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Efficacy of induction therapy and its impact on the development of delayed graft function in kidney transplant recipients: a single-center retrospective analysis

Böbrek nakli hastalarında indüksiyon tedavisinin etkinliği ve gecikmiş greft fonksiyonu gelişimine etkisi: tek merkezli retrospektif bir analiz

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Abstract

Purpose: This study aimed to evaluate the impact of two different induction therapies-Basiliximab and ATG-Fresenius (ATG-F)-on early outcomes and the development of delayed graft function (DGF) in kidney transplant recipients from living or deceased donors at a single center.

Matherials and methods: A total of 33 patients over 18 years old who underwent kidney transplantation at a single center between February 2022 and February 2025 were analyzed. Body mass index (BMI), demographic data, transplant characteristics, and complications were recorded. DGF was defined as requiring dialysis within the first seven postoperative days. Statistical analyses were performed using the t-test or Mann-Whitney U test for continuous variables and the Chi-square test for categorical variables, with $p<0.05$ considered significant.

Results: The mean age of recipients was 39.8±11.9 years; there were 10 females and 23 males. The mean BMI was 24.5±3 kg/m². Sixteen patients (14/16 Basiliximab) received living-donor kidneys, while 17 (17/17 ATG-F) received deceased-donor kidneys. Cold ischemia time was 1.1±0.2 hours for living-donor grafts versus 11.6±2.0 hours for deceased donors ($p=0.001$). Similarly, Pre-transplant dialysis duration was significantly longer in deceased-donor recipients (2.5±2.6 vs. 9.4±4.8 years, $p=0.001$). Overall, 30.3% (10/33) of patients developed DGF, predominantly in those with longer ischemia and dialysis times.

Conclusion: In deceased-donor kidney transplant recipients, prolonged cold ischemia and pre-transplant dialysis duration increase the incidence of DGF. The use of ATG-F in patients with high immunologic risk appears to be beneficial and is consistent with the existing literature. However, the limited sample size makes it difficult to clarify the impact of induction therapy on DGF; therefore, larger prospective studies are needed.

Keywords: Kidney transplant, end-stage renal disease, hemodialysis.

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Öz

Amaç: Bu çalışma, tek merkezde canlı veya kadavradan böbrek nakli yapılan hastalarda iki farklı indüksiyon tedavisinin-Basiliksimab ve ATG-Fresenius (ATG-F)-erken dönem sonuçları ve gecikmiş greft fonksiyonu (DGF) gelişimi üzerindeki etkilerini değerlendirmeyi amaçlamaktadır.

Gereç ve yöntem: Şubat 2022 ile Şubat 2025 tarihleri arasında, tek bir merkezde böbrek nakli yapılan 18 yaş üzeri toplam 33 hasta retrospektif olarak incelendi. Vücut kitle indeksi (VKİ), demografik veriler, nakil özellikleri ve komplikasyonlar kaydedildi. DGF, transplantasyonu takiben ilk yedi gün içinde diyalize ihtiyaç duyulması şeklinde tanımlandı. Sürekli değişkenler için normal dağılıma göre t-testi veya Mann-Whitney U testi, kategorik değişkenler için ise Ki-kare testi kullanıldı. $p<0,05$ istatistiksel olarak anlamlı kabul edildi.

Bulgular: Hastaların yaş ortalaması 39,8±11,9 yıl olup; 10'u kadın, 23'ü erkekti. Ortalama VKİ 24,5±3 kg/m² idi. Canlı verici grubundaki 16 hastanın 14'üne Basiliksimab, kadaverik gruptaki 17 hastanın tamamına ATG-F uygulanmıştır. Soğuk iskemi süresi, canlı vericili greftlerde 1,1±0,2 saat; kadavradan alınan greftlerde ise 11,6±2,0 saat olarak bulunmuştur ($p=0,001$). Benzer şekilde, transplantasyon öncesi diyaliz süresi de kadavra verici alıcılarında anlamlı derecede daha uzundu (2,5±2,6 yıla karşı 9,4±4,8 yıl; $p=0,001$).

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Genel olarak hastaların %30,3'ünde (10/33) DGF gelişmiş olup, bu hastalarda iskemi ve diyaliz süreleri anlamlı derecede daha uzundu.
Sonuç: Kadavradan böbrek nakli yapılan hastalarda uzamış soğuk iskemi ve transplantasyon öncesi diyaliz süresi, DGF gelişme insidansını artırmaktadır. Yüksek immünolojik riske sahip hastalarda ATG-F kullanımının faydalı olabileceği mevcut literatür ile uyumludur. Ancak, sınırlı hasta sayısı, indüksiyon tedavisinin DGF üzerindeki etkisini netleştirmeyi güçleştirmektedir; bu nedenle daha geniş prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Böbrek nakli, son dönem böbrek hastalığı, hemodiyaliz.

