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Clinical Frailty Scale and Charlson Comorbidity Index as Predictors of Hospitalization and

Mortality Risk after Kidney Transplant Failure

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Abstract

Introduction and Objectives: Kidney transplant (KT) recipients who experience graft failure and return to dialysis face a higher risk of adverse outcomes. This study aimed to identify risk factors for hospitalization and mortality two years post-graft failure. Materials and Methods: We conducted a retrospective cohort study of end-stage kidney disease patients who initiated hemodialysis following graft failure between January 2019 and December 2020. The Clinical Frailty Scale (CFS) and the Charlson Comorbidity Index (CCI) were assessed for each patient at the time of graft loss. The primary outcomes were hospitalization and all-cause mortality over a two-year follow-up period. Results: A total of 107 patients were included, with a mean age of 55 years and a mean graft survival of 134 months. The two-year hospitalization rate was 37.4%, with lower residual diuresis and higher CFS identified as independent risk factors. The two-year mortality rate was 16.8%. A multivariate regression model, explaining 82% of the variance, confirmed that higher CCI, higher CFS, and lower residual diuresis significantly increased mortality risk. A CCI cut-off of ≥ 8 (AUC 0.95) further stratified patients at elevated mortality risk. Immunological and transplant-related variables did not influence mortality or hospitalization risk. Conclusions: In this cohort, frailty defined by CFS was associated with hospitalization and mortality, while comorbidity burden evaluated by CCI was strongly related to mortality. These tools may help personalize the care of patients with a failing graft.

Keywords: Charlson Comorbidity Index; Clinical Frailty Scale; Graft failure; Hospitalization; Kidney transplantation; Mortality;

Abbreviations:

AUC – area under the curve

CCI - Charlson Comorbidity Index

CI – confidence interval

CFS - Clinical Frailty Scale

CKD – chronic kidney disease

CV – cardiovascular risk

ESKD – end-stage kidney disease

ESC - European Society of Cardiology

H - hemodialysis

KT – kidney transplantation

IS – immunosuppression

RKF – residual kidney function

Introduction

The last decade has witnessed a significant improvement in short-term kidney transplantation outcomes, but long-term graft survival remains suboptimal, with the mean graft survival rate at 10 years ranging from 50% to 70%. [1,2]Additionally, the increasing patient lifespan and better access to healthcare have led to a growing population of kidney transplant (KT) recipients who experience graft failure and return to dialysis, which is currently the fourth leading cause of incident dialysis. [3,4]

Patients with end-stage kidney disease (ESKD) who begin dialysis after graft loss encounter various complications and face an increased burden of morbidity beyond chronic kidney disease (CKD). Previous studies have indicated lower quality of life scores, a higher incidence of depression, increased hospitalizations, and notably higher mortality rates. [5–8] Certain characteristics of this patient group may contribute to the poorer outcomes observed, including prolonged CKD duration and ongoing exposure to immunosuppression (IS), which is linked to an increased risk of life-threatening infections [9], endocrine and metabolic dysfunction [10], and specific types of neoplasms [11].

Considering the aging global population and the improved survival rates of KT recipients, we are witnessing a growing number of older, frailer patients with more comorbidities returning to dialysis, which might also influence the increased morbidity and mortality rates post-graft failure. [12].

The Clinical Frailty Scale (CFS) and the Charlson Comorbidity Index (CCI) have been utilized to assess frailty and clinical outcomes in patients with ESKD, including dialysis, KT recipients, and those under conservative care management. [13–17] Frailty, a multisystem clinical syndrome resulting from the accumulation of vascular, inflammatory, and age-related challenges, is increasingly prevalent in the CKD hemodialysis (HD) population and significantly impacts clinical outcomes such as hospitalization, institutionalization, decreased quality of life, and mortality. [18] The CCI score serves as a valid index with strong discriminatory power in predicting survival at the onset of dialysis. [17] For patients facing high morbidity and mortality rates following graft loss, these indices offer valuable tools for multidisciplinary decision-making regarding whether to initiate dialysis or pursue conservative kidney management, engaging both patients and their families [16,19].

The community of physicians involved in caring for KT recipients is increasingly aware of the importance of managing post-graft loss. Still, coordination with dialysis nephrologists, conservative care teams, and timely referrals for retransplantation remains suboptimal. [21] Despite the high morbidity and mortality observed in this patient population, the systematic assessment of frailty and comorbidities is still scarce. Consequently, the potential role of these factors in guiding therapeutic decisions and informing prognosis has been underexplored. [22,23]

The primary aim of our study was to identify predictors of mortality and hospitalization over a two-year period among ESKD with a failed graft who initiated HD, focusing on comorbidity and frailty scores.

Methods:

We performed an observational retrospective cohort study of ESKD patients with graft failure who started HD between January 2019 and December 2020 at Coimbra University Hospital, a large tertiary care centre in Portugal. Our study was carried out following the Declaration of Helsinki and approved by the ethics committee of Coimbra University Hospital (#CE-002-2020). Given the study's retrospective nature, sample size, and outcome of our sample population, the same committee waived the need for informed consent.

