



Health-Related Quality of Life in Older Kidney Transplant Recipients: A National Cohort Study of Short- and Longer-Term Outcomes

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Rationale & Objective: Assessing the optimal therapy for older patients (aged ≥ 65 years) with end-stage kidney disease requires knowledge of longevity and health-related quality of life (HRQoL) outcomes. Kidney transplantation prolongs survival but its long-term impact on HRQoL in older recipients is not well defined. We aimed to prospectively evaluate HRQoL changes from enlisting until 3 years posttransplantation and examine pretransplantation predictors of posttransplantation outcomes.

Study Design: Prospective cohort study.

Setting & Participants: Patients 65 years and older enlisted at the Norwegian National Transplant Center between January 2013 and November 2016.

Predictors: Kidney transplantation, dialysis vintage, and pretransplantation comorbidity assessed using the Liu Comorbidity Index.

Outcomes: HRQoL, assessed using the Kidney Disease Quality of Life Short Form, version 1.3.

Analytical Approach: HRQoL scores obtained at 3 years posttransplantation were compared with those obtained pretransplantation and after 1 year using a paired-sample *t* test. Multivariable linear mixed-effect models were used to identify possible predictors of HRQoL changes over time.

Results: Among 289 patients included, 220 (mean age, 71.5 years) had undergone transplantation and 136 had completed the 3-year HRQoL follow-up by October 2020. Posttransplant HRQoL, both generic and kidney specific, substantially improved and the benefit persisted for 3 years. For wait-listed candidates remaining on dialysis, HRQoL gradually deteriorated, and recipients who died within 3 years posttransplantation experienced no improvement during the first year. Moderately elevated pretransplantation comorbidity scores and prolonged dialysis vintage independently predicted poor HRQoL outcomes posttransplantation. Recipients receiving dialysis for 1 year or longer with pretransplantation comorbidity scores ≥ 7 experienced a marked and sustained physical deterioration after transplantation.

Limitations: Homogenous and highly selected population.

Conclusions: Transplantation is associated with a sustained HRQoL improvement and should be the preferred treatment for selected older patients. The value of a pretransplant comorbidity score to predict posttransplantation outcomes warrants further evaluation and may improve the selection process.

Visual Abstract included

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Kidney Med. 3(6):974-983. Published online July 22, 2021.

doi: 10.1016/j.xkme.2021.05.007

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The optimal kidney replacement therapy for the increasing population of older patients (aged ≥ 65 years) with end-stage kidney disease¹ is not well defined. Although eligible older transplant recipients have been reported to survive longer than matched dialysis patients,^{2,3} recent studies have failed to demonstrate any significant survival benefit of kidney transplantation compared with dialysis.^{4,5} Older recipients are at increased risk for early postoperative adverse events,⁶ and the allocation of organs from extended criteria donors and donors after cardiac death is associated with impaired survival.^{7,8} Given that specific evidence-based treatment guidelines are lacking,⁶ it is often debated whether kidney transplantation should be recommended in the elderly.⁹

Although patients with kidney disease have been reported to be predominantly concerned about their quality of life,¹⁰ most studies comparing different kidney replacement therapy alternatives have mainly focused on patient and graft survival, whereas patient-reported health-

related quality-of-life (HRQoL) outcomes are either underreported or completely lacking in kidney transplant studies.¹¹ Additionally, HRQoL outcomes serve as prognostic markers, with poor scores indicating increased risk for worse outcomes.¹² Given the current organ scarcity, transplants should primarily be allocated to patients who are expected to take full advantage of transplantation.¹³ Thus, in addition to life expectancy, knowledge of posttransplantation HRQoL changes over time is of major importance.

In older transplant candidates, HRQoL declines due to prolonged wait-listing¹⁴ and age-related comorbid conditions,¹⁵ whereas early posttransplantation, the generic HRQoL domains have been reported to improve.^{16,17} The long-term impact of kidney transplantation on older recipients' HRQoL has not been previously prospectively assessed. The primary aim of the current study was to prospectively evaluate HRQoL changes until 3 years posttransplantation in recipients 65 years and older at enlisting.

PLAIN-LANGUAGE SUMMARY

Assessing the optimal treatment for the growing population of older patients in need of kidney replacement therapy requires knowledge of health-related quality of life (HRQoL) outcomes, as well as survival. This study evaluated HRQoL changes from acceptance for transplantation, during waitlisting, and until 3 years post-transplantation. The results indicate that transplant recipients, in contrast to patients who did not undergo transplantation who are receiving dialysis, substantially improved their HRQoL outcomes shortly after transplantation, and the benefit persisted at least for 3 years. Recipients receiving dialysis for less than 1 year with low pretransplantation comorbidity experienced the best outcomes. Kidney transplantation should be encouraged in carefully selected older patients and available organs for transplantation should be allocated to patients who are expected to experience favorable outcomes.

The secondary aim was to identify potential pretransplant predictors of posttransplantation HRQoL outcomes.

