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Przeszczepienie nerki u starszych biorców - czynniki ryzyka, powikłania i implikacje kliniczne. Przegląd literatury i badania własne

Rozprawa na stopień doktora nauk medycznych i nauk o zdrowiu

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1. Barbachowska-Kubik A, Gozdowska J, Durlik M. Kidney Transplantation in Older Recipients: One-Year Outcomes and Complications from a Single-Center Experience. J Clin Med. 2025 Sep 17;14(18):6545. doi: 10.3390/jcm14186545. PMID: 41010748; PMCID: PMC12471075

   Współczynnik oddziaływania (IF) 2,9; punktacja MNiSW 140

2. Barbachowska-Kubik AM, Gozdowska J, Kosieradzki M, Durlik M. Risk Factors for Development of Post-Transplant Diabetes Mellitus After Kidney Transplantation and Comparison Between Older and Younger Recipients in the Early Post-Transplantation Period: A Single-Center Study. Ann Transplant. 2025 Nov 4;30:e949855. doi: 10.12659/AOT.949855. PMID: 41185395; PMCID: PMC12598774

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3. Barbachowska A, Gozdowska J, Durlik M. Kidney Transplantation in Older Recipients Regarding Surgical and Clinical Complications, Outcomes, and Survival: A Literature Review. Geriatrics (Basel). 2024 Nov 20;9(6):151. doi: 10.3390/geriatrics9060151. PMID: 39584952; PMCID: PMC11587128

   Współczynnik oddziaływania (IF) 2,1; punktacja MNiSW 20

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Spis treści

1. Wykaz stosowanych skrótów

BKV - wirus BK (ang. BK polyomavirus)

BMI - wskaźnik masy ciała (ang. body mass index)

BPAR - ostre odrzucanie potwierdzone biopsyjnie (ang. biopsy-proven acute rejection)

CMV - wirus cytomegalii (ang. cytomegalovirus)

DGF - opóźniona czynność nerki przeszczepionej (ang. delayed graft function)

eGFR - szacunkowy wskaźnik filtracji kłębuszkowej (ang. estimated glomerular filtration rate)

ESRD - schyłkowa niewydolność nerek (ang. end-stage renal disease)

IGF - natychmiastowa czynność przeszczepu (ang. immediate graft function)

KTx - przeszczepienie nerki (ang. kidney transplantation)

PNF - pierwotny brak czynności przeszczepu (ang. primary non-function)

PTDM - cukrzyca potransplantacyjna (ang. post-transplant diabetes mellitus)

2. Streszczenie w języku polskim

Przeszczepienie nerki (KTx), będące jak dotąd najskuteczniejszą metodą leczenia schyłkowej niewydolności nerek (ESRD), coraz częściej dotyczy pacjentów w starszym wieku. Zjawisko to wynika zarówno ze starzenia się populacji, jak i z poprawy opieki medycznej, umożliwiającej kwalifikowanie do transplantacji osób w coraz bardziej zaawansowanym wieku. Jest to grupa pacjentów charakteryzująca się większą liczbą chorób towarzyszących, a w wybranych przypadkach zespołem kruchości i zaburzeniami poznawczymi. Ponadto, stosowana immunosupresja dodatkowo nasila fizjologiczny i postępujący wraz z wiekiem proces dysfunkcji układu immunologicznego. Powyższe czynniki mogą wpłynąć na wystąpienie wczesnych powikłań klinicznych i chirurgicznych oraz na funkcję nerki przeszczepionej i jej przeżycie. Dostępna literatura w wielu aspektach pozostaje niejednoznaczna, co budzi potrzebę prowadzenia dalszych badań w tym zakresie. Dodatkowo, jak dotąd nie ustalono jednoznacznych kryteriów określających starszego biorcę, dlatego w pracach prezentowane są różne kryteria wiekowe w zależności od przyjętej definicji.

Niniejszą rozprawę doktorską tworzy cykl trzech publikacji. Przeprowadzone badania miały na celu: 1) ocenę wieku biorcy jako istotnego czynnika determinującego wczesne powikłania kliniczne i chirurgiczne, funkcjonowanie nerki przeszczepionej oraz przeżycie pacjenta i narządu we wczesnym okresie po transplantacji; 2) wpływ cukrzycy potransplantacyjnej (PTDM) u starszych pacjentów na wystąpienie powikłań oraz na funkcję nerki we wczesnym okresie po przeszczepieniu; 3) zbadanie czynników ryzyka rozwoju PTDM, które w większym stopniu dotyczą starszych biorców i wymagają odrębnej analizy. Starszy biorca został określony jako osoba ≥60 roku życia, zgodnie z definicją Organizacji Narodów Zjednoczonych.

Do pierwszego, retrospektywnego, obserwacyjnego badania włączono 270 pacjentów, którzy zostali zakwalifikowani do przeszczepienia nerki w okresie: styczeń 2021- kwiecień 2024. Biorcy zostali podzieleni na dwie grupy w zależności od wieku (grupa ≥60 lat i grupa <60 lat), a następnie porównano ich pod kątem wczesnych powikłań klinicznych i chirurgicznych, funkcji i przeżycia nerki przeszczepionej oraz przeżycia pacjentów. Okres obserwacji wynosił 12 miesięcy.

Kolejne badanie, również retrospektywne, obserwacyjne, dotyczyło 218 pacjentów po przeszczepieniu nerki w okresie: styczeń 2021- luty 2024. W pierwszej części badania pacjentów podzielono na dwie grupy w zależności od wystąpienia PTDM, a następnie oceniono czynniki ryzyka rozwoju PTDM. W drugiej części badania spośród pacjentów z PTDM (n=55) wyłoniono dwie podgrupy w zależności od wieku (grupa osób ≥60 lat i grupa osób <60 lat), a następnie porównano je ze sobą pod kątem czynności nerki przeszczepionej oraz występowania powikłań klinicznych.

Przegląd literatury będący ostatnim z cyklu publikacji do rozprawy doktorskiej został stworzony z myślą o podsumowaniu opublikowanych dotychczas badań dotyczących wyników przeszczepienia u starszych biorców oraz najczęściej obserwowanych powikłań. Miał też na celu wskazanie obszarów, które do tej pory nie zostały dokładnie zbadane.

Wyniki pierwszej publikacji wykazały, że starsi biorcy charakteryzowali się istotnie większym BMI (MD = 1,77; CI95 [0,63; 2,91], p = 0,002), częściej występowała u nich cukrzyca (34,7% vs 11,8%, RR = 2,94; CI95 [1,79; 4,82], p < 0,001) i choroby sercowo-naczyniowe (37,3% vs 7,2%, RR = 5,20; CI95 [2,90; 9,32], p < 0,001). Starsi pacjenci częściej otrzymywali nerki od dawców zmarłych (grupa ≥60 lat: 94,7%, grupa <60 lat: 72,3%, p<0,001) i od dawców o rozszerzonych kryteriach akceptacji (54,9% vs. 13,5%, RR = 4,08; CI95 [2,55; 6,51], p < 0,001). Dodatkowo, nerki otrzymywane przez biorców ≥60 lat miały średnio o 1 punkt więcej w skali Remuzziego, co odpowiada bardziej zaawansowanym zmianom histologicznym, niż narządy przeszczepiane młodszym chorym (MD = 1,00; CI95 [0,00; 1,00], p < 0,001). U starszych pacjentów częściej występowały: powikłania chirurgiczne (30,7% vs 16,9%; RR = 1,81; CI95 [1,14; 2,87], p = 0.020), w tym przede wszystkim powikłania naczyniowe (14,7%) i urologiczne (13,3%); powikłania infekcyjne (p = *0.019*), wśród których dominowały zakażenia dróg moczowych, a główną etiologią były bakterie; zdarzenia sercowo-naczyniowe (18,7% vs 8,2%; RR = 2,28; CI95 [1,17; 4,43], p = 0,025), spośród których najczęściej występowała arytmia; oraz opóźniona czynność nerki przeszczepionej (DGF) (p < 0,001). U biorców ≥60 lat częściej rozpoznawano PTDM (p<0,001). Szacunkowy wskaźnik filtracji kłębuszkowej (eGFR) był istotnie niższy u pacjentów ≥60 lat, zarówno w dniu wypisania ze szpitala po pierwotnej hospitalizacji (MD = −6,50; CI95 [−13,00; −3,00], p = 0,004), jak i po rocznej obserwacji (MD = −11,79; CI95 [−17,32; −6,25], p < 0,001); eGFR po 12 miesiącach wynosił w grupie ≥60 lat 45,02 ± 19,36 ml/min/1,73 m² vs w grupie <60

lat 56,81 ± 20,48 ml/min/1,73 m². Roczne przeżycie przeszczepu nerkowego i pacjentów było porównywalne w obu badanych grupach. W grupie starszych biorców wynosiło odpowiednio 94,7% (przeżycie nerki przeszczepionej) i 96,9% (przeżycie pacjenta), natomiast w grupie młodszych osób odpowiednio: 97,3% i 98,5%. Nie wykazano różnicy pomiędzy grupami w zakresie występowania ostrego odrzucania potwierdzonego biopsją (BPAR) (p=0,840), replikacji wirusa cytomegalii (CMV) (p=0,186) i replikacji wirusa BK (BKV) (p=0,595).

W drugiej publikacji wykazano, że na rozwój PTDM miały istotny wpływ: wiek (OR=1,07; CI95 [1,04; 1,10], p<0,001); zwiększony wskaźnik masy ciała (BMI) (OR=1,15; CI95[1,07; 1,25], p<0.001); hipomagnezemia (OR=2,34, CI95[1,19; 4,57, p<0,0013); hipertriglicerydemia (OR=1,01; CI95[1,00; 1,01], p<0,001); hipercholesterolemia (OR=1,01; CI95[1,00; 1,02], p<0,001). Nie wykazano korelacji pomiędzy wystąpieniem PTDM, a stosowaniem indukcji przed przeszczepieniem (tymoglobulina (p=0,261) lub bazyliksymab (p=0,825)), leczeniem BPAR pulsami z glikokortykosteroidów (p=0,157) oraz średnich wartości takrolimusu we krwi w okresie obserwacji (p=0,885). Porównanie starszych i młodszych biorców z PTDM nie wykazało istotnych różnic w zakresie wczesnych powikłań infekcyjnych (p=0,188), replikacji wirusa CMV (p=0,718) i wirusa BK (p=0,443), ostrego odrzucania potwierdzonego biopsją nerki (p=0,773). Stężenie kreatyniny w surowicy pozostawało porównywalne pomiędzy grupami w obserwacji 6 miesięcznej i wynosiło odpowiednio 1,6 mg/dl w grupie ≥ 60 lat i 1,45 mg/dl u pacjentów <60 lat (*p=0,137*).

Przeszczepienie nerki u biorców w wieku ≥60 lat jest procedurą bezpieczną, zapewniającą dobre krótkoterminowe wyniki w zakresie przeżycia pacjentów i nerki. W rocznej obserwacji funkcja nerki przeszczepionej była statystycznie gorsza u starszych pacjentów, jednak wyniki te pozostawały w akceptowalnym zakresie klinicznym. Starsi biorcy powinni być uważnie monitorowani pod kątem powikłań chirurgicznych. Powikłania infekcyjne, również częściej występowały w tej grupie pacjentów. Uwzględniając wyniki własne oraz dane z przeglądu literatury, które także wskazują na powikłania infekcyjne jako główną przyczynę zgonów u starszych biorców, należy podkreślić konieczność szybkiej diagnostyki i interwencji medycznej w tej grupie chorych. Z uwagi na zwiększone ryzyko zdarzeń sercowo-naczyniowych oraz cukrzycy potransplantacyjnej, pacjenci ≥60 lat wymagają szczegółowych i regularnych badań, w celu wczesnego wykrycia i wdrożenia odpowiedniego leczenia.

Badania nad wczesnymi powikłaniami i czynnością nerki przeszczepionej u starszych biorców stanowią punkt wyjścia do dalszych badań ukierunkowanych na długoterminowe wyniki przeszczepienia, w tym funkcjonowanie nerki przeszczepionej i przeżycie pacjentów.

3. Streszczenie w języku angielskim

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.

4. Wstęp

Przeszczepienie nerki (KTx) jest jak dotąd najskuteczniejszą metodą leczenia schyłkowej niewydolności nerek (ESRD) [1]. W porównaniu do pacjentów dializowanych, przeszczepienie nerki nie tylko wydłuża przeżycie pacjentów, ale zwiększa również jakość ich życia, niezależnie od wieku [2-4]. Biorąc pod uwagę ogólny trend starzenia się społeczeństwa, w tym polskiego, szacuje się, że pomiędzy 2015 a 2050 rokiem, odsetek ludności powyżej 60 roku życia zwiększy się z 12% do aż 22% [5]. Zależność ta jest też obserwowana wśród biorców przeszczepu nerki. Wg ERA Registry Study liczba biorców powyżej 65 roku życia wzrosła z 18% w 2010 roku do aż 28% w roku 2019 [6]. Starsi pacjenci charakteryzują się przede wszystkim większą współchorobowością, ale również zespołem kruchości i często demencją, przez co stanowią grupę chorych, która wymaga kompleksowego i zindywidualizowanego podejścia. Ponadto są to chorzy, u których można spodziewać się większej liczby powikłań klinicznych, jak również chirurgicznych, a stosowana immunosupresja może wywołać dużo więcej działań niepożądanych.

W literaturze nie istnieje jedna, powszechnie akceptowana definicja wieku wyznaczającego starszego biorcę przeszczepu nerki, a w dostępnych publikacjach przedstawione są różne kryteria wiekowe. Według Organizacji Narodów Zjednoczonych starszy wiek zdefiniowany jest jako ≥60 lat [7], z kolei Centers for Disease Control podaje próg ≥65 lat [8]. W publikacjach naukowych dotyczących KTx duża część autorów przyjmuje kryterium ≥60 lat, ale pojawiają się też prace, w których granica starszego wieku zostaje przesunięta do >70 lat [9,10]. Należy przy tym podkreślić, że przewidywana długość życia biorców przeszczepu nerki >60 lat jest porównywalna z długością życia osób >75 lat w populacji ogólnej [11].

Powikłania po KTx można podzielić na chirurgiczne i kliniczne, do których należą-zaburzenia metaboliczne (w szczególności cukrzyca potransplantacyjna (PTDM)), powikłania kardiologiczne, infekcyjne (w tym reaktywacja cytomegalowirusa (CMV) i wirusa BK (BKV)) oraz ostre odrzucanie nerki potwierdzone biopsją (BPAR). Istotnym parametrem jest również czas od operacji przeszczepienia nerki (a dokładniej wytworzenia zespoleń naczyniowych) do podjęcia przez nią funkcji. Wyróżnia się natychmiastową czynność przeszczepu (IGF), opóźnione podjęcie czynności nerki

przeszczepionej (DGF) wymagające zabiegów dializy w ciągu tygodnia po operacji oraz pierwotny brak czynności nerki przeszczepionej (PNF).

Jednym z istotnych elementów różnicujących młodszych i starszych biorców jest dobór dawcy. Pacjenci w starszym wieku częściej otrzymują nerkę od dawcy zmarłego i dawcy o rozszerzonych kryteriach akceptacji [6,12,13], co potencjalnie wpływa na podjęcie czynności nerki przeszczepionej bezpośrednio po operacji, ale też na funkcjonowanie narządu w dalszej obserwacji. Literatura pozostaje w tej kwestii niejednoznaczna. W części badań nie stwierdzono różnicy w występowaniu DGF pomiędzy różnymi grupami wiekowymi [10,14,15], z kolei niektórzy autorzy obserwowali większe ryzyko DGF wśród osób starszych [14,16].

