Scientific Research Publishing

Open Journal of Nephrology, 2024, 14, 240-252
https://www.scirp.org/journal/ojneph
ISSN Online: 2164-2869
ISSN Print: 2164-2842

Return to Dialysis after Kidney Graft Failure

Ikram Ftaimi, Soukaina Sakab, Manal Chattahi, Tarik Bouattar, Loubna Benamar, Rabia Bayahia, Naima Ouzeddoun

Service de Néphrologie-Dialyse-Transplantationrénale, CHU Ibn Sina, Rabat Université Mohammed V, Rabat, Morocco
Email: ikram.ickow@gmail.com

How to cite this paper: Ftaimi, I., Sakab, S., Chattahi, M., Bouattar, T., Benamar, L., Bayahia, R. and Ouzeddoun, N. (2024) Return to Dialysis after Kidney Graft Failure. *Open Journal of Nephrology*, **14**, 240-252.
https://doi.org/10.4236/ojneph.2024.142023

Received: March 30, 2024
Accepted: June 22, 2024
Published: June 25, 2024

Abstract

Introduction: The transition period from renal transplantation to dialysis is associated with high morbidity and mortality. The aim of this study is to describe the clinical and paraclinical characteristics, therapeutic management and evolutionary profile of patients returning to dialysis after kidney graft failure. **Material and Methods:** This was a retrospective, descriptive study conducted in the Nephrology-Dialysis-Renal Transplant Department at university hospital IbnSina between January 1998 and December 2021. We included all renal transplant recipients who had experienced kidney graft dysfunction and returned to dialysis. Patients with a follow-up after return to dialysis of less than 1 year were excluded. **Results:** Among 166 renal transplant recipients, 20 returned to dialysis after a median renal graft life of 85.5 months [42 - 186], corresponding to a prevalence of 12%. The mean age of our patients was 38.7 ± 11.9 years, with a M/F sex ratio of 2.3. Dialysis was initiated urgently in 10 patients (50%). Hemodialysis was the most commonly used modality (75%). Central venous catheterization was used in 35% of cases, including tunneled catheters. General condition is impaired in all patients, with persistent hypertension in 70% of cases. Mean uremia was 2.35 ± 0.8 g/l, mean creatinine 116 ± 48.3 mg/l, giving a mean GFR of 5.1 ± 2.2 ml/min. Mean albuminemia was 32.9 ± 6 g/l and mean hemoglobinemia 8.6 ± 1.9 g/dl. During the first year of follow-up, none of the patients died. However, 13 patients required hospitalization, with a mean length of stay of 15 days. Eight patients were hospitalized for infections and 5 for renal graft intolerance syndrome. After a mean follow-up of 22 months, 6 patients were detransplanted following graft necrosis. **Conclusion:** Return to dialysis after RT is fraught with a high rate of complications. The management of these patients must be optimized to improve their vital prognosis and quality of life.

Keywords

Kidney Graft Failure, Dialysis, Detransplantation, Immunosuppression

1. Introduction

The number of patients returning to dialysis after kidney graft failure is increasing, because of limited survival of the kidney graft, increased number of kidney transplantations and decreased access to a new transplantation due to immunisation [1].

According to several recent studies, kidney graft failure is the fourth leading cause to dialysis initiation [2] [3].

This transition period from renal transplantation to dialysis is associated with high high risk of complications. Indeed, patients on dialysis after kidney graft failure are reported to have a higher mortality rate than those who retain a functional graft [1].

This is explained by an inflammatory state due to the allograft, leading to anemia via erythropoietin resistance and hypoalbuminemia.

In addition, maintaining immunosuppressive therapy after return to dialysis in order to preserve residual kidney graft function and prevent graft necrosis increases the risk of infectionandtumors [4].

Psychological difficulties have also been reported in these patients following the change of care teams, but especially due to the end of autonomy related to renal transplantation [5].

This finding should draw attention to the importance of monitoring these patients during this period.

Much has been written regarding the risks incurred by this population. However, no clearly defined management strategy is available: the timing of dialysis initiation is not well defined, the management of immunosuppressive drugs is not standardised and indication for detransplantation remains controversial.

In the light of the data, we undertook a study of patients returning to dialysis after kidney graft failure in our center.

We describe the clinical and paraclinical characteristics, therapeutic management and evolutionary profile of those patients.