METHODS**Study Design**

The prospective cohort study Health-Related Quality of Life in ESKD Patients Older Than 65 years, also known as Question 65, is designed to evaluate HRQoL in older kidney transplant recipients from enlisting until 10 years posttransplantation.¹⁴ The study is conducted at the Norwegian National Transplant Center at Oslo University Hospital, to which all transplant candidates are referred and evaluated.

A baseline questionnaire was completed at study inclusion and thereafter at every 6 months until kidney transplantation, permanent withdrawal from the wait-list, or death. Posttransplantation, HRQoL outcomes are collected at 10 weeks, 6 months, and 1, 3, 5, 7, and 10-years until graft loss or death.

The current study evaluated HRQoL outcomes from baseline until 3 years posttransplantation. For the transplant recipient group, the last HRQoL reference values pretransplantation were compared with those obtained at 1 and 3 years posttransplantation. Included candidates who did not undergo transplantation who were receiving maintenance dialysis served as controls, and baseline HRQoL scores were compared with scores obtained at 1 and 2 years after dialysis initiation.

All questionnaires were sent by mail to the patient's residence, and in case of no response, a single reminder was sent after 3 to 4 weeks. Supplemental data relevant to

the study were retrieved from Oslo University Hospital and the Norwegian Renal Registry.

The study was approved by the Regional Committee for Medical and Health Research Ethics, South East Norway (2012/527), and followed the regulations of the Helsinki Declaration. All participants were informed and signed a consent form before their inclusion in the study.

Study Population

All patients 65 years and older who were enlisted between January 2013 and November 2016 were invited to participate. Sufficient Norwegian language skills and intact cognitive functions, evaluated by the local nephrologist during the pretransplantation workup, were prerequisites for inclusion.

Health-Related Quality of Life

HRQoL outcomes were assessed using the Kidney Disease Quality of Life Short Form (KDQOL-SF), version 1.3, questionnaire. This self-reported instrument was developed for patients receiving dialysis¹⁸ and has been validated in kidney transplantation.¹⁹ The generic 36-Item Short Form Health Survey (SF-36)²⁰ includes 35 items divided into 8 domains: physical function, role limitation due to physical problems, bodily pain, general health, vitality, social function, role limitation due to emotional problems, and mental health. The last item reports health transition during the last year.²⁰ Missing items were substituted with the mean score of the completed items in the same domain when at least half the items in a multi-item domain were answered.²¹

The kidney-specific instrument (KDQOL)¹⁸ includes 43 items divided into 11 domains: symptoms, effect of kidney disease, burden of kidney disease, work status, cognitive function, quality of social interaction, sexual function, sleep, social support, dialysis staff encouragement, and patient satisfaction. The final item, total health, is scored on a 0 to 10 numeric scale, from worse to best possible score.¹⁸ KDQOL-SF items were converted on a 0 to 100 possible range, with higher scores reflecting better HRQoL.²² No substitution of missing data was performed for the kidney-specific items.²²

Both instruments were translated into Norwegian.^{23,24} The KDQOL has been validated in a Scandinavian population²⁵ and Norwegian reference values have been established for the SF-36.^{26,27} Population norms, published in 2018,²⁷ were used in the current study for calculations of z scores, allowing valid comparisons with the general population.

Additional Items

Five additional items relevant to posttransplantation issues were added to the 3-year follow-up questionnaire: to what extent the pretransplantation expectations were fulfilled, individuals' perceptions of graft function, the psychological

distress of living as a transplant recipient, side effects of immunosuppression, and whether the participants, after having experienced kidney transplantation, would choose it again as the preferred treatment.

Comorbidity

The Liu Comorbidity Index (LCI)²⁸ was developed based on data from a US dialysis population with a mean age of 65 years and has been reported to predict survival in older patients receiving dialysis²⁹ and post-kidney transplantation.³⁰ LCI score ranges from 0 to 21 (Table S1). Our study population was categorized into 4 comorbidity groups based on LCI scores (0-3, 4-6, 7-9, and ≥ 10), as previously described.²⁸

Statistical Analysis

Descriptive continuous data are presented as mean \pm standard deviation (SD) if normally distributed or as median with 25th-75th percentiles if skewed. Categorical data are presented as percentages.

Independent-sample *t* tests were used to estimate differences in continuous variables between different groups. A paired-sample *t* test was used to estimate HRQoL changes within groups between 2 time points. Chi-squared test was used for categorical variables. $P \leq 0.05$ was considered statistically significant. Differences of a half SD (0.5 SD) from HRQoL mean scores,³¹ and *z* scores ≥ 0.5 from the population norms were used as thresholds for clinical significance.

Linear mixed-effect models were used to evaluate the time development of HRQoL (pre-kidney transplantation, 6 months, and 1 and 3 years post-kidney transplantation). HRQoL domains were defined as outcome variables, and fixed effects for time were used as categorical variables of interest. Sex, age at kidney transplantation, marital status dichotomized to married/partnered or not, LCI scores as continuous and categorical variables, dialysis vintage, wait-listing time, estimated glomerular filtration rate at 10 weeks and at 1 year post-kidney transplantation, and living donor kidney transplantation were included in univariable analysis. Variables yielding $P \leq 0.25$ ³² were included as fixed factors in the multivariable model along with variables of known clinical importance. A backward manual elimination procedure was performed to identify significant predictors of HRQoL changes over time. All models included random intercepts and an unstructured covariance matrix; the random slope was included in the model only when it significantly contributed to its improvement. Clinical factors that correlated ≥ 0.7 were not included in the model to avoid multicollinearity.