Funkcjonowanie nerki po przeszczepieniu u starszych biorców pozostaje niedostatecznie zbadane. Ziaja J. i współautorzy, w dziesięcioletniej obserwacji nie wykazali istotnych różnic w szacunkowym współczynniku przesączania kłębuszkowego (eGFR) w populacji osób >60 roku życia (eGFR po 1 roku obserwacji w grupie ≥60 lat vs <60 lat: 55,6 vs 56,9 mL/min/1,73 m2; *p*=0,41 i analogicznie po 10 latach eGFR 48,9 vs 47,6 mL/min/1,73 m2; *p*=0.12) [17]. Podobne wyniki uzyskali Skrabaka D. i współautorzy w trzymiesięcznej obserwacji [18].

Przeżycie nerki przeszczepionej jest za to dobrze opisanym zagadnieniem w pracach badawczych. W większości z nich krótkoterminowe wyniki KTx nie różnią się pomiędzy grupami wiekowymi [10,19,20]. W długoterminowych obserwacjach występuje gorsze ogólne przeżycie przeszczepu u starszych biorców, co jest głównie związane ze zwiększoną liczbą zgonów z funkcjonującym przeszczepem [10,19,20]. Co istotne, niezależne badania nie wykazały różnicy w zakresie przeżycia nerki przeszczepionej z cenzurowaniem zgonów (death-censored graft survival) [9,21,22].

Przeżywalność starszych pacjentów po KTx zmienia się wraz z długością obserwacji, co jest związane z długością oczekiwanych lat życia. Ziaja J. i współautorzy wykazali, że w pierwszym roku po KTx odsetek przeżycia starszych pacjentów nie różni się istotnie w porównaniu z młodszymi biorcami (pacjenci ≥60 roku życia – 93% vs pacjenci <60 lat – 96,2%; *p*=0,200), jednak w dziesięcioletniej obserwacji przeżycie starszych biorców istotnie zmniejszyło się (pacjenci ≥60 roku życia - 69,5% vs pacjenci <60 lat - 82,2%; *p*=0.01) [17]. Podobne wnioski zostały opisane w innych publikacjach [8,14,18,21].

Powikłania chirurgiczne po KTx pozostają bardzo istotnym zagadnieniem, mogącym wydłużyć pierwszą hospitalizację oraz wpłynąć na długoterminowe funkcjonowanie nerki przeszczepionej. Zagadnienie to nie zostało jak dotąd szerzej opisane w literaturze, jednak część publikacji wskazuje na wyższy wskaźnik powikłań wśród starszych pacjentów [14,23]. Brak jest również jednoznacznych badań opisujących poszczególne typy powikłań chirurgicznych (urologiczne, naczyniowe oraz związane z gojeniem rany pooperacyjnej). Na uwagę zasługuje praca Hernandeza D. i współautorów, w której wykazano korelację między starszym wiekiem a ryzykiem wystąpienia nieszczelności moczowodowo-pęcherzowej [24].

Powikłania infekcyjne stanowią, obok chorób sercowo-naczyniowych i nowotworów, jedną z głównych przyczyn zgonów pacjentów po KTx [10,18,25]. Wraz z wiekiem dochodzi do stopniowego osłabienia odpowiedzi immunologicznej (immunosenescencji), dlatego infekcje wśród starszych biorców stanowią groźną, potencjalnie śmiertelną grupę powikłań. Dotyczy to szczególnie pierwszego roku po KTx kiedy dawki stosowanej immunosupresji są największe [26]. Wśród głównych przyczyn infekcji wymieniane są bakterie, natomiast najczęstszym miejscem zakażenia są drogi moczowe [27,28]. Ważnym aspektem pozostaje wpływ infekcji na wydłużenie i potrzebę ponownych hospitalizacji oraz potencjalny wpływ na funkcjonowanie nerki przeszczepionej. Kolejnym elementem wchodzącym w skład powikłań infekcyjnych są infekcje CMV i BKV. Zarówno w przypadku CMV, jak i BKV sugerowano związek między starszym wiekiem i większym ryzykiem reaktywacji zakażenia [21,29], jednak dane w tym zakresie pozostają niejednoznaczne i wymagają dalszych badań.

Ostre odrzucanie przeszczepionej nerki pozostaje istotnym powikłaniem klinicznym. Potencjalny wpływ na jego pojawienie się może mieć wspomniana wcześniej immunosenescencja, jak również stosowanie indukcji w postaci tymoglobuliny czy basiliximabu przed operacją przeszczepienia nerki. Badania porównujące obecność BPAR pomiędzy młodszymi i starszymi pacjentami pozostają jednak niejednoznaczne. Doucet B. i współautorzy wskazują na rzadsze występowanie BPAR w grupie starszych biorców nerki przeszczepionej od żywego dawcy [10], z kolei w inne badania nie wykazały takiej zależności [14,25,30].

Cukrzyca potransplantacyjna (PTDM) stanowi jedno z najczęstszych powikłań metabolicznych po KTx. Odsetek jej występowania jest zróżnicowany i waha się od 4% do 25% [31], chociaż raportowano też wartości sięgające 40% [32]. Ponieważ wiek jest jednym z niemodyfikowalnych czynników ryzyka wystąpienia zarówno cukrzycy typu II

jak i PTDM, można oczekiwać, że powikłanie to będzie częściej występować wśród starszych biorców przeszczepu. Dostępne publikacje potwierdzają powyższe przypuszczenie [21,33]. Brakuje jednak badań porównujących starszą i młodszą grupę pacjentów z PTDM, szczególnie pod kątem funkcjonowania przeszczepionej nerki oraz współwystępowania innych powikłań po KTx takich jak obecność replikacji wirusa CMV i BKV.

Powikłania kardiologiczne, będące jedną z wiodących przyczyn zgonów po KTx [10,18,25], stanowią bardzo ważną grupę powikłań. Wiek jest udowodnionym czynnikiem ryzyka wystąpienia chorób sercowo-naczyniowych [34], przez co starsi biorcy są szczególnie narażeni na ich wystąpienie. Kolejnymi opisywanymi czynnikami ryzyka wśród pacjentów po KTx są płeć męska i aktywne palenie papierosów [35]. Dodatkowo wykazano, że pacjenci po KTx od żywego dawcy mieli mniejsze ryzyko powikłań kardiologicznych w porównaniu z pacjentami po KTx od dawcy zmarłego [35]. W dostępnej literaturze powikłania kardiologiczne są zazwyczaj ujęte jako całość i brakuje publikacji opisujących występowanie poszczególnych rodzajów powikłań, dlatego konieczne są dalsze badania w tym kierunku.

Przedstawiony cykl publikacji koncentruje się na powikłaniach klinicznych i chirurgicznych oraz na wynikach przeszczepienia nerki u starszych pacjentów we wczesnym okresie po KTx. Dwa pierwsze artykuły dotyczą pacjentów po KTx hospitalizowanych w Klinice Transplantologii, Immunologii, Nefrologii i Chorób Wewnętrznych Warszawskiego Uniwersytetu Medycznego.

W pierwszej publikacji (Barbachowska-Kubik A, Gozdowska J, Durlik M. Kidney Transplantation in Older Recipients: One-Year Outcomes and Complications from a Single-Center Experience. J Clin Med. 2025 Sep 17;14(18):6545. doi: 10.3390/jcm14186545. PMID: 41010748; PMCID: PMC12471075) porównano wyniki przeszczepienia nerki u pacjentów $\geq$60 roku życia z pacjentami poniżej 60 roku życia, ze szczególnym uwzględnieniem powikłań klinicznych, chirurgicznych, przeżycia i funkcji nerki przeszczepionej oraz przeżycia pacjentów.

Kolejna publikacja (Barbachowska-Kubik AM, Gozdowska J, Kosieradzki M, Durlik M. Risk Factors for Development of Post-Transplant Diabetes Mellitus After Kidney Transplantation and Comparison Between Older and Younger Recipients in the Early Post-Transplantation Period: A Single-Center Study. Ann Transplant. 2025 Nov 4;30:e949855. doi: 10.12659/AOT.949855. PMID: 41185395) przedstawia wyniki

analizy czynników ryzyka związanych z wystąpieniem potransplantacyjnej cukrzycy (PTDM) oraz porównuje ze sobą dwie grupy pacjentów z PTDM (pacjenci ≥60 roku życia z pacjentami <60 roku życia).

Ostatnia publikacja (Barbachowska A, Gozdowska J, Durlik M. Kidney Transplantation in Older Recipients Regarding Surgical and Clinical Complications, Outcomes, and Survival: A Literature Review. Geriatrics (Basel). 2024 Nov 20;9(6):151. doi: 10.3390/geriatrics9060151. PMID: 39584952; PMCID: PMC11587128) stanowi przegląd literatury opisujący wyniki dotychczas przeprowadzonych i opublikowanych badań w zakresie powikłań klinicznych i chirurgicznych u starszych biorców po KTx.

5. Założenia i cel pracy

Rosnąca liczba starszych biorców wynika ze starzenia się populacji oraz wzrostu liczby pacjentów w podeszłym wieku kwalifikowanych do przeszczepienia nerki. Jest to grupa charakteryzująca się większym obciążeniem chorobami współistniejącymi, co może mieć wpływ na wczesne powikłania oraz wyniki przeszczepienia. W dostępnej literaturze wyniki transplantacji u pacjentów w podeszłym wieku pozostają niejednoznaczne, szczególnie w zakresie wczesnych powikłań oraz czynników determinujących funkcję przeszczepu.

W związku z tym założenia pracy były następujące:

1. Wiek biorcy stanowi istotny czynnik determinujący wczesne powikłania kliniczne i chirurgiczne, funkcjonowanie nerki przeszczepionej, przeżycie pacjenta i narządu we wczesnym okresie po transplantacji.
2. Cukrzyca potransplantacyjna (PTDM) u starszych pacjentów wpływa na obecność powikłań oraz funkcję nerki we wczesnym okresie po przeszczepieniu.
3. Czynniki ryzyka rozwoju PTDM w większym stopniu dotyczą starszych biorców i wymagają odrębnej analizy.
4. Za starszego biorcę przyjęto pacjenta w wieku ≥60 lat, zgodnie z definicją stosowaną przez Organizację Narodów Zjednoczonych.

Cele pracy:

1. Ocena bezpieczeństwa występowania wczesnych powikłań klinicznych i chirurgicznych oraz funkcji nerki przeszczepionej, a także przeżycia pacjenta i narządu w rocznej obserwacji po transplantacji.
2. Identyfikacja czynników ryzyka rozwoju PTDM we wczesnym okresie po przeszczepieniu nerki.
3. Porównanie starszych biorców z PTDM z młodszymi pacjentami pod względem występowania powikłań klinicznych oraz wczesnej funkcji nerki przeszczepionej w 6-miesięcznym okresie po transplantacji.

6. Kopie opublikowanych prac

1. Barbachowska-Kubik A, Gozdowska J, Durlik M. Kidney Transplantation in Older Recipients: One-Year Outcomes and Complications from a Single-Center Experience. J Clin Med. 2025 Sep 17;14(18):6545. doi: 10.3390/jcm14186545. PMID: 41010748; PMCID: PMC12471075

2. Barbachowska-Kubik AM, Gozdowska J, Kosieradzki M, Durlik M. Risk Factors for Development of Post-Transplant Diabetes Mellitus After Kidney Transplantation and Comparison Between Older and Younger Recipients in the Early Post-Transplantation Period: A Single-Center Study. Ann Transplant. 2025 Nov 4;30:e949855. doi: 10.12659/AOT.949855. PMID: 41185395; PMCID: PMC12598774

3. Barbachowska A, Gozdowska J, Durlik M. Kidney Transplantation in Older Recipients Regarding Surgical and Clinical Complications, Outcomes, and Survival: A Literature Review. Geriatrics (Basel). 2024 Nov 20;9(6):151. doi: 10.3390/geriatrics9060151. PMID: 39584952; PMCID: PMC11587128

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Kidney Transplantation in Older Recipients: One-Year Outcomes and Complications from a Single-Center Experience

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Abstract

Background/Objectives: Each year, the number of kidney transplants (KT) performed in older recipients continues to rise. The process of aging may impact early post-transplant outcomes. The aim of this study was to analyze one-year outcomes, clinical and surgical complications, as well as patient and graft survival in senior recipients. **Methods**: This retrospective, observational study included a total of 270 participants who underwent KT during the period between January 2021 and April 2024. Recipients were divided into two groups: the older group (≥60 years; n = 75) and the younger group (<60 years; n = 195) and then analyzed during a one-year follow-up period. **Results**: Older recipients were characterized by a higher body mass index (MD = 1.77, CI95 [0.63; 2.91], $p = 0.002$), suffered more often from diabetes mellitus (RR = 2.94, CI95 [1.79; 4.82], $p < 0.001$), cardiovascular diseases (RR = 5.20, CI95 [2.90; 9.32], $p < 0.001$) and were more likely to receive a kidney from older (MD = 12.37, CI95 [8.94; 15.80], $p < 0.001$) deceased ($p < 0.001$) donors. Senior patients had more infections ($p = 0.019$) and surgical complications (RR = 1.81, CI95 [1.14; 2.87], $p = 0.020$), more cardiac events (RR = 2.28, CI95 [1.17; 4.43], $p = 0.025$), and a higher incidence of delayed graft function ($p < 0.001$) compared to younger patients. The estimated glomerular filtration rate (eGFR) was significantly lower in the older group both at initial hospital discharge (MD = −6.50, CI95 [−13.00; −3.00], $p = 0.004$) and at one-year follow-up (MD = −11.79, CI95 [−17.32; −6.25], $p < 0.001$). No differences were observed in the incidence of biopsy-proven acute rejection, cytomegalovirus replication, and polyomavirus replication. One-year patient and graft survival was 97.3% and 94.7% in the older group, and 98.5% and 96.9% in the younger group, respectively. **Conclusions**: Kidney transplantation in older recipients is safe in the short term. Although eGFR was lower in the older group, it remained within an acceptable range.

Keywords: clinical complications; graft survival; kidney transplantation; older kidney recipients; patient survival; surgical complications

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1. Introduction

Kidney transplantation (KT) remains the most effective treatment of end-stage kidney disease (ESKD) [1]. Moreover, compared to patients on dialysis, kidney transplant recipients have a longer expected lifespan across all age groups [2].

Although the percentage of kidney transplants is still the highest among younger patients (15% in the 20–44-year age group vs. 4% in the 65–74-year age group), each year the number of kidney transplants in older recipients is growing [2,3]. One of the reasons for that is the aging of the population. According to the World Health Organization (WHO),

by 2050, 22% of the world's population will be over 60 years of age [4]. The aging process affects most organs and systems. Additionally, older individuals often present with multiple comorbidities—such as diabetes mellitus (DM), cardiovascular diseases (CVD), and frailty- all of which may reflect on early post-kidney transplant surgical and clinical complications, as well as patient and graft-survival. Therefore, the older kidney transplant recipients may require a distinct clinical approach that takes these variables into account. Previous studies present inconclusive findings, especially regarding surgical complications and biopsy-proven acute rejection. Moreover, several aspects (for instance, cardiac complications, presence of cytomegalovirus replication, or polyomavirus replication) need further investigation. This single-center study aimed to analyze early (one-year) post-transplant outcomes, clinical and surgical complications, as well as patient and graft survival in senior patients.