Patients over 18 years old who had at least two appointments with a transplant nephrologist the year before HD initiation were included. Patients with a previous graft, multiorgan transplant, or graft failure within the first month post-transplant were excluded. Demographic data, comorbidities, and transplant-related variables, including biopsy-proven rejections according to Banff 2017 criteria, were collected from patient records. We have also accessed patients IS withdrawal scheme post-graft failure. Laboratorial values, including serum albumin, hemoglobin and parathormone levels were registered in the last appointment post graft failure.

The estimated glomerular filtration rate (eGFR) at graft failure was defined by the CKD-EPI formula. Whether planned or unplanned, the decision on start dialysis was based on clinical and laboratory parameters. An urgent HD start was defined as the need to begin HD imminently or within 48 hours after presentation to the Emergency Room. An unplanned start was defined as the absence of autologous vascular access and/or the requirement for hospitalization to start HD. Residual diuresis was defined as the 24-hour urinary output (mL/day) at the last nephrology appointment.

Comorbidities, frailty, and cardiovascular risk assessment

To classify patients' cumulative comorbidities and frailty risk, we utilized the 2014 revised CCI [24,25] and the CFS [26] (Supplementary table 1 and supplementary table 2). To determine CCI and CFS, we relied on the information provided by the assistant nephrologist during the last nephrology appointment before graft failure, with a mean time to graft failure of 23 ± 14 days.

For baseline cardiovascular (CV) risk, we referenced the European Society of Cardiology (ESC) guidelines. [27] Because our focus was solely on ESKD patients, who are classified as very high risk for CVD, we further stratified CV risk irrespective of kidney disease. Based on the ESC guidelines, we divided CV risk categories into High (ESC's very high and high risk) and Low (ESC's moderate and low risk). All patients had at least one echocardiogram in the year before graft failure, as it is part of our KT follow-up routine, which allowed us to classify patients as having heart failure with or without preserved ejection fraction.

Follow-up and primary endpoints

We followed our cohort for two years, and the primary endpoints were all-cause hospitalization and mortality. Hospitalization was defined as an admission to our inpatient facility for medical observation, treatment, or care, with a minimum stay of 24 hours. We registered the number of hospitalizations by patient, cause, and duration. The cause of hospitalization was classified as infectious, CV, graft intolerance syndrome or neoplasia, based on the primary reason for admission documented in the medical records. For mortality, the cause of death was established according to the patient's registries and classified as infectious cause, CV events, neoplasms, and others.

Statistical analysis

Statistical analysis was performed using IBM-SPSS Statistics v22, and the confidence interval (CI) was set at 95%. A *p*-value < 0.05 was considered statistically significant. Categorical variables were described as relative frequency (absolute frequency). Continuous data (including the CCI and CFS) were defined as mean

± standard deviation. T-tests were used to compare the means of normally distributed variables between groups, and the χ2 test was used to compare the prevalence of categorical variables of interest. A comparison of continuous variables is presented as Pearson coefficient (r). Logistic regression analysis was used to evaluate hospitalization risk, and Cox regression analysis was used to assess mortality risk factors. The variables considered in the multivariate models were those statistically significant in univariate analysis and clinically relevant variables. The receiver operating characteristic (ROC) curves and Youden index were used to identify a cut-off point for variables of interest that predicted higher mortality and hospitalization risk.

Results

Demographic Data and Baseline Characteristics at the Start of Hemodialysis

A total of 107 patients met the inclusion and exclusion criteria and were included, with their demographic data summarized in Table 1. There was a male predominance, and the mean age at graft loss was 55.9 ± 13.3 years. The IS therapy before HD initiation varied: Fifty-three patients (49%) were on double therapy with steroids and calcineurin inhibitors; 37 patients (35%) were on triple IS with calcineurin inhibitors, mycophenolate, and steroids; and 17 patients (16%) had an IS regimen with mTOR inhibitors. After graft loss, all patients on a triple IS regimen suspended mycophenolate immediately. Regarding calcineurin inhibitors, 14 patients who were candidates for retransplantation and were not HLA sensitized at graft loss maintained calcineurin inhibitors for six months in addition to prednisolone. All patients maintained 5mg prednisolone for at least one year. There was a high prevalence of significant CV comorbidities such as hypertension, heart failure, and diabetes, with an average duration of diabetes of 11.5 ± 6.7 years. This is reflected in more than half of the patients presenting with a high ESC CV score. The mean graft survival time was approximately 11 years (133.8 ± 93.4 months), and the leading cause of graft loss was presumed chronic allograft nephropathy. The majority of patients (N=76, 71%) had an unplanned HD start, and of these, a large proportion (N=46 patients, 60.5%) had urgent initiation, mainly due to hypervolemia (N=41, 90%).

Hospitalization

We recorded 48 hospitalizations (0.44 events per patient) and a hospitalization rate of 37.4% (n=40) at two years of follow-up, with a median hospitalization stay of 17.6 days (IQR 1-22). The most common causes of hospitalization were infections (58.3%, n=28), especially respiratory and urinary tract infections, followed by CV events (29%, n=14), and four patients were hospitalized due to graft intolerance syndrome (Table 2).

