Prehabilitation for kidney transplant candidates: Is it time?

Xingxing S. Cheng | Jonathan N. Myers | Glenn M. Chertow | Ralph Rabkin | Khin N. Chan | Yu Chen | Jane C. Tan

1 Division of Nephrology, Department of Medicine, Stanford University, Palo Alto, CA, USA
2 Division of Cardiology, Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA
3 Research Service, Veterans Administration Health Care System, Palo Alto, CA, USA

Correspondence
Jane C. Tan, MD, PhD, Division of Nephrology, Department of Medicine, Stanford University, Palo Alto, CA, USA.
Email: janetan@stanford.edu

Abstract
Many patients become frail with diminished cardiorespiratory fitness while awaiting kidney transplantation. Frailty and poor fitness powerfully predict mortality, transplant graft survival, and healthcare utilization after kidney transplantation. Efforts to intervene with post-transplant physical therapy have been met with limited success, in large part due to high study dropout. We reviewed the literature on chronic kidney disease and exercise to propose a clinical framework for physical therapy interventions to improve fitness, scheduled for before the transplant. This framework may lead to better patient retention and compliance, and thus demonstrate better efficacy in mitigating the effects of frailty and poor fitness after kidney transplantation.

KEYWORDS
elderly, end-stage renal disease, exercise, fitness, frailty, kidney transplant, physical therapy, transplant outcomes

1 INTRODUCTION
A growing body of research has demonstrated that an individual’s fitness level powerfully predicts outcomes associated with elective surgical interventions. Thus is born the concept of “prehabilitation”: an exercise-based therapy program which aims to improve an individual’s fitness prior to surgery and result in better outcomes after the surgery. This review seeks to apply this paradigm to patients with end-stage renal disease (ESRD) awaiting kidney transplantation. Efforts to improve post-transplant outcomes have typically focused on post-transplant interventions. We suggest that intervening before the transplant may be a uniquely fruitful avenue to explore. In this study, we first summarize the evidence on the importance of functional status in patients with ESRD and the efficacy of surgical prehabilitation, and then discuss the unique challenges, especially logistical, in applying this paradigm to the kidney transplant population.

2 MEASURES OF PHYSICAL FUNCTION
Prehabilitation aims to improve physical function. Physical function is a very broad term related to two key concepts: frailty and cardiorespiratory fitness.
Frailty is a clinical syndrome of decreased physiologic reserve and diminished capacity to respond to health stressors. Originally described as an adverse consequence of aging, frailty is increasingly recognized as a significant feature of myriad of chronic diseases, including chronic kidney disease (CKD). The most common and best validated way to quantify frailty is the multidimensional Fried criteria, a collection of phenotypic features, both measured (low grip strength, low walking speed) and self-reported (exhaustion, weight loss, and low physical activity level assessed by a standardize questionnaire and transformed into kilocalories per week). In her original work, Fried et al. demonstrated that meeting three or more of these criteria predicted incident falls, worsening mobility or disability, hospitalization,
and death in elderly persons over 3 years. Subsequent studies in multiple populations have confirmed the predictive power of these criteria.³

Physical function, in contrast, refers to a person’s ability to perform physical tasks. An examination of the five frailty criteria listed above reveals that four are at least partly related to poor physical function. Clinically, physical function is often assessed by directly observing the person undertaking specific tests. The Short Physical Performance Battery (SPPB), one of the most commonly used instruments, encompasses three tests that assess standing balance, walking speed, and ability to rise from a chair.⁵ It is therefore predominantly a test of lower extremity muscle strength,⁶ and is a reliable predictor of short-term mortality and nursing home admission in elderly persons.⁵

Cardiorespiratory fitness is a physiological attribute that quantifies an individual’s ability to deliver and utilize oxygen for physical work.⁷ It is related to physical function, in that it assesses a patient’s maximal capacity to perform physical activities. The gold standard for quantifying cardiorespiratory fitness is peak oxygen uptake (peak VO₂).⁸ defined as:

\[
\text{Peak VO}_2 = HR_{\text{max}} \times SV_{\text{max}} \times (C_{\text{VO}_2} - C_{\text{O}_2})_{\text{max}}
\]

where HR is heart rate, SV is stroke volume, and \(C_{\text{VO}_2} - C_{\text{O}_2}\) is the arteriovenous oxygen content difference. Peak VO₂ is a measure of an individual’s maximal aerobic capacity.⁷ It is either measured directly or estimated from the maximal work rate. Most reports in the literature report this measure in one of two forms: (i) a numerical value in milliliters of oxygen per kilogram of body weight per minute; or (ii) a percentage of the age-, sex-, and size-adjusted predicted value. Peak VO₂ is a powerful predictor of all-cause mortality and cardiovascular events⁸ and may even predict death better than traditional cardiovascular risk factors.⁹ Despite these advantages, the direct measurement of peak VO₂ requires specialized equipment and personnel. A well-validated alternative to (proxy for) peak VO₂ is the 6-minute walk test, widely used as a surrogate endpoint for physical function in chronic cardiopulmonary conditions.¹⁰ Use of the 6-minute walk test to assess cardiopulmonary fitness in CKD is less well established.