2. Materials and Methods

2.1. Study Population

In this retrospective observational study, we analyzed patients who underwent kidney transplantation at Infant Jesus Clinical Hospital, Warsaw, Poland, during the period between January 2021 and April 2024. A total of 405 kidney transplant procedures (KTs) were performed. Patients who were ≥18 years of age received a first, single-organ kidney transplant, and had no prior history of transplantation were included in further research. The exclusion criteria included multi-organ transplantation, KT following another non-kidney solid organ transplant, and transfer to a different center during the follow-up period, which resulted from the nationwide mandatory organ allocation framework for kidney transplantation. The study included 270 patients. Participants were divided into two groups according to age (older recipients ≥60 years, n = 75; younger recipients <60 years, n = 195) and then compared. All information was accessed through medical records and laboratory test results. The selection process of the study cohort is outlined in the STROBE flow diagram (Figure 1).

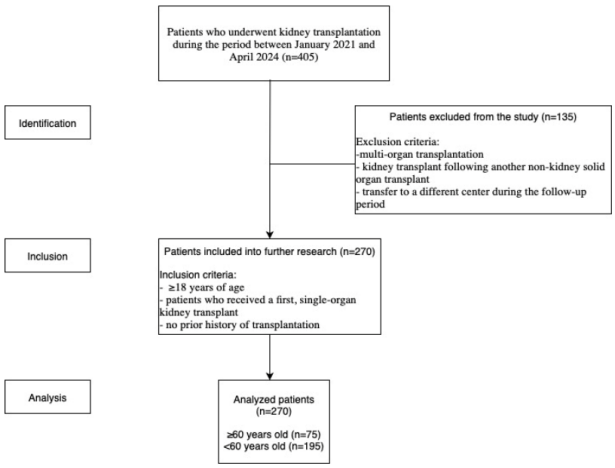

Figure 1. STROBE Flow Chart of Patient Inclusion and Exclusion Criteria during 12-month observational period.

Our data included demographics, cause of ESKD, type of dialysis (if applicable), duration of dialysis, comorbidities at the time of transplantation, and type of immunosuppressive regimens. Donor-related data such as age, sex, body mass index (BMI), comorbidities (diabetes mellitus, hypertension, cardiovascular diseases), donor type (living or deceased), as well as panel reactive antibody (PRA), human leukocyte antigen (HLA) mismatches, and Remuzzi score in zero-time kidney biopsy were also considered in the analysis.

Outcome variables included surgical complications, clinical complications such as newly diagnosed post-transplant diabetes mellitus, biopsy-proven acute rejection (BPAR), infection that occurred during the initial hospitalization, infections which required hospitalization during the follow-up period, cardiac events, cytomegalovirus replication, and polyomavirus replication, length of initial hospitalization, number of hospitalizations during the follow-up period, patient and graft survival and post-transplant graft function.

The follow-up period was 12 months. The study was conducted in full accordance with the principles of the Declaration of Helsinki and the Declaration of Istanbul.

2.2. Definitions

Older patients were defined as those aged ≥60 years, based on the United Nations definition [5].

An expanded criteria donor was defined as a deceased donor aged over 60 years, or a donor aged over 50 years with at least two of the following: hypertension, serum creatinine ≥ 0.133 mmol/L, or death due to stroke. The Remuzzi score was calculated by the addition of four different parameters: glomerular global sclerosis (0–3), tubular atrophy (0–3), interstitial fibrosis (0–3), arterial and arteriolar narrowing (0–3). It was included in the analysis to assess graft quality at the time of transplantation, as well as to evaluate the extent of chronic histological injury, which could influence graft function. Infection was diagnosed based on positive cultures and laboratory findings, caused by bacterial, viral, or fungal pathogens. Throughout the follow-up period, during both the initial hospitalization and any subsequent infection-related hospitalizations, the site of infection (e.g., urinary tract, wound, pneumonia, or sepsis of unknown origin) and the specific pathogen (bacteria, virus, fungus, or unidentified) were identified. Polyomavirus replication was determined in serum samples. Both polyomavirus replication and cytomegalovirus replication were monitored in the third month post-transplant, and subsequently every 3 to 6 months or in the presence of symptoms suggestive of viremia. The diagnosis of BPAR was made based on histological findings obtained during the protocol biopsy at 3 months post-transplant or when acute rejection was clinically suspected. Graft function was assessed based on the: primary non-function (PNF), presence of delayed graft function (DGF) and immediate graft function (IGF), as well as serum creatinine (sCr) and estimated glomerular filtration rate (eGFR), both measured at the end of initial hospitalization and after 12 months. Surgical complications, defined as postoperative events directly related to the surgical procedure that required surgical intervention, were divided into 3 subgroups: vascular (which included renal graft vessel thrombosis, renal graft vessel stenosis; iliac artery dissection, iliac artery thrombosis and iliac artery pseudoaneurysm), urological (urinal leakage, ureteral obstruction, lymphocele) and those related to surgical wound healing (wound dehiscence, wound infection, wound prolonged healing). Delayed graft function (DGF) was defined as the need for dialysis within the first week after KT. Immediate graft function (IGF) was defined as a functioning allograft immediately post-transplant, characterized by the appearance of diuresis, a progressive decrease in serum creatinine and no requirement for dialysis within the first 7 days. Primary non- function (PNF) was defined as the complete absence of graft function following transplantation, with the patient remaining dialysis-dependent. Post-transplant diabetes mellitus (PTDM) was

diagnosed based on the 2013 International Consensus Meeting on Post-transplant Diabetes Mellitus and included fasting glucose > 7 mmol/L on more than one occasion or random glucose > 11.1 mmol/L with symptoms or 2-h glucose after a 75-g OGTT of >11.1 mmol/L or hemoglobin A1c (HbA1c) ≥ 6.5% [6]. Cardiac events, defined as clinically significant cardiovascular complications occurring within 12 months after transplantation, included myocardial infarction, ischemic heart disease, new-onset congestive heart failure, and arrhythmia. The standard immunosuppressive regimen consisted of a calcineurin inhibitor (tacrolimus or cyclosporine), mycophenolate mofetil (MMF), and corticosteroids. The choice of induction therapy depended on the patient's immunological risk and comorbidities: no induction was used in low-risk recipients, basiliximab in those with intermediate risk, and thymoglobulin (ATG) in high-risk recipients. Immunosuppressive treatment was not modified based on recipient age.

2.3. Statistical Analysis

Continuous variables were summarized as mean ± standard deviation (SD) or median and interquartile range (IQR), depending on normality. Categorical variables were presented as n (%). Normality was evaluated with the Shapiro-Wilk test, along with assessments of skewness and kurtosis. Levene's test was applied to assess homogeneity of variances. Comparisons between age groups were made with Student's *t*-test, Welch *t*-test, Mann-Whitney U test, Pearson's chi-square test or Fisher's exact test, as appropriate. Mean/median difference (MD) was used to measure the difference between age groups in case of continuous variables and relative risk (RR) was used to measure the difference in case of proportions, both MD and RR were presented with 95% confidence intervals (CI). Alpha of 0.05 was used for statistical significance. All analyses were performed using R software (R4.4.2).

3. Results

3.1. Demographics

Of the 405 KT procedures, 270 patients met the inclusion criteria and were included in the final analysis. Recipients were divided into two groups based on their age: the older group (≥60 years) and the younger group (<60 years). The older group consisted of 75 patients (28%; 29 females (38.7%) and 46 males (61.3%)) with the mean age of 65 years, while the younger group was represented by 195 patients (72%; 80 females (41%) and 115 males (59%)), with a mean age of 41 years. Recipients in the older group had a significantly higher body mass index (BMI) (MD = 1.77, CI95 [0.63; 2.91], $p = 0.002$), more often suffered from diabetes mellitus (DM) (34.7% vs. 11.8%, RR = 2.94, CI95 [1.79; 4.82], $p < 0.001$) and cardiovascular diseases (37.3% vs. 7.2%, RR = 5.20, CI95 [2.90; 9.32], $p < 0.001$). The etiology of end-stage kidney disease (ESKD) differed between the groups, $p < 0.001$. Diabetes mellitus (DM), autosomal dominant polycystic kidney disease (ADPKD), hypertension (HT) and undetermined causes were more frequent among patients ≥60 years compared to patients <60 years (DM: 17.3% vs. 9.2%, ADPKD: 16.0% vs. 13.3%, HT: 8.0% vs. 4.1%, undetermined:25.3 vs. 7.7%). Chronic glomerulonephritis was the main cause of ESKD among patients <60 years.

All patients received a standard immunosuppression protocol consisting of steroids, calcineurin inhibitors (CNI), and mycophenolate acid. Induction immunosuppression was used more frequently in younger recipients compared to the older ones ($p = 0.014$). Sixty-one patients (22.5%) received thymoglobulin (ATG) induction therapy, 10.6% from the older group (8 recipients) and 27.1% from the younger group (53 recipients). Thirty patients (11%) received basiliximab prior to transplantation, 12% from the older group (9 recipients) and 10.7% from the younger group (21 patients).

3.2. Clinical Complications

Table 2 presents a comparison of post-transplant outcomes and complications between the two groups. The Remuzzi score was higher by 1.00 among patients aged ≥60 years (MD = 1.00, CI95 [0.00; 1.00], $p < 0.001$). The mean Remuzzi score was 2.53 in the older group and 1.47 in the younger group. The first hospitalization was longer by 5 days on average among patients ≥60 years (MD = 5.00, CI95 [2.00; 6.00], $p < 0.001$). The older group had a higher infection rate in the early postoperative period compared to the younger group; however, the p-value of 0.057 does not meet the standard criterion for statistical significance ($p < 0.05$), though it suggests a marginal or borderline effect. The most common site of infection in both groups was the urinary tract. Patients aged ≥60 years had more hospitalizations within 12 months compared to patients <60 years (MD = 1.00, CI95 [0.00; 1.00], $p = 0.002$). Moreover, the proportion of patients hospitalized due to infection was 65% higher among patients ≥60 years compared to patients < 60 years (34.7% vs. 21.0%, RR = 1.65, CI95 [1.09; 2.49], $p = 0.030$). Bacteria were the most common cause of infection, and the urinary tract was the main site of the infection in both groups. A significant difference was confirmed for PTDM occurrence, $p < 0.001$. PTDM was more common in the group ≥60 years compared to the group <60 years (PTDM: 29.3% vs. 20.5%). Cardiac events were twice as common among patients ≥60 years compared to patients <60 years (18.7% vs. 8.2%, RR = 2.28, CI95 [1.17; 4.43], $p = 0.025$). Arrhythmia was the most common cardiac complication in both groups. No statistically significant differences were found in terms of cytomegalovirus (CMV) and polyomavirus (BKV) replication, as well as biopsy proven acute rejection (BPAR).

Table 2. Comparison of post-transplantation outcomes and complications between groups.

Variable	Patients <60 years	Patients ≥60 years	MD/RR (95% CI)	*p*
No of hospitalizations within 12 months	1.00 (0.00;2.00)	2.00 (1.00;3.00)	1.00 (0.00;1.00)	0.002
Proportion of patients hospitalized due to infection within 12 months	41 (21.0)	26 (34.7)	1.65 (1.09;2.49)	0.030
Bacterial	32 (16.4)	20 (26.7)	1.62 (0.99;2.66)	0.082
Viral	6 (3.1)	4 (5.3)	1.73 (0.50;5.97)	0.472
Not identified	8 (4.1)	9 (12.0)	2.92 (1.17;7.30)	0.035
Fungal	3 (1.5)	1 (1.3)	0.87 (0.09;8.20)	>0.999
Infection-related hospitalizations (per patient/year) *	0.00 (0.00;0.00)	0.00 (0.00;1.00)	0.00 (0.00;0.00)	0.019
Surgical complication	33 (16.9)	23 (30.7)	1.81 (1.14;2.87)	0.020
Vascular	13 (6.7)	11 (14.7)	2.20 (1.03;4.69)	0.067
Urological	15 (7.7)	10 (13.3)	1.73 (0.82;3.69)	0.231
Wound	9 (4.6)	4 (5.3)	1.16 (0.37;3.64)	0.759
Graft function				
Immediate Graft Function (IGF)	128 (65.6)	29 (38.7)	-	<0.001
Delayed graft function (DGF)	65 (33.3)	43 (57.3)		
Primary non-function (PNF)	2 (1.0)	3 (4.0)		
DGF length, days	4.00 (2.00;7.00)	4.00 (3.00;6.50)	0.00 (−1.00;1.00)	0.693
BPAR	43 (22.1)	15 (20.0)	0.91 (0.54;1.53)	0.840
PTDM	40 (20.5)	22 (29.3)	-	<0.001
no DM after Tx	132 (67.7)	28 (37.3)		
Cardiac events	16 (8.2)	14 (18.7)	2.28 (1.17;4.43)	0.025
Arrhythmia	10 (5.1)	8 (10.7)	2.08 (0.85;5.07)	0.173
MI	3 (1.5)	3 (4.0)	2.60 (0.54;12.60)	0.353
New onset HF	4 (2.1)	3 (4.0)	1.95 (0.45;8.51)	0.401

Table 2. *Cont.*

Variable	Patients <60 years	Patients ≥60 years	MD/RR (95% CI)	*p*
CMV replication	36 (18.5)	20 (26.7)	1.44 (0.90;2.33)	0.186
BKV replication	27 (13.8)	13 (17.3)	1.25 (0.68;2.29)	0.595
Remuzzi score [0–12]	1.00 (0.00;2.00)	2.00 (1.00;3.00)	1.00 (0.00;1.00)	<0.001
Remuzzi score (mean)	1.47	2.53	-	-
sCr at 12 months follow-up	1.40 (1.10;1.77)	1.55 (1.10;2.00)	0.15 (−0.04;0.25)	0.165
eGFR at 12 months follow-up	56.81 ± 20.48	45.02 ± 19.36	−11.79 (−17.32;−6.25)	<0.001
Patient's death within 12 months	3 (1.5)	2 (2.7)	1.73 (0.30;10.17)	0.620
Patient's 12 months survival	192 (98.5)	73 (97.3)	0.99 (0.95;1.03)	0.620
Graft 12 months survival	189 (96.9)	71 (94.7)	0.98 (0.92;1.04)	0.472
Characteristics regarding initial hospitalization				
Length of initial hospitalization, days	14.00 (10.00;21.00)	19.00 (13.00;27.00)	5.00 (2.00;6.00)	<0.001
sCr at discharge	1.61 (1.29;2.15)	1.68 (1.30;2.20)	0.06 (−0.10;0.21)	0.520
eGFR at discharge	46.00 (33.00;62.25)	39.50 (25.50;56.25)	−6.50 (−13.00;−3.00)	0.004
Infection during 1st hospitalization	60 (30.8)	33 (44.0)	1.43 (1.03;1.99)	0.057
Urinary tract infection	41 (21.0)	26 (34.7)	1.65 (1.09;2.49)	0.030
Wound infection (during	1 (0.5)	2 (2.7)	5.20 (0.48;56.50)	0.188
Other	19 (9.7)	6 (8.0)	0.82 (0.34;1.98)	0.835

BKV—BK polyomavirus, BPAR—biopsy-proven acute rejection, CI—confidence interval, CMV—cytomegalovirus, DGF—delayed graft function, DM—diabetes mellitus, eGFR—estimated glomerular filtration rate, IGF—immediate graft function, MD—mean or median difference (≥60 years vs. <60 years), No—number, PNF—primary non-function, PTDM—post-transplant diabetes mellitus, RR—relative risk (≥60 years vs. <60 years), sCr—serum creatinine, Tx—transplantation. Data presented as mean ± SD or median (IQR) in case of numeric variables, depending on distribution and n (%) in case of categorical variables. Groups compared with t-Student test, Mann-Whitney U test, Pearson's chi-square test or Fisher's exact test, as appropriate. * Infection-related hospitalizations are shown as mean events per patient/year. Values reported as "0.00" indicate mean values < 0.01 after rounding.