2. Material and Methods

This is a retrospective, descriptive, monocentric study conducted in the Nephrology-Dialysis-Transplantation Department of IbnSina University Hospital in Rabat.

The study period is spread over 23 years, from January 1998 to December 2021.

We included all kidney transplant patients followed in our unit who presented a kidney graft dysfunction and returned to dialysis.

We excluded from this study kidney transplant patients with a follow-up after return to dialysis less than 1 year.

Variables and definitions:

We analyzed the demographic, clinical, paraclinical, therapeutic and evolutionary data of these patients.

Data were collected from medical files in the renal transplant unit, and the analysis of the data concerned 3 periods:

- The period of dialysis before renal transplantation.
- The period of renal transplantation.

For which the analysis was essentially descriptive.

- The period of return to dialysis after renal transplantation.

This period was analyzed in terms of the patients' age, their comorbidities, their clinical examination and the results of biological tests. We also recorded the modality and the circumstances of the return to dialysis as well as the need to place a central venous catheter.

We noted the dosage of the immunosuppressive treatment, *i.e.* anti-metabolite, anticalcineurin and corticosteroids at Day 0, day of the return to dialysis, at 1 month, 3 months, 6 months and 1 year.

We defined early cessation of immunosuppressive therapy as cessation of anti-metabolite and anticalcineurin before 120 days after return to dialysis.

We also reported infectious episodes, the hospitalisation requirement, the occurrence of rejection and the need for detransplantation.

We judged patient outcomes based on the occurrence of infection, graft intolerance syndrome, need for detransplantation, detection of HLA antibodies, and patient survival at 1 year.

The statistical analysis was carried out using JAMOVI software version 2.3.21.0.

Quantitative variables are expressed as means and standard deviation, median and interquartile range, and qualitative variables as number and percentage.

The data are compared using the Chi-2 test or Fisher's exact test.

3. Results

Among 166 kidney transplant patients, we identified 20 patients who returned to dialysis during the inclusion period, corresponding to a prevalence of 12%.

The mean age of our patients at the time of return to dialysis was 38.7 ± 11.9 years, with a sex ratio M/F of 2.3.

1) Period of dialysis before renal transplantation

Initial nephropathy was glomerular in 3 patients: 1 case of membranous nephropathy and 2 cases with IgA nephropathy. Nephroangiosclerosis, Alport syndrome and polycystic kidney disease were noted in 1 case each.

Chronic tubulointerstitial nephritis was involved in 3 patients. While the initial nephropathy remained undetermined in 11 patients.

The most frequent dialysis modality before renal transplantation was haemodialysis for 19 patients with a mean dialysis duration of 34.5 ± 29.5 months.

2) Period of renal transplantation:

Three patients received a kidney from a brain-dead donor (BDE) and 17 patients from a living donor, with a median kidney graft survival time of 85.5 months [42 - 186].

The causes of kidney graft dysfunction are listed in Table 1.

3) Period of return to dialysis after renal transplantation:

The clinical characteristics of patients after return to dialysis are summarised in Table 1 and the biological data in Table 2.

At the time of return to dialysis, 14 patients (70%) remained hypertensive with more than 3 antihypertensive treatments, 2 patients had heart disease (10%) and only 1 patient developed a new-onset diabetes after transplant (NODAT) (5%). Chronic smoking was reported in only one patient (5%).

The average BMI of our patients was 22 kg/m^2 ± 3, with extremes ranging from 18.3 to 26 kg/m^2. In addition, 4 patients presented psychological disorders requiring psychiatric follow-up (20%).

Biologically, an inflammatory syndrome was found in the majority of our patients with a median C-reactive protein (CRP) of 15.5 [3.8 - 27].

The initiation of dialysis was urgent in 10 patients (50%), with a low average GFR of 5.1 ml/min/1.73m^2. This dialysis was carried out using a central venous catheter in 7 patients (35%), one of whom was tunnelled, while 8 patients had a previously prepared AVF. Once the emergency was over and after education sessions, 15 patients opted for HD and 5 for PD.

Regarding the management of immunosuppressive therapy, we kept oral corticosteroid therapy at low dose (5 mg/d) for the first year. The antiproliferative agent is reduced by 50% per month until discontinuation and the anticalcineurin is reduced by 1mg every two weeks for tacrolimus and 25 mg every two weeks for ciclosporin until discontinuation.

Thus, weaning from mycophenolatemofetil (MMF) and anticalcineurins is achieved progressively over a period of 3 months and 5 months respectively. Three patients were allowed to stop immunosuppressive treatment early without clinical consequences on the kidney graft (Figure 1).