The additional items were coded as ordinal variables on a 4-range scale and further dichotomized into positive and negative outcomes. The logistic regression model included all these variables and HRQoL scores obtained at 1 year post-kidney transplantation.

RESULTS

Study Population

Among 437 eligible wait-listed patients 65 years and older, 289 (66%) were included in the study. Nonincluded patients were younger (mean age, 69.8 vs 71.1 years; $P = 0.02$); otherwise, no differences were observed between the groups. Demographic and clinical characteristics of the study population are presented in Table 1.

By October 2020, a total of 220 participants underwent transplantation; 194 (88%) more than 3 years ago. Among them, 13 experienced graft loss (6 subsequently died) and 27 patients died with a functional graft. Of 154 eligible recipients, 136 (88%) completed the 3-year HRQoL questionnaire (Fig 1).

Compared with deceased recipients, survivors tended to be younger, with less pretransplantation comorbidity and shorter dialysis vintage, and more often underwent transplantation pre-emptively. Although male participants, when compared with females, had higher LCI scores (3.0 vs 1.5; $P < 0.001$) and increased prevalence of cardiovascular disease (63.2% vs 36.6%; $P = 0.004$) and any comorbid conditions (82% vs 61%; $P = 0.008$), they experienced shorter waiting times (13.0 vs 17.4 months; $P = 0.01$).

Candidates who did not undergo transplantation who were receiving dialysis ($N = 69$) had higher LCI scores and prevalence of cardiovascular disease and tended to be older and more prone to have diabetes than transplant recipients. During follow-up, 20 (29%) died and 40 (58%) were withdrawn from the wait-list.

HRQoL in Survivors After a 3-Year Follow-up

For recipients who completed the 3-year follow-up, reference HRQoL scores, obtained during the last 6 months pre-kidney transplantation, were compared with scores obtained at the end of year 3 post-kidney transplantation. At 3 years posttransplantation, all generic and kidney-specific HRQoL domains had improved (Fig 2). The increase in the domains of general health, vitality, effect, and burden of kidney disease was clinically significant. The score of total health increased early and remained stable throughout the third year.

Between posttransplantation years 1 and 3, recipients who underwent transplantation at 70 years or older ($N = 81$) declined in statistical but not in clinical significance in the domains of physical function, bodily pain, general health, vitality, symptoms, and effect of kidney disease. The decrease in physical function (-2.2 vs -8.7 ; $P = 0.06$) and bodily pain (-1.3 vs -11.2 ; $P = 0.03$) scores were less marked in recipients who underwent transplantation at the age of 65 to 70 years ($N = 55$). The crude generic and kidney-specific HRQoL scores for transplanted survivors and deceased recipients are shown in Table S2.

HRQoL in Deceased Transplant Recipients

At the end of the first year, recipients who subsequently died between 12 and 36 months posttransplantation ($N = 13$)