3.3. Surgical Complications

The proportion of surgical complications was higher among the older group (30.7% vs. 16.9%, RR = 1.81, CI95 [1.14; 2.87], $p = 0.020$). The two main complications were vascular (14.7% in the older group vs. 6.7% in the younger group) and urological (13.3% in the older group vs. 7.7% in the younger group).

3.4. Graft Function

A significant difference between groups was confirmed for graft function, $p < 0.001$. Primary non-function (PNF) was observed in three patients aged ≥60 years and two patients aged <60 years. Immediate graft function was less frequent in the ≥60 group compared to <60 group (38.7% vs. 65.6%), consequently delayed graft function was more frequent in the ≥60 group (57.3% vs. 33.3%). There was no statistical difference in the duration of DGF. The estimated glomerular filtration rate (eGFR) at hospital discharge after KT was lower among patients ≥60 years compared to patients <60 years (MD = −6.50, CI95 [−13.00; −3.00], $p = 0.004$). Similarly, eGFR at 12 months follow-up was lower in the older group (MD = −11.79, CI95 [−17.32; −6.25], $p < 0.001$). Figure 2 presents the distribution of serum creatinine (sCr) and eGFR at both discharge and 12 months post-transplantation, split by age group (<60 years and ≥60 years).

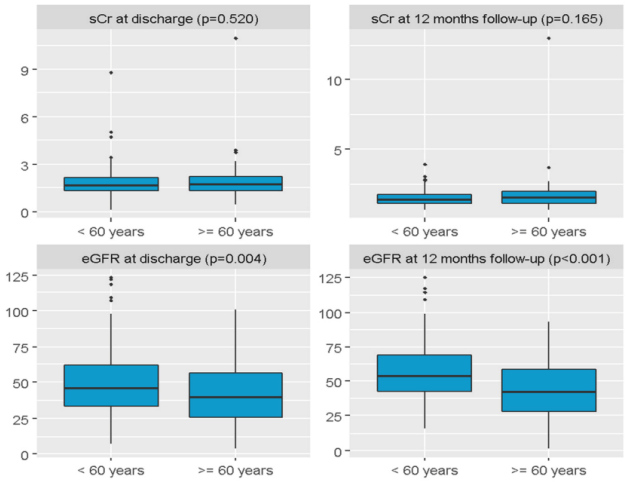

Figure 2. Boxplot charts presenting distribution of serum creatinine and estimated glomerular filtration rate at both discharge and 12 months after the transplantation in split to patients < 60 years and patients ≥ 60 years. sCr—serum creatinine; eGFR—estimated glomerular filtration rate (mL/min/1.73 m^2).

3.5. Survival Analysis

One-year patient and graft survival rates were comparable between the two groups (one-year patient survival: RR 0.99, 95% CI: [0.95–1.03]; $p = 0.62$; one-year graft survival: RR 0.98, 92% CI: [0.92–1.03]; $p = 0.472$). One-year patient survival was 97.3% in the older group and 98.5% in the younger group. One-year graft survival in patients ≥60 years of age was 94.7% and 96.9% in patients <60 years.

4. Discussion

This single-center retrospective study aimed to evaluate one-year outcomes, as well as clinical and surgical complications, in older kidney transplant recipients in comparison to younger patients. Numerous differences were found between the groups; however, our main findings indicate that kidney transplantation in older recipients is relatively safe and beneficial in the short-term perspective.

Among baseline characteristics of the patients, donor age was significantly higher in older recipients compared to younger ones, in both LDKT and DDKT groups. Expanded-criteria donors were also more often allocated to patients ≥60 years of age. Moreover, it was reflected in the Remuzzi score which was higher by 1.00 point compared to patients <60 years of age. This presents the tendency to allocate marginal donors, such as older individuals, to older KT recipients [7,8].

Since age is a well-known risk factor not only for type 2 diabetes mellitus in the general population, but also for post-transplant diabetes mellitus, it is not surprising that this correlation was also found in our study. PTDM was present in 29.3% patients aged ≥60 years, and in 20.5% of patients aged <60 years ($p < 0.001$), which corresponds with the outcomes of other studies [9,10].

Infectious complications are particularly important, as they are one of the main causes of death with a functioning graft in older kidney transplant recipients [11,12]. Different percentages of infections in older recipients have been reported, with some reaching as

high as 92.3% within the first year after kidney transplantation [13]. In our study, infection in the early postoperative period did not meet the threshold for statistical significance; however, the number of hospitalizations due to infection during the follow-up period was significantly higher among older patients. Similar to Kim et al., the most common causative pathogens were bacteria, and the most frequent site was the urinary tract [14].

Cytomegalovirus replication/disease has been associated with lower death-censored graft survival in the first year after KT [15]. In a large, retrospective study conducted by Deina et al., age was identified as one of the risk factors for CMV infection [15]. Jankowska et al. also observed a trend toward more CMV infections in the older population [9]. However, different studies did not reach the same conclusion [16,17]. In our study, cytomegalovirus (CMV) infection did not differ between older and younger recipients, although it might be due to the relatively small group of participants and a short follow-up period.

Another viral infection which remains a challenging aspect after the kidney transplantation is BK polyomavirus (BKV) nephropathy. Although it has been associated with older recipient age, the level of evidence remains low [18]. In this study, no correlation between age and BKV replication was proven. Additionally, there are not many studies addressing the subject of BKV nephropathy in older kidney transplant recipients, thus more research is needed in this field.

Various studies have been inconclusive in terms of biopsy-proven acute rejection (BPAR). Doucet et al. found BPAR less frequent in older patients, which could be expected, when taking into consideration age-related changes in the immune system [19]. In contrast, some studies did not observe a significant difference in PBAR occurrence [11,16,20]. In our study, BPAR was also similar between both groups (22.1% of younger patients and 20% of older patients). It is plausible that the use of induction immunosuppression, particularly thymoglobulin, which was more frequently administered to younger patients (27.1% vs. 10.7%), contributed to the observed outcomes. Additionally, over time, more differences in terms of the immunosuppression approach might be observed, with a tendency to reduce calcineurin inhibitors in older patients. Thus, there is a need for more research in this regard.

In this study, cardiac events in the post-transplantation period were twice as common among patients $\geq$60 years compared to patients <60 years. Interestingly, in both groups, newly diagnosed arrhythmia was the main cardiac complication. In research conducted by Gozdowska et al. [21], living donor kidney transplant recipients were at lower risk of cardiovascular complications, compared to deceased donor kidney transplant recipients, of which the highest risk was during the first year. Not surprisingly, age, male gender, and frequent smokers were associated with a higher risk of such events [21]. It is common knowledge that PTDM, as well as type 2 diabetes mellitus, often followed by micro- and macroangiopathy conditions more often observed in the older group- could be additional important factors explaining the observed outcomes. Since cardiovascular diseases remain one of the leading causes of death in older kidney transplant recipients [11,12,20,22], there should be more careful pretransplant evaluation, focusing on cardiovascular diseases.

Similarly to other studies [11,23], delayed graft function (DGF) was more frequently observed in the group $\geq$60 years; however, there was no difference in terms of duration of DGF. Kidney graft function, measured with the eGFR formula, was poorer in older recipients at the end of first hospitalization, as well as after 12-month follow-up. However, in both groups, eGFR increased during that time. In our opinion, eGFR of 45 mL/min/1.73 m^2 at the end of the first year post-KT is still an acceptable outcome for older recipients.

Another important aspect which has been a major concern in terms of KT in senior patients, is surgical complications. Many studies, including ours, have indeed observed an

increased number of complications in older recipients [11,24]. Hernandez et al., in a study conducted on 870 cadaveric kidney transplants, reported that older recipients were more prone to urinary leak [25], which corresponds to our study results, where patients ≥60 years of age tended to have urologic complications. The reason for this remains unclear; however, it might be connected with elevated BMI and longer time on dialysis, both of which are more often present in senior patients [24,25]. In addition, it is possible that a higher number of surgical complications has influenced the initial hospital stay, which was on average 5 days longer in senior patients.

In our study, one-year patient survival and one-year graft survival were comparable between both groups. Therefore, in the short-term observation KT in senior recipients might be considered both beneficial and safe. Furthermore, Silva et al., in a retrospective study, did not find a correlation between age and one-year mortality [22]. Naturally, over time, patient survival rates tend to favor young recipients due to their longer life expectancy [9,11,19], and survival rates among older recipients decrease. However, in a study conducted by Jankowska et al., death-censored graft survival did not differ between the groups [9].

Our findings highlight key differences between younger and older recipients, particularly in terms of surgical complications, infection rates, PTDM occurrence and cardiac events. All of them were more likely presented in older recipients, and had an impact on graft function, which highlighted the need for careful monitoring of this group, particularly in the early post-transplant period.

The study has a number of limitations. Firstly, it is a single-center study with a relatively small group of participants (75 older and 195 younger KT recipients), which limits the extrapolation of the results to other populations. Furthermore, the disproportion in group sizes (the smaller number of senior patients compared to younger ones), as well as in donor characteristics (markedly fewer LDKT and more DDKT among older recipients) limits the strength of comparisons between the groups. Subsequently, the retrospective nature of the research influences the reliability of available data, or the lack of them, which limits the scope of the results. Another limitation of our study is the lack of data on functional outcomes such as frailty, independence, or nutritional status, which could further characterize the benefits and risks of kidney transplantation in older recipients. Lastly, the cut-off age of 60 years was used to distinguish between older and younger patients, while many studies have used the age of 65 years or even higher. Our choice was made based on the United Nations definition, which in our opinion is a reliable source. Moreover, expected remaining years of life for KT recipients aged >60 years are similar to those of people older than 75 years old in the general population [2].

5. Conclusions

Surgical complications, with emphasis on urological problems, DGF, and infectious complications are more common in patients aged ≥60 years. Thus, a careful approach should be applied in this group. PTDM and cardiac events are also more frequently observed in senior patients. No significant differences in terms of CMV replication, BKV replication, and BPAR were detected. The estimated glomerular filtration rate was lower in the older group, although it remained an acceptable outcome. One-year patient and graft survival were comparable between both groups, which indicates that kidney transplantation in older recipients is a relatively safe procedure.

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Abbreviations

The following abbreviations are used in this manuscript:

ADPKD	autosomal dominant polycystic kidney disease
ATG	thymoglobulin
BPAR	biopsy-proven acute rejection
BMI	body mass index
BKV	polyomavirus BK
CNI	calcineurin inhibitors
CMV	cytomegalovirus
CVD	cardiovascular diseases
DGF	delayed graft function
DDKT	deceased donor kidney transplant
DM	diabetes mellitus
eGFR	estimated glomerular filtration rate
ESKD	end-stage kidney disease
HD	hemodialysis
HLA	human leukocyte antigen
HT	hypertension
IGF	immediate graft function
IQR	interquartile range
KT	kidney transplants
LDKT	living donor kidney transplant
MD	mean/median difference
No	number
PRA	panel reactive antibody
PNF	primary non-function
PTDM	post-transplant diabetes mellitus
RR	relative risk
SD	standard deviation
sCr	serum creatinine
Tx	transplantation

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Risk Factors for Development of Post-Transplant Diabetes Mellitus After Kidney Transplantation and Comparison Between Older and Younger Recipients in the Early Post-Transplantation Period: A Single-Center Study

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Background: Diabetes mellitus after kidney transplantation (post-transplant diabetes mellitus PTDM) is a commonly observed metabolic complication. Its incidence ranges from 4% to 25%. The aim of this study was to analyze potential risk factors associated with PTDM in kidney transplant recipients. Additionally, the study focused on determining differences between older and younger patients with PTDM.

Material/Methods: In this retrospective study, we screened 375 patients who received a kidney transplant between January 2021 and February 2024. PTDM was defined based on the 2013 International Consensus Meeting on Post-transplant Diabetes Mellitus. Kidney transplant recipients who developed PTDM were compared with patients without PTDM, and then patients with PTDM were divided into 2 subgroups based on age (≥60 years, and <60 years), and compared.

Results: The data of 218 kidney transplant recipients were analyzed. Of those, 55 patients (25%) developed PTDM. Age ($p<0.001$), elevated body mass index ($p<0.001$), hypomagnesemia ($p<0.013$), hypertriglyceridemia ($p<0.001$), and hypercholesterolemia ($p<0.001$) were significant risk factors for PTDM occurrence. A comparison between older and younger patients with PTDM did not reveal significant differences in terms of BMI, hypomagnesemia, hypertriglyceridemia, and hypercholesterolemia.

Conclusions: PTDM is a common complication after kidney transplantation. Older age showed the strongest association with PTDM. Patients who are at high risk should be carefully monitored and treated aggressively if the diabetes develops.
More research comparing older and younger patients with PTDM is needed so that a better and more individualized approaches can be implemented.

Keywords: Transplantation • Diabetes Mellitus • Risk Factors

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Introduction

Kidney transplantation is considered the most effective treatment for end-stage chronic kidney disease (ESKD) [1], but various complications can occur after this procedure.

Post-transplant diabetes mellitus (PTDM) is one of these complications and is a commonly observed metabolic disorder [2].

PTDM is defined as newly diagnosed diabetes mellitus in the post-transplant setting, irrespective of whether it was present but undetected before transplantation [3]. Diabetes mellitus after transplantation was first described in 1964 among kidney transplant recipients [4], and since then the nomenclature of this disease has changed many times. In 2014, the International Expert Panel, consisting of transplant nephrologists, diabetologists, and clinical scientists, recommended changing the terminology from new-onset diabetes after transplantation (NODAT) to post-transplant diabetes mellitus (PTDM). This change was due to the high prevalence of undiagnosed pre-transplant diabetes mellitus [4].

The incidence of PTDM ranges from 4% to 25% [2], but higher rates have also been reported (up to 40%) [5].

Various modifiable and non-modifiable risk factors for PTDM have been reported. Some of them are the same as risk factors for type 2 diabetes mellitus (DM), and include Black and Hispanic ethnicity, age, elevated BMI, family history of diabetes, and male sex. Other reported risk factors are specific to solid organ transplantation and include hypomagnesemia, a history of biopsy-proven acute rejection (BPAR), use of steroids and calcineurin inhibitors (CNI), cytomegalovirus (CMV) infection, hepatitis C, and certain human leukocyte antigen (HLA) types [6]. Moreover, genetic and epigenetic polymorphisms have also been also associated with PTDM [7].

The occurrence of PTDM has a significant impact on quality of life and mortality. Diabetes after transplantation has been associated with worse patient and graft survival [8-11 and it can also promote other transplant complications such as cardiovascular diseases, infections, and impaired wound healing [12,13].

Although knowledge about risk factors leading to PTDM has improved, there is still a need for further research. Furthermore, patients with PTDM may require tailored management strategies. For example, older individuals with PTDM might be at higher risk of cardiovascular events, which warrants a different approach to follow-up and treatment in this subgroup. This topic has not been comprehensively addressed in the literature, which highlight the need for further investigation.

Thus, the aim of this single-center study, performed at Infant Jesus Clinical Hospital Warsaw, Poland, was to analyze potential risk factors associated with PTDM in kidney transplant recipients. Additionally, we compared older and younger patients with PTDM, seeking to determine differences between these groups and to assess the need for a dedicated approach.