During the first year of follow up, 13 patients (65%) required one or two hospitalisations, with an average duration of hospitalisation of 15 days. Eight patients were hospitalised for infections: 4 cases of tuberculosis, 3 case of dialysis catheter related infection and 1 case of peritonitis in PD. The evolution was favorable for all patients after appropriate antibiotic therapy.

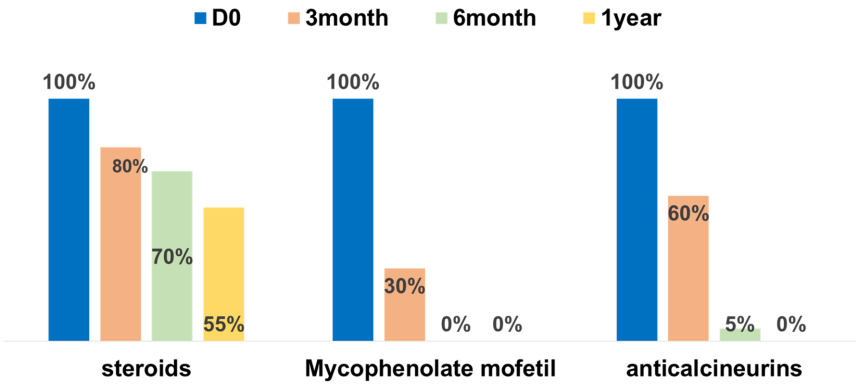

Figure 1. Management of immunosuppressive therapy.

Table 1. Characteristics of patients after return to dialysis.

Variables	Value
Age of patients at return to dialysis (in years)[a]	38.7 ± 11.9
Gender[b]	
Male	14 (70%)
Female	6 (30%)
IMC (kg/m²)[a]	22 ± 3
Comorbidities[b]	
NODAT	1 (5%)
Hypertension	14 (70%)
Heart disease	2 (10%)
Smoking	1 (5%)
Depression	4 (20%)
Causes of kidney graft dysfunction[b]	
Rejection	15 (75%)
Recurrence of initial nephropathy	3 (15%)
Toxicity of anticalcineurins	1 (5%)
Graft renal vein thrombosis	1 (5%)
Lifetime of kidney graft (in months)[c]	85.5 [42 - 186]
Urgent initiation of dialysis after renal transplantation[b]	10 (50%)
Post-transplantation dialysis modality[b]	
HD	15 (75%)
PD	5 (25%)
Hemodialysis vascular access[b]	
Catheter	7 (35%)
AVF	8 (40%)
Hospitalisation (patients)[b]	13 (65%)
Duration of hospital stay (in days)[a]	15 ± 7.19
Infection[b]	
Tuberculosis	4 (8%)
Catheter related infection	3 (13%)
Peritonitis in PD	1 (5%)
Kidney graft intolerance syndrome[b]	
Total	8 (40%)
During the 1st year	5 (25%)
Detransplantation[b]	6 (30%)
Death[b]	1 (5%)

[a]Expressed as mean ± standard deviation, [b]Expressed as number (percentage), [c]Expressed as median [interquartile range].

Table 2. Biological characteristics of patients returning to dialysis.

Variables	Value
Uremia (g/l)[a]	2.35 ± 0.8
Creatinine serum level (mg/l)[a]	116 ± 48.3
GFR (ml/min)[a]	5.1 ± 2.2
Kalemia (mEq/l)[a]	4.75 ± 0.7
Alkaline reserve (mEq/l)[a]	15.7 ± 6.7
Natremia (mEq/l)[a]	133± 5.1
Calcemia (mg/l)[a]	81.4 ± 8.7
Phosphorus (mg/l)[a]	58.5 ± 20
Uricemia (mg/l)[a]	80.3 ± 24.1
Albumin serum level (g/l)[a]	32.9 ± 6
Haemoglobin serum level (g/dl)[a]	8.6 ± 1.9
C-reactive protein (mg/l)[b]	15.5 [3.8 - 27]

[a]Expressed as mean ± standard deviation, [b]Expressed as median [interquartiles].

After a mean follow-up of 22 months, 8 patients presented a kidney graft intolerance syndrome, 5 of them during the first year.

