

Clinical and pathological analysis of cases with graft nephrectomy after renal transplantation

Böbrek nakli sonrası greft nefrektomi olgularının klinik ve patolojik analizi

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Özet

Amaç: Böbrek transplantasyonunun en sık komplikasyonu olan greft yetmezliği vakalarının sayısı, artan böbrek nakli ameliyatları nedeniyle artmaktadır. Greft nefrektomi, içerdiği yüksek komplikasyon riski nedeniyle greft yetmezliği olan renal transplant alıcılarında son tedavi seçeneğidir. Bu çalışmanın amacı, greft nefrektomi yapılan hastalarda klinik özellikleri, nefrektomi nedenlerini, eksplante edilen greftin patolojik analizini ve cerrahi komplikasyonları değerlendirmektir.

Gereç ve Yöntemler: Merkezimizde 2010-2020 yılları arasında farklı nedenlerle greft nefrektomi geçiren 38 alıcı, retrospektif olarak incelendi. Alıcılar ameliyat zamanına göre iki gruba ayrıldı; klinik ve patolojik özellikleri retrospektif olarak incelendi. Erken greft nefrektomi grubunu, nakil ameliyatından sonraki ilk 6 ayda greft nefrektomi geçiren hastalar, geç greft nefrektomi grubunu ise, ameliyattan 6 ay sonra greft nefrektomi geçiren hastalar oluşturmaktaydı.

Bulgular: Erken greft nefrektomi endikasyonları çoğunlukla vasküler, cerrahi problemler ve enfeksiyon iken, geç greft nefrektomi endikasyonları rejeksiyon ve enfeksiyondü. Rejeksiyon açısından iki grup arasında istatistiksel olarak anlamlı bir fark vardı. Greft sağkalımı, postoperatif vasküler ve cerrahi komplikasyon oranları erken grupta daha yüksekti (sırasıyla $p = 0,011$ ve $p = 0,005$). Panel Reaktif Antikor (PRA) pozitifliği değerlendirildi ve iki grup arasında immünolojik risk açısından fark gözlenmedi.

Abstract

Objective: The number of cases with graft failure, which is the most frequent complication of renal transplantation, is increasing due to the increasing number of kidney transplant surgeries. Graft nephrectomy is the last treatment option in renal transplant recipients with graft failure due to the high complication risk it entails. The aim of the present study is to evaluate the clinical characteristics, etiologies for nephrectomy, pathological analysis of explanted graft, and surgical complications in recipients with graft nephrectomy.

Material and Methods: We retrospectively analyzed 38 recipients who had undergone graft nephrectomy for different reasons in the center since 2010. The recipients were divided into two groups, according to the time of surgery, with characteristics analyzed retrospectively. The early graft nephrectomy group consisted of patients who had undergone graft nephrectomy in the first 6 months after transplant surgery; the late graft nephrectomy group consisted of patients who had undergone graft nephrectomy more than 6 months after surgery.

Results: Indications for early graft nephrectomy were mostly vascular, surgical problems, and infection, whereas indications for late graft nephrectomy were rejection and infection. There was a statistically significant difference between the two groups with respect to rejection. The rate of graft survival, post-operative vascular and surgical complications were higher in the early group ($p=0.011$, and $p=0.005$, respectively). Panel Reactive Anti-

This study was approved by the Clinical Research Ethics Committee of Yeniüzyıl University (Approval number: 1436. Date: Aug 20, 2020). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

Sonuç: Greft nefrektomi yüksek morbidite ve mortalite oranlarına sahip olduğundan, potansiyel ciddi komplikasyonları önlemek için sadece seçilmiş vakalarda, gerektiğinde uygulanmalıdır.

Anahtar Kelimeler: Greft, nefrektomi, böbrek, renal, transplantasyon, komplikasyonlar.

body (PRA) positivity was evaluated, and no difference was observed between the two groups in terms of immunological risk.

Conclusions: As graft nephrectomy has high morbidity and mortality rates, it should only be applied in selected cases, where necessary, in order to prevent potentially serious complications.

Keywords: Graft, nephrectomy, kidney, transplantation, complications.