### 3 | FRAILTY AND PHYSICAL FUNCTION IN KIDNEY TRANSPLANT CANDIDATES

Kim et al.¹¹ recently reviewed the mechanisms linking frailty and CKD. Muscle wasting is common in patients with advanced CKD due to uremia, medication side effects, altered neuropeptide signaling,¹² and impaired taste/smell, predisposing patients to anorexia and protein energy wasting. Other contributing factors include inflammation, oxidative stress, catabolic/anabolic hormone imbalance, metabolic acidosis, and other cellular alterations in the uremic milieu.¹¹

Frailty rises in prevalence as CKD progresses from non-dialysis-requiring to dialysis-requiring CKD, or ESRD. Two cross-sectional analyses utilizing data from the Third National Health and Nutrition Evaluation Survey¹³ and the Chronic Renal Insufficiency Cohort¹⁴ demonstrated that frailty was present in approximately 20% of persons with non-dialysis-requiring CKD. In multiple prospective studies of ESRD cohorts in the United States (US), the frailty phenotype is present in up to 70% of persons and associated with an approximately twofold increase in mortality.¹⁵⁻¹⁷

One may expect kidney transplant candidates to demonstrate better physical function owing to the rigorous screening process for transplant candidacy. However, two US studies suggest that frailty and poor physical function still afflict kidney transplant candidates and may exert an influence even after the kidney transplant. In a national cohort of patients from the Dialysis Morbidity and Mortality Study (DMMS) who initiated ESRD therapy in 1996-1997, the investigators quantified physical function based on responses to the SF-36 physical functioning scale, which was 10 items from the Kidney Disease Quality of Life-Short Term (KDQOL) survey assessing the extent to which the patient’s health limits typical daily activities.¹⁸ Of the 366 patients who received a transplant within 24 months of dialysis initiation, a lower pre-transplant physical functioning score was significantly associated with a higher risk of post-transplant hospitalization and death. A methodologic limitation was that physical function was quantified via patient self-report, rather than objective measurement, in this study. Reassuringly, in an assessment of physical function in Frequent Hemodialysis Network (FHN) trial participants, the self-report-based SF-36 and the objectively obtained SPPB score appeared to agree,¹⁹ suggesting that physical function assessments based on patient self-report are at least partially valid in patients with ESRD.

In a second study, investigators prospectively assessed for the presence of frailty at the time of transplant using the Fried criteria in 537 kidney transplant recipients from a single center between 2008 and 2013.²⁰ Although the mean age of this cohort was only 53 years, 19.9% met criteria for frailty and 33% for “pre-frailty” (defined as having two of five criteria). After adjusting for confounders, frailty was independently associated with a 94% higher risk of delayed graft function,²¹ 61% higher risk of early hospital readmission,²² and 117% higher risk of death within 5 years.²⁰ The magnitudes of the effect sizes in this study are comparable to those in the aforementioned ESRD studies. This study powerfully demonstrates the link between frailty and kidney transplant outcomes.

### 4 | CARDIORESPIRATORY FITNESS IN KIDNEY TRANSPLANT CANDIDATES

In contrast to frailty, cardiorespiratory fitness has not been extensively studied in patients with ESRD, partly because the latter requires specialized testing and cannot be quantified using patient self-report. Nonetheless, as the association between cardiorespiratory fitness and mortality is very robust in non-kidney disease populations,⁹ ²³,²⁴ one expects the relation to hold in ESRD as well.

A few studies have tested the hypothesis that persons with CKD have reduced cardiorespiratory fitness compared to persons with normal or near normal kidney function. In a cohort of 5812 male veterans with no baseline CKD, measured exercise capacity was inversely
Two possible explanations exist for this interesting observation: (i) exercise may have salutary effects on cardiovascular and metabolic parameters that help delay the onset of CKD; or (ii) the higher apparent CKD incidence may result from an under-diagnosis of baseline CKD (by the serum creatinine-based criteria) in less active veterans. In a study of 175 ambulatory patients on chronic hemodialysis, with a mean follow-up of approximately 3.5 years, peak VO₂ < 17.5 mL/min/kg (median) was strongly associated with mortality.