Table 1 presents patients' clinical and laboratory features with and without hospitalizations. Identified risk factors for hospitalization included lower diuresis, lower albumin levels, the presence of a central venous catheter (CVC), higher CFS, and higher CCI scores. Age, gender, baseline CV risk, specific comorbidities (neoplasms, diabetes, heart failure), transplant-related, and immunological variables did not influence the hospitalization rate at two years. Our multivariate model (Table 3) explained 39.2% of the sample's variance and showed that residual diuresis volume and CFS at graft loss were the only significant parameters increasing hospitalization risk. Residual diuresis was correlated with CV hospitalizations, as these patients had a significantly lower residual diuresis volume (mean difference (df) = -423.1 mL/day, p=0.02). Patients with unplanned HD initiation (df = 7.7 days, p=0.0004), higher CFS (r=0.345, p=0.002), and higher CCI (r=0.257, p=0.03) had significantly more prolonged hospitalizations.

Mortality

The cohort's one-year and two-year mortality rates were 10.3% (n=11) and 16.8% (n=18), respectively and death occurred on average 9.3 ± 5.7 months post-graft loss. The leading causes of mortality were infection (55.5%, N=10), with four cases of SarsCov-2 pneumonia, followed by CV death (28%, N=5) (Table 2). Table 1 displays the differences in variable distribution for two-year mortality in our cohort. Mortality was significantly associated with older age, lower diuresis, lower albumin levels, higher CFS, higher CCI scores, and hospitalization. The mortality rate was also higher among patients with diabetes, heart failure, high CV risk, and unplanned HD initiation. Transplant-related variables, such as estimated glomerular filtration rate at HD start, months of graft survival, donor characteristics, induction, maintenance IS, and previous graft rejection episodes, did not associate with the two-year mortality rate. Our Cox regression model for mortality achieved statistical significance, explaining 83% of the variance in the studied outcome. It confirmed the relevance of the CCI, CFS, and lower residual diuresis volume in increasing mortality risk (Table 3). After adjusting for confounding variables, a cut-off value for CCI ≥ 8 (sensitivity 94.4%, specificity

84.9%, area under the curve (AUC) 0.95) was found to predict a higher two-year mortality risk (Figure 1). Kaplan-Meier curves for patients with a CCI ≥ 8 (N=30) or ≤ 7 (N=77) are shown in Figure 2.

Discussion

To our knowledge, this study is the first to examine the relationship between frailty, comorbidity, and outcomes in patients with a failing kidney graft who are initiating HD. Over a two-year follow-up period, 37.4% of patients were hospitalized (0.44 events per patient), most commonly due to infection and CV events. Frailty, measured by the CFS, was significantly associated with hospitalization (OR 1.99), highlighting its relevance in predicting post-graft morbidity. In contrast, no significant correlation was found between CCI and hospitalization. Given that the mean time to death was 9.3 ± 5.7 months and that CV-related were the second most common cause, we hypothesize that mortality acted as a competing risk, thereby reducing the likelihood of subsequent hospitalization. Eighteen patients (17%) died during follow-up, most within the first year. Severe infections were the leading cause of death, aligning with previously published data. [22] Both CFS and CCI emerged as independent predictors of mortality, as reported in native kidney ESKD. [28,29.] A cut-off CCI score of ≥8, provided good sensitivity and specificity for two-year mortality risk.

Frailty in ESKD patients with failing grafts is an emerging concern. As graft survival increases and the transplant population ages, comorbidities—particularly CV disease—accumulate. [30] In a large study by Gill et al., older age, diabetes, peripheral vascular disease, heart failure, and low serum albumin were the strongest predictors of post-graft failure mortality. [22] Other large cohorts have similarly reported high rates of hospitalization and mortality, especially in the first year [8,31,32]. However, tools for stratifying patients using frailty and comorbidity scores remain underdeveloped.

Personalizing care for patients with failed allografts has become a key recommendation in recent transplant guidelines. [21] KT recipients face unique risks due to prolonged IS and complex trajectories of CKD. In a previous work from our group that compared KT recipients with native ESKD patients, we found similar mortality rates despite KT recipients being about 10 years younger—emphasizing the complexity of their risk profile. [33]

Identifying frail patients at the point of graft failure creates opportunities to intervene early—potentially reducing infection- and CV-related deaths. It also allows tailored discussions around all available post-graft therapies, including conservative kidney management. In native CKD, patients over 80 with high comorbidity and poor functional status may have similar life expectancies, whether managed with dialysis or conservatively. [34] We found that older diabetic patients with high CCI scores had a mean survival of only 9 months after starting dialysis, underscoring the importance of considering non-dialysis options. However, none of our patients were referred for conservative care. Managing conservative care post-graft failure presents unique challenges, including ongoing IS. [19] While maintaining IS can preserve residual kidney function (RKF) and prevent graft intolerance syndrome—a subclinical inflammatory state that increases morbidity—it also raises risks of infection, malignancy, and metabolic complications. [35–37] In our cohort, continued calcineurin inhibitor (CNI) use was not associated with increased hospitalizations and was inversely correlated with hospitalization and mortality, aligning with recent meta-analyses. [38] These findings support individualized IS tapering, with low-dose steroids potentially reducing intolerance syndrome and anuria risk.