INTRODUCTION

Renal transplantation (RT) is the best treatment method for end-stage kidney disease (1-4). The number of allograft insufficiency cases, which is the most frequent complication of RT, is also increasing due to the increasing number of kidney transplant surgeries (2,5,6). The failure rate of RT is between 12-22% and 44-59% over 3 and 10 years, respectively (7). The risk factors and mechanisms of graft failure vary in association with the length of time following RT (8-10). A failed transplant increases morbidity and mortality by provoking an inflammatory response. It also provokes intolerable symptoms in patients (8). Due to the fact that graft nephrectomy may also result in morbidity and mortality, it should only be applied as a life-saving option in RT recipients in cases of graft failure (11). Acute rejection, as well as vascular and surgical problems, have been stated as the foremost indications in the early graft nephrectomy groups. Chronic rejections have started been to be played a leading role in the late nephrectomy groups (12,13).

The aim of the present study is to compare the clinical and pathological characteristics of the recipients who underwent graft nephrectomy after RT at our center.

MATERIAL AND METHODS

Between 2010 and 2020, 2380 RTs have been performed at our transplantation center. A renal graft was obtained from a living donor in 1958 RTs, and from a deceased donor in the remaining 422. We retrospectively evaluated 38 recipients that underwent graft nephrectomy for different reasons. The patients were divided into two groups, according to the time of the surgery, and their clinical and histopathological characteristics were analyzed retrospectively. The group of re-

cipients, who had undergone graft nephrectomy more than 6 months after RT, was referred to as the “late graft nephrectomy” group; whereas the group of recipients who had undergone graft nephrectomy in the first 6 months after the RT was referred to as the “early graft nephrectomy” group.

Our immunosuppressive maintenance regimen consisted of Tacrolimus, Mycophenolate mofetil or Mycophenolic acid, and Prednisone. We used ATG or IL-2 receptor antagonist (Basiliximab) for induction therapy. Patients received pulse steroid treatment in acute rejection episodes. When the acute rejection attack was resistant to steroid treatment, polyclonal or monoclonal antibodies were started.

Statistical Analysis

The Shapiro-Wilk test was used for assessing whether the variables followed a normal distribution or not. Continuous variables were presented as median (minimum: maximum) and mean±standard deviation values. Categorical variables were reported as n (%). The Pearson Chi-Square test and Fisher’s exact test were used for comparison of the categorical variables. SPSS (IBM Corp. Released 2012, IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp.) was used for statistical analysis, and a p-value <0.05 was considered statistically significant.

RESULTS

There were 23 males and 15 females with a mean age of 41.93 ± 13.8 years. The early graft nephrectomy group consisted of 16 recipients, while the late nephrectomy group consisted of 22. The median age of the early graft nephrectomy group was 51.5±14.2 years (range: 20 to 65 years), and the median age of the late graft

nephrectomy was 29.5 ± 12.9 years (range; 17 to 61 years). The average age of the donors was 43.4 ± 13.8 years (range: 23 to 72 years). RTS was performed from a living donor in 29 recipients and from a deceased donor in the remaining 9. The ratios of living donor/deceased donor in the early and late groups were 9/7 and 20/2, respectively. Before RT, 35 recipients were under hemodialysis, 1 recipient was under peritoneal dialysis, while the remaining 2 were preemptive. Median dialysis time in the early group was 40 months (range 2 to 156 months), whereas it was 19 months (range: 0 to 105 months) in the late group. Median graft survival was 1 month (range: 0 to 6 months) in the early group and 34 months (range: 7 to 95 months) in the late group. In terms of immunological risk, there were 7 (43.8%) PRA (+) patients in the early group and 5 (22.7%) in the late group. There was no significant difference between the groups ($p=0.169$). The clinical characteristics of the graft nephrectomy recipients are summarized in Table 1. The most common disease for renal failure was hypertension, glomerulonephritis and diabetes mellitus. The details are demonstrated in Table 2. There was no statistically significant difference between the groups in terms of primary diseases ($p>0.05$).

The most common indications for graft nephrectomy were chronic rejection. There was a statistically significant difference between the two groups with respect to rejection. In the early group, the rate of graft survival was statistically significantly higher; compared with the late group ($p=0.011$). There was a significant difference between the groups in terms of vascular and surgical complications. Vascular and surgical complications were higher in the early group ($p=0.005$). No statistically significant difference was found between the groups in terms of infection and other graft nephrectomy indications ($p>0.05$) (Table 3). All of the recipients with chronic rejection belonged to the late nephrectomy group. The most common causes for nephrectomy were hematuria, fever, anemia, and pain in the allograft. The most common nephrectomy indications for the recipients with vascular and surgical problems observed in the early graft nephrectomy group were renal vein thrombosis ($n = 3$) and renal artery thrombosis ($n = 2$) (Table 3).