Similarly, kidney transplant candidates have diminished cardiorespiratory fitness. Of 240 kidney transplant candidates in the United Kingdom, 135 (56%) had a peak VO₂ lower than 40% of age-predicted. Over a 5-year follow-up, 124 patients received a kidney transplant. A low peak VO₂ was strongly associated with all-cause mortality, including post-transplant mortality. Furthermore, a lower peak VO₂ was associated with intensive care unit admission (due to hemodynamic instability) after kidney transplant. Interestingly, despite these findings, the mortality benefit conferred by kidney transplantation (relative to remaining on dialysis) was more pronounced in the group with lower peak VO₂.

An ongoing exercise intervention study (Protein signaling, Exercise and Renal Failure in the Elderly: a Clinical Trial, or PERFECT) at our institution is testing the effect of home-based exercise therapy in patients 55 years or older with ESRD. We compared the baseline characteristics of transplant candidates against non-candidates: in no measure did the two groups differ (Figure 1). Interestingly, peak VO₂ did not appear to differ between the two groups: transplant candidates were just as impaired as non-transplant candidates (mean peak VO₂ ≈ 60% of predicted). This finding must be interpreted with caution, given the very small sample size and selection bias (only ≈ 10% of our study participants had peak VO₂ lower than 40% of age-predicted, compared to 56% in Ting et al. study). However, if verified with larger studies, it may suggest that peak VO₂ is independent of other clinical surrogates commonly used to establish transplant candidacy and, given its performance in discriminating successful, uncomplicated transplant outcomes from less successful ones, could be more widely used in pre-transplant risk stratification.

Taken together, these studies defined physical function along two different paths (frailty and cardiorespiratory fitness), but arrived at a similar conclusion: Poor physical function before kidney transplant is common and is associated with higher mortality, morbidity, and healthcare utilization after kidney transplant. Peak VO₂ may be an especially robust marker for risk stratification in kidney transplant candidates.

5 | PHYSICAL REHABILITATION IN PATIENTS WITH END-STAGE RENAL DISEASE

Multiple small interventional studies, most with 30 or fewer subjects per arm, have investigated the effect of exercise programs in patients with ESRD. Many studies reported only intermediate outcomes. Table 1 summarizes the key studies that reported physical function endpoints as the primary outcome. A few observations include the following:

1. The most common intervention was exercise delivered during dialysis treatment (“intradialytic”), probably due to ease of delivery. The second most common intervention was in-center aerobic exercise on non-dialysis days. Home-based regimens are the least extensively studied.

2. Attrition, that is, dropout rate, ranged from 5 to 50%, and was 10 to 15% in the two largest, best-conducted studies on intradialytic exercise. Exercise duration was 12 weeks in both studies. In the largest study on home-based exercise, which was 24 weeks in duration, dropout approached 30% in the intervention arm.

3. Efficacy of the intervention varied from study to study. Overall, exercise intervention appeared to improve physical function, but the magnitude was modest compared to the high level of baseline impairment.

![FIGURE 1](image-url) Measures of cardiorespiratory fitness (peak VO₂, 6-minute walk test) and proximal muscle strength in 18 candidates and 10 non-candidates for kidney transplantation. Each outcome is expressed as a percentage of the age- and sex-predicted value.
### Table 1
A summary of key randomized controlled trials comparing exercise vs regular care in dialysis-dependent patients that directly assess effects on directly measured indices of physical function. Only studies with at least 10 patients per arm are included. Table is partly adopted from systemic reviews by Barcellos et al.32 and Cheema et al.33 Main results refer to change in intervention group compared to control. *P*-values refer to the significance of the difference between the intervention and control groups.

