Frailty, cognitive impairment and quality of life in older people with kidney transplants, more than a scale: Narrative Review.

Zulay Milena Quiroga Trillos 1, Martha Patricia Rodriguez 1.

1. Postgraduate Department of Geriatrics, Faculty of Medicine, Pontificia Universidad Javeriana, Bogotá, Colombia.

Abstract

Introduction: With the increase in the number of deceased donors over 65, transplant programs have been developed for older people with the least frailty at the time of transplant.

Objective of the review: This article is a narrative review to show the importance of frailty and cognitive impairment as parameters for decision-making about a kidney transplant in an older adult.

Essential points of the review:

- Cognitive impairment can precede frailty by months, so its early detection and treatment prevents the progression to frailty.
- Frailty has two types: responsive and refractory; both types must be treated intensively during the waiting time on the transplant list.
- The transplant significantly improves frailty in three months, although there is a higher incidence of comorbidities in this postoperative recovery time.
- Both frailty and cognitive impairment are reversible and largely depend on high protein nutrition and increased muscle mass.

Conclusion: Kidney transplantation in older people is an increasingly accessible option, but research is needed to unify eligibility criteria and improve results.

Keywords:

MESH: Frailty; Kidney Transplantation; Mortality; Muscle, Skeletal; Aged; Elderly Nutrition Renal Dialysis.
Chronic kidney disease (CKD) is a progressive and irreversible condition and a significant cause of death and disability, and its prevalence increases with age [1, 2]. In Colombia, the average age of patients on hemodialysis is 61 years, and hemodialysis is the fifth leading cause of death in older adults. The mortality rate for CKD stage 5 is 14.55 cases per 100,000 inhabitants [3]. Globally, the number of dialysis patients is estimated to increase to 4.9 million by 2030 [4]. Dialysis patients have a 10-fold higher risk of death than the general population, with notably higher hospitalization rates and poorer health-related quality of life [3].

In recent years, with the increase in deceased donors over 65 years of age [6], transplant programs for older adults have been developed to transplant a graft from an older adult into a senior recipient without frailty, which has led to an increase in waiting lists for kidney transplantation in older adults [2].

The selection process for kidney transplantation in older adults is more complex than in younger patients. Factors considered include age, sex, comorbidities, frailty, cognitive status, and quality of life [8, 9]. Additionally, excluding older adults from clinical studies limits the evidence-based medical information available to this population [9].

Understanding these geriatric syndromes is critical for appropriate patient selection for kidney transplantation. However, few guidelines help physicians make decisions in this context. Therefore, deepening our understanding of frailty, cognitive impairment, and quality of life in older adults with CKD is essential. This will help improve patient selection for kidney transplantation and reduce the impact of complications in the clinical setting [10].

Definition of fragility
Frailty is a geriatric syndrome characterized by decreased functional reserve, leading to vulnerability to stressors [11].

The FRAIL frailty scale (Table 1), developed by Dr. Linda Fried et al. [12], comprises five criteria: unintentional weight loss, fatigue, low physical activity, low grip strength, and slow walking speed. Frailty is a dynamic and changing condition that can be reversible if detected and treated early [13]. Frailty predicts future complications and adverse clinical outcomes, such as increased mortality, prolonged hospital stay, functional decline, and disability.

Furthermore, frail patients have a higher risk of postoperative morbidity and mortality [14].

Definition of cognitive impairment
Cognitive impairment is one of the components of frailty; therefore, there is an association between physical frailty and cognitive impairment, presenting a higher incidence of functional disability, poor quality of life, and mortality [16].

Consequently, in older patients with kidney disease, early detection of cognitive deterioration is necessary through screening tests, which identify cognitive decline promptly, thus preventing the evolution toward frailty [17].

The most commonly used screening scales are the Montreal Cognitive Assessment (MoCA) and the Mini-Mental State Examination (MMSE) [18]. These scales evaluate the individual’s behavior, orientation, attitude, perception, judgment, abstraction, and cognition [19, 20].

Quality of life
Health-related quality of life (HRQoL) is the value a person assigns to their life, considering their functional status, limitations, perceptions, and social opportunities. These factors can be influenced by diseases, injuries, treatments, and health policies [21].