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Introduction

Chronic kidney disease (CKD), which has become a significant public health problem worldwide, is an important cause of morbidity and mortality [1]. After end-stage renal disease (ESRD) develops, renal replacement therapy becomes necessary, and kidney transplantation is currently the most preferred replacement approach [2]. Kidney transplantation improves patients' quality of life, reduces treatment costs, and increases patient survival. Significant advances in immunosuppressive therapy in recent years have considerably improved graft and patient survival rates [3, 4], yet graft rejection remains a major complication both in the early and late postoperative periods [5].

Immunosuppressive regimens are used to prevent rejection. Rejection episodes have an adverse effect on graft survival and are important determinants of graft failure. Antilymphocyte biological agents for induction therapy are widely used immediately before, during, or after the kidney transplant operation. Commonly used induction therapies include T lymphocyte-depleting agents (rabbit or horse anti-thymocyte globulin [rATG], alemtuzumab) or a non-depleting IL-2 receptor antagonist (IL2RA) (basiliximab), high-dose calcineurin inhibitors, and high-dose methylprednisolone [6, 7].

The first randomized studies demonstrated that both rATG and IL2RA induction reduce early acute rejection. They also recommended routine use of IL2RA induction as first-line therapy after renal transplantation while reserving ATG for high-risk cases. In patients at high immunological risk, ATG induction can reduce the relative risk of acute rejection by almost 50% compared to IL2RA [8].

A general trend toward increased use of induction therapy in solid organ transplantation (except liver transplantation) has been observed over the past two decades [4]. The use of rATG in induction therapy has also risen. However, the optimal regimen and duration of immunosuppression remain unknown [5].

For deceased donor kidney transplants, induction therapy has become more clearly established, while its use in living donor kidney transplantation is still somewhat debated. Living donor transplantation is generally considered less risky than deceased donor transplantation [6], but there are also studies showing opposite results.

The transplant recipient's immunological status, HLA mismatches, panel-reactive antibody (PRA) levels, donor-specific antibodies (DSA), donor age, etiology of chronic kidney disease, and cold ischemia time all play a role in the selection and dosing of induction therapy. Cost, availability, and side effects are also important considerations. Basiliximab and ATG-Fresenius (ATG-F, also known as Grafalon) have long been used as induction agents at our transplant center. In addition, all patients routinely receive high-dose methylprednisolone, calcineurin inhibitors, and mycophenolic acid (or mycophenolate mofetil). The aim of this study was to present the outcomes of kidney transplant induction therapy.

Materials and methods

Sample selection

This retrospective study included patients over the age of 18 who received a kidney transplant from a living or deceased donor at the PAUTF University Hospital transplant center between February 2022 and February 2025. Patients with missing data and pediatric cases were excluded.

Data collection

For all kidney transplant recipients, we gathered the following data from the hospital's electronic records: age, sex, body mass index (BMI), cause of ESRD, comorbidities, prior dialysis type and duration, the time from starting renal replacement therapy to transplantation, donor age and type (living or deceased), cold ischemia time, immunological profiles, and the initial immunosuppressive therapy regimen. Postoperative medical complications were noted, including DGF, leukopenia, neutropenia, severe neutropenia, thrombocytopenia, the day on which serum creatinine fell below three times its baseline, and discharge creatinine levels.

DGF was defined as the need for hemodialysis within seven days following kidney transplantation. Leukopenia was defined as WBC <3000/mm^3. Neutropenia was defined as an absolute neutrophil count <1500 cells/μL, and severe neutropenia as <500 cells/μL.

Immunosuppressive therapy regimen

Two main groups were formed based on induction therapy with Basiliximab or ATG-F.

Basiliximab group: Given to low-immunological-risk patients with PRA <20% (if <70 years old) or <50% (if ≥70 years old) and no DSA, dosed at 20 mg immediately before and four days after kidney transplantation.

ATG-F group: Given to high-risk patients (factors such as higher PRA, immunological mismatch, etc.). All patients also received standard induction and maintenance immunosuppressive therapy: corticosteroids, mycophenolic acid (or mycophenolate mofetil), and a calcineurin inhibitor (tacrolimus).

Ethics approval was obtained from the Pamukkale University Non-Interventional Clinical Research Ethics Committee (approval date: 04.02.2025/03, approval no: E-60116787-020-643233).