| Author, year | Country | Duration (weeks) | Dropout | Physical function outcomes | Main results |
|--------------|---------|------------------|---------|----------------------------|--------------|
| **Intradialytic aerobic or mixed aerobic and resistance exercise** | | | | | |
| Akiba 199534 | Japan | 12 | I: 4/10 C: 0/10 | Peak VO2 | ↓ in C, no Δ in I |
| DePaul 200235 | Canada | 12 | I: 5/20 C: 4/18 | Submaximal exercise test 6 MW | ↑ (P=.02) No Δ |
| Painter 200236 | US | 20 | I+C: 17/65 | Peak VO2 | ↑ (P=.028) |
| Van Nisstelen 200537 | Netherlands | 12 | I: 7/53 C: 0/43 | Peak VO2 | ↑10% (P=.14) |
| Kouidi 200938 | Greece | 40 | I: 3/32 C: 2/31 | Peak VO2 | ↑ 29% (P<.001) |
| Reboredo 201239 | Brazil | 12 | I: 2/14 C: 2/14 | Peak VO2 | No Δ |
| Dobsak 201240 | US | 20 | I: NR/11 C: NR/10 | 6 MW Lower body strength | ↑ (P=.016) ↑ (P=.033) |
| Giannaki 201341 | Greece | 24 | I: 0/12 C: 0/12 | STS | ↑ (P=.05) |
| Bohm 201442 | Canada | 24 | I: 7/30 C: 1/30 | Peak VO2 6 MW | No Δ No Δ |
| Liao 201643 | Taiwan | 12 | I: NR/20 C: NR/20 | 6 MW | ↑ (P<.05) |
| **Non-dialysis day, outpatient aerobic, or mixed aerobic and resistance exercise** | | | | | |
| Goldberg 198344 | US | 48 | I: NR/14 C: NR/11 | Peak VO2 | ↑17-21% (P<.01) |
| Kouidi 199745 | Greece | 24 | I: 4/24 C: 1/12 | Peak VO2 | ↑38% (P<.05) |
| Deligiannis 199946 | Greece | 24 | I: NR/30 C: NR/30 | Peak VO2 | ↑41% (P<.05) |
| Koufaki 200247 | UK | 12 | I: 8/26 C: 7/22 | Peak VO2 | ↑ 21% (P<.0001) |
| Konstantinidou 200248 | Greece | 24 | I: 5/16 C: 0/12 | Peak VO2 | ↑43% (P<.05) |
| Tsuyuki 200349 | Japan | 20 | I: NR/17 C: NR/12 | Peak VO2 | ↑ (P<.05) |
| Molsted 200450 | Denmark | 20 | I: 11/22 C: 2/11 | Peak VO2 | ↑11% (P<.012) |
| **Home-based aerobic or mixed aerobic and resistance exercise** | | | | | |
| Koh 201051 | Australia | 24 | I: 5/20 C: 6/22 | 6 MW Grip strength | No Δ No Δ |
| Manfredini 201752 | Italy | 24 | I: 47/151 C: 22/145 | 6 MW STS | ↑ (P<.001) ↑ (P=.001) |
| **Resistance exercise only** | | | | | |
| Johansen 200653 | US | 12 | I: 4/39 C: 5/39 | Lower body strength | ↑ (P<.0001) |
| Cheema 200754 | US | 12 | I: 4/24 C: 1/25 | Muscle strength 6 MW | ↑ 20% (P=.002) No Δ |
| Chen 201055 | US | 24 | I: 6/25 C: 5/25 | SPPB Lower body strength | ↑21% (P=.03) ↑45% (P=.0001) |

(Continues)
No trial specifically looked at kidney transplant candidates. This likely reflects the logistic challenges related to tailoring interventions for kidney transplant candidates. Transplant centers seldom form long-term relationships with patients prior to their actual transplant procedure. General nephrologists focus on the care of patients with ESRD and may not be attuned to transplant-specific needs. As such, the only studies on exercise and physical rehabilitation in transplant recipients were performed by transplant centers and enrolled patients after their kidney transplant.

The largest such study took place between 1995 and 1997 and randomized 167 patients one month after kidney transplant to usual care vs individualized, home-based cardiovascular exercise. Dropout rate was 42%, mostly due to loss of follow-up and loss of interest. Intervention resulted in a higher percentage of patients reporting being physically active (67% vs 36%) and a higher increase in percentage of age-predicted physical activity level in the control groups appeared to decrease post-transplant. Dishearteningly, however, physical activity level in the control groups appeared to decrease post-transplant and dropout from the intervention arm was very common. While discouraging, these attrition rates are similar to most cardiac rehabilitation programs. To our knowledge, no such studies have been performed.