Material and Methods

Study Population

In this retrospective, observational study we analyzed data from patients who underwent kidney transplant (KT) between January 2021 and February 2024. A total of 375 KTs were performed. Patients who received single-organ kidney transplant without prior history of diabetes mellitus were included. The exclusion criteria included multi-organ transplantation, pre-existing diabetes mellitus (DM), conversion from cyclosporine to tacrolimus during the follow-up period (the timing of conversion to cyclosporine varied significantly between individuals, making it difficult to accurately describe and interpret their immunosuppressive exposure), and transferring to a different center during the follow-up period (which resulted from the nationwide mandatory organ allocation framework for kidney transplantation, by which patients were transferred to other centers at various time points and could not be systematically followed by our center, which prevented consistent data collection). We excluded 157 recipients from the study, after applying the exclusion criteria. A homogeneous group of 218 White patients was analyzed.

All data were accessed through medical records and laboratory test results obtained during hospitalizations, outpatient clinic visits, and from transplant registry data. Our data included demographics, comorbidities, transplant characteristics, type of induction therapy (if applicable), treatment of biopsy-proven acute rejection (if applicable), polyomavirus replication, cytomegalovirus replication, laboratory test results (cholesterol, magnesium, triglycerides, tacrolimus, serum creatinine, uric acid), and type of treatment for PTDM. The follow-up period was 6 months. The study was conducted in full accordance with the principles of the Declaration of Helsinki and the Declaration of Istanbul, and informed consent was obtained from all participants.

Definitions

Post-transplant diabetes mellitus was diagnosed based on the 2013 International Consensus Meeting on Post-transplant Diabetes Mellitus, and included symptoms of hyperglycemia (polydipsia, polyuria, and unintentional weight loss) with random blood glucose ≥200 mg/dl, fasting plasma glucose

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≥126 mg/dl, or two-hour plasma glucose ≥200 mg/dl during oral glucose tolerance test (OGTT). Since hemoglobin A1C (HbA1C) was not recommended as a screening test in the early post-transplant period, it was not used as a diagnostic tool [5]. The diagnosis of PTDM was made only after the patient had been on maintenance immunosuppression treatment for at least 3 months after transplantation). The diagnosis of BPAR was made based on histological findings obtained during the protocol biopsy at 3 months after transplant or when acute rejection was clinically suspected. Biopsy-proven acute rejection was treated with 500 mg of methylprednisolone for 3 consecutive days. Older patients were defined as those aged ≥60 years, based on United Nations definition.

Serum magnesium, uric acid, tacrolimus, cholesterol, and triglyceride levels were obtained during the follow-up period and are presented as mean values over the first 6 months. Hypertriglyceridemia was defined as serum triglyceride levels ≥150 mg/dL (reference rage <150 mg/dL), hypomagnesemia as serum magnesium levels <1.6 mg/dL (reference range 1.6-2.4 mg/dL), and hypercholesterolemia as total cholesterol levels ≥190 mg/dL (reference range <190 mg/dL) or current use of lipid-lowering medication. Hyperuricemia was defined as serum uric acid >6.8 mg/dL (reference range 3.4-6.8 mg/dL) or current use of uric acid-lowering agents. Participants were considered to have dyslipidemia and/or hypomagnesemia and/or hyperuricemia if any of the above criteria were met. Both polyomavirus replication and cytomegalovirus replication were monitored in the third and sixth months after transplant or in the presence of symptoms suggestive of viremia.

Statistical Analysis

Continuous variables were summarized as mean±standard deviation (SD) or median and interquartile range (IQR), while categorical variables were presented as n (%). Normality was evaluated with the Shapiro–Wilk test, supported by assessments of skewness and kurtosis. Levene's test was applied to assess homogeneity of variances. Comparisons between groups were made with the *t* test, Mann-Whitney U test, Pearson's chi-square test, or Fisher's exact test, as appropriate. Two-step logistic regression analysis was performed to identify risk factors for post-transplant diabetes mellitus. Variables for the multivariate model were selected based on p-value threshold of <0.25 [14], and a stepwise approach was used for final variables selection. Potential confounders were identified a priori based on clinical relevance and literature review, and were included in the multivariable logistic regression model alongside variables meeting the p-value threshold of <0.25 in univariate analysis. This approach allowed adjustment for potential confounding effects when estimating the independent association between each variable and PTDM risk. Logistic regression was chosen due to the binary nature of the outcome (presence/absence of PTDM) and its ability to control for multiple covariates simultaneously. Model fit was assessed using Nagelkerke R2 and Hosmer and Lemeshow goodness of fit (GOF) test. Variance inflation factors (VIF) were calculated to verify multicollinearity. Receiver operating characteristic (ROC) analysis was conducted to evaluate the prognostic performance of the selected variables for PTDM. Optimal cut-offs were indicated with the Youden method. A significance level (alpha) of 0.05 was used for statistical significance. All analyses were performed using R software (R4.1.2).

Results

Characteristics of Study Groups and Comparison of Study Subgroups

Of the 375 KT procedures, 218 (58%) patients were included in the study. Among them 131 (60.09%) were male and 87 (39.91%) were female.

In the study group, 189 patients (87%) underwent their first kidney transplantation, while 29 (13%) had received a second transplant. The mean age of all recipients was 45.5 years. Fifty-five patients (25%) developed PTDM (26 women and 29 men; 47.3% vs 52.7%). Of these, 24 (44%) patients were aged ≥60 years (12 women and 12 men).

All patients received a standard immunosuppression protocol consisting of steroids, calcineurin inhibitors (CNI)-tacrolimus, and mycophenolate acid. Seventy-five patients included in the study (34%) received induction therapy of thymoglobulin (ATG), and 24 patients (11%) received basiliximab prior to transplantation.

The group with PTDM was compared with those without PTDM in terms of clinical and laboratory data. Subsequently, patients who developed PTDM were divided into 2 subgroups according to age (< 60 years and ≥60 years), and comparisons between them were conducted.

Compared to patients without PTDM, patients with PTDM were significantly older (MD=11.11, CI95 [7.19; 15.03], p<0.001), and had significantly higher BMI (MD=2.46, CI95 [1.20; 3.71], p<0.001). The proportion of patients with age above or equal 60 years was significantly higher among those with PTDM (43.6% vs 12.9%, p<0.001). A comparison between patients with PTDM and patients without PTDM is presented in **Table 1**.

Risk Factors of PTDM – Logistic Regression Analysis

In the univariate analysis, advanced age significantly increased the odds of PTDM (OR=1.07, CI95 [1.04; 1.10], p<0.001).

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Table 1. Characteristics and comparison of study groups.

Variable	PTDM (n=55)	Non-PTDM (n=163)	MD/effect size	p-value
Sex, Female, n (%)	26 (47.3)	61 (37.4)	–	0.258
Age, years, mean±SD	54.04±12.38	42.93±12.88	11.11 (7.19; 15.03)	<0.001
Age ≥60 years, n (%)	24 (43.6)	21 (12.9)	–	<0.001
Thymoglobulin, n (%)	15 (27.3)	60 (36.8)	–	0.261
Basiliximab, n (%)	7 (12.7)	17 (10.4)	–	0.825
GKS pulses, n (%)	10 (18.2)	16 (9.8)	–	0.157
Month of PTDM, mean±SD	2.73±1.80	–	–	–
Insulin-based therapy, n (%)	15 (27.3)	0 (0.0)	–	<0.001
Antidiabetic drugs, n (%)	43 (78.2)	1 (0.6)	–	<0.001
BMI, kg/m^2, mean±SD	26.49±4.56	24.04±3.90	2.46 (1.20; 3.71)	<0.001
HD, n (%)	52 (94.5)	152 (93.3)	–	>0.999
PD, n (%)	4 (7.3)	18 (11.0)	–	0.587
DDKT, n (%)	44 (80.0)	127 (77.9)	–	0.892
LDKT, n (%)	11 (20.0)	36 (22.1)	–	0.892
TG, mg/dL, median (IQR)	203.0 (150.5; 296.0)	141.0 (108.5; 197.0)	62.00 (32.00; 85.00)	<0.001
Hypertriglyceridemia, n (%)	51 (92.7)	106 (65.0)	–	<0.001
Lipid-lowering treatment, n (%)	28 (50.9)	57 (35.0)	–	0.053
Cholesterol, mg/dL, mean±SD	208.64±54.40	182.47±45.48	26.16 (11.45; 40.88)	0.001
Hypercholesterolemia, n (%)	45 (81.8)	101 (62.0)	–	0.011
Tacrolimus, ng/mL, mean±SD	11.83±2.04	11.79±1.83	0.04 (-0.54; 0.62)	0.885
Uric acid, mg/dL, median (IQR)	6.80 (6.00; 8.40)	6.60 (5.60; 7.60)	0.20 (-0.10; 0.90)	0.117
Treatment for hyperuricemia, n (%)	18 (32.7)	43 (26.4)	–	0.464
Hyperuricemia, n (%)	34 (61.8)	94 (57.7)	–	0.702
Magnesium, mg/dL, median (IQR)	1.70 (1.50; 1.80)	1.90 (1.70; 2.10)	-0.20 (-0.30; -0.10)	<0.001
Hypomagnesemia, n (%)	20 (36.4)	32 (19.6)	–	0.020
Creatinine, mg/dL, median (IQR)	1.50 (1.15; 2.00)	1.50 (1.19; 1.85)	0.00 (-0.10; 0.20)	0.671
BPAR, n (%)	10 (18.2)	16 (9.8)	–	0.157
CMV, n (%)	8 (14.5)	17 (10.4)	–	0.559
BKV, n (%)	8 (14.5)	10 (6.1)	–	0.094

BMI – body mass index, CI – confidence interval, DDKT – deceased donor kidney transplantation, GKS pulses – methylprednisolone pulses, HD – hemodialysis, IQR – interquartile range, LDKT – living donor kidney transplantation, MD – mean or median difference (with PTDM vs without PTDM), PD – peritoneal dialysis, SD – standard deviation, TG – triglycerides. Groups compared with the *t* test[1], Mann-Whitney U test[2], Pearson's chi-square test, or Fisher's exact test[3], as appropriate.

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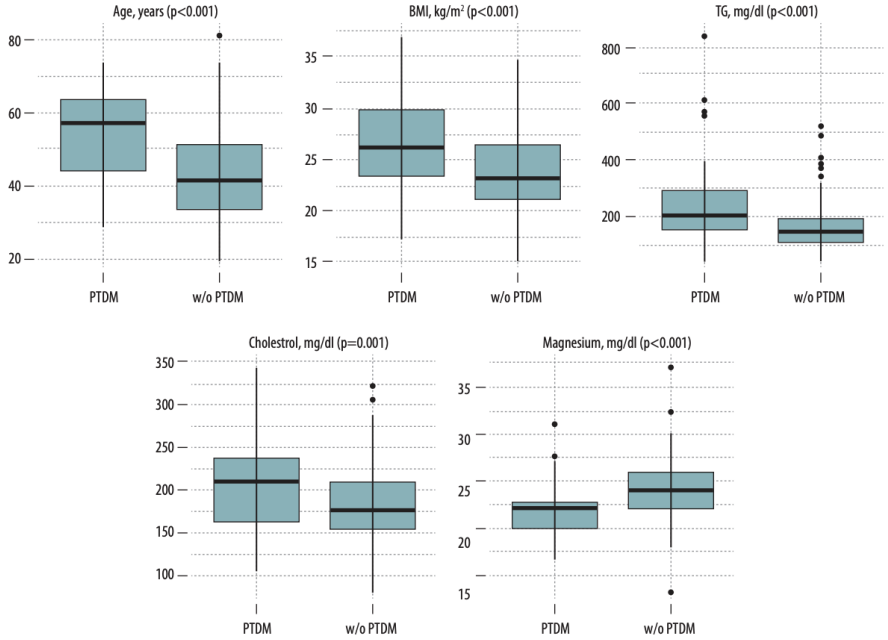

Figure 1. Boxplot charts presenting distribution of continuous variables which proved to differ significantly between patients with PTDM and patients without PTDM. *Figure created using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).*

Additionally, patients aged 60 years or above had 5-fold higher odds of PTDM than patients below 60 years (OR=5.24, CI95 [2.60; 10.68], p<0.001). Other risk factors associated with PTDM occurrence were higher BMI (OR=1.15, CI95 [1.07; 1.25], p<0.001), hypertriglyceridemia (OR=1.01, CI95 [1.00; 1.01], p<0.001), hypercholesterolemia (OR=1.01, CI95 [1.00; 1.02], p<0.001), and hypomagnesemia (OR=2.34, CI95 [1.19; 4.57], p=0.013). No correlation between sex, type of donor, type of dialysis, hyperuricemia, induction therapy, presence and treatment of acute rejection, and mean tacrolimus level was observed. **Figure 1** presents boxplot charts illustrating the distribution of variables significantly different between patients with PTDM and those without PTDM.

Multivariate logistic regression model confirmed that age had a significant impact on the odds of PTDM. Each additional year increased the odds of PTDM by 8% (OR=1.08, CI95 [1.04; 1.11], p<0.001). The odds of PTDM were 12% higher for each 1 kg/m² increase in BMI (OR=1.12, CI95 [1.02; 1.23], p=0.026). The concentration of triglycerides slightly influenced the odds of PTDM (OR=1.00, CI95 [1.00; 1.01], p=0.046). Hypertriglyceridemia increased the odds of PTDM by 4-fold (OR=3.54, CI95 [1.12; 13.93], p=0.045). Higher magnesium concentrations reduced the odds of PTDM by 88% (OR=0.12, CI95 [0.03; 0.46], p=0.003). **Table 2** presents the outcomes of logistic regression analysis for PTDM.

Receiver Operating Characteristics (ROC) analysis

Receiver operating characteristics (ROC) analysis was conducted to evaluate the predictive ability of selected parameters for PTDM. The highest AUC (area under the curve), which referred to best prognostic properties, was found for age (AUC=0.733, CI95 [0.658; 0.809]) with a cut-off of 48.5 years. Patients above the cut-off were predicted to develop PTDM with a sensitivity of 71% and a specificity of 69%. AUC values for other variables ranged from 0.638 (presence of hypertriglyceridemia) to 0.693 (concentration of triglycerides), indicating moderate predictive ability. The results are summarized in **Table 3**.

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Table 2. Outcome of logistic regression analysis for PTDM.

Variable	Univariate models			Multivariate model		
	OR	95% CI	p	OR	95% CI	p
Sex, Female (vs male)	1.50	0.81-2.78	0.198	–	–	–
Age, years	1.07	1.04-1.10	<0.001	1.08	1.04-1.11	<0.001
Age ≥60 years (vs <60 years)	5.24	2.60-10.68	<0.001	–	–	–
Thymoglobulin	0.64	0.32-1.24	0.200	–	–	–
Basiliximab	1.25	0.46-3.09	0.638	–	–	–
Methylprednisolone pulses	2.04	0.84-4.76	0.103	–	–	–
BMI, kg/m^2	1.15	1.07-1.25	<0.001	1.12	1.02-1.23	0.026
Triglycerides, mg/dl	1.01	1.00-1.01	<0.001	1.00	1.00-1.01	0.046
Hypertriglyceridemia	6.86	2.63-23.51	<0.001	3.54	1.12-13.93	0.045
Cholesterol, mg/dl	1.01	1.00-1.02	<0.001	1.01	1.00-1.01	0.111
Hypercholesterolaemia	2.76	1.34-6.16	0.008	–	–	–
Mean tacrolimus level	1.01	0.86-1.19	0.884	–	–	–
Uric acid, mg/dl	1.17	0.98-1.41	0.091	–	–	–
Hyperuricemia	1.19	0.64-2.25	0.589	–	–	–
Mean magnesium levels mg/dl	0.10	0.03-0.32	<0.001	0.12	0.03-0.46	0.003
Hypomagnesemia	2.34	1.19-4.57	0.013	–	–	–
BPAR	2.04	0.84-4.76	0.103	–	–	–

MI – body mass index; BPAR – biopsy-proven acute rejection; CI – confidence interval; DDKT – deceased donor kidney transplantation; LDKT – living donor kidney transplantation; OR – odds ratio.