Advanced Chronic Kidney Disease Units have been established to enhance the quality of life, survival, and morbilidy in ESKD. [39] The British Transplantation Society recommends dedicated low-clearance transplant clinics offering multidisciplinary tailored care to reduce unplanned dialysis starts and promote early decision-making on dialysis, conservative care, or re-transplantation. [40,41] More recent studies show better survival rates in patients returning to dialysis, which might reflect the shift of care and the focus on ESKD post graft failure.[42,43] Considering our study results, a low-clearance clinic is being developed for KT patients.

Our study was limited by its retrospective nature and small sample size, including the small number of hospitalization and mortality events that likely affected statistical power. We also lacked data on peritoneal dialysis starts, which may influence outcomes via preserved RKF. Additionally, missing that on induction therapy and donor characteristics further limits the analysis. It is also essential to notice that the study was performed during the SarsCoV-2 pandemic, which had a generally negative impact on the care of chronic patients [44]

In conclusion, our findings highlight the importance of frailty and comorbidity in shaping outcomes after kidney graft failure. Patients with a CCI ≥8 face the highest risk of early mortality, particularly in the first-year post-failure. Early identification of at-risk individuals when eGFR declines below 20 mL/min/1.73m² can facilitate smoother transitions, better IS management, tailored symptom control, and proactive re-transplantation or conservative care planning.

1. Poggio ED, Augustine JJ, Arrigain S, Brennan DC, Schold JD. Long-term kidney transplant graft survival-Making progress when most needed. *Am J Transplant*. 2021;21(8):2824-2832. doi:10.1111/AJT.16463

2. Meier-Kriesche HU, Schold JD, Kaplan B. Long-term renal allograft survival: have we made significant progress or is it time to rethink our analytic and therapeutic strategies? *Am J Transplant*. 2004;4(8):1289-1295. doi:10.1111/J.1600-6143.2004.00515.X

3. Boenink R, Astley ME, Huijben JA, et al. The ERA Registry Annual Report 2019: summary and age comparisons. *Clin Kidney J*. 2021;15(3):452-472. doi:10.1093/CKJ/SFAB273

4. Lentine KL, Smith JM, Hart A, et al. OPTN/SRTR 2020 Annual Data Report: Kidney. *Am J Transplant*. 2022;22 Suppl 2(S2):21-136. doi:10.1111/AJT.16982

5. Huml AM, Sehgal AR. Hemodialysis Quality Metrics in the First Year Following a Failed Kidney Transplant. *Am J Nephrol*. 2019;50(3):161-167. doi:10.1159/000501605

6. Huml AM, Wakam GK, Schold JD. Does the Transplant System Fail Patients Following Kidney Allograft Loss? *American Journal of Kidney Diseases*. 2025;85(3):267-269. doi:10.1053/j.ajkd.2024.12.001

7. Kawaguchi T, Hamano T, Masakane I, et al. Association of kidney transplantation with mortality on hemodialysis after graft failure. *Journal of Nephrology 2021 34:2*. 2021;34(2):521-530. doi:10.1007/S40620-020-00929-4

8. Lam NN, Boyne DJ, Quinn RR, et al. Mortality and Morbidity in Kidney Transplant Recipients With a Failing Graft: A Matched Cohort Study. *Can J Kidney Health Dis*. 2020;7:2054358120908677. doi:10.1177/2054358120908677

9. Fishman JA, Costa SF, Alexander BD. Infection in Kidney Transplant Recipients. *Kidney Transplantation - Principles and Practice*. Published online January 1, 2019:517. doi:10.1016/B978-0-323-53186-3.00031-0

10. Gosmanova EO, Tangpricha V, Gosmanov AR. Endocrine-metabolic pathophysiologic conditions and treatment approaches after kidney transplantation. *Endocr Pract*. 2012;18(4):579-590. doi:10.4158/12016.RA

11. Agraharkar ML, Cinclair RD, Kuo YF, Daller JA, Shahinian VB. Risk of malignancy with long-term immunosuppression in renal transplant recipients. *Kidney Int*. 2004;66(1):383-389. doi:10.1111/J.1523-1755.2004.00741.X

12. Quint EE, Zogaj D, Banning LBD, et al. Frailty and Kidney Transplantation: A Systematic Review and Meta-analysis. *Transplant Direct*. 2021;7(6):E701. doi:10.1097/TXD.0000000000001156

13. Kennard AL, Rainsford S, Glasgow NJ, Talaulikar GS. Use of frailty assessment instruments in nephrology populations: a scoping review. *BMC Geriatr*. 2023;23(1). doi:10.1186/S12877-023-04101-Y

14. Roshanravan B, Robinson-Cohen C, Patel K V., et al. Association between physical performance and all-cause mortality in CKD. *J Am Soc Nephrol*. 2013;24(5):822-830. doi:10.1681/ASN.2012070702