Table 1. Demographic and Clinical Characteristics of the Study Population

	Kidney Transplantation (N = 220)	Non-Kidney Transplantation (N = 69)	P	3 y (N = 136)	Deceased (N = 33)	P
Male sex	154 (70%)	42 (60.9%)	0.18	95 (69.9%)	25 (75.8%)	0.53
Age, y	70.8±4.0	71.8±4.5	0.07	71.5±4.1	71.8±4.2	0.09
Marital status						
Married	174 (79.1%)	48 (69.6%)	0.31	112 (82.4%)	22 (66.7%)	0.98
Single	11 (5.0%)	5 (7.2%)		2 (1.5%)	3 (9.1%)	
Divorced	17 (7.7%)	9 (13.0%)		10 (7.4%)	6 (18.2%)	
Widowed	18 (8.2%)	7 (10.1%)		12 (8.8%)	2 (6.1%)	
Comorbid conditions						
CVD	116 (52.7%)	47 (68.1%)	0.03 ^a	75 (55.1%)	22 (66.7%)	0.33
Diabetes	52 (23.6%)	24 (34.8%)	0.08	31 (22.8%)	7 (21.2%)	0.82
COPD	21 (9.5%)	5 (7.2%)	0.64	10 (7.4%)	6 (18.2%)	0.05
GI bleeding	22 (10.0%)	6 (8.7%)	>0.99	15 (11.0%)	4 (12.1%)	0.77
Liver disease	2 (0.9%)	1 (1.4%)	0.56	0	0	>0.99
Cancer	51 (23.2%)	20 (29.0%)	0.34	30 (22.1%)	8 (24.2%)	0.82
No comorbidity	51 (23.2%)	12 (17.4%)	0.40	33 (24.3%)	4 (12.1%)	0.24
LCI score	2.63±2.4	3.6±2.8	0.01 ^a	2.6±2.4	3.5±2.3	0.06
LCI group						
0-3	153 (69.5%)	36 (52.2%)	<0.001 ^a	98 (72.1%)	15 (45.5%)	0.06
4-6	52 (23.6%)	25 (36.2%)		29 (21.3%)	15 (45.5%)	
7-9	12 (5.5%)	4 (5.8%)		8 (5.9%)	2 (6.1%)	
≥10	3 (1.4%)	4 (5.8%)		1 (0.7%)	1 (3.0%)	
Dialysis status						
Pre-emptive	57 (25.9%)			43 (31.6%)	3 (9.1%)	0.01 ^a
Hemodialysis	124 (56.4%)			70 (51.5%)	29 (87.9%)	<0.001 ^a
Peritoneal dialysis	39 (17.7%)			23 (16.9%)	1 (3.0%)	0.03 ^a
Dialysis vintage, mo						
LD kidney transplantation	14.2 [6.9, 24.0]			9.8 [6.2, 24.0]	15.1 [13.6, 16.5]	0.97
DBD kidney transplantation	30.4±17.7			23.9±11.9	37.2±22.5	0.01 ^a
Waitlisting DBD kidney transplantation, mo	17.9±12.8	65.3±17.9	<0.001 ^a	16.8±8.4	18.7±12.4	0.05 ^a
Time from baseline HRQoL to kidney transplantation, mo	12.6±11.7			8.8±7.6	14.1±10.4	0.007 ^a
LD	30 (13.6%)			26 (19.1%)	2 (6.1%)	0.18
Donor age, y						
LD	51.7±11.7			51.3±11.6	49.0±11.3	0.74
DBD	66.5±10.5			65.3±11.0	68.4±9.5	0.27
eGFR y 1, mL/min/1.73 m ²	47.5±14.7			47.4±14.8	46.8±14.8	0.86
eGFR y 3, mL/min/1.73 m ²				51.1±16.7		

Note: Values expressed as number (percent), mean ± standard deviation, and median [25th, 75th percentiles].

Abbreviations and Definitions: CVD, cardiovascular disease includes congestive heart failure, coronary vascular disease/myocardial infarction, arrhythmia, cerebrovascular disease, and peripheral vascular disease; COPD, chronic obstructive pulmonary disease; DBD, deceased brain-dead donor; eGFR, estimated glomerular filtration rate by Chronic Kidney Disease Epidemiology Collaboration equation; GI, gastrointestinal; HRQoL, health-related quality of life; LCI, Liu Comorbidity Index; LD, living donor.

^aStatistically significant.

deteriorated in all the generic and improved only nonsignificantly in the kidney-specific HRQoL domains. There was no difference observed in pretransplantation HRQoL scores between deceased and surviving recipients. However, deceased recipients lacked HRQoL improvement during the first posttransplantation year and maintained their generic HRQoL at the pretransplantation level until death (Fig S1).

HRQoL in Candidates Who Did Not Undergo Transplantation Who Were Receiving Maintenance Dialysis

Wait-listed candidates who did not undergo transplantation who were receiving dialysis deteriorated in all HRQoL domains, at least in the first 2 years following dialysis initiation, with an accelerated pace after the first year (Fig S2). The generic HRQoL outcomes were

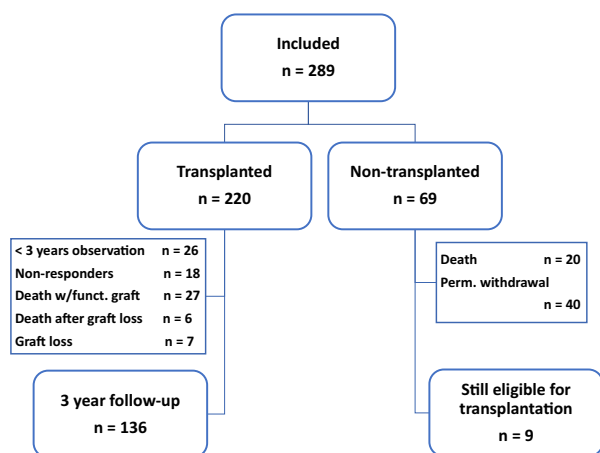


Figure 1. Flow chart of the study. Abbreviations: funct, functioning; Perm, permanent.

especially affected, and when compared with baseline scores, the domains of physical function (49.3 vs 62.1; $P = 0.04$), vitality (35.4 vs 45.0; $P = 0.003$), and mental health (65.7 vs 74.1; $P = 0.003$) were significantly impaired after 2 years.

HRQoL in Living Donor Kidney Transplantation

During follow-up, recipients of living donor kidney transplants ($N = 26$) improved significantly in all HRQoL outcomes except for bodily pain, cognitive function, quality of social interaction, sex, and social support. Compared with deceased donor kidney transplantation, living donor kidney transplantation was associated with shorter dialysis vintage (14.6 vs 23.9 months; $P < 0.001$), younger donor age (51.3 vs 65.3 years; $P < 0.001$), and improved physical function between the first and third posttransplantation years (1.2 vs -8.0 ; $P = 0.03$).

