

Abstract

Long-term outcomes of kidney transplantation

Introduction:

Kidney transplant recipients who maintain satisfactory graft function for more than 25 years after transplantation represent a rare and clinically distinct population. Evidence regarding these patients remains limited, largely owing to the small size of available cohorts and the retrospective nature of most studies, which often rely on medical records spanning several decades. Studying patients with sustained graft function beyond 25 years may help identify factors associated with long-term graft survival and function. This may improve understanding of the factors associated with long-term graft survival and function and help inform strategies to improve long-term transplantation outcomes.

Aim of the Study:

The aim of this doctoral dissertation was to assess the factors associated with the long-term outcomes of kidney transplantation, with particular emphasis on determinants of very long-term kidney graft survival.

Materials and Methods:

The dissertation is based on three scientific publications that together constitute a coherent research program.

Stage I included a cohort of 45 kidney transplant recipients with a well-functioning graft ≥ 25 years after transplantation, without a comparative group. This preliminary report focused on relationships between laboratory and perioperative parameters, particularly kidney function and hemoglobin (HGB) and serum creatinine levels at 10 years after kidney transplantation (KTx).

Stage II extended this descriptive analysis to 59 patients with exceptionally long-term graft survival. It provided a detailed description of immunosuppressive treatment and the long-term clinical course. This study also did not include a control group and focused on the characteristics of patients at such a distant time point after transplantation, addressing the limited amount of published evidence concerning this specific patient population.

Stage III was designed as a comparative study of patients with graft survival >25 years and a control group of patients who experienced early graft loss within 10 years of transplantation. The medical records of 120 kidney transplant recipients were retrospectively analyzed, including 59 patients with very long-term graft survival and 61 patients who experienced loss of graft function within a maximum of 10 years after transplantation, necessitating the reinitiation of hemodialysis. In all participants, the analyzed transplant was the first and only organ transplantation performed during the observation period. To minimize the potential impact of changes in transplantation practices over time, only patients who underwent transplantation during the same period, between 1980 and 1995, were included. The entire study population consisted of individuals of Polish nationality. This stage involved formal hypothesis testing and the use of multivariable models. It therefore differed qualitatively from the preceding descriptive studies, which justified its separate presentation.

The study was conducted in accordance with the principles of the Declaration of Helsinki and applicable legal regulations. The study protocol received a positive opinion from the Bioethics Committee of the Medical University of Warsaw (approval no. AKBE/167/2022).

Results:

The predominant cause of end-stage kidney disease among patients with exceptionally long graft survival was chronic glomerulonephritis. The vast majority of transplants were performed using organs obtained from deceased donors; only one graft was obtained from a living donor. Both recipients and donors constituted a relatively young population. The mean recipient age at transplantation was 31.6 years, while the mean donor age was 32.8 years.

During long-term follow-up, hypertension was diagnosed in 93% of patients, compared with 88% before transplantation. Disorders of glucose metabolism were relatively uncommon and affected 12% of patients after transplantation. The most frequently used and longest-maintained immunosuppressive agents were prednisone, azathioprine, and cyclosporine.

Cold ischemia time (CIT) was the strongest factor associated with long-term graft survival. CIT was shorter in patients with long-term graft function than in those who experienced graft failure requiring renal replacement therapy (1281.8 ± 473.9 vs. 1764.8 ± 564.9 min; $p = 0.016$; mean difference, 483 min). Longer CIT was associated with

a higher risk of early graft loss (per 60-minute increase: adjusted OR 1.29; 95% CI 1.02–1.63; $p = 0.032$).

Patients with good long-term graft function required anti-rejection treatment less frequently during the first year after transplantation (≥ 1 course of anti-rejection therapy: 40.7% vs. 63.9%; $p = 0.017$). This group also demonstrated more favorable early kidney function parameters, including lower serum creatinine concentrations at 6 months, 1 year, and 5 years after transplantation (all $p \leq 0.004$), as well as higher hemoglobin concentrations at 5 years ($p < 0.001$).

In an exploratory univariable landmark analysis, serum creatinine concentration at 6 months demonstrated moderate discriminatory ability for distinguishing between the two groups (AUC 0.739).

Although metabolic and cardiovascular factors were clinically relevant to the long-term care of kidney transplant recipients, they showed less prognostic importance in the analyzed model than parameters related to graft quality and early immune-mediated injury. Hypertension and other metabolic complications were common in the study population; however, when appropriately managed, they did not appear to substantially limit long-term graft function.

Conclusions:

The findings highlight the importance of the early post-transplant period, particularly the first year, in determining very long-term outcomes, including graft survival exceeding 25 years.

The results emphasize the importance of minimizing cold ischemia time, preventing immune-mediated graft injury during the first year after transplantation, and routinely monitoring early markers of kidney function, particularly serum creatinine at 6–12 months. Optimization of cardiometabolic risk factors may also contribute to improved long-term graft outcomes.

Very long-term kidney graft survival depends on a coordinated approach that combines early graft protection with consistent long-term monitoring and management of systemic factors affecting graft function.