The nephrectomy technique was extracapsular in the early group, whereas it was subcapsular in the late group. The surgical complication rate was 43.75% in the early graft nephrectomy group and 18.18% in the late graft nephrectomy group (Table 4). Although surgical complications were higher in the early graft nephrectomy group, there was no statistically significant difference between the groups ($p=0.147$). Furthermore, there was no statistically significant difference between the groups in terms of bleeding status, wound infection, and sepsis ($p=0.291$, $p=0.624$, and $p= 0.066$, respectively).

According to the histopathologic examinations of graft nephrectomy specimens, there was a statistically significant difference between the two groups in terms of acute and chronic cellular (T-cell) rejection. The acute cellular (T-cell) rejection rate was higher in the early group ($p=0.021$), while the chronic rejection rate was higher in the late group ($p=0.002$). No statistically significant difference was found between the groups in terms of acute humoral (B- cell) rejection and acute humoral + cellular rejection ($p> 0.05$). Histopathological analyses are demonstrated in Table 5.

In induction treatment, ATG was used in 34 recipients, and IL-2 receptor antagonist (Basiliximab) was used in the remaining 4. There were no surgical complications in 4 recipients who were induced, IL2 receptor antagonists. Hemorrhage due to mycotic aneurysm rupture and renal vein thrombosis were detected in two recipients who received ATG therapy for rejection. Graft nephrectomy was performed on the 25th day in the recipient who had developed bleeding due to mycotic aneurysm rupture, and in the 2nd month in the recipient who had developed renal vein thrombosis. Additionally, renal artery thrombosis was seen in two recipients who had received ATG, and graft nephrectomy was performed on the 2nd and 8th days after RT. In the late nephrectomy group, graft nephrectomy was performed in a recipient due to the detection of plasmacytoma in the graft.

Mortality was observed in 4 of the 38 recipients. The remaining 34 recipients continued their lives with weekly hemodialysis programs. All 4 mortalities were observed in the early graft nephrectomy group. Post-operative complications occurred in 11 recipients.

Post-operative bleeding and vascular complications were observed in 4 patients, which resulted in mortality in two patients. The other two patients with hemorrhage recovered with blood transfusion and conservative follow-ups. Of the 4 recipients with hemorrhage, 3 were in the early nephrectomy group, and 1 was in the late nephrectomy group. Surgical site infection was seen

in 4 recipients, 3 in the late nephrectomy group and 1 in the early nephrectomy group. All recipients' wounds were primarily closed after recovery with open-wound dressing and antibiotic treatment. Three recipients developed sepsis in the post-operative period. All of the recipients with sepsis were in the early nephrectomy group.

Table 1. The clinical characteristics of the graft nephrectomy patients

	Total (n=38)	Early Graft Nephrectomy Group (n=16)	Late Graft Nephrectomy Group (n=22)
Recipient age	40.39±13,81	51.50 (20:65)	29.50(17:61)
Recipient sex			
Female	15(39.47%)	9(56.25%)	6(27.27%)
Male	23(60.53%)	7(43.75%)	16(72.73%)
Donor age	43.47±13,82	48.06±13.76	40.14±13.19
Transplant Type			
Living Donor	29(76.32%)	9(56.25%)	20(90.91%)
Deceased Donor	9(23.68%)	7(43.75%)	2(9.09%)
Dialysis Modality			
Preemptive	2(5.26%)	0	2(9.09%)
Hemodialysis	35(92.11%)	16(100%)	19(86.36%)
Peritoneal Dialysis	1(2.63%)	0	1(4.55%)
Dialysis Duration (months)	24(0:156)	40(2:156)	19(0:105)
Graft Survival (months)	10(0:95)	1(0:6)	34(7:95)
Mortality			
Yes	4(10.53%)	4(25%)	0
No	34(89.47%)	12(75%)	22(100%)
PRA			
No	26(68.42%)	9(56.25%)	17(77.27%)
Class I	5(13.16%)	2(12.50%)	3(13.64%)
Class II	5(13.16%)	3(18.75%)	2(9.09%)
Class I + Class II	2(5.26%)	2(12.50%)	0

Data were presented as median (minimum: maximum), mean±standard deviation and n(%).