15. 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(4):984-994. doi:10.1111/AJT.15198

16. Iyasere O, Brown EA, Johansson L, et al. Quality of life with conservative care compared with assisted peritoneal dialysis and haemodialysis. *Clin Kidney J*. 2018;12(2):262-268. doi:10.1093/CKJ/SFY059

17. Anderson RT, Cleek H, Pajouhi AS, et al. Prediction of Risk of Death for Patients Starting Dialysis: A Systematic Review and Meta-Analysis. *Clin J Am Soc Nephrol*. 2019;14(8):1213-1227. doi:10.2215/CJN.00050119

18. McAdams-Demarco MA, Law A, Salter ML, et al. Frailty as a novel predictor of mortality and hospitalization in individuals of all ages undergoing hemodialysis. *J Am Geriatr Soc*. 2013;61(6):896-901. doi:10.1111/JGS.12266

19. Murakami N, Reich AJ, Pavlakis M, Lakin JR. Conservative Kidney Management in Kidney Transplant Populations. *Semin Nephrol*. 2023;43(1). doi:10.1016/J.SEMNEPHROL.2023.151401

20. Lubetzky M, Tantisattamo E, Molnar MZ, et al. The failing kidney allograft: A review and recommendations for the care and management of a complex group of patients. *Am J Transplant*. 2021;21(9):2937-2949. doi:10.1111/AJT.16717

21. Josephson MA, Becker Y, Budde K, et al. Challenges in the management of the kidney allograft: from decline to failure: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int*. 2023;104(6):1076-1091. doi:10.1016/J.KINT.2023.05.010/ATTACHMENT/D817E860-D903-4E62-8163-A893CD93468D/MMC1.PDF

22. Gill JS, Abichandani R, Kausz AT, Pereira BJG. Mortality after kidney transplant failure: The impact of non-immunologic factors. *Kidney Int*. 2002;62(5):1875-1883. doi:10.1046/J.1523-1755.2002.00640.X

23. Leal R, Pardinhas C, Martinho A, Sá HO, Figueiredo A, Alves R. Challenges in the Management of the Patient with a Failing Kidney Graft: A Narrative Review. *J Clin Med*. 2022;11(20). doi:10.3390/jcm11206108

24. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40(5):373-383. doi:10.1016/0021-9681(87)90171-8

25. Frenkel WJ, Jongerius EJ, Mandjes-Van Uitert MJ, Van Munster BC, De Rooij SE. Validation of the Charlson Comorbidity Index in acutely hospitalized elderly adults: a prospective cohort study. *J Am Geriatr Soc*. 2014;62(2):342-346. doi:10.1111/JGS.12635

26. Sternberg SA, Schwartz AW, Karunananthan S, Bergman H, Mark Clarfield A. The identification of frailty: a systematic literature review. *J Am Geriatr Soc*. 2011;59(11):2129-2138. doi:10.1111/J.1532-5415.2011.03597.X

27. Visseren F, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. *Eur Heart J*. 2021;42(34):3227-3337. doi:10.1093/EURHEARTJ/EHAB484

28. Alfaadhel TA, Soroka SD, Kiberd BA, Landry D, Moorhouse P, Tennankore KK. Frailty and mortality in dialysis: evaluation of a clinical frailty scale. *Clin J Am Soc Nephrol*. 2015;10(5):832-840. doi:10.2215/CJN.07760814

29. Oki R, Hamasaki Y, Tsuji S, et al. Clinical frailty assessment might be associated with mortality in incident dialysis patients. *Scientific Reports 2022 12:1*. 2022;12(1):1-9. doi:10.1038/s41598-022-22483-8

30. Alfieri C, Malvica S, Cesari M, et al. Frailty in kidney transplantation: a review on its evaluation, variation and long-term impact. *Clin Kidney J*. 2022;15(11):2020-2026. doi:10.1093/CKJ/SFAC149

31. Rao PS, Schaubel DE, Jia X, Li S, Port FK, Saran R. Survival on dialysis post-kidney transplant failure: results from the Scientific Registry of Transplant Recipients. *Am J Kidney Dis*. 2007;49(2):294-300. doi:10.1053/j.ajkd.2006.11.022

32. Kabani R, Quinn RR, Palmer S, et al. Risk of death following kidney allograft failure: a systematic review and meta-analysis of cohort studies. *Nephrol Dial Transplant*. 2014;29(9):1778-1786. doi:10.1093/NDT/GFU205

33. Silva AR, Guedes Marques M, Rodrigues L, et al. Chronic kidney disease management in patients with a failing graft: a comparative study with incident non-transplant hemodialysis patients. *Ren Fail*. 2025;47(1). doi:10.1080/0886022X.2024.2447791

34. Chou A, Li KC, Brown MA. Survival of Older Patients With Advanced CKD Managed Without Dialysis: A Narrative Review. *Kidney Med*. 2022;4(5). doi:10.1016/J.XKME.2022.100447

