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Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu

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Kidney Transplantation in Older Recipients: Risk Factors, Complications, and Clinical Implications. A Literature Review and Original Research

Kidney transplantation (KTx), the most effective treatment for end-stage renal disease (ESRD), is increasingly performed in older recipients. This reflects both the demographic aging of the population, and improvement in medical care, which allow to qualify patients of progressively advanced age for transplantation. Older candidates are characterized by a greater burden of comorbidities, and in selected cases, frailty, and cognitive impairment. In addition, immunosuppression may further exacerbate the age-associated decline in immune function. Those factors might influence the occurrence of early clinical and surgical complications, as well as the function and survival of the transplanted kidney. The existing literature remains inconclusive in several aspects, highlighting the need for further investigation. Moreover, there is no universally accepted definition of an "older recipient", resulting in heterogeneous age thresholds across studies.

This doctoral dissertation comprises a cycle of three publications. The aims of the studies were to: 1) evaluate recipient age as a determinant of early clinical and surgical complications, renal graft function, and short-term patient and graft survival; 2) assess the impact of early post-transplant diabetes mellitus (PTDM) in older recipients on early complications and renal graft function; 3) identify risk factors for PTDM, particularly those more relevant to older patients. An older recipient was defined as a patient aged ≥60 years, in accordance with the United Nations classification.

The first retrospective observational study included 270 kidney transplant recipients qualified between January 2021 and April 2024. Patients were divided into two groups based on age (≥60 years and <60 years) and compared in terms of early clinical and surgical complications, graft function, patient and graft survival during 12 months of follow-up.

The second retrospective observational study included 218 kidney transplant recipients from January 2021 to February 2024. In the first part, patients were stratified based on the development of PTDM and risk factors for PTDM were analyzed. In the second part, recipients

with PTDM (n=55) were stratified by age (≥60 years vs. <60 years), and the groups were compared for early clinical complications and graft function.
The final publication - literature review- summarized current evidence on outcomes of kidney transplantation in older recipients, and the most frequently observed complications. It also identified research gaps requiring further investigation.

In the first study, older recipients had a significantly higher BMI (MD = 1.77; 95% CI [0.63; 2.91], p = 0.002), a higher prevalence of diabetes mellitus (34.7% vs 11.8%, RR = 2.94; 95% CI [1.79; 4.82], p < 0.001), and more frequent cardiovascular disease (37.3% vs 7.2%, RR = 5.20; 95% CI [2.90; 9.32], p < 0.001). Older patients more often received kidneys from deceased donors (≤60 years: 94.7% vs. <60 years: 72.3%, p<0.001) and from expanded criteria donors (54.9% vs. 13.5%, RR = 4.08, CI95 [2.55; 6.51], p < 0.001). Kidneys transplanted to recipients ≥60 years had on average one point higher Remuzzi score, which corresponds to more advanced histologic changes, compared with grafts transplanted to younger patients (MD = 1.00, CI95 [0.00; 1.00], p < 0.001). Older recipients more frequently experienced surgical complications (30.7% vs 16.9%; RR = 1.81, CI95 [1.14; 2.87], p = 0.020), with vascular (14.7%) and urological (13.3%) complications being the most common; infectious complications (p=0.019), predominantly urinary tract infections, the main etiology was bacterial; cardiovascular events (18.7% vs 8.2%; RR = 2.28, CI95 [1.17; 4.43], p = 0.025), most commonly arrhythmias; and delayed graft function (DGF) (p <0.001). PTDM was more frequently diagnosed in recipients ≥60 years (p <0.001). Estimated glomerular filtration rate (eGFR) was significantly lower in the older recipients at discharge after initial hospitalization (MD = −6.50, CI95 [−13.00; −3.00], p = 0.004), and after 12 months (MD = −11.79, CI95 [−17.32; −6.25], p < 0.001); eGFR at 12 months was 45.02 ± 19.36 ml/min/1,73 m² in the older group vs. 56.81 ± 20.48 ml/min/1,73 m² in the younger group. One-year graft and patient survival were comparable between groups: 94.7% and 96.9% in older recipients vs. 97.3% and 98.5% in younger recipients. No significant differences were observed in biopsy-proven acute rejection (BPAR) (p=0.840), cytomegalovirus (CMV) replication (p=0.186), or BK virus (BKV) replication (p=0.595).
In the second publication, significant predictors of PTDM included age (OR=1.07, CI95 [1.04; 1.10], p<0.001); higher body mass index (BMI) (OR=1.15, CI95[1.07; 1.25], p<0.001); hypomagnesemia (OR=2.34, CI95[1.19; 4.57, p<0.0013); hypertriglyceridemia (OR=1.01, CI95[1.00; 1.01], p<0.001); hypercholesterolemia (OR=1.01, CI95[1.00; 1.02], p<0.001). No association was found between PTDM occurrence and induction therapy (thymoglobulin

(p=0.261) or basiliximab (p=0.825), treatment of BPAR with glycocorticoid pulses (p=0.157), or mean tacrolimus levels (p=0.885). Among patients with PTDM, no significant differences were observed between older and younger recipients in early infectious complications (p=0.188), CMV (p=0.718) or BKV replication (p=0.443), and BPAR (p=0.773). Serum creatinine levels were comparable after 6 months of follow-up (1.60 mg/dl in patients ≥60 years vs. 1.45 mg/dl in those <60 years) (p=0.137).

Kidney transplantation in recipients aged ≥60 years is a safe procedure, providing favorable short-term patient and graft outcomes. Although graft function after 12 months was statistically lower in older recipients, the values remained within clinically acceptable limits. Older recipients require careful monitoring for surgical complications. Infectious complications - also more common in this group - necessitate prompt diagnosis and management, particularly given evidence from both the literature review and our own study indicating their contribution to mortality in older transplant recipients. Due to the increased risk of cardiovascular events and PTDM, recipients aged ≥60 years require regular and targeted clinical assessments for early detection and treatment.

Research on early complications and graft function in older kidney transplant recipients serves as a foundation for future studies focusing on long-term outcomes, including graft function and patient survival.