For this reason, HRQOL must be evaluated multidimensionally, considering physical, psychological, social, and environmental aspects.

The SF-36 questionnaire [22] is the most commonly used instrument to measure HRQoL. It consists of 36 questions that cover the following scales:

<table>
<thead>
<tr>
<th>Physical function</th>
</tr>
</thead>
<tbody>
<tr>
<td>physical role</td>
</tr>
<tr>
<td>Bodyside</td>
</tr>
<tr>
<td>General Health</td>
</tr>
<tr>
<td>Vitality</td>
</tr>
<tr>
<td>Social function</td>
</tr>
<tr>
<td>Emotional role</td>
</tr>
<tr>
<td>Mental health</td>
</tr>
</tbody>
</table>

Table 1. FRAIL Scale [15]

<table>
<thead>
<tr>
<th>Fatigue</th>
<th>In the last 4 weeks, how tired have you felt?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All the time</td>
</tr>
<tr>
<td></td>
<td>Most of the time</td>
</tr>
<tr>
<td></td>
<td>Some of the time</td>
</tr>
<tr>
<td></td>
<td>Very little time</td>
</tr>
<tr>
<td></td>
<td>No time</td>
</tr>
</tbody>
</table>

Endurance

You alone, without aid such as a cane or walker: Do you have difficulty climbing ten steps (a staircase)?

| Yes              |
| No               |

Wandering

You alone, without any aid such as a cane or walker: Do you have difficulty walking 100 meters (Two blocks) without resting?

| Yes              |
| No               |

Diseases

Has any doctor told you that you have any of these diseases?
High blood pressure, Diabetes, Cancer (excluding skin cancer), Chronic obstructive pulmonary disease, Ischemic heart disease, Congestive heart failure, Angina, Asthma, Arthritis (Includes osteoarthritis and rheumatoid arthritis), Vascular stroke, chronic kidney disease.

Score if it is 5 or more.

<table>
<thead>
<tr>
<th>Weightloss</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>How much did you weigh 1 year ago?</td>
<td></td>
</tr>
<tr>
<td>Percent weight change [(weight 1 year ago-Current weight)/Weight 1 year ago] × 100</td>
<td></td>
</tr>
<tr>
<td>Weight loss &gt; or = 5%</td>
<td></td>
</tr>
<tr>
<td>Weight loss &lt; or = 4%</td>
<td></td>
</tr>
<tr>
<td>Each positive value will be scored with 1 point. 0 points = Robust, 1 or 2 points = Prefragile, = or &gt; 3 points = fragile.</td>
<td></td>
</tr>
</tbody>
</table>

The K/DOQI guidelines recommend that all patients with a glomerular filtration rate (GFR) less than 60 mL/min be evaluated for HRQoL. HRQoL is related to morbidity and mortality and can help make treatment decisions [23] (Figure 1).

**Figure 1.** Relationships between frailty, cognitive impairment, and quality of life in older patients with kidney transplants.

Kidney transplant

**Fragility**

Fragility is very common in patients in hemodialysis programs; approximately 50% have a diagnosis of frailty, and up to 21% of patients are on the waiting list [9]. Kidney transplants improve the life expectancy of older people compared to dialysis by 3.8 years [24], but older patients are less likely to be on waiting lists [25]. This could be because transplant eligibility factors are not standardized [26].

Frailty is a risk factor for older chronic kidney disease (CKD) patients. Frail patients are more vulnerable to transplant stressors and are at higher risk for postoperative complications. Studies have shown that up to 30.1% of transplant recipients with frailty have a hospital admission 30 days after the transplant, which increases mortality and graft loss [29]. However, frail patients can also benefit from kidney transplantation. One study found that frail patients who underwent kidney transplantation improved their physical function more rapidly than non-frail patients in the first three months [29] due to increased physical activity and improved nutritional status.

Frailty is a dynamic process that may worsen after transplantation but improves significantly over time, beginning in the third month after transplantation [30].