Table 3. Outcome of receiver operating characteristics (ROC) assessing quality of selected parameters to predict PTDM.

Variable	Cut-off*	AUC (95% CI)	Sensitivity	Specificity	PPV	NPV	Accuracy	p
Age, years	48.50	0.733 (0.658; 0.811)	0.71	0.69	0.44	0.88	0.70	<0.001
BMI, kg/m^2	27.48	0.662 (0.580; 0.744)	0.45	0.82	0.45	0.82	0.72	<0.001
Triglycerides, mg/dl	175.50	0.693 (0.602; 0.773)	0.65	0.69	0.41	0.85	0.68	<0.001
Hypertriglyceridemia	–	0.638 (0.587; 0.687)	0.93	0.35	0.32	0.93	0.50	<0.001
Magnesium, mg/dl	1.89	0.684 (0.606; 0.763)	0.78	0.52	0.36	0.88	0.59	<0.001

AUC – area under curve; CI – confidence interval; NPV – negative predictive value; PPV – positive predictive value. * Only for continuous parameters.

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Table 4. Comparison of patients aged ≥60 years vs patients aged <60 years with PTDM.

Variable	Patients with PTDM aged ≥60 years	Patients with PTDM aged <60 years	MD (95% CI)	p
N	24 (100.0)	31 (100.0)	–	–
Thymoglobulin, n (%)	4 (16.7)	11 (35.5)	–	0.212
Basiliximab, n (%)	3 (12.5)	4 (12.9)	–	>0.999[3]
GKS, n (%)	5 (20.8)	5 (16.1)	–	0.733[3]
Insulin-based therapy, n (%)	6 (25.0)	9 (29.0)	–	0.978
Antidiabetic drugs, n (%)	19 (79.2)	24 (77.4)	–	>0.999
Infection within 6 months, n (%)	16 (66.7)	14 (45.2)	–	0.188
Triglycerides, mg/dl, median (IQR)	188.00 (151.25; 238.50)	245.00 (152.50; 339.00)	-57.00 (-111.00; 17.00)	0.169[2]
Cholesterol, mg/dl, mean±SD	219.83±51.50	199.97±55.82	19.87 (-9.58; 49.31)	0.182[1]
Creatinine mg/dl, median (IQR)	1.60 (1.40; 2.02)	1.45 (1.00; 1.85)	0.15 (-0.10; 0.60)	0.137[2]
BPAR, n (%)	5 (20.8)	5 (16.1)	–	0.733[3]
CMV, n (%)	4 (16.7)	4 (12.9)	–	0.718[3]
BKV, n (%)	2 (8.3)	6 (19.4)	–	0.443[3]

BKV – polyomavirus replication; BPAR – biopsy-proven acute rejection; CI – confidence interval; CMV – cytomegalovirus replication; GKS – additional methylprednisolone pulses; IQR – interquartile range; MD – mean or median difference (≥60 years vs <60 years); SD – standard deviation. Groups were compared with the *t* test[1], Mann-Whitney U test[2], Pearson's chi-square test, or Fisher's exact test[3], as appropriate.

Comparison of Patients with PTDM Aged ≥60 Years and Patients with PTDM Aged <60 Years

The younger group was compared with older group in terms of induction therapy, type of PTDM treatment (insulin vs oral medications), infection occurrence, cytomegalovirus (CMV) replication, and polyomavirus (BKV) replication, creatinine level after 6 months, presence of biopsy-proven acute rejection, and levels of cholesterol and triglycerides. No significant difference was found between patients with PTDM aged ≥60 years and patients with PTDM aged <60 years (p>0.05). Results are presented in **Table 4**.

Discussion

Post-transplant diabetes mellitus is a common complication after kidney transplantation. In our study, 25% developed this metabolic disorder, which is quite high, but it agrees with other studies [12,15]. The incidence of PTDM ranges from 10% to 25% [2,16]. This wide variation may result from lack of a standard definition of PTDM, duration of follow-up, and the presence of modifiable and non-modifiable risk factors in kidney transplant recipients in homogenous cohorts. The present study found that the risk factors advanced age, higher BMI, hypertriglyceridemia, hypercholesterolemia, and hypomagnesemia were associated with PTDM, consistent with previous studies [17].

Since age is a well-known non-modifiable risk factor of type 2 diabetes mellitus [18], it is not surprising that we found a higher risk of PTDM for KT patients. Patient age was the strongest risk factor, with a cut-off of 48.5 years. Additionally, the subgroup of older recipients (aged 60 years or above) had 5 times higher odds of PTDM than patients below 60 years (p<0.001). Comparable conclusions were reported in other studies [19-21].

Consistent with trends in the general population, elevated BMI was a significant risk factor for PTDM in our study. The mechanisms responsible for insulin resistance in obese (BMI >30 kg/m^2) and overweight (BMI >25 kg/m^2) patients are not fully understood, but may be the consequence of a chronic inflammatory state caused by excessive fat tissue, which stimulates macrophage recruitment to adipocytes and the release

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of proinflammatory adipokines, leading to downregulation of insulin signaling [22]. Furthermore, adipose tissue produces tumor necrosis factor-alpha (TNF-α) and its activation is associated with insulin resistance due to reduced expression of insulin-sensitive transporters [23].

Some studies suggest that post-transplant weight gain is also a risk factor of PTDM [21,24]. Another important aspect might be the body fat distribution. Cron et al demonstrated that PTDM was strongly associated with central obesity [25]. In a study performed by von Düring et al, visceral fat tissue was correlated with PTDM and hyperglycemia early after transplantation [26]. Thus, it might be essential to monitor not only BMI, but also waist circumference in KT recipients.

Our study also showed that elevated triglyceride levels were associated with PTDM, perhaps due to the association between hypertriglyceridemia and insulin resistance, which can then lead to diabetes [27].

Hypomagnesemia has been found to be related to increased risk of PTDM, although the underlying mechanism remains unclear [12,28]. Lower magnesium level impacts insulin signaling [29], but it also might be the effect of calcineurin inhibitor treatment, which is considered to be a risk factor for PTDM [30]. Moreover, Augusto et al reported that pre-transplant, rather than post-transplant, hypomagnesemia was an independent risk factor of PTDM [31]. The same results were shown by Xu et al [32]. In our study, post-transplant hypomagnesemia was an independent risk factor of development of PTDM, although pre-transplant serum magnesium levels should also be taken into consideration in further research.

Our study revealed that hypercholesterolemia was associated with PTDM. Sinangil et al, also revealed positive correlation between elevated total cholesterol level and LDL-C (low-density lipoprotein cholesterol) in patients with PTDM [33]. On the contrary some studies found out that the rise of TG/HDL-C (triglyceride/high-density lipoprotein cholesterol) ratio and lower HDL-C were increasing risk of diabetes mellitus in KT recipients [22,28].

The impact of cholesterol and its fractions on PTDM might be because excess cholesterol accumulation leads to β-cell dysfunction, thus impairing glucose tolerance, and affecting insulin secretion. Moreover, islet cholesterol deposition can cause increased islet amyloid polypeptide aggregation, and increased islet amyloid formation, thus further deteriorating β-cell function and affecting glucose homeostasis [26,34,35].

Numerous studies suggest that immunosuppression therapy, particularly calcineurin inhibitors, and steroids, may contribute to PTDM development in a dose-dependent manner [30,32,36].

However, in our study, no correlation was found between mean post-transplant tacrolimus levels, additional steroid doses (used to treat BPAR), and PTDM. This may be due to the short follow-up period, and the low incidence of BPAR, which has limited statistical significance.

In the final stage of the study, we divided the group who developed PTDM into 2 subgroups based on age (≥60 years of age, and <60 years of age), and then compared them.

There was no significant difference in regard to BPAR, CMV infection, BKV infection, or type of PTDM treatment (insulin vs oral medications). Mean creatinine level at the end of follow-up period was 1.6 mg/dl for older patients, and 1.4 mg/dl for younger patients, which in our opinion is similar, and acceptable outcome. Revanur et al, in a retrospective study, revealed that survival of patients over the age of 55 years with PTDM was similar to the control group. On the contrary, KT recipients under 55 years of age with PTDM were associated with a much higher risk of death. No differences in graft survival or acute rejection were found [8]. Comparison between older and younger KT recipients with PTDM has not been extensively studied. More research on differences between PTDM patients is needed, ideally with a longer follow-up, thus an adequate patient-specific approach can be performed. We plan to address this in our future work.

This study has a number of limitations. Firstly, it is a single-center study with only 218 White participants, from which 55 developed PTDM, which limits extrapolation of the results to other populations. Moreover, many patients (42%) were excluded due to variable timing of tacrolimus-to-cyclosporine conversion or transfer to other facilities, which precluded consistent follow-up and could limit the generalizability of our findings.

This was a retrospective study with database analysis; therefore, the reliability or lack of available data limits the scope of the results.

The follow-up period was relatively short compared to other studies; therefore, some factors (eg, immunosuppression) might have long-term pro-diabetogenic effects which were not observed in this study. Additional studies with prolonged observation are needed to validate these findings, and we are already planning a follow-up study with extended observation. Lastly, we enrolled a relatively small group of older and younger patients with PTDM (24 and 31 recipients, respectively).

Conclusions

Advanced age had the strongest association with PTDM. Elevated BMI, hypomagnesemia, and hypercholesterolemia also increased the risk of PTDM. No significant differences in terms

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of serum creatinine level, CMV infection, BKV infection, BPAR, or type of PTDM treatment (insulin vs oral medications) were detected in younger or older recipients with PTDM. PTDM influences patient and graft survival, and increases risk of cardiovascular diseases. More research is necessary to establish modifiable risk factors to help prevent PTDM [8,9,37]. Additionally, KT recipients with non-modifiable risk factors should be regularly screened for PTDM, and aggressive treatment is needed if they develop diabetes, to minimise the risk of complications. Furthermore, close monitoring and management of modifiable risk factors, such as BMI and cholesterol and triglyceride levels, in high-risk patients is crucial, highlighting the importance of personalized preventive strategies in clinical practice. Practical recommendations, including screening protocols and lifestyle interventions, may help clinicians mitigate PTDM risk. More research comparing older and younger patients with PTDM is needed, focusing on long-term risks such as BPAR, CMV/BKV replication, and cardiac events, thereby providing a better and more individualized approach.

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Declaration of Figures' Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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Review

Kidney Transplantation in Older Recipients Regarding Surgical and Clinical Complications, Outcomes, and Survival: A Literature Review

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Abstract: Context: The best treatment for end-stage chronic kidney disease (ESKD) is kidney transplantation (KT). As a result of an aging population, each year more kidney transplants in older adults are performed. Nevertheless, older recipients, characterized by more comorbidities and frailty, raise concerns about the outcomes, potential complications, and the general approach. **Aim**: The aim of this literature review was to study the outcomes, graft and patient survival, as well as common complications, to establish safety and increase awareness of the potential complications of kidney transplantation in the older population. **Methods**: PubMed and Google scholar databases were searched. The cut-off age defining an old patient was 60 years. The inclusion criteria were as follows: first kidney transplantation, and studies in English language. The exclusion criteria were as follows: more than one organ transplant, dual transplants, articles published before 2015, meta-analysis, reviews, letter to the editor, case reports, and studies published only as a conference abstract. Comparative and noncomparative studies addressing patient survival, death-censored graft survival, surgical complications, and clinical complications, such as delayed graft function (DGF) and biopsy proven acute rejection (PBAR), were included. **Results**: After screening the papers, 17 studies met the inclusion criteria and were included for review. Eleven papers compared older recipients with younger recipients and in six papers only older patients were analysed. Two studies used paired deceased donors to eliminate donor bias. The rest of the studies used either deceased donors or both living and deceased donors. The majority of patients were male (61.83%) and received a kidney from a deceased donor (58.08%). **Conclusions**: Kidney transplantation is safe and can be beneficial for recipients over 60 years of age. Older patients suffered more infectious complications, which were also one of the main reasons for death. Most studies did not show a significant difference in death-censored graft survival compared to the younger population. More research is needed to establish the prevalence of surgical complications, and some clinical complications.

Keywords: older kidney recipients; complications; survival; outcomes

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1. Introduction

Kidney transplantation (KT) is by far the most effective way of treating end-stage chronic kidney disease (ESKD) [1]. Compared to dialysis, it prolongs patients' life and improves quality of life [2–4]. Those outcomes also apply to patients over 60 years of age, regardless of donor characteristics [4,5]. Considering the ageing of the population in many countries—for example, in Poland, from 2005 to 2022, the percentage of people over 60 years of age increased from 17.2%, to 25.9% [6]—analogously, a growing number of older patients with ESKD is also observed [7,8]. Thus, the number of older patients on the waiting list, as well as kidney recipients, is constantly increasing [9–11]. This group, characterised by more comorbidities, frailty, and often dementia, requires a wide-spectrum and individual approach. This relates not only to which patient should be put on the waiting list, but also how to manage the patient after kidney transplant.

In this literature review, aspects such as post-surgical and clinical complications, mortality, and patient and graft survival after transplantation were considered. The main aim of this review was to establish whether kidney transplant is safe for the older population, and also which aspects are the most important when approaching older patients.

2. Methods

In May and June of 2024, PubMed and Google scholar databases were searched using the terms: "older recipients", "kidney transplant", "kidney transplantation outcomes", "clinical complications", "surgical complications", and "survival". In this literature review, the United Nations definition was adopted, thus we were looking for articles that presented patients aged above 60. Other inclusion criteria were first kidney transplantation, and studies in English language. Studies that included more than one organ transplant (multi-organ transplants), dual transplants, or were published before 2015 were excluded. All types of articles were eligible for inclusion except for meta-analysis, review, letter to editor, case report, and studies published only as a conference abstract. The literature search was conducted by a single reviewer. Using the databases mentioned above, the articles were screened by title and abstract to determine if they fulfilled the criteria. Further elimination was made after reading the full text, in regard to the above criteria.

2.1. Study and Participant Characteristics

In the presented studies, different cut-off points were established to define older recipients. Eight studies used the age of 60 as the cut-off point, three studies used the age of 65, three studies used the age of 70, one study used the age of 75, and one study used the age of 80. Ten studies compared the older population with younger kidney recipients (excluding paediatric patients). Shi et al. [12] compared older recipients with older, dialysis patients. Six studies were non-comparable and presented outcomes of kidney transplantation in older recipients. Two studies used paired deceased donors to eliminate donor bias. The remaining studies used either deceased donors (four studies) or both living and deceased donors (eleven studies). All studies were retrospective studies and used data obtained from the patients' medical records. Seven studies were from Europe, four from Asia, three from Australia and New Zealand, two from South America, and one from North America.

2.2. Characteristics of Patients

This article reviewed 17 studies, assessing a total of 32,231 recipients, including 5252 older recipients. The majority of patients were male (61.83% of all recipients; 65.91% of older patients). Most patients received a kidney from a deceased donor (58.08% of all recipients; 72.99% of older recipients).

3. Analysis of Included Studies

Table 1 presents the characteristics and main findings of the studies used in the literature review.

Table 1. Summary of studies used in the literature review.