The clinical symptomatology was suggestive of kidney graft sensitivity in 8 cases, associated with haematuria in 6 cases and resistant hypertension in 2 cases. All patients had an elevated CRP, averaging 92.9 ± 76.6 mg/l with extremes between 25 and 207 mg/l. Doppler ultrasound of the kidney graft performed in all patients showed infiltration of the graft associated with foci of pyelonephritis in 2 patients.

Increasing the dose of steroids from 5 to 20 mg improved the clinical signs in 2 patients, while 6 patients required detransplantation. The histological examination of the graft showed foci of necrosis in 5 patients and pyonephrosis in one patient.

The evolution was favorable for all patients after detransplantation with a regression of clinical symptoms, normalization of blood pressure and resolution of the biological inflammatory syndrome.

Despite the deteriorated condition of the patients at the time of initiation of dialysis, only one death occurred after 16 months following a covid-19 infection.

In statistical analysis, the comparison between the early weaned group of immunosuppresive therapy (<120 days) and the late weaned group (>120 days) showed a significant association between the prolongation of immunosuppressive therapy beyond 120 days and the occurrence of infection ($p < 0.05$) (**Table 3**).

In terms of psychological care, our patients experienced psychological difficulties during the period of transition. The beginning of dialysis marks a period of adaptation, as the patient's rhythm of life is affected by the frequency of dialysis sessions.

Table 3. Risk factors associated with duration of immunosuppressive therapy.

Variables	Weaning IS > 120 jours		p-Value *Chi*-2	p-Value Fisher
	No n = 17	Yes n = 3		
Death	1 (6%)	0 (0%)	0.6	1
Infection	**5 (29%)**	**3 (100%)**	**0.02**	**0.049**
Detransplantation	6 (35%)	0 (0%)	0.2	0.52
Graft intolerance syndrome	8 (47%)	0 (0%)	0.1	0.24
Detection of HLA antibodies	12 (70%)	3 (100%)	0.2	0.53

IS: Immunosuppressive therapy; HLA: Human leukocyte antigen.

The majority of patients felt nervous, stressed, anxious, had no desire for anything, and experienced mood swings. Some of them were restless and had sleeping difficulties.

Four patients were depressed, refused dialysis and required psychiatric follow-up.

These psychological difficulties can be attributed to changes in medical teams, from the transplant doctor to the dialysis doctor, but mostly due to the loss of autonomy provided by the kidney transplant.

4. Discussion

4.1. Initiation of Dialysis: Circumstances and Modalities

The optimal time to start dialysis after kidney graft failure is not clearly defined in the literature. Some authors start dialysis early to avoid uremic complications, others delay dialysis until the onset of clinical signs [4] [5].

A cohort study by the United States Renal Data System (USRDS) registry showed that high GFR at dialysis initiation is associated with an increased risk of mortality of 4% for each ml/min/1.73m^2 (HR: 1.04, 95% - CI: 1.02 - 1.06) [6]. However, this study is biased since patients with comorbidities are those who started dialysis early.

Molnar *et al.* used a propensity score to evaluate outcomes of 747 patients with kidney graft failure. According to the adjusted model, GFR did not emerge as a risk factor for mortality. (HR: 1.02, 95% IC: 0.96 - 1.07). However, higher mortality was noted in young and healthy patients. The conclusion of this study is that there is no benefit to initiate dialysis early [7]. These results are in agreement with those of the IDEAL study [8].

In our study, 10 patients initiated dialysis urgently with a mean GFR of 5 ml/min/1.73m^2. We expect a lower percentage of urgent dialysis since all our patients are followed regularly and closely. This underlines the difficulty of nephrologists to manage these patients who are for the majority reticent to return to dialysis.

Thus, the initiation of dialysis for patients with kidney graft dysfunction must take into account not only the GFR but also the clinical status of patients, their comorbidities and the existence of symptoms related to graft dysfunction.

Dialysis modality offered to patients with kidney graft dysfunction is debated in the literature. Many studies have compared HD with PD and have shown equal survival with both techniques [9]-[12].

4.2. Management of Immunosuppressive Therapy

The management of immunosuppression after return to dialysis is a real challenge for nephrologists. In the absence of recommendations, practices vary from one centre to another.

Some propose to withdraw the immunosuppressive therapy in order to avoid its side effects, 76 while others carry out a gradual weaning. In fact, both approaches have their benefits and risks.

Indeed, maintaining immunosuppression after kidney graft dysfunction preserves residual graft function, prevents graft intolerance syndrome and avoids HLA immunisation. On the other hand, this immunosuppression increases the risk of infections and complications [13]-[15].