Table 2. Reasons for renal failure

(n=38)	Early Graft Nephrectomy Group (n=16)	Late Graft Nephrectomy Group (n=22)	p-value
DM			
Present (n=5)	3(18.75%)	2(9.09%)	0.632 ^b
Absent (n=33)	13(81.25%)	20(90.91%)	
HT			
Present (n=12)	6(37.50%)	6(27.27%)	0,503 ^a
Absent (n=26)	10(62.50%)	16(72.73%)	
GN			
Present (n=7)	3(18.75%)	4(18.18%)	>0,99 ^b
Absent (n=31)	13(81.25%)	18(81.82%)	
ADPCD			
Present (n=1)	1(6.25%)	0	0,421 ^b
Absent (n=37)	15(93.75%)	22(100%)	
Obstructive uropathy			
Present (n=1)	0	1(4.55%)	>0,99 ^b
Absent (n=37)	16(100%)	21(95.45%)	
Hereditary disease			
Present (n=1)	1(6.25%)	0	0,421 ^b
Absent (n=37)	15(93.75%)	22(100%)	
Unknown			
Present (n=10)	2(12.50%)	8(36.36%)	0,143 ^b
Absent (n=28)	14(87.50%)	14(63.64%)	
Other			
Present (n=1)	0	1(4.55%)	>0,99 ^b
Absent (n=37)	16(100%)	21(95.45%)	

Data were presented as n(%).**a:** Chi-Square Test, **b:** Fisher's exact test

DM: Diabetes mellitus, **HT:** Hypertension, **GN:** Glomerulonephritis,

ADPCD: Autosomal Dominant Polycystic Kidney Disease

Table 3. Indications of graft nephrectomy

(n=38)	Early Graft Nephrectomy Group (n=16)	Late Graft Nephrectomy Group (n=22)	p-value
Rejection			
Present (n=21)	5(31.25%)	16(72.73%)	0.011^a
Absent (n=17)	11(68.75%)	6(27.27%)	
Infection			
Present (n=6)	3(18.75%)	3(13.64%)	0,682 ^b
Absent(n=32)	13(81.25%)	19(86.36%)	
Vascular and Surgical Problems			
Present (n=8)	7(43.75%)	1(4.55%)	0,005^b
Absent (n=30)	9(56.25%)	21(95.45%)	
Other			
Present (n=3)	1(6.25%)	2(9.09%)	>0,99 ^b
Absent (n=35)	15(93.75%)	20(90.91%)	

Data were presented as n(%). **b**: Chi-Square Test, **d**: Fisher's exact test

Table 4. Post-operative surgical complications

(n=38)	Early Graft Nephrectomy Group (n=16)	Late Graft Nephrectomy Group (n=22)	p-value
Hemorrhage			
Present (n=4)	3(18.75%)	1(4.55%)	0.291 ^b
Absent (n=34)	13(81.25%)	21(95.45%)	
Surgical site infection			
Present (n=4)	1(6.25%)	3(13.64%)	0.624 ^b
Absent (n=34)	15(93.75%)	19(86.36%)	
Sepsis			
Present (n=3)	3(18.75%)	0	0.066 ^b
Absent (n=35)	13(81.25%)	22(100%)	

Data were presented as n(%). **b**: Fisher's exact test

Table 5. Histopathologic analyses of graft nephrectomy specimens

(n=38)	Early Graft Nephrectomy Group (n=16)	Late Graft Nephrectomy Group (n=22)	p-value
Acute Humoral (B-cell) Rejection			
Present (n=11)	6(37.50%)	5(22.73%)	0.471 ^b
Absent (n=27)	10(62.50%)	17(77.27%)	
Acute Cellular (T-cell) Rejection			
Present (n=9)	7(43.75%)	2(9.09%)	0.021^b
Absent (n=29)	9(56.25%)	20(90.91%)	
Acute Humoral+Cellular Rejection			
Present (n=8)	3(18.75%)	5(22.73%)	>0.99 ^b
Absent (n=30)	13(81.25%)	17(77.27%)	
Chronic Rejection			
Present (n=10)	0	10(45.45%)	0.002^b
Absent (n=28)	16(100%)	12(54.55%)	

Data were presented as n(%). **b**: Fisher's exact test

DISCUSSION

In the present study, we categorized 38 graft nephrectomy patients whose operations were performed at our center according to the time of nephrectomy and shared our experiences.