Statistical analysis

All statistical analyses were performed using the SPSS 27.0 software. Normality of distribution was assessed with the Kolmogorov-Smirnov test. Descriptive statistics for continuous variables were expressed as mean ± standard deviation for normally distributed data or as median (minimum-maximum) for non-normally distributed data. Categorical variables were expressed as frequency and percentage. For group comparisons, we used the independent two-sample t-test for normally distributed variables and the Chi-square independence test for categorical data. Statistical significance was set at $p<0.05$.

Results

Thirty-three patients who underwent kidney transplantation were included in the study. Their demographic characteristics are shown in Table 1. The cohort included 10 women and 23 men, with a mean age of 39.8±11.9 years and a mean BMI of 24.5±3 kg/m^2. When classified by donor type, 16 patients (48.5%) received kidneys from living donors, and 17 (51.5%) from deceased donors. DGF was observed in 10 patients (30.3%). Factors affecting the development of DGF are shown in Table 2.

Among both living-donor and deceased-donor recipients, the most common blood group was A Rh(+) (33.3%). No statistically significant relationship was found between blood group and DGF (p=0.757, cs=1.184). When recipients were evaluated according to tissue matching:

In terms of induction therapy, Basiliximab was used in 14 of the living-donor transplants and ATG in 2 (12.5%). All deceased-donor recipients received ATG induction. For maintenance immunosuppression, all recipients received corticosteroids + tacrolimus + mycophenolate mofetil.

Table 1. Demographic characteristics of patients receiving living-donor or deceased-donor kidney transplants

		Donor		*p*
		Living donor	**Deceased donor**	
Recipient Sex (n / %)	**Female**	3 (18.8%)	7 (43.8%)	0.127 (cs=2.327)
	Male	13 (81.3%)	9 (56.3%)	
Recipient age (year)	**Mean ± S.D**	38.25±14.63	41.41±8.94	0.456 (t=-0.744)
	Med (IQR)	38.5 (24-49.5)	40 (36-49)	
	min-max	18-67	24-56	
BMI (kg/m²)	**Mean ± S.D**	24.06±4.34	25.02±3.23	0.472 (t=-0.729)
	Med (IQR)	24.2 (20.5-27.95)	25.4 (22.05-28.05)	
	min-max	15-30	20 - 29.1	
Cold ischemia time	**Mean ± S.D**	0.61±0.23	11.61±2	0.0001* (z=-4.911)
	Med (IQR)	0.55 (0.5-0.57)	11.52 (10.38-13.39)	
	min-max	0.4-1.15	8.17-15.2	
Pre-transplant dialysis duration (year)	**Mean ± S.D**	2.53±2.6	9.41±4.85	0.0001* (z=-4.321)
	Med (IQR)	2 (1-3)	8 (6-11.5)	
	min-max	0-11	3-22	
Donor age (year)	**Mean ± S.D**	43±10.05	41.94±18.76	0.84 (t=0.204)
	Med (IQR)	41.5 (36.25-52.5)	46 (22-58)	
	min-max	25-60	14-70	
Donor sex (n / %)	**Female**	3 (18.8%)	5 (29.4%)	0.688 γ
	Male	13 (81.3%)	12 (70.6%)	

*p<0.05 statistically significant, S.D: Standard Deviation, Med (IQR): Median (25^{th}-75^{th} percentiles), z: Mann Whitney U test
t: Independent samples t test, cs: Chi-square test, γ: Fisher exact test, BMI: Body Mass Index

Table 2. Factors affecting patients requiring dialysis in the first week after transplantation (DGF)