A number of intervention trials have tested the effects of prehabilitation on function and perioperative outcomes. Most trials were performed in the setting of cardiothoracic and orthopedic surgeries, which directly affect the primary organ systems defining fitness (ie, cardiovascular and musculoskeletal systems). They report significant improvements in short-term (length of hospitalization, postoperative complications) and long-term (functional capacity, quality of life) outcomes. Data for intra-abdominal surgeries, which are likely more applicable to kidney allograft implantations, are less robust (Table 2). Three of the six studies (50%) summarized reported a modest (<15%) improvement in cardiopulmonary fitness from a 3- to 8-week exercise intervention compared to controls. Most of the interventions lasted for 4 weeks or shorter, in contrast to the longer intervention periods in ESRD trials (see previous section). Adherence was variable, but better adherence to prehabilitation was reported compared to post-operative rehabilitation in one study. Because they are particularly prone to functional decline and muscle wasting, patients with ESRD awaiting kidney transplantation may be ideally suited for prehabilitation programs. To our knowledge, no such studies have been performed.

7 | A NEW PARADIGM: PREHABILITATION FOR KIDNEY TRANSPLANTATION

We therefore propose a new paradigm for the clinical operation of transplant programs: prehabilitation for kidney transplantation. Potential advantages of prehabilitation over post-transplant rehabilitation include the following:

1. Frailty and depressed cardiopulmonary fitness are strongly associated with increased peri- and post-transplant mortality, morbidity, and healthcare utilization. As many adverse events post-transplant, including rehospitalization, appear to be clustered in the early post-operative period, a better initial time to intervene may be before kidney transplantation.

2. Post-transplant care is becoming more complex. Given the growing organ scarcity and longer wait time, more elderly and medically complex patients are opting for more marginal organs, thus increasing the likelihood of delayed graft function and other transplant-related complications recovery from which may be prolonged.
Surgical literature supports the use of prehabilitation for high-risk patients. Many transplant candidates potentially fit the phenotype of high-risk patients who stand to benefit from prehabilitation.

Physical activity falls off in the first year post-transplant, and post-transplant exercise programs are met with high dropout rates. These results may reflect the reality that the period immediately post-transplant is likely to be affected by life events, such as returning to school or work, that divert time and energy away from exercise. In contrast, transplant candidates are frequently the most motivated to take active measures to improve their health and therefore the likelihood of transplantation. This forms an ideal window of opportunity to recruit patients into self-driven efforts to modify health-related behavior, such as exercise, that pay health dividends well into the future.

A few questions remain unanswered by the current literature and should be prioritized by research efforts:

1. What is the optimal patient population to target? The ideal population should be patients who have functional impairment that is both associated with adverse outcomes and amenable to intervention. A reasonable starting point would be to target elderly individuals who meet the frailty criteria or have a peak VO₂ below 40% of predicted. The next objective would be establishing whether prehabilitation in these patients improves transplant outcomes.

2. What is the optimal prehabilitation regimen? Most studies on patients with ESRD thus far have focused on intradialytic exercise programs, which may be difficult for transplant centers to implement. Outpatient exercise programs on non-dialysis days may be burdensome to patient schedules. Home-based therapies may be ideal, especially for patients located far from their transplant centers. Motivating patients and ensuring adherence will be the keys to the success of these home-based programs.

3. What is the optimal timing for a prehabilitation regimen? Aside from living donations, timing of kidney transplantation is inherently unpredictable. The point at which patients either have high enough kidney allocation scores to receive deceased donor offers, identified by transplant centers locally, or have live donors who are fully evaluated, forms the natural intervention point. Even then, timing prehabilitation relative to surgery is nearly impossible: too early and dropout may be high, too late and benefit may be minimal.

4. What are the financial costs of implementing exercise programs? While prehabilitation programs may potentially improve patient outcomes and reduce post-transplant healthcare utilization, cost data and formal cost-effectiveness analyses are missing. Uncovering how to deliver prehabilitation most efficiently and utilize existing infrastructure will be crucial to ensuring the feasibility of such programs.

To meaningfully improve long-term outcomes for kidney transplant recipients, intervention trials to test the efficacy of prehabilitation programs are necessary but not sufficient. Each transplant center will need to devise ways to integrate physical function assessments and exercise interventions into routine clinical operations, including pre-transplant evaluation and waitlist management. We have summarized instruments for physical function assessment in Table 3. As can be seen from the table, a gradient exists from the best-validated but most resource-intensive to administer instruments (i.e., exercise testing) to the less-validated but easiest to administer instruments (i.e., SF-36 Physical Function subscale, which can be administered remotely without any staff supervision). At
### TABLE 3  A summary of commonly used instruments for assessing frailty, physical function, and/or cardiorespiratory fitness