Author	Country	Recruitment Period	Recipients Age	Total Number of KT	Donor	Control Group Age (If Presents)	Main Outcomes
Gheith [11]	Kuwait	2000–2014	>60	962	DDKT and LDKT, DDKT predominated in control group and LDKT dominated in older patients	40–60	BPAR was less common for older patients No significant differences regarding patient and graft survival were observed between groups
Heldal [13]	Norway	1990–2005	≥70	1326	DDKT and LDKT	60–69 45–54	No differences in death-censored graft survival between three groups
Doucet [14]	Australia and New Zealand	2000–2015	≥70	10,651	DDKT and LDKT	18–69	Worse patients' survival and graft outcomes in older group Comparable rates of DGF between groups Lower rates of ABMR in older living donor kidney recipients
Orlandi [15]	Brazil	1998–2010	>60	732	DDKT and LDKT	18–60	Diabetes mellitus was risk factor of kidney graft loss and higher mortality in older patients
Ko [16]	Korea	2009–2012	>60	4966	DDKT and LDKT	<60	KT in older recipients can be associated with worse graft or patient survival High sensitization is less significant impact in older patients Old age is risk factor of higher mortality, mostly due to infection and desensitization therapy
Skrabaka [17]	Poland	1998–2018	>60	350	Paired deceased donor	<60	No difference in regard to surgical and clinical complications between groups No significant difference in patient and graft survival between groups Old age as risk factor of early postoperative infectious complication
Yoo [18]	Korea	1997–2012	>60	3565	DDKT and LDKT	<60	Worse recipients' survival in older group No difference in death-censored allograft survival between younger and older recipients
So [19]	Australia	2006–2016	≥65	802	DDKT and LDKT	-	Prevalent vascular disease and peritoneal dialysis are risk factors associated with poorer outcome of KT for older recipients 5-year graft and patient survival exceeded 75%
Adani [20]	Italy	1993–2016	>65	109	DDKT	-	KT is safe, feasible, and has good graft survival for older people Recipients age ≥ 71 have higher mortality and higher incidence of graft loss Main causes of death: infectious, tumours, cardiovascular disease
Saucedo-Crespo [21]	USA	2003–2013	≥70	2624	DDKT and LDKT	<70	Acceptable outcome of graft and patient survival in KT recipients age ≥ 70 Caution listing older patient with BMI > 30 kg/m^2, PRA > 20%, CABG, PVD Death as the main factor of graft loss in recipients age ≥ 70
Kim [22]	Korea	2014–2017	≥60	3738	DDKT and LDKT	<60	older patients had higher incidence of early post-transplant infections older recipients have more mycobacterial infections, coinfections, and multiple site infections

Table 1. *Cont.*

Author	Country	Recruitment Period	Recipients Age	Total Number of KT	Donor	Control Group Age (If Presents)	Main Outcomes
Silva [23]	Portugal	2011–2020	≥65	147	DDKT and LDKT	-	Cautious pretransplant evaluation is needed for older patients Factors such as cold ischemia time, increased donor age, cardiovascular disease, DGF, early cardiovascular complication post KT, early rehospitalizations, peritoneal dialysis, have positive correlation to 1-year mortality in older patients
Shi [12]	Australia	2009–2019	>70	930	DDKT and LDKT		>70 dialysis patients on the waiting list Early post-transplant mortality is higher for older patients compared to patients on dialysis; however, in long term approach, survival of KT recipients is higher
Neri [24]	Italy	2004–2014	>60	452	DDKT	-	Increasing age was risk factor for patient and graft survival BPAR and neoplasia are associate with worse graft survival
Cabrera [25]	Uruguay	2002–2015	≥75	138	Similarly aged DDKT	-	Recipients ≥ 75 years of age can benefit from KT using grafts from extremely aged or deceased donors in comparison to patients remaining on dialysis or listed for transplantation
Jankowska [26]	Poland	1994–2016	≥60	328	Paired deceased donor	<60	No difference in one-year patient survival, one-year graft survival, DGF, BPAR, death-censored graft survival between two groups Older patients have significantly worse patients and graft survival in long-term
Lønning [27]	Norway	1983–2015	≥80	47	DDKT	-	KT from living donor can be beneficial for older recipients 5-year survival rate was 55% for recipients ≥ 80 yo

Abbreviations: DDKT—deceased-donor kidney transplant, LDKT—living-donor kidney transplant, KT—kidney transplant, BPAR—biopsy-proven acute rejection, DGF—delayed graft function, CABG—coronary artery bypass grafting, PVD—peripheral vascular disease.

Gheith et al. studied a total of 962 patients, divided in two groups based on age: one group of 252 patients older than 60 years of age (mean age 65.5), and second group of 710 adults (mean age 49.3). Recipients received kidneys from both deceased and living donors. DDKT predominated in the younger group and LDKT dominated in older patients. PTDM was higher in the younger group (24% vs. 17%, $p = 0.53$); however, diabetes mellitus was more common in the older group. More micro- and macro-angiopathy appeared in the older group. Patients and graft survival were comparable between the older and younger recipients ($p > 0.5$). Older recipients were characterised by much higher cardiovascular risks, and a higher number of malignancies, but fewer episodes of BPAR ($p < 0.5$) [11].

Heldal et al. divided 1326 patients, based on age, into three subgroups (age $\geq$ 70; age 60–69; age 45–54). Recipients received kidneys from deceased and living donors. No significant difference was observed in death-censored graft survival between all groups (89% in septuagenarians, 88% in seniors; 90% in younger adults). Five-year actuarial patient survival was 56% in the septuagenarians, 72% in the senior group; 91% in the younger group ($p < 0.001$) [13].

In the Doucet et al. study, 299 adults over 70 years of age were compared to 12,684 adults between the ages of 18 and 69. Recipients received kidneys both from deceased and living donors. Older patients had worse one- and five-year survival compared to the younger group (96–97% and 79–81% vs. 97–99% and 90–95%). DGF was comparable between the two groups ($p = 0.029$). Older patients who received a kidney from living donors had lower rates of BPAR ($p = 0.02$) [14].

Orlandi et al. studied a total of 732 patients, divided into two equal groups based on age. The first group included patients over 60 years of age, and the second group had patients between the ages of 18 and 60 years. Diabetes mellitus and prioritisation, but surprisingly not age, were independent risk factors of kidney graft loss. Five-year and ten-year patient survival was lower in the older group (76.6% vs. 87.7% and 54.8% vs. 84.3%; $p < 0.001$). Death with functioning graft was the main reason for graft loss in older recipients. The main causes of death were infections, cardiovascular events, and malignancy. Surgical complications and DGF were more common in the older group. BPAR was similar between the two groups (24.6% vs. 29.5%; $p = 0.134$) [15].

Ko et al. compared a group of 356 patients above the age of 60 with a control group of 4610 younger adults. Recipients received kidneys from deceased and living donors. No significant difference between the two groups was observed in terms of BPAR ($p = 0.808$). Age was an independent risk factor for death-censored graft failure in the overall study population, and in LDKT recipients, but not in DDKT recipients. The main causes of death were once again infections, cardiovascular events, and malignancy. The mortality caused by infection was much higher in the older group than in the control group ($p < 0.001$) [16].

Skrabaka et al. studied 350 patients divided into two equal groups using the same deceased organ donor to establish early post-transplant complications. The cut-off age used in this study was over 60 years and below 60 years. The older group was characterised by a higher body mass index and a higher occurrence of diabetes mellitus and cardiovascular diseases (CVD). In the three-month period studied, no significant difference was observed regarding surgical (20.6% vs. 24%) and clinical complications (28.6% vs. 27.4%), patient survival (95.4% vs. 97.1%), or graft survival (93.1% vs. 95.4%). Age, duration of dialysis, pretransplant diabetes mellitus, and CVD were risk factors for infectious complication in both groups [17].

Yoo et al., in a cohort study, analysed the clinical outcomes of kidney transplantation in the Korean population. A total of 3565 patients, divided into five subgroups based on age (18–29, 30–39, 40–49, 50–59, >60), received grafts from either deceased or living donors. In the older group (age > 60 years) diabetes mellitus and ischemic heart disease were significantly higher compared to the other groups. The recipients' survival rate was lower in the older group ($p = 0.001$). The main cause of death was infection. BPAR and death-censored graft survival were comparable between all groups ($p = 0.104$; $p = 0.501$) [18].

So et al. examined long-term patients and graft outcomes. Participants over 65 years of age (median age 68 years) received graft from deceased and living donors. One-year and five-year patients' survival rates were 95.1% and 79%. Moreover, prevalent vascular disease and peritoneal dialysis were risk factors associated with a poorer outcome of KT for older recipients [19].

Adani et al., in a retrospective study, analysed the outcome of KT in recipients over 65 years of age. Two subgroups were selected based on age (65–70; 71–76). All participants received a graft from a deceased donor. Three main causes of death observed during the study were, as previously mentioned, infections, tumours, and cardiovascular diseases. At one, three, five, and ten years, patient survival was 89%, 84%, 72%, and 45%. At one, three, five, and ten years, graft survival was 100%, 97%, 89%, and 84%. Recipients aged $\geq$ 71 had higher mortality and graft loss compared to the group aged between 65–70 [20].

Saucedo-Crespo et al. compared two groups of patients, defined by an age of greater or equal to 70 years (mean age 73.2 years), and below 70 years (mean age 50.9 years). One-, three-, and five-year patient survival rates were lower in the older group (95% vs. 98%; 86% vs. 95%; 77% vs. 90%; $p = 0.001$). Death was the main factor of graft loss in recipients aged $\geq$ 70 [21].

Kim et al. studied risk factors and the clinical impact of early post-transplant infection. A total of 3738 patients were divided based on age, with one group equal to or older than 60 years, and another group younger than 60 years. Older recipients had a higher incidence of early post-transplant infections compared to the younger group (22.7% vs. 16.9%), and they more often suffered from mycobacterial infections, coinfections, and multiple site infections. For both groups, bacteria were the most common pathogen causing the infection, and the most frequent site of infection was the urinary tract [22].

In Silva et al.'s study, patients' short-term survival in 147 recipients aged $\geq$ 65 years was examined. Patients received kidneys from both deceased and living donors. Factors such as cold ischemia time, increased donor age, cardiovascular disease, DGF, early cardiovascular complication post-KT, early rehospitalizations, and peritoneal dialysis were positively correlated with one-year mortality in older patients [23].

Shi et al., in a matched paired analysis, compared the survival of kidney transplantation with ongoing dialysis for 930 patients over 70 years of age. The research showed that shortly after KT mortality is higher compared to that of people on dialysis. One-year survival rates were similar between the two groups; however, after one year the survival rate was progressively higher in the transplantation group. The main causes of death in both groups were cardiovascular diseases [12].

Neri et al. analysed 452 recipients aged greater than 60 years who received a kidney from a deceased donor. One-, three-, and five-year patients' survival were 98.7%; 93%; 89%. One-, three-, and five-year grafts' survival were 94.4%, 87.9%, 81.4%. Age was a risk factor for both patient and graft survival. Moreover, BPAR and neoplasia were correlated with worse graft survival [24].

Cabrera et al. studied older patients with a cut-off age of $\geq$75 years, which is higher compared to most presented studies. Patients received kidneys from similarly aged, deceased donors. One- and five-year patients' survival rates, as well as grafts' survival rates were 82.1%, 60.1%, and 95.6%, 93.1%. In 8.0% of patients, primary graft non-function was observed. Infection was the main cause of death [25].

Jankowska et al. studied 328 patients divided equally into two groups based on age. One group was $\geq$60 years of age, and the second group was <60 years of age. Patients received a kidney from a paired deceased donor. In the research, no significant difference was observed regarding one-year patient survival, one-year graft survival, DGF, BPAR, or death-censored graft survival between the two groups. Elderly patients had significantly worse patient and graft survival in the long-term. The main causes of death after one year were neoplasia, cardiovascular diseases, and infections [26].

Lønning et al. conducted a study in which two groups of KT recipients were compared in terms of graft and patient survival. All patients received a kidney from deceased donors.

The first group was ≥80 years of age and the second group was 70–79 years of age. Contrary to other studies, both groups included the older population. No significant difference was observed regarding death-censored graft survival. The five-year patients' survival was 55% for recipients ≥80 years of age [27].

4. Discussion

4.1. Definition of Older Population

The definition of older people remains unclear since there are different cut-off points. The World Health Organization (WHO) defines it as people over 65 years of age (in developed countries). On the other hand, the United Nations points to the age of 60 years. In the medical literature relating to kidney transplants, different cut-off points were also included. For example, in the Middle East Single-Centre retrospective study, the older patients were defined as >60 years old [11], while the study from Norway reported on outcomes in recipients over 70 years of age [13]. The presented studies clearly indicate that kidney transplantation can be beneficial for older recipients; however, some complications—for example, infections—can be observed more frequently in the older population. Thus, clarification in terms of the definition of older kidney recipients is needed.

4.2. Surgical Complications

Surgical complications are defined as any incident related to the procedure of surgical transplantation of the graft. Scrabaca et al., in the three-month follow-up period after transplantation, did not observe any difference between older patients and younger recipients [17]. Similar results were observed in a study performed by Jankowska et al. [26]. On the other hand, Orlando et al., in a long-term observational study, proved that older patients have indeed a higher incidence of surgical complications. The most commonly observed were surgical wound dehiscence, urinary fistula, hernia, and dilated bladder [16]. Moreover, the research comparing the Eurotransplant Kidney Allocation System (ETKAS)—a regular program which allocates organs to patients on the waiting list—with the Eurotransplant Senior Program (ESP)—the program in which patients over 65 years of age receive kidneys from deceased donors 65 years and above—indicated that the ESP had a higher rate of surgical complications [28]. Any kind of surgical complication prolongs hospitalisation and also hinder the rehabilitation process, which is essential for older patients. There is a need for more studies about surgical complications, with emphasis on each type of complication.

4.3. Clinical Complications

Clinical complications can be described as the ones observed shortly after kidney transplant and in long-term outcomes. In this article, we focus on biopsy-proven acute rejection (BPAR), delayed graft function (DGF), post-transplant diabetes mellitus (PTDM), and infectious complications.

4.3.1. Delayed Graft Function (DGF)

Delayed graft function (DGF) is defined as a requirement for dialysis within seven days after transplantation due to the lack of immediate function of the graft [29]. No difference between the occurrence of DGF in older and younger groups was found in the presented studies [11,14,15,17,26].

4.3.2. Biopsy Proven Acute Rejection

It is clear that, during the ageing process, all body systems, including the immune system, becomes less efficient; therefore, acute rejection in older kidney recipients could be less often observed. However, presented studies are inconclusive in this regard. In a retrospective study performed by Orlandi et al., the incidence of acute rejection in both older and younger recipients was comparable [15]. Similar results were observed in three other studies [13,16,26]. However, Doucet et al. indicated that older patients who received a kidney from living donors had lower rates of acute rejection [14].

4.3.3. Infectious Complication

Infectious complications can be very dangerous, not only shortly after kidney transplantation, but also in the long-term perspective. They are one of the main reasons for death with a functioning graft [13,15,16,18,20,23]. Infectious complications are more often seen in older recipients [22]. The urinary tract is the main site of infection shortly after transplantation [22,23]. The most common pathogens are bacteria. Interestingly, older patients are more frequently exposed to mycobacterial infection, co-infection, and multiple site infections after the first six months post-transplantation [22].

4.3.4. Post-Transplant Diabetes Mellitus

Post-transplant diabetes mellitus has not been a thoroughly examined complication in the presented studies. The reason for this may be the fact that a significant number of older patients already have diabetes mellitus, compared with younger recipients (47.14% vs. 23.3%) [11,14–17,21,22,27,28]. Only in one study was the number of PTDM higher in older recipients [26]. In contrast to the study by Jankowska et al., the Single-Centre Middle East research observed a higher incidence of PTDM in younger patients, although more micro- and macro-angiopathies were present in the older population [11]. There is no doubt that more research is required to establish whether PTDM is a widespread complication in older patients.