		No DGF	DGF	*p*
Recipient age (year)	**Mean ± S.D**	38.57±13.22	42.9±8.12	0.346 (t=-0.956)
	Med (IQR)	38 (30-50)	41 (37.75-49.25)	
	min-max	18-67	29-56	
Donor age (year)	**Mean ± S.D**	40.48±12.62	47±19.3	0.256 (t=-1.158)
	Med (IQR)	39 (33-51)	53 (25-61.25)	
	min-max	18-60	14-70	
BMI	**Mean ± S.D**	23.78±3.96	26.34±2.72	0.073 (t=-1.855)
	Med (IQR)	24 (20.5-27.8)	26.95 (24.95-28.48)	
	min-max	15-30	20-29.1	
Cold ischemia time	**Mean ± S.D**	3.92±5.23	11.71±2.04	0.0001* (z=-3.338)
	Med (IQR)	0.55 (0.5-10.28)	11.75 (10.23-13.43)	
	min-max	0.4-14.48	8.58-15.2	
Pre-transplant dialysis duration (year)	**Mean ± S.D**	3.76±3.28	11.4±4.99	0.0001* (z=-3.755)
	Med (IQR)	3 (2-5)	10.5 (7.75-14.75)	
	min-max	0-12	6-22	
PRA Class I	**negative**	20 (87%)	10 (100%)	0.536 γ
	pozitive	3 (13%)	0 (0%)	
PRA Class II	**negative**	22 (95.7%)	9 (90%)	0.521 γ
	pozitive	1 (4.3%)	1 (10%)	
HLA matches	**0**	2 (8.7%)	0 (0%)	0.082 (cs=9.78)
	1	6 (26.1%)	2 (20%)	
	2	5 (21.7%)	7 (70%)	
	3	5 (21.7%)	1 (10%)	
	4	3 (13%)	0 (0%)	
	6	2 (8.7%)	0 (0%)	
A	**0**	10 (45.5%)	8 (88.9%)	0.047* (cs=6.119)
	1	9 (40.9%)	1 (11.1%)	
	2	3 (13.6%)	0 (0%)	
B	**0**	9 (40.9%)	3 (33.3%)	0.41 (cs=1.781)
	1	11 (50%)	6 (66.7%)	
	2	2 (9.1%)	0 (0%)	
DR	**0**	7 (31.8%)	0 (0%)	0.017* (cs=8.102)
	1	9 (40.9%)	8 (88.9%)	
	2	6 (27.3%)	1 (11.1%)	
Donor	**Living**	16 (69.6%)	0 (0%)	0.0001* γ
	Deceased	7 (30.4%)	10 (100%)	
Nephrectomy	**Left**	16 (69.6%)	3 (30%)	0.057
	Right	7 (30.4%)	7 (70%)	
ATG	**0**	14 (60.9%)	0 (0%)	0.001* γ
	1	9 (39.1%)	10 (100%)	
Basilixumab	**0**	8 (34.8)	10 (100%)	0.0001* γ
	1	15 (65.2)	0 (0%)	

*p<0.05 statistically significant, S.D: Standard Deviation, Med (IQR): Median (25^{th}-75^{th} percentiles), z: Mann Whitney U test
t: Independent samples t test, cs: Chi-square test, γ: Fisher exact test, BMI: Body Mass Index, PRA: Panel Reactive Antibody
HLA: Human Leukocyte Antigen, ATG: Antithymocyte Globulin

Discussion

In this study, we examined early outcomes and the impact on DGF of different induction therapies used in patients who received kidney transplants from living or deceased donors. Our findings showed that 30.3% of the overall patient group developed DGF, particularly among those who received kidneys from deceased donors and had longer cold ischemia time and pre-transplant dialysis durations. The literature similarly reports that prolonged cold ischemia and pre-transplant dialysis duration increase the risk of not only graft dysfunction but also graft loss [3, 4]. This accumulation of high immunological and clinical risk may render the kidney more vulnerable in the postoperative adaptation period.

In the present study, Basiliximab was generally chosen for living-donor transplants, whereas ATG-F was used in deceased-donor transplants that were considered higher risk (prolonged pre-transplant dialysis duration, potential immunological mismatches, etc.). The frequent observation of DGF in the ATG-F group does not imply that ATG-F alone causes DGF; rather, it suggests that these recipients already presented more unfavorable baseline clinical and immunological conditions. Therefore, with the limited number of patients and the retrospective design of our study, drawing definitive conclusions about a direct effect of the induction regimen on DGF etiology is challenging. However, previous studies also emphasize the effectiveness of T-lymphocyte-depleting agents (e.g., rATG, ATG-F) in reducing the incidence of acute rejection in high-risk patients [6-8].

Our study observed that patients who developed DGF had a slightly higher mean BMI, although it did not reach statistical significance, making it difficult to draw firm conclusions on the role of BMI in DGF. Similarly, age and certain immunological parameters (HLA matches, PRA status) showed some influence on DGF but did not reach statistical significance. However, previous reports have noted that advanced age, high BMI, or insufficient HLA matching could negatively affect graft function [3, 5]. The trends observed in our study may not have achieved statistical significance due to the small sample size and heterogeneity of the study population.

In conclusion, our findings demonstrate that extended cold ischemia and pre-transplant dialysis duration are major determinants of DGF in deceased-donor kidney recipients. In living-donor recipients, giving basiliximab to those with a lower immunological risk profile might be associated with fewer early DGF events. Nonetheless, it is important to note that such differences may largely stem from the distinct baseline clinical and immunological risk profiles between the two recipient groups. Prospective, large-sample, and multicenter studies are needed to more clearly elucidate the impact of different induction strategies on DGF and long-term graft survival. Such research will provide valuable data for reducing early complications and identifying optimal immunosuppressive approaches in high-risk patient populations.

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Conflict of interest: No conflict of interest was declared by the authors

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