Several studies have evaluated the impact of immunosuppression on patients undergoing dialysis after kidney graft dysfunction (**Table 4**).

In our study, 8 patients developed graft intolerance syndrome after a mean follow-up time of 22 months, 6 of them required detransplantation, without any statistical correlation with early withdrawal of immunosuppressive therapy.

Table 4. Studies analysing the management of immunosuppression.

Authors/Year	Cohort size	Results
Augustine *et al.* 2012 [16]	**119**	Withdrawal of immunosuppressive therapy was predictive of HLA immunisation (P = 0.004), graft intolerance syndrome and detransplantation (P < 0.001).
Kosmoliaptsis *et al.* 2014 [17]	**131**	Maintaining two immunosuppressive drugs reduces significantly the risk of developing HLA antibodies.
Martin *et al.* 2021 [18]	**134**	Continued immunosuppressive therapy did not improve HLA immunisation or outcomes of the second kidney graft, but reduced significantly the risk of detransplantation (P = 0.01).
Knoll *et al.* 2022 [19]	**269**	Continued immunosuppression is not associated with a higher risk of death or hospitalisation for infection, but remains insufficient to prevent HLA immunisation and graft intolerance syndrome.

However, infection was statistically higher in patients with prolonged immunosuppression over 120 days (P = 0.02). Almost half of these infections were due to dialysis catheter related infection (3/8). Their occurrence could be prevented by early creation of a vascular access for patients with graft dysfunction as soon as a GFR of 20 ml/min/1.73m^2.

4.3. Detransplantation

The detransplant rate after kidney graft failure varies widely from one centre to another. According to the USRDS, the probability of detransplantation at 1 week, 3 months, 6 months and 1 year after graft dysfunction is respectively 5.3%, 17.6%, 25%, and 30.9% [20]. Thus, 89.3% of detransplants are performed within the first year [21].

There is no systematic recommendation for detransplantation after return to dialysis [22]-[24]. The majority of centres follow indications that are related either to the kidney graft or to immunosuppression (**Table 5**).

A less invasive alternative to detransplantation described in 1993 by Lorenzo *et al.*, is kidney graft embolisation [25].

In 2018, a meta-analysis and systematic review compared detransplantation to graft embolisation in 2421 patients in terms of morbidity and mortality. They found that mortality and morbidity in the detransplantation group were higher compared to the embolisation group. However, 20% of patients required subsequent detransplantation [26]. This result may be of interest for patients with a high surgical risk.

4.4. Patients Surviving on Dialysis after Kidney Graft Failure

Survival of patients with graft failure is poor, estimated at 40% at 10 years compared to 75% for patients with a functional graft [27]. The most common causes of death reported in the literature are infections and cardiovascular disease [28]-[30].

Table 5. Indications for detransplantation afterkidney graft failure [15] [18] [19] [24] [31].

Absolute indications	Relative indications
Primary non-function of renal allograft	Early graft loss (<6 - 12 months)
Acute rejection resistant to immunosuppression	Resistant BK virus nephropathy
Severe graft pyelonephritis/urosepsis	
Graft lymphoproliferative syndrome	
Refractory graft intolerance syndrome	
Graft vascular complications: Hemorrhage/Thrombosis	
Creating space for a second graft	

In fact, patients with a dysfunctional graft tend to have hypoalbuminemia, anemia and resistance to erythropoietin in the context of chronic inflammation, which may increase the risk of death [32]-[34].

In addition, these patients have a long history of uraemia and immunosuppressive therapy which increases the risk of cardiovascular disease, diabetes, infections and cancer [35] [36].

Management of these modifiable risk factors may improve survival in such patients.

The use of central venous catheters in two-thirds of patients returning to dialysis after kidney graft dysfunction contributes to a significant rate of catheter related infections [6] [27] [37]-[39]. Thus, the creation of a permanent vascular access could reduce the morbidity and mortality linked to infections [30].

A significant increase in cardiovascular events has been reported in patients maintained on immunosuppression, which increases the risk of mortality by 4.9 times (95% CI: 1.8 - 13.5), mainly by myocardial infarction [40]. Assessment and treatment of cardiovascular risk factors is essential to improve patient survival.

In our cohort, we report one death due to infection after 16 months follow up: this was an acute respiratory distress syndrome related to the COVID-19 pandemic.

