North Am Ed* 2013;**381**:752–62.
44. Lee HJ, Son YJ. Prevalence and associated factors of frailty and mortality in patients with end-stage renal disease undergoing hemodialysis: a systematic review and meta-analysis. *Int J Environ Res Public Health* 2021;**18**:3471.
45. Nixon AC, Bampouras TM, Pendleton N *et al*. Diagnostic accuracy of frailty screening methods in advanced chronic kidney disease. *Nephron* 2019;**141**:147–55.
46. Worthen G, Tennankore K. frailty screening in chronic kidney disease: current perspectives. *Int J Nephrol Renovasc Dis* 2019;**12**:229–39.
47. Bangalore S, Maron DJ, O'Brien SM *et al*. Management of coronary disease in patients with advanced kidney disease. *N Engl J Med* 2020;**382**:1608–18.
48. Sharif A. The argument for abolishing cardiac screening of asymptomatic kidney transplant candidates. *Am J Kidney Dis* 2020;**75**:946–54.
49. Parker SG, McCue P, Phelps K *et al*. What is Comprehensive Geriatric Assessment (CGA)? An umbrella review. *Age Ageing* 2018;**47**:149–55.
50. Ellis G, Whitehead MA, O'Neill D *et al*. Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev* 2011;Cd006211.
51. Veronese N, Custodero C, Demurtas J *et al*. Comprehensive geriatric assessment in older people: an umbrella review of health outcomes. *Age Ageing* 2022;**51**:afac104.
52. van Loon IN, Goto NA, Boereboom FTJ *et al*. Geriatric assessment and the relation with mortality and hospitalizations in older patients starting dialysis. *Nephron* 2019;**143**:108–19.
53. Nixon AC, Brown J, Brotherton A *et al*. Implementation of a frailty screening programme and Geriatric Assessment Service in a nephrology centre: a quality improvement project. *J Nephrol* 2021;**34**:1215–24.
54. Hall RK, Haines C, Gorbatkin SM *et al*. Incorporating geriatric assessment into a nephrology clinic: preliminary data from two models of care. *J Am Geriatr Soc* 2016;**64**:2154–8.
55. Voorend CGN, Joosten H, Berkhout-Byrne NC *et al*. Design of a consensus-based geriatric assessment tailored for older chronic kidney disease patients: results of a pragmatic approach. *Eur Geriatr Med* 2021;**12**:931–42.
56. Wu HHL, Woywodt A, Nixon AC. Frailty and the potential kidney transplant recipient: time for a more holistic assessment? *Kidney360* 2020;**1**:685–90.
57. Wilkinson TJ, Miksza J, Zaccardi F *et al*. Associations between frailty trajectories and cardiovascular, renal, and mortality outcomes in chronic kidney disease. *J Cachexia Sarcopenia Muscle* 2022;**13**:2426–35.
58. *Frailty Toolkit*. https://www.england.nhs.uk/rightcare/wp-content/uploads/sites/40/2019/07/frailty-toolkit-june-2019-v1.pdf (13 February 2023, date last accessed).
59. Johansen KL, Dalrymple LS, Delgado C *et al*. Factors associated with frailty and its trajectory among patients on hemodialysis. *Clin J Am Soc Nephrol* 2017;**12**:1100–8.
60. Nixon AC, Bampouras TM, Gooch HJ *et al*. Home-based exercise for people living with frailty and chronic kidney disease: a mixed-methods pilot randomised controlled trial. *PLoS One* 2021;**16**:e0251652.
61. Young HML, March DS, Highton PJ *et al*. Exercise for people living with frailty and receiving haemodialysis: a mixed-methods randomised controlled feasibility study. *BMJ Open* 2020;**10**:e041227.
62. Lorenz EC, Hickson LJ, Weatherly RM *et al*. Protocolized exercise improves frailty parameters and lower extremity impairment: a promising prehabilitation strategy for kidney transplant candidates. *Clin Transplant* 2020;**34**:e14017.