4.4. Patent Mortality, Graft Loss, and Patient Survival

As could be presumed, patient mortality in older patients was higher than in younger groups [13,15,18]. The cause of that is not only the age, but also the commonly observed comorbidities in the older population, such as coronary artery disease, diabetes mellitus, and hypertension. Factors associated with a greater risk of all-cause death are prevalent coronary artery disease, cerebrovascular disease, increasing ischemic time, donor age, delayed graft function, and peritoneal dialysis pre-transplantation [19]. The three most common causes of death are infectious diseases, cardiovascular diseases, and cancer [13,15,16,18,20,23–26]. No difference between death-censored graft survival in various groups was observed [11,13,17,18,26]. Recipient age, BPACR, and surgical complications were identified as risk factors for death-censored graft survival [24]. Regarding patient survival in the three-month follow-up, the older and younger groups were comparable [13,17]. However, the long-term survival varied in favour of younger patients. Orlandi et al. indicated lower survival in the older group after five years (76.6% vs. 87.7%) and ten years (54.8% vs. 84.3%). [15]. The same result was observed in an Australia and New Zealand Dialysis and Transplant Registry Study after a one-year (96% vs. 97%), three-year (84% vs. 93%), and five-year (79% vs. 90%) follow-up [14]. In a Norwegian study, five-year survival for recipients over 80 years of age was 55%, which can still be presumed to be an acceptable outcome [27]. What seems to be an important aspect of patient survival, though, is the comparison between older patients on dialysis, and after kidney transplantation. Shi et al. conducted such a study and the results clearly indicated that, shortly after transplantation, the risk of mortality was indeed higher for KT patients, and this was mainly due to infectious complications. However, after the first year, the survival of KT recipients steadily improved compared to patients on dialysis (five-year survival of 80% vs. 53%, and a ten-year survival of 53% vs. 17%) [12].

4.5. Frailty

Frailty is defined as a clinically recognisable state of increased vulnerability resulting from ageing-associated decline in reserve and function across many physiological systems, which leads to an inability to cope with everyday or acute stressors [30]. There are multiple scores used to assess frailty; however, two of them seem to be particularly significant. The first one is the Fried frailty score (phenotype score), and the second one is the frailty score (deficit accumulation score). Fried et al. defined frailty as meeting three or more out of five criteria indicating decreased strength: weakness (low grip strength), low energy, slowed

walking speed, low physical activity, and unintentional weight loss (≥4.5 kg in the past year) [30,31]. The deficit accumulation index contains about 50 health-associated deficits, including cognitive function, physical function, functionality, and laboratory test results. The more deficits that are present, the greater the severity of frailty becomes. This scale is also more complex than the phenotype score and requires more laboratory tests [32]. Frailty is an important aspect when approaching older kidney recipients, especially because it is considered a modifiable risk factor and can be treated [33]. It increases mortality and also lowers health-related quality of life [34]. Moreover, it can increase the risk of DGF [35]. In the presented studies, frailty was not widely discussed, thus more studies are needed to establish an accurate approach, not only to kidney transplantation recipients, but also to patients on the waiting list.

4.6. Study Limitations

This study has potential limitations. Firstly, its reliance on only two databases, and secondly, the manual verification of excessive amounts of data, make the retrieval process vulnerable to omissions.

5. Conclusions

In this literature review, the findings indicate that older kidney transplant recipients have higher mortality, and worse overall survival compared to the younger groups; however, most of the presented studies did not show worse death-censored graft survival. Infectious complications are often observed in older adults and are one of the main causes of death. No difference between the occurrence of DGF and BPAR was observed. More studies are necessary to establish the incidence of surgical complications, as well as some clinical complications, such as post-transplant diabetes mellitus and cytomegalovirus infection. There is also a great need for studies to include frailty and other geriatric impairments occurring in older recipients, which may contribute to some post-transplant complications and affect patient survival. Kidney transplantation can be beneficial for selected older patients; however, each patient requires a careful approach, especially with regard to their comorbidities.

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7. Podsumowanie i wnioski

Starsi biorcy po przeszczepieniu nerki stanowią szczególną grupę pacjentów wymagającą wnikliwej oceny klinicznej. Przeprowadzone analizy potwierdziły bezpieczeństwo transplantacji w tej populacji i korzystne wyniki wczesnej funkcji przeszczepu. Analiza statystyczna pozwoliła na identyfikację powikłań klinicznych i chirurgicznych, które częściej obserwowano u pacjentów w podeszłym wieku. Do najistotniejszych powikłań obserwowanych u starszych pacjentów należały powikłania chirurgiczne (a wśród nich powikłania naczyniowe i urologiczne), infekcje o etiologii bakteryjnej, z głównym punktem wyjścia z dróg moczowych, cukrzyca potransplantacyjna, opóźniona czynność nerki przeszczepionej oraz zdarzenia sercowo-naczyniowe.

W kolejnym etapie oceniono czynniki ryzyka rozwoju PTDM u wszystkich poddanych analizie biorców, ze szczególnym uwzględnieniem biorców ≥60 roku życia. Wiek, podwyższone BMI, hipomagnezemia, hipertriglicerydemia i hipercholesterolemia istotnie zwiększały ryzyko wystąpienia tej choroby. Co istotne, regresja logistyczna wykazała największy wpływ wieku na rozwój PTDM, przez co pacjenci w podeszłym wieku pozostają szczególnie narażoną grupą.

W analizie porównawczej starszych i młodszych biorców z PTDM nie stwierdzono czynników istotnie pogarszających wczesną funkcję nerki przeszczepionej u starszych pacjentów.

Przedstawione wyniki badań własnych pozostają zgodne z obserwacjami opisanymi w przeglądzie literatury i wskazują zarówno na niebezpieczeństwa jak i korzyści płynące z przeszczepienia nerki u pacjentów ≥60 roku życia. Opisane wczesne powikłania i funkcja przeszczepu stanowi dobry punkt wyjścia w kierunku dalszych badań nad długoterminowymi skutkami przeszczepienia nerki u starszych biorców.

Wnioski:

1. Wczesne wyniki przeszczepienia nerki u pacjentów w wieku ≥60 lat charakteryzują się częstszym występowaniem wybranych powikłań klinicznych i chirurgicznych. W rocznej obserwacji wykazano w tej grupie niższą, choć nadal

klinicznie akceptowalną, funkcję nerki przeszczepionej w porównaniu z młodszymi biorcami.

2. Pacjenci w wieku ≥60 lat pozostają szczególnie narażeni na rozwój PTDM, co podkreśla konieczność ich regularnego monitorowania.
3. Wśród biorców u których rozwinęła się PTDM wczesna funkcja nerki przeszczepionej oraz częstość powikłań nie różnią się istotnie w analizowanych grupach wiekowych.
4. Przeżywalność pacjentów i nerki przeszczepionej pozostaje na porównywalnym, akceptowalnym klinicznie poziomie, co potwierdza zasadność kwalifikowania pacjentów w wieku ≥60 lat do KTx.
5. Przedstawione wyniki wskazują na konieczność indywidualizacji postępowania oraz ścisłego monitorowania powikłań u starszych biorców.

8. Piśmiennictwo

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9. Opinia Komisji Bioetycznej

Komisja Bioetyczna
przy Warszawskim Uniwersytecie Medycznym

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e-mail: komisja.bioetyczna@wum.edu.pl
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Warszawa, dnia 14.04.2025

AKBE/ 95 / 2025

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Klinika Transplantacji, Immunologii, Nefrologii
i Chorób Wewnętrznych,
ul. Nowogrodzka 59,
02-006 Warszawa

OŚWIADCZENIE

Niniejszym oświadczam, że Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym w dniu 14 kwietnia 2025r. przyjęła do wiadomości informację na temat badania pt. "Wczesne wyniki przeszczepienia nerki u starszych biorców w wieku ≥60 lat-badanie jednoośrodkowe, retrospektywne."
Przedstawione badanie nie stanowi eksperymentu medycznego w rozumieniu art. 21ust.1 ustawy z dnia 5 grudnia 1996 r. o zawodach lekarza i lekarza dentysty (Dz.U. z 2018r poz.617) i nie wymaga uzyskania opinii Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym, o której mowa w art. 29 ust.1 ww. ustawy.

Przewodnicząca Komisji Bioetycznej

Prof. dr hab. n. med. Magdalena Kuźma –Kozakiewicz

Komisja Bioetyczna
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Warszawa, dnia 20.01.2025

AKBE/ 1 / 2025

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OŚWIADCZENIE

Niniejszym oświadczam, że Komisja Bioetyczna przy Warszawskim Uniwersytecie Medycznym w dniu 20 stycznia 2025r. przyjęła do wiadomości informację na temat badania pt. "Czynniki ryzyka rozwoju cukrzycy potransplantacyjnej u biorców przeszczepu nerkowego oraz porównanie pomiędzy starszymi i młodszymi biorcami po przeszczepieniu nerki z cukrzycą potransplantacyjną." Przedstawione badanie nie stanowi eksperymentu medycznego w rozumieniu art. 21ust.1 ustawy z dnia 5 grudnia 1996 r. o zawodach lekarza i lekarza dentysty (Dz.U. z 2018r poz.617) i nie wymaga uzyskania opinii Komisji Bioetycznej przy Warszawskim Uniwersytecie Medycznym, o której mowa w art. 29 ust.1 ww. ustawy.

Przewodnicząca Komisji Bioetycznej

Prof. dr hab. n. med. Magdalena Kuźma –Kozakiewicz

10. Oświadczenia współautorów

Warszawa, 17.11.2025
(miejscowość, data)

prof. dr hab. n. med. Magdalena Durlik
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. "Kidney Transplantation in Older Recipients: One-Year Outcomes and Complications from a Single-Center Experience" oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: edycja i ostateczna akceptacja manuskryptu. Mój udział procentowy w przygotowaniu publikacji określam jako 5 %.

Wkład lek. Aleksandry Barbachowskiej-Kubik w powstawanie publikacji określam jako 80%,
(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji artykułu, metodyki, zebranie i analizę danych, interpretację wyników, napisanie manuskryptu

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji)*

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik
(imię i nazwisko kandydata do stopnia)

.....
(podpis oświadczającego)

Warszawa, 17.11.2025
(miejscowość, data)

dr hab. n. med. Jolanta Gozdowska
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. "Kidney Transplantation in Older Recipients: One-Year Outcomes and Complications from a Single-Center Experience" oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: nadzór merytoryczny nad koncepcją publikacji, metodyką oraz interpretacją wyników, edycja i ostateczna akceptacja manuskryptu.

Mój udział procentowy w przygotowaniu publikacji określam jako 15 %.

Wkład lek. Aleksandry Barbachowskiej-Kubik w powstawanie publikacji określam jako 80%,

(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji artykułu, metodyki, zebranie i analizę danych, interpretację wyników, napisanie manuskryptu

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji)*

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik

(imię i nazwisko kandydata do stopnia)

J. Gozdowska
.....
(podpis oświadczającego)

Warszawa, 17.11.2025
(miejscowość, data)

prof. dr hab. n. med. Maciej Kosieradzki
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. "Risk Factors for Development of Post-Transplant Diabetes Mellitus After Kidney Transplantation and Comparison Between Older and Younger Recipients in the Early Post-Transplantation Period: A Single-Center Study" oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: edycja i ostateczna akceptacja manuskryptu. Mój udział procentowy w przygotowaniu publikacji określam jako 5 %.

Wkład lek. Aleksandry Barbachowskiej-Kubik w powstawanie publikacji określam jako 75%,
(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji artykułu, metodyki, zebranie i analizę danych, interpretację wyników, napisanie manuskryptu

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji)*

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik
(imię i nazwisko kandydata do stopnia)

ORDYNATOR - KIEROWNIK KLINIKI Chirurgii Ogólnej i Transplantacyjnej UCK WUM SKDJ
Prof. dr hab. n. med. Maciej Kosieradzki

.....
(podpis oświadczającego)

Warszawa, 17.11.2025
(miejscowość, data)

prof. dr hab. n. med. Magdalena Durlik
(imię i nazwisko)

OŚWIADCZENIE

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Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik
(imię i nazwisko kandydata do stopnia)

M Durlik
.....
(podpis oświadczającego)

Warszawa, 17.11.2025
(miejscowość, data)

dr hab. n. med. Jolanta Gozdowska
(imię i nazwisko)

OŚWIADCZENIE

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Wkład lek. Aleksandry Barbachowskiej-Kubik w powstawanie publikacji określam jako 75%,
(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji artykułu, metodyki, zebranie i analizę danych, interpretację wyników, napisanie manuskryptu

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Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik
(imię i nazwisko kandydata do stopnia)

J. Gozdowska
.....
(podpis oświadczającego)

Warszawa, 17.11.2025
(miejscowość, data)

prof. dr hab. n. med. Magdalena Durlik
(imię i nazwisko)

OŚWIADCZENIE

Jako współautor pracy pt. "Kidney Transplantation in Older Recipients Regarding Surgical and Clinical Complications, Outcomes, and Survival: A Literature Review" oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: edycja i ostateczna akceptacja manuskryptu.

Mój udział procentowy w przygotowaniu publikacji określam jako 5 %.

Wkład lek. Aleksandry Barbachowskiej-Kubik w powstawanie publikacji określam jako 80%,
(imię i nazwisko kandydata do stopnia)

obejmował on: przygotowanie koncepcji artykułu, metodyki, zebranie i analizę danych, interpretację wyników, napisanie manuskryptu

(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji)*

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik
(imię i nazwisko kandydata do stopnia)

M Durlik

(podpis oświadczającego)

Warszawa, 17.11.2025
(miejscowość, data)

dr hab. n. med. Jolanta Gozdowska
(imię i nazwisko)

OŚWIADCZENIE

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(merytoryczny opis wkładu kandydata do stopnia w powstanie publikacji)*

Jednocześnie wyrażam zgodę na wykorzystanie w/w pracy jako część rozprawy doktorskiej lek. Aleksandry Barbachowskiej-Kubik
(imię i nazwisko kandydata do stopnia)

J. Gozdowska
.....
(podpis oświadczającego)

Warszawa, 17.11.2025

(miejscowość, data)

Lek. Aleksandra Barbachowska-Kubik

(imię i nazwisko)

OŚWIADCZENIE

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Mój udział procentowy w przygotowaniu publikacji określam jako 80%.

Aleksandra Barbachowska-Kubik

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

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OŚWIADCZENIE

Jako współautor pracy pt. „Risk Factors for Development of Post-Transplant Diabetes Mellitus After Kidney Transplantation and Comparison Between Older and Younger Recipients in the Early Post-Transplantation Period: A Single-Center Study" oświadczam, iż mój własny wkład merytoryczny w przygotowanie, przeprowadzenie i opracowanie badań oraz przedstawienie pracy w formie publikacji stanowi: przygotowanie koncepcji artykułu, metodyki, zebranie i analizę danych, interpretację wyników, napisanie manuskryptu.

Mój udział procentowy w przygotowaniu publikacji określam jako 75%.

Aleksandra Barbachowska-Kubik

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników

Warszawa, 17.11.2025

(miejscowość, data)

Lek. Aleksandra Barbachowska-Kubik

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OŚWIADCZENIE

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Aleksandra Barbachowska-Kubik

(podpis oświadczającego)

*w szczególności udziału w przygotowaniu koncepcji, metodyki, wykonaniu badań, interpretacji wyników