4.5. Limits of the Study

Our study has several limits: the retrospective nature of the study exposes us to missing data, the small sample size, and the essentially descriptive analysis of data which limits the scientific contribution of this work.

However, these data could improve the management of these patients during this delicate transition period and consequently improve their vital prognosis.

5. Conclusion

The transition from kidney graft to dialysis is associated with high morbidity and mortality [28]-[30] [38]. However, there are no practical recommendations for the management of these patients. We believe that adequate preparation for dialysis initiation, early management of comorbidities and creation of a vascular access could improve outcomes and reduce risks in this population.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Mourad, G., Szwarc, I. and Buzançais, A. (2016) Dialysis after Graft Failure: How to Improve Survival? *Néphrologie & Thérapeutique*, **12**, S89-S94. https://doi.org/10.1016/j.nephro.2016.01.007

[2] Boenink, R., Astley, M.E., Huijben, J.A., Stel, V.S., Kerschbaum, J., Ots-Rosenberg,

M., Åsberg, A.A., Lopot, F., Golan, E., De la Nuez, P.C., *et al.* (2022) The ERA Registry Annual Report 2019: Summary and Age Comparisons. *Clinical Kidney Journal*, **15**, 452-472. https://doi.org/10.1093/ckj/sfab273

[3] Lentine, K.L., Smith, J.M., Hart, A., Miller, J., Skeans, M.A., Larkin, L., Robinson, A., Gauntt, K., Israni, A.K., Hirose, R., *et al.* (2022) OPTN/SRTR 2020 Annual Data Report: Kidney. *American Journal of Transplantation*, **22**, 21-136. https://doi.org/10.1111/ajt.16982

[4] Lobbedez, T., Lecouf, A., Ficheux, M., Henri, P., Hurault de Ligny, B. and Ryckelynck, J.-P. (2007) Le retour en dialyse après échec de transplantation rénale. *Néphrologie & Thérapeutique*, **3**, 238-241. https://doi.org/10.1016/S1769-7255(07)78754-0

[5] Pedrazzini, B., Golshayan, D. and Teta, D. (2018) Retour en dialyse après transplantation rénale: Une étude rétrospective dans le canton de Vaud. Revue Médicale Suisse, **4**, 430-434. https://doi.org/10.53738/REVMED.2018.14.595.0430

[6] Gill, J.S., Abichandani, R., Kausz, A.T., *et al.* (2002) Mortality after Kidney Transplant Failure: The Impact of Non-Immunologic Factors. *Kidney International*, **62**, 1875-1883. https://doi.org/10.1046/j.1523-1755.2002.00640.x

[7] Molnar, M.Z., Streja, E., Kovesdy, C.P., *et al.* (2012) Estimated Glomerular Filtration Rate at Reinitiation of Dialysis and Mortality in Failed Kidney Transplant Recipients. *Nephrology Dialysis Transplantation*, **27**, 2913-2921. https://doi.org/10.1093/ndt/gfs004

[8] Cooper, B.A., Branley, P., Bulfone, L., *et al.* (2010) A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis. *The New England Journal of Medicine*, **363**, 609-619. https://doi.org/10.1056/NEJMoa1000552

[9] Davies, S.J. (2001) Peritoneal Dialysis in the Patient with a Failing Renal Allograft. *Peritoneal Dialysis International*, **21**, 280-284. https://doi.org/10.1177/089686080102103S49

[10] De Jonge, H., Bammens, B., Lemahieu, W., *et al.* (2006) Comparison of Peritoneal Dialysis and Haemodialysis after Renal Transplant Failure. *Nephrology Dialysis Transplantation*, **21**, 1669-1674. https://doi.org/10.1093/ndt/gfl010

[11] Perl, J., Dong, J., Rose, C., Jassal, S.V. and Gill, J.S. (2013) Is Dialysis Modality a Factor in the Survival of Patients Initiating Dialysis after Kidney Transplant Failure? *Peritoneal Dialysis International*, **33**, 618-628. https://doi.org/10.3747/pdi.2012.00280

[12] Salazar, A.M., Chávez, C.O., Álvarez, T.G., Mañanes, C.M., Wu, J., Ureña, A.D., Muñoz, J.N., López, J.M.C., Fernández, F.V. and Blanca, A.M. (2018) Returning to Dialysis after Kidney Transplant Failure. Does the Dialysis Treatment Modality Influence the Survival Prognosis? *Transplantation*, **102**, S537. https://