63. McAdams-DeMarco MA, Ying H, Van Pilsum Rasmussen S *et al*. Prehabilitation prior to kidney transplantation: results from a pilot study. *Clin Transplant* 2019;**33**:e13450.
64. Beetham KS, Krishnasamy R, Stanton T *et al*. Effect of a 3-year lifestyle intervention in patients with chronic kidney disease: a randomized clinical trial. *J Am Soc Nephrol* 2022;**33**:431.
65. Chang J, Gao Y, Fang X-Y *et al*. Individualized intervention for frail non-dialysis elderly patients with chronic kidney disease: protocol for a randomized controlled trial. *BMC Geriatr* 2020;**20**:159.
66. Pérez-Sáez MJ, Morgado-Pérez A, Faura A *et al*. The FRAILMar Study Protocol: frailty in patients with advanced chronic kidney disease awaiting kidney transplantation. a randomized clinical trial of multimodal prehabilitation. *Front Med (Lausanne)* 2021;**8**:675049.
67. Anderson BM, Dutton M, Day E *et al*. Frailty Intervention Trial iN End-Stage patientS on haemodialysis (FITNESS): study protocol for a randomised controlled trial. *Trials* 2018;**19**:457.

68. Chu NM, Deng A, Ying H *et al*. Dynamic frailty before kidney transplantation-time of measurement matters. *Transplantation* 2019;**103**:1700–4.
69. Shrestha P, Van Pilsum Rasmussen SE, King EA *et al*. Defining the ethical considerations surrounding kidney transplantation for frail and cognitively impaired patients: a Delphi study of geriatric transplant experts. *BMC Geriatr* 2022;**22**:566.
70. Shrestha P, Van Pilsum Rasmussen SE, Fazal M *et al*. Patient perspectives on the use of frailty, cognitive function, and age in kidney transplant evaluation. *AJOB Empir Bioeth* 2022;**13**:263–74.
71. Howell SJ, Nair S. Measuring frailty in the older surgical patient: the case for evidence synthesis. *Br J Anaesth* 2021;**126**:763–7.
72. Pan E, Bloomfield K, Boyd M. Resilience, not frailty: a qualitative study of the perceptions of older adults towards "frailty". *Int J Older People Nurs* 2019;**14**:e12261.
73. Ekwegh U, Dean J. Improving care planning and communication for frail older persons across the primary-secondary care interface. *Future Healthc J* 2020;**7**:e23–6.
74. Cheng XS, Myers JN, Chertow GM *et al*. Prehabilitation for kidney transplant candidates: is it time? *Clin Transplant* 2017;**31**:e13020.
75. Kennedy C. *Exercise to Treat Frailty and Decreased Physical Function in Transplant Candidates (ClinicalTrials.gov Identifier: NCT03535584)*. https://www.clinicaltrials.gov/ct2/show/NCT03535584?term=frailty&cond=transplantation&draw=2&rank=3 (13 February, 2023, date last accessed).
76. Knight T, Atkin C, Martin FC *et al*. Frailty assessment and acute frailty service provision in the UK: results of a national 'day of care' survey. *BMC Geriatr* 2022;**22**:19.
77. Centre for Perioperative Care, British Geriatrics Society. *Guideline for Perioperative Care for People Living with Frailty Undergoing Elective and Emergency Surgery*. Centre for Perioperative Care, 2021. https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fcpoc.org.uk%2Fguidelines-resources-guidelines%2Fperioperative-care-people-living-frailty&data=05%7C01%7Cmara%40jhu.edu%7C031866d6358445fc035708db0dd3b4d9%7C9fa4f438b1e6473b803f86f8aedf0dec%7C0%7C0%7C638118975158967306%7CUnknown%7CTWFpbGZsb3d8eyJWIjoiMC4wLjAwMDAiLCJQIjoiV2luMzIiLCJBTiI6Ik1haWwiLCJXVCI6Mn0%3D%7C3000%7C%7C%7C&sdata=YDqTciWcvUGyEfjLLUyuvg2W3IV5Pz4y0pYjJgmfAFU%3D&reserved=0 (13 February, 2023, date last accessed).