35. del Moral Cuesta CL, Foz SG, Pereda DG, et al. Immunosuppression with calcineurin inhibitor after renal transplant failure inhibits allosensitization. *Biomedicines*. 2020;8(4). doi:10.3390/biomedicines8040072

36. Martin K, Cantwell L, Barraclough KA, et al. Prolonged immunosuppression does not improve risk of sensitization or likelihood of retransplantation after kidney transplant graft failure. *Transpl Int*. 2021;34(11):2353-2362. doi:10.1111/TRI.13998

37. Ryu H, Kim YC, Moon JJ, et al. Weaning Immunosuppressant in Patients with Failing Kidney Grafts and The Outcomes: A Single-Center Retrospective Cohort Study. *Sci Rep*. 2020;10(1). doi:10.1038/s41598-020-63266-3

38. Elgenidy A, Shemies RS, Atef M, et al. Revisiting maintenance immunosuppression in patients with renal transplant failure: early weaning of immunosuppression versus

prolonged maintenance—systematic review and meta-analysis. *J Nephrol*. 2023;36(2):537-550. doi:10.1007/s40620-022-01458-y

39. Prieto-Velasco M, del Pino y Pino MD, Buades Fuster JM, et al. Advanced Chronic Kidney Disease Units in Spain: a national survey on standards of structure, resources, results and patient safety. *Nefrologia*. 2020;40(6):608-622. doi:10.1016/J.NEFRO.2020.06.006

40. Evans RDR, Bekele S, Campbell SM, et al. Assessment of a Dedicated Transplant Low Clearance Clinic and Patient Outcomes on Dialysis After Renal Allograft Loss at 2 UK Transplant Centers. *Transplant Direct*. 2018;4(6):e352. doi:10.1097/TXD.0000000000000788

41. Arshad A, Jackson-Spence F, Sharif A. Development and evaluation of dedicated low clearance transplant clinics for patients with failing kidney transplants. *J Ren Care*. 2019;45(1):51-58. doi:10.1111/JORC.12268

42. Khairallah P, Lorenz EC, Waterman A, et al. Trends in Kidney Allograft Failure Among First-Time Transplant Recipients in the United States. *Am J Kidney Dis*. 2025;85(3). doi:10.1053/J.AJKD.2024.09.005

43. Varas J, Pérez-Saez MJ, Ramos R, et al. Returning to haemodialysis after kidney allograft failure: a survival study with propensity score matching. *Nephrology Dialysis Transplantation*. 2019;34(4):667-672. doi:10.1093/NDT/GFY215

44. Danhieux K, Buffel V, Pairon A, et al. The impact of COVID-19 on chronic care according to providers: a qualitative study among primary care practices in Belgium. *BMC Fam Pract*. 2020;21(1):1-6. doi:10.1186/S12875-020-01326-3/PEER-REVIEW

Tables and Figures

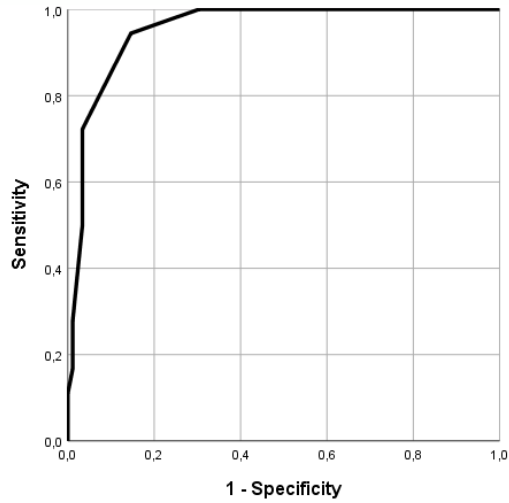**Figure 1. ROC analysis of the Charlson Comorbidity Index (CCI) in respect to mortality**

Figure 2. Kaplan-meier survival curves for patients amongst patients with a CCI≤ 7 (N=77) and ≥8 (N=30)
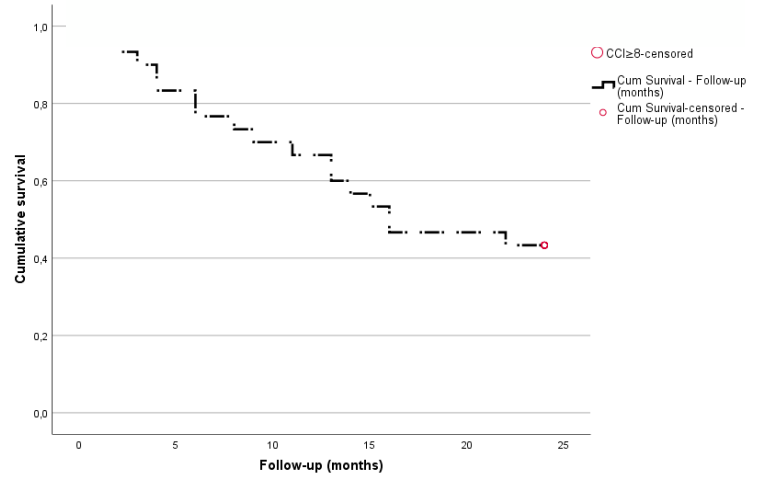
Table 1 – Demographic, clinical, and laboratory characteristics of kidney transplant recipients with graft loss.