To improve transplant survival in older patients, it is essential to identify and address risk factors for frailty, such as the risk of falls and malnutrition [31]. It is necessary to mention that frailty has two types: responsive frailty, the most common defect characterized by a decreased functional reserve that can be reversed with appropriate interventions. For example, patients with responsive frailty can improve their strength and functional capacity with muscle-building exercises, high-protein nutrition, and medical care. The second type is refractory frailty, a more severe form of frailty that is more resistant to interventions. Patients with refractory frailty may have underlying health problems that contribute to their frailty, such as chronic illness, malnutrition, depression, or severe cognitive loss. This raises a research question: if patients with refractory frailty compared to patients with responsive frailty have worse posttransplant outcomes at the 1-year follow-up, subsequent studies should differentiate these study groups.

**Cognitive impairment**

In patients with chronic kidney disease (CKD), cognitive impairment is multifactorial and associated with an increased risk of cerebrovascular disease; kidney disease is also a risk factor for cognitive impairment [29]. Approximately 53% of kidney transplant patients have mild to moderate cognitive impairment [33]. This can make it difficult to follow instructions and comply with medical treatments, reducing your chances of an effective transplant or losing posttransplant adherence [17]. Posttransplant follow-up studies have shown that frail and non-frail recipients experience short-term cognitive improvement after transplant. This information is useful for more careful monitoring of cognitive function in patients with frailty, both before and after transplant. This also constitutes evidence that allows patients with mild cognitive impairment to be included on waiting lists [34].

**Health-related quality of life**

Although renal replacement therapies efficiently improve health-related quality of life (HRQoL), they do not reach the patient's levels before entering dialysis programs [35]. Even kidney transplantation significantly improves HRQoL but fails to restore pre-CKD levels [36]. Compared to the general population, 60% of older transplant patients have a similar HRQoL to the general population, and 40% have a greater impact on anxiety and muscle weakness [38]. Therefore,
psychological support is important to reduce anxiety and fear of disease progression and death. In addition to rehabilitation programs to strengthen muscle mass [39].

Other scales

It is important to know that the scales that assess cognitive impairment have different sensitivities; for example, the MM scale determines that the majority of patients on the waiting list have cognitive impairment (mild or moderate), while the MoCA scale determines that 55% of patients on the waiting list have cognitive impairment [33]. Likewise, in the senior clinical setting, the single “Timed standing and walking test” or the “Comprehensive Geriatric Assessment (CGA)” scale is widely used instead of the FRAIL scale for the diagnosis of frailty. Each transplant team should include a specific assessment of frailty, quality of life, and cognitive impairment in each elderly patient entering the kidney transplant preparation program. No studies compare frailty scales prospectively in this group of patients, which constitutes a line of research to follow in the future.

Conclusion

Kidney transplantation is an increasingly accessible therapeutic option for older people with stage 5-d chronic kidney disease. This is due to the improvement in life expectancy and quality of life of transplant patients compared to those receiving dialysis. However, eligibility criteria for kidney transplantation in older people should be adjusted to consider age-related factors, such as frailty and cognitive decline. These geriatric syndromes can be reversible and improve transplant patients’ quality of life. Therefore, further research is required to unify frailty and cognitive impairment thresholds for kidney transplant eligibility. Intervention programs are also needed to improve functionality and decrease post-transplant complications in older people.

Abbreviations

HRQoL: Health-related quality of life.
CKD: Chronic kidney disease.

Supplementary information

Supplementary materials have not been declared.

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Author contributions

Zulay Milena Quiroga Trillos: Conceptualization, Data curation, Formal analysis, Funding acquisition, Research, Methodology, Project administration, Resources, Software, Writing – original draft.
Martha Patricia Rodríguez: Conceptualization, Supervision, Validation, Visualization, Writing: review and editing.
All the authors have read and approved the final version of the manuscript.

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Consent for publication

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Conflicts of interest

The authors report having no conflicts of interest.

Author information

Zulay Milena Quiroga Trillos: Geriatrics Resident. Faculty of Medicine, Pontifical Javeriana University.
Martha Patricia Rodríguez: Assistant teacher. Javeriana University Pontifical Faculty of Medicine- San Ignacio University Hospital, Bogotá, DC, Colombia – Master in Bioethics International University of Valencia, Spain.

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