| Instrument | Assesses | Description | Strengths & weaknesses |
|------------|----------|-------------|------------------------|
| Fried criteria<sup>22</sup> | Frailty | 5 aspects: 1. Self-reported 10 lb unintentional weight loss in the last year; 2. Self-reported exhaustion; 3. Low physical activity ascertained from 2-week version of Minnesota Leisure Time Physical Activity Questionnaire<sup>71</sup>; 4. Measured handgrip weakness; 5. Measured 15-feet timed walk | Strengths: • Extensively validated in multiple settings, including kidney transplantation  Weaknesses: • Requires specialized equipment |
| Modified fried criteria<sup>72,73</sup> | Frailty | Similar to fried, except measured handgrip weakness and 15-feet timed walk are substituted with a score <75 on the SF-36 Physical Function scale (10-item questionnaire) | Strengths: • Validated in ESRD  • Does not require specialized equipment  • Less time-consuming to administer than Fried criteria  Weaknesses: • Relies entirely on self-report  • Ordinal outcome (frailty vs none): difficult to track progress with physical therapy |
| 10-item physical function subscale in SF-36<sup>72,73</sup> | Physical function | 10 questions asking how impaired a patient is in performing activities such as carrying groceries or climbing stairs | Strengths: • Validated in ESRD  • Does not require specialized equipment  • Easy to administer  Weaknesses: • Relies entirely on self-report |
| Short physical performance battery<sup>19</sup> | Physical function | 3 simple office tests: 1. Balance 2. Gait speed 3. Chair stand | Strengths: • Extensively validated in rehabilitation and prehabilitation settings  • Does not require special equipment  Weaknesses: • No validation in kidney transplant setting |
| Exercise testing for peak VO<sub>2</sub><sup>29</sup> | Cardiorespiratory fitness | Administered in an exercise laboratory on a treadmill | Strengths: • Extensively validated in multiple settings, including kidney transplantation  Weaknesses: • Requires dedicated equipment and personnel  • May not be safe in patients with unstable cardiac disease |
| 6-minute walk test<sup>52</sup> | Physical function cardiorespiratory fitness | Distance covered during walking back and forth along a 72-feet course for 6 minutes as quickly as possible | Strengths: • Extensively validated in rehabilitation and prehabilitation settings  • Does not require specialized equipment  • Outcome in many exercise in ESRD trials  Weaknesses: • No validation in kidney transplant setting |
| Sit-to-stand test<sup>52</sup> | Physical function | 2 versions: 5-STS: time it takes to perform chair-stand 5 times 30-STS: number of chair-stands performed in 30 seconds | Strengths: • Extensively validated in rehabilitation and prehabilitation settings  • Does not require specialized equipment  • Outcome in many exercise in ESRD trials  Weaknesses: • No validation in kidney transplant setting |

SF-36, 36-item short form health survey.
Assessment Clinic (TRAC) to re-evaluate patients who are approaching transplantation, including physical function evaluation \(77\) (Table 4). These tests into our clinic workflow demonstrated feasibility: A nurse coordinater is able to complete the tests within 15-20 minutes.

At our institution, where wait time to a kidney transplant may be 7 years or longer, we have launched a Transplant Readiness Assessment Clinic (TRAC) to re-evaluate patients who are approaching transplantation, including physical function evaluation \(77\) (Table 4). Part of TRAC’s operational platform includes teaching patients to use the pre-existing electronic communication portal to communicate with the transplant center. Home-based exercise therapy, for the reasons described previously, are optimal for our patient population. We have involved the investigators of the PERFECT study to enroll eligible patients in their home-based exercise therapy clinical trial. Our future directions include obtaining normative data on physical function tests in the transplant candidate population, identifying the highest-risk cohort, and broadly implementing home-based exercise therapy with the assistance of the electronic communication portal.

In summary, the growing number of elderly and medically complex patients on the kidney transplant waitlist poses unique challenges to optimizing transplant outcomes, especially under resource constraints present in every health system. For such patients, kidney transplant is a “once and for all” process with little opportunity for post hoc salvaging. \(78\) Evidence supports the critical role of functional status, especially cardiorespiratory fitness, in modulating post-transplant outcomes. Ample surgical experience suggests that prehabilitation may be an effective way to improve functional status. We acknowledge the considerable challenges to a paradigm shift and share our center’s preliminary experience in overcoming some of the practical and logistical barriers. Identifying the target population, selecting an effective exercise regimen, identifying the optimal timing of prehabilitation, and incorporating prehabilitation into routine clinical operations should be priorities for the transplant community.

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**CONFLICT OF INTEREST**

None.

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