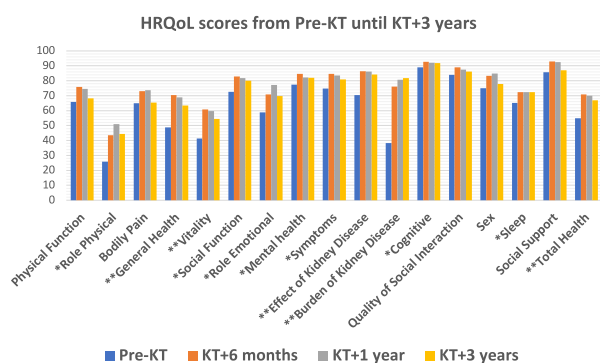


Figure 2. Development of health-related quality of life (HRQoL) scores from pretransplantation until the end of year 3 posttransplantation. *Statistically significant and **clinically significant improvement. Abbreviation: KT, kidney transplantation.

Linear Mixed-Effect Models Regression Analysis

The linear mixed-effect model regression, including all transplant recipients ($N = 220$), are presented in [Tables S3](#) and [S4](#). Pretransplantation LCI score was the most persistent predictor of posttransplantation HRQoL. Each per-unit increase in LCI scores and LCI scores ≥ 7 consistently predicted poor outcomes in nearly all the generic and kidney-specific domains ([Fig 3](#)). Longer dialysis vintage was independently associated with worse posttransplantation physical function ([Fig S3](#)), and this effect was enhanced with increasing LCI scores. Recipients with both LCI scores ≥ 7 and dialysis for 1 year or longer ($N = 14$) experienced the worst physical outcomes posttransplantation ([Fig 4](#)). Older age and living donor kidney transplantation were positively associated with social and mental functioning.

Significant interaction effects were also observed between time and sex for physical function, time, and LCI score for mental health, and time and age for quality of social interaction and total health.

Comparison With the General Population

SF-36 scores at 3 years posttransplantation, adjusted for age and sex, albeit lower, did not differ significantly from the Norwegian population norms except for the domain of physical function (z score = -0.64) in men ([Fig S4](#)).

Additional Items

Pretransplantation expectations were accomplished in 82% of older recipients, and 97% experienced a well-functioning kidney. Side effects of immunosuppression and psychological distress related to kidney transplantation were considered to be of minor importance by 76% of recipients. Overall, 99% of study participants who underwent transplantation would opt again for kidney transplantation.

DISCUSSION

In the present study, kidney transplant recipients older than 65 years at enlisting, with a functioning graft, improved early posttransplantation in both generic and kidney-specific HRQoL outcomes, and the benefits extended at least for 3 years. Recipients of living donor kidney transplants with short waiting time experienced the most favorable outcomes. Prolonged dialysis vintage and elevated pretransplantation comorbidity scores were associated with a marked and sustained physical deterioration posttransplantation. This national cohort study is to our knowledge the first to prospectively and longitudinally evaluate the impact of transplantation on HRQoL outcomes in older patients.

Posttransplantation HRQoL alterations followed distinct patterns among different patient groups. Recipients surviving for at least 3 years improved substantially in almost all HRQoL domains, whereas recipients who died within 36 months posttransplantation experienced no

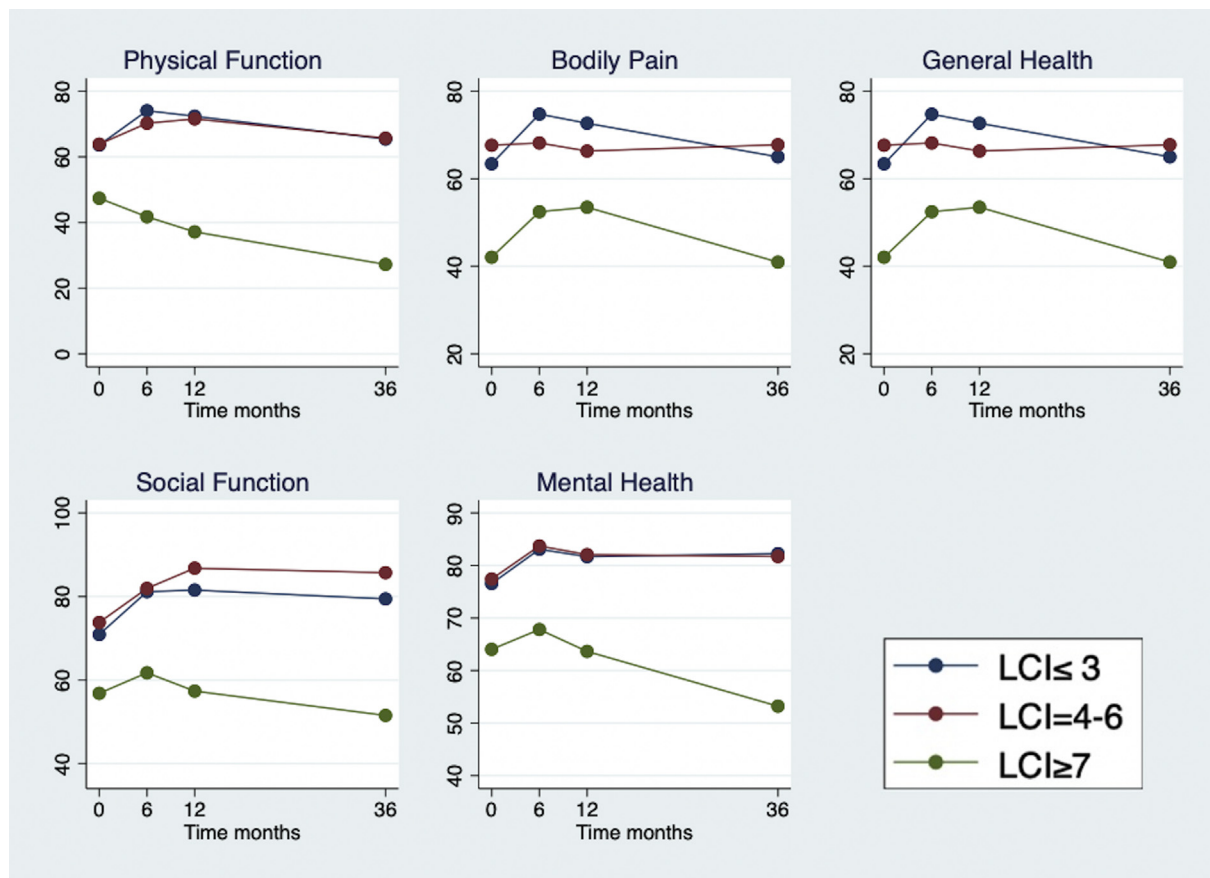


Figure 3. Posttransplantation generic health-related quality of life outcomes by Liu Comorbidity Index (LCI) score.

improvement during the first year. These findings are novel and imply that posttransplantation HRQoL measurements may identify older recipients at risk for adverse outcomes. Wait-listed candidates who did not undergo transplantation who were receiving dialysis perceived worse HRQoL, and the generic scores obtained at 2 years after enlisting were significantly impaired compared with baseline scores.

In older recipients, HRQoL posttransplantation has been reported to improve predominantly in social, emotional, and mental functioning.^{16,33} We observed that the posttransplantation HRQoL benefits comprised all the generic and kidney-specific outcomes, including physical functioning, and were extended throughout the third posttransplantation year, as reported in younger recipients.³⁴ At the end of the third year, age- and sex-adjusted SF-36 scores were comparable to the Norwegian general population²⁷ except for impaired physical function in males, as previously reported.¹⁶ In line with our results, older transplant recipients have been reported to confirm that kidney transplantation was the correct decision, while health problems and worries about the transplant were of minor importance.^{35,36}

Between the first and third posttransplantation years, physical function declined in recipients who were older than 70 years at transplantation. This observation

corroborates previous reports^{16,37} and most likely represents an age-related impairment in physical functioning. In the general population, increasing age beyond 65 years is associated with accelerated decline in physical function.³⁸ Younger recipients have also been reported to deteriorate in physical function long-term posttransplantation^{39,40} but this is attributed to long-standing immunosuppression rather than age.³⁹ In accordance with previous findings,^{16,35,41} we describe posttransplant social, mental, and general health perception to be excellent.

Recipients who died between 12 and 36 months maintained their 1-year posttransplantation HRQoL at the pretransplantation level, which indicates a possible association between impaired posttransplantation HRQoL and risk for adverse outcomes. In younger recipients, poor HRQoL, both pre- and posttransplantation, has been associated with increased mortality after kidney transplantation,^{42,43} whereas in our study, no difference was observed in pretransplantation HRQoL scores between survivors and nonsurvivors. It is likely that in the elderly, assessment of functional status is confounded by the normal age-induced physical impairment³⁸ and proper pretransplantation evaluation may additionally require measures of frailty,⁴⁴ which are not included in our study. The lack of HRQoL improvement in deceased recipients warrants cautious interpretation because the analysis is

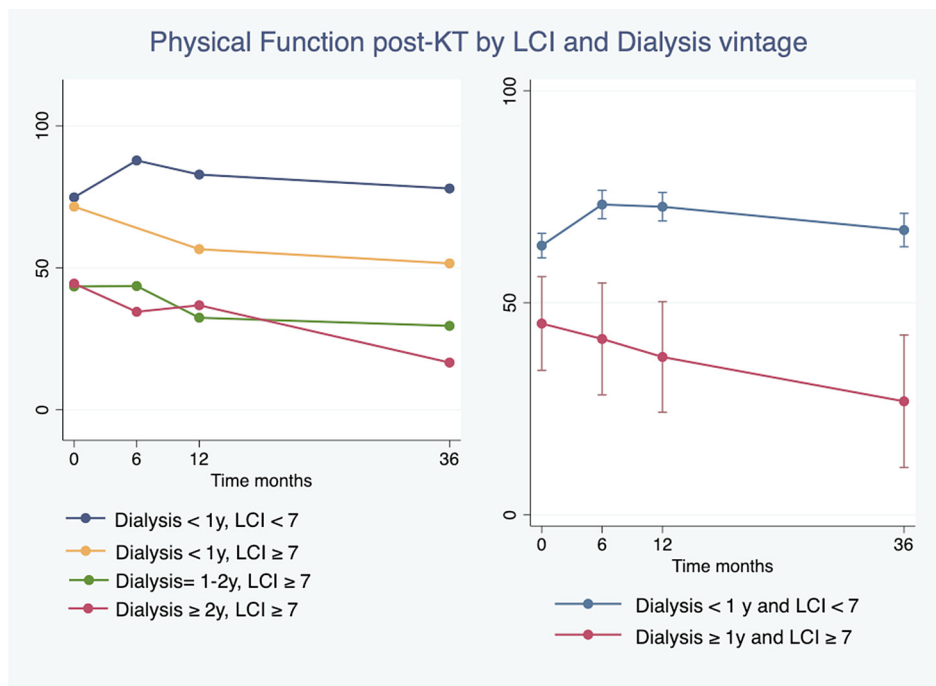


Figure 4. Posttransplantation physical function (PF). Interaction effect of Liu Comorbidity Index (LCI) score with time receiving dialysis. Abbreviation: KT, kidney transplantation.

based on few observations and is not adjusted for posttransplantation events that might have accounted for the observed outcome. Although not yet confirmed, we support the implementation of regular posttransplantation HRQoL measurements in the follow-up of older recipients, which may prove useful in identifying individuals at risk for impaired outcomes.

Prolonged dialysis vintage was associated with poor HRQoL. Older candidates who did not undergo transplantation receiving dialysis gradually declined in all HRQoL outcomes, and 2 years after enlisting, the generic domains of physical, mental, and social functioning were significantly impaired compared with the baseline. Most study participants who did not undergo transplantation were either deceased (29%) or withdrawn from the list (58%) during the 3-year follow-up. It is well documented that HRQoL deteriorates in older wait-listed candidates,¹⁴ with an accelerated pace of physical decline during the first 2 years after dialysis initiation.⁴³ Worse physical function has also been reported to increase the risk for temporary inactivation from the waiting list.⁴³

As previously described,³⁵ older transplant candidates remaining on dialysis for 1 year or longer experienced worse physical function posttransplantation than patients who were dialyzed for less than 1 year. Interestingly, we observed that the rate of physical decline accelerated as pretransplantation comorbidity score increased. Individuals with both LCI scores ≥ 7 and dialysis for 1 year or longer experienced the worst physical outcomes.

Accordingly, moderately elevated pretransplantation LCI scores consistently predicted poor physical, mental, social,

and kidney-specific HRQoL outcomes posttransplantation. Elevated LCI score has also been reported to predict intensive care admission and reduced survival in kidney transplant recipients older than 55 years.³⁰ Although pretransplantation comorbidity measured using other indexes has been associated with impaired physical status³⁵ and reduced patient and graft survival,^{43,45} it has not been found to independently predict survival in kidney recipients 70 years and older.⁴⁶ Our finding is novel and indicates that a single pretransplantation comorbidity index may predict both life expectancy and well-being in older recipients. Additionally, the negative effect of longer dialysis vintage on posttransplant physical function was significantly enhanced by elevated LCI scores. Whether the assessment of pretransplantation comorbidity by LCI can prove useful during the selection of older transplant candidates should be further evaluated.

During follow-up, 17% of older transplant recipients died. Due to increased comorbidity and age, posttransplantation survival is reduced in older versus younger recipients.^{47,48} This discrepancy is further amplified by the 'old for old' organ allocation policy,¹³ giving rise to a debate of whether older recipients receiving older organs actually may benefit more from remaining on dialysis than receiving a kidney transplant.^{4,49} Due to organ scarcity, identifying reliable predictors of posttransplantation outcomes is essential for the efficient use of all available transplants. In the current study, the pretransplantation comorbidity score and dialysis vintage were increased in recipients who died within 3 years posttransplantation, which corroborates previous reports.⁴ Besides HRQoL

impairment, dialysis vintage of 2 years or longer has also been recognized as the strongest modifiable factor⁵⁰ of reduced survival in older recipients.⁴ Our results indicate that older wait-listed candidates dialyzed 1 year or longer or with elevated pretransplantation comorbid conditions are at increased risk for adverse outcomes and should be thoroughly informed and carefully re-evaluated on a regular basis.

Our study has several strengths. To our knowledge, it is the first prospective study to longitudinally evaluate HRQoL outcomes in older kidney transplant recipients, making possible the distinction between short-, medium-, and longer-term outcomes and eliminating recall bias. Furthermore, it is a national study, conducted from the only Norwegian transplant center, ensuring uniform evaluation and treatment protocols and the representativeness of the study population. All data are self-reported and always collected at the patient's residence, which minimizes the collection and interpretation biases. A high response rate of 88% ensures that all outcomes are reported. A large sample size provides robust results.