	TOTAL N=107	Hospitalized N=40	Non-hospitalized N=67	p	Non-survivors N=18	Survivors N=89	p
Demographic data							
Age, years (mean±sd)	55.9 ± 13.3	56.7 ± 12.7	55.4 ± 13.7	0.60	64.9 ± 8.7	54.0 ± 13.5	0.001
Male (n, (%))	75 (70.1)	30 (75)	45 (67.2)	0.51	12 (66.7)	63 (70.7)	0.78
Caucasian (n, (%))	104 (97.2)	40 (100)	64 (95.5)	0.29	18 (100)	86 (96.6)	1.0
Transplant related data							
Deceased donor (n, (%))	104 (97.2)	39 (97.5)	65 (97.0)	1.0	18 (100)	86 (96.6)	1.0
ECD donor	19 (17.8)	7 (17.5)	12 (17.9)	0.95	4 (22.2)	10 (15.7)	0.51
IS before graft failure				0.911			0.716
Triple IS with antiproliperative, CNI and steroids (n, (%))	37 (35)	13 (32.5)	24 (36)		6 (33)	31 (35)	
Double IS with CNI and steroids (n, (%))	53 (49)	20 (50)	33 (49)		8 (44.4)	45 (50.5)	
IS with mTOR inhibitors (n, (%))	17 (16)	7 (17.5)	10 (15)		4 (22.2)	13 (14.6)	
Previous acute rejection (n, (%))	28 (26.2)	9 (22.5)	19 (28.3)	0.65	3 (16.7)	25 (28.1)	0.33
Comorbidities							
Hypertension (n, (%))	73 (68.2)	27 (67.5)	46 (68.7)	0.8	12 (66.7)	61 (68.6)	0.63
Heart failure (n, (%))	43 (40.2)	20 (50.0)	23 (34.3)	0.15	14 (77.8)	29 (32.9)	0.001
LVEF≤40% heart failure (n, (%))	11 (10.2)	7 (20.0)	3 (4.5)	0.06	2 (11.1)	9 (10.1)	1.0
Diabetes (n, (%))	42 (39.3)	16 (40.0)	26 (38.8)	1.0	15 (83.3)	27 (30.3)	<0.001
Insulin treated diabetes (n, (%))	27 (25.2)	10 (25.0)	17 (25.3)	1.0	11 (61.1)	16 (17.9)	0.001
Neoplasm(n, (%))	21 (19.6)	7 (17.5)	14 (20.9)	0.8	6 (33.3)	15 (16.8)	0.11
Clinical scores							
High CV risk score (n, (%))	57 (53.5)	22 (55.0)	35 (52.2)	0.84	17 (94.4)	40 (44.9)	<0.001

Clinical Frailty Scale (mean±sd)	3.3 ± 1.6	3.9 ± 1.7	2.9 ± 1.4	0.002	5.4 ± 1.1	2.9 ± 1.4	<0.001
Charlson Comorbidity Index (mean±sd)	6.2 ± 2.6	6.9 ± 2.7	5.6 ± 2.5	0.02	9.8 ± 1.9	5.4 ± 2.1	<0.001
Hospitalization (n, (%))	40 (37.4)				12 (66.7)	28 (31.5)	0.007
Graft failure scores							
Graft survival (months) (mean±SD)	133.8±934	136.5 ± 90.6	132.2 ± 95.6	0.82	117.3 ± 63.1	137.1 ± 98.3	0.28
eGFR at dialysis start, mL/min/1.73m^2 (mean±sd)	10.3±2.8	10.3 ± 2.8	10.3 ± 2.8	0.99	9.8 ± 2.7	10.5 ± 2.8	0.31
Residual diuresis (mL/day) (median (IQR))	600 (0-1200)	0 (0-750)	1000 (0-1500)	<0.0001	0 (0-600)	900 (0-1400)	<0.0001
Unplanned HD start (n, (%))	76 (71.0)	25 (62.5)	51 (76.1)	0.18	18 (100)	58 (65.1)	0.001
Urgent HD start (n, (%))	46 (43.0)	18 (45)	28 (42)	0.76	18 (100)	28 (31.4)	<0.001
Arteriovenous fistula/graft (n, (%))	56 (52.3)	15 (37.5)	41 (61.2)	0.027	5 (27.8)	51 (57.3)	0.037
Maintained CNI post graft failure (n, (%))	14 (13)	5 (12.5)	9 (13.4)	1.00	1 (6)	13 (15)	0.46
Laboratorial values							
Serum albumin (g/dL (mean±SD))	3.4±0.6	3.2 ± 0.5	3.5 ± 0.5	0.03	2.8 ± 0.4	3.5 ± 0.5	<0.001
Albumin <3,5g/dL (n, (%))	49 (45.7)	24 (60.0)	24 (35.8)	0.007	18 (100)	31 (34.8)	<0.001
Hemoglobin, g/dL (mean±SD)	9.6±0.8	9.6 ± 0.8	9.6 ± 0.8	0.77	54.0 ± 13.5	54.0 ± 13.5	0.68
Hemoglobin<10g/dL (n, (%))	79 (73.8)	29 (72.5)	50 (74.6)	0.82	12 (66.7)	67 (75.2)	0.55
iPTH, IU/mL (mean±SD)	601.9±354.1	526.0 ± 244.1	640.6 ± 395.2	0.10	555.1 ± 295.1	611.4 ± 366.1	0.54