In the literature, the morbidity rate observed in transplant nephrectomy has been reported to be between 0 - 83%. Hemorrhage and infection were the most frequently observed complications (7,11-15). Mortality rates ranged from 1.2% to 39%, and most were due to sepsis (7,14,16). In the present study, mortality was observed in 4 patients (10%), which was consistent with other studies in the literature. Some studies have reported high complication rates in early nephrectomy groups compared to late nephrectomy groups (17,18). On the other hand, high major complications rates were also reported in other studies. No major complications were observed in the early graft nephrectomy groups 19. In the present study, post-operative complications were observed in 11 recipients (29%), and the rate was higher in the early group. However, there was no statistically significant difference between the early and late groups ($p=0.147$). The major surgical complication in our series was hemorrhage, and the mortality rate in these recipients was 18%. These results are inconsistent with the literature.

Previous studies demonstrated that acute rejection was the most common etiological factor in early graft nephrectomy (6,18). In the present study, acute cellular rejection was the most common etiological factor in the early graft nephrectomy group, in accordance with the literature. Previous studies stated that, in the late nephrectomy group, the most common cause of nephrectomy was chronic rejection, known as graft intolerance syndrome (20,21). In the present study, in accordance with the literature, all 10 chronic rejections were detected in the late graft nephrectomy group.

Transplant recipients have an increased risk of hemorrhage as a result of sepsis compared to the general population due to the immunosuppressive agents they receive (22). In the present study, as induction therapy, anti-thymocyte globulin (ATG) was applied to 34 recipients, whereas four recipients received the IL2 receptor antagonist (Basiliximab). ATG and pulse steroids were

administered in all hyperacute and acute rejection episodes. There were no surgical complications in 4 recipients who were induced, IL2 receptor antagonists. In a study by Mazzuchi et al., ATG treatment used in acute rejection recipients was stated to be associated with hemorrhage complications (19). In the present study, a recipient who received ATG treatment for 5 days due to acute cellular rejection underwent surgery on the 25th day due to a mycotic aneurysm rupture. Renal vein thrombosis was observed on the 52nd day in another recipient who had ATG and five-day pulse steroid treatment due to cellular rejection. A nephrectomy was performed in the second month. In a third recipient, who had received preoperative ATG due to PRA positivity, renal artery thrombosis was detected in the primary non-functional kidney one day after nephrectomy. Renal artery thrombosis was observed on the 8th day in another recipient, who received ATG and three-day pulse steroid treatment due to cellular rejection.

Post-transplantation lymphoproliferative disorder (PTLD) is a complication of organ transplantation (23). Monomorphic PTLD, which is similar to extramedullary plasmacytoma, is rare and, according to the WHO classification, is referred to as "Plasmacytoma-like PTLD. It accounts for <2% of TLDs (24). In the literature, only a few cases of PTLD confined to the kidney were reported (25,26). In the present study, graft nephrectomy was performed due to the detection of plasmacytoma in a graft kidney in the late group.

CONCLUSION

In conclusion, graft nephrectomy has substantially high morbidity and mortality rates. Although the number of RT and rejections are increasing day by day, the application of graft nephrectomy should only be undertaken in selected, necessary cases. Medical treatment should be the priority in all cases of graft failure, and recipients who undergo nephrectomy should be evaluated in detail in the pre and post-operative periods.

Conflict of Interest

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

Ethical Approval

The study was approved by the Clinical Research Ethics Committee of Yenyüzyıl University (Approval number: 1436. Date: Aug 20, 2020) and written informed consent was received from all participants. The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions

Conception and design; MS, UPH, Data acquisition; MS, UPH, Data analysis and interpretation; MS, UPH, Drafting the manuscript; MS, UPH, Critical revision of the manuscript for scientific and factual content; MS, UPH, Statistical analysis; MS, UPH, Supervision; MS, UPH.

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