However, our findings cannot be generalized to the whole kidney replacement therapy advanced age population because participants in this study were predominately White, had relatively short waiting times, and fulfilled stringent medical requirements to be enlisted and undergo transplantation. Thus, selection bias cannot be ruled out. As per protocol design, recipients who experienced graft loss were excluded from the study, not allowing any evaluation of the impact of graft loss on HRQoL. Older kidney transplant recipients are per definition a frail population. Frailty was not assessed in our study but because all recipients fulfilled the medical requirements for enlisting, it is unlikely that this has significantly confounded our findings. Posttransplantation HRQoL impairment in non-survivors must be interpreted cautiously because the lack of adjustment for posttransplantation events and quality of the graft (Kidney Donor Profile Index) limits the generalizability of our results.

HRQoL assessment by KDQOL-SF does not necessarily capture all issues relevant to transplantation or advanced age. Nevertheless, it has been validated in transplant recipients and is the most-used tool for HRQoL measurements in all ages, ensuring the reliability and accuracy of the derived results. Comorbidity was assessed by using only the LCI and did not allow direct comparisons with other studies. Its association with the widely used Charlson Comorbidity Index⁵¹ should be evaluated in future studies.

HRQoL improved substantially in older kidney transplant recipients and the benefit persisted for at least 3 years after transplantation. Recipients who died within 3 years posttransplantation experienced no HRQoL improvement during the first year, indicating that impaired posttransplantation HRQoL may be related to poor outcomes. Candidates who did not undergo transplantation remaining on dialysis deteriorated in all HRQoL domains. Longer dialysis vintage was independently associated with posttransplantation

physical decline, and elevated pretransplantation comorbidity score consistently predicted poor HRQoL. Kidney transplantation should be encouraged in carefully selected older patients and, when possible, with living donor kidney transplantation and short wait-listing time. Further research is required to optimize the selection process and identify reliable pretransplantation predictors of overall long-term clinical outcomes.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Changes in health-related quality-of-life scores during the first year posttransplantation for survivors versus deceased recipients.

Figure S2: Health-related quality-of-life scores for wait-listed candidates on dialysis, from enlisting until 2 years after dialysis initiation.

Figure S3: Posttransplantation physical function by time spent on dialysis.

Figure S4: SF-36 scores 3 years after kidney transplantation compared with the age-matched general Norwegian population, presented as z score.

Table S1: Liu Comorbidity Index.

Table S2: Health-related quality-of-life scores from pretransplantation until the end of the third year posttransplantation for survivors (N = 136) and until the end of the first year posttransplantation for deceased recipients (N = 13).

Table S3: Linear mixed-effect regression analysis (multivariable) at 6 months and 1 and 3 years after kidney transplantation for SF-36 (N = 220).

Table S4: Linear mixed-effect regression analysis (multivariable) at 6 months and 1 and 3 years after kidney transplantation for KDQOL (N = 220).

ARTICLE INFORMATION

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Support: This project was funded by South-Eastern Norway Regional Health Authority. The funders did not participate in study design; collection, analysis and interpretation of data; writing the report; and the decision to submit the report for publication.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Acknowledgements: Data from the Norwegian Renal Registry were provided by Professor Anders Åsberg. The study is registered at www.clinicaltrials.gov (NCT01760733).

Peer Review: Received January 12, 2021. Evaluated by 2 external peer reviewers, with direct editorial input by the Statistical Editor and the Editor-in-Chief. Accepted in revised form May 23, 2021.

Data Sharing: Deidentified individual participant data underlying the results presented in the manuscript are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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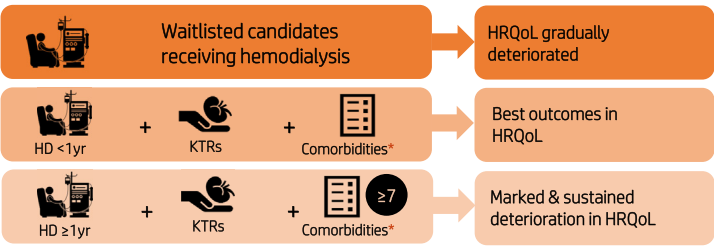
What is the Health - Related Quality of Life (HRQoL) in older kidney transplant recipients?



Norwegian National Transplant Center

- Prospective Cohort Study
- Jan 2013 - Nov 2016
- 222 Kidney Transplant Recipients (KTRs)
- Age ≥ 65 yrs

220 pts with mean age of 71.5 yrs
 136 pts with 3 yrs HRQoL assessed until Oct 2020



*as measured by the Liu comorbidity index

HRQoL assessed by Kidney Disease Quality of Life Short Form Version 1.3

HRQoL substantial improved and benefit persists for 3 yrs
 KTRs

Conclusion: Transplantation is associated with a sustained HRQoL improvement and should be the preferred treatment for selected older patients

Reference: Tsarpali V, Midtvedt K, Lønning K et al. Health-related quality of life in older kidney transplant recipients: a national cohort study of short and longer-term outcomes. *Kidney Medicine*, 2021.
 Visual Abstract by Anju Yadav MD FASN @docanjuyadav