Sd: standard deviation, IS: immunosuppression; mTOR: mammalian target of rapamycin inhibitors; LVEF: left ventricular ejection fraction; CV: cardiovascular; eGFR: estimated glomerular filtration rate; HD: hemodialysis. iPTH: intact parathormone

Table 2. Causes of hospitalization and death

Hospitalization (N=48)	
Cause	N (%)
Infection	28 (58.3)
Respiratory tract infection	13
Urinary tract infection	8
Abdominal infection	3
Central venous catheter infection	2
Other	2
Cardiovascular	14 (29.2)
Acute myocardial infarction	6
Heart failure	4
Peripheral arterial disease	2
Valvular hear disease	2
Other	6 (12.5)
Graft intolerance syndrome	4
Neoplasia	2
Mortality (N=18)	
Infection	10 (55.5)
Respiratory	6
Gastrointestinal	2
Fungal	2
Cardiovascular	5 (28)
Acute myocardial infarction	3
Sudden death	2
Other	3 (16.5)
Neoplasia	2
Unknown	1

Table 3. Multivariate regression analysis of hospitalization and mortality risk.

	Hospitalization Risk				Mortality Risk			
	OR	Sig	95%CI		HR	Sig	95%CI	
			Lower	Upper			Lower	Upper
Age	0.967	0.199	0.919	1.018	1.050	0.305	0.909	1.358
Diabetes	2.579	0.126	0.767	8.671	3.47	0.08	0.84	14.3
Heart Failure	1.339	0.646	0.386	4.644	6.177	0.409	0.082	155.531
Charlson Comorbidity Index	1.21	0.264	0.866	1.696	4.555	0.001	1.68	15.99
Clinical Frailty Scale	1.990	0.01	1.167	3.393	2.45	0.012	1.22	4.93
Hospitalization					3.785	0.459	0.019	5.996
Serum Albumin	1.42	0.50	0.51	4.00	0.635	0.745	0.085	3.156
Diuresis (mL/day)	0.999	0.010	0.998	0.999	0.994	0.030	0.989	0.999
Urgent HD	5.65	0.14	0.82	19.55	2.01	0.64	0.23	2.77
Arteriovenous fistula/graft	2.572	0.186	0.976	6.774	0.657	0.264	0.051	3.471

OR: odds ratio; Sig: significance; CI: confidence interval. Age, Charlson Comorbidy Index, Clinical Frailty Score, and diuresis were treated has continuous variables.

Supplementary material

Supplementary Table 1. Calculation of the Charlson Comorbidity Index. Table adapted from Charlson ME et al (15). AIDS: adquired immunodeficiency syndrome

Score	Comorbidity
1	Previous acute myocardial infarction Congestive heart failure Peripheral vascular disease Cerebrovascular disease Dementia Chronic pulmonary disease Connective tissue disease Peptic ulcer disease Mild liver disease (without portal hypertension) Diabetes without end-organ damage
2	Hemiplegia Moderate or severe chronic kidney disease Diabetes with end-organ damage Tumor without metastasis Leukemia Lymphoma
3	Moderate to severe liver disease
6	Metastatic solid tumor AIDS

Supplementary Table 2. Clinical Frailty Scale; adapted from Sternberg SA, et al (17).

Score	Definition
1	Very Fit: People who are robust, active, energetic, and motivated. These people commonly exercise regularly. They are among the fittest for their age.
2	Well: People who have no severe disease symptoms but are less fit than category 1. They exercise or are very active occasionally, e.g., seasonally.
3	Managing Well: People whose medical problems are well-controlled but are not regularly active beyond routine walking.
4	Living With Very Mild Frailty: Previously named "Vulnerable," While not dependent on others for daily help, symptoms often limit activities. A common complaint is being "slowed-up" and being tired during the day.
5	Living with Mild Frailty: These people usually have more evident slowing and need help in higher-order instrumental activities of daily living (IADLs) such as finance, transportation, heavy housework, and medication management. Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation, and housekeeping.
6	Living With Moderate Frailty: People need help with all outside activities and housekeeping. Inside often have problems with stairs, need help with bathing, and may need minimal assistance with dressing.
7	Living With Severe Frailty: Completely dependent for cognitive and physical personal care. However, they seem stable and not at high risk of dying (within six months).
8	Living with Very Severe Frailty: Completely dependent for personal care and approaching end of life. Typically they could not recover even from minor illnesses.
9	Terminally Ill: Approaching the end of life. This category applies to people with a life expectancy of under six months who are not otherwise living with severe frailty. (Many terminally ill people can still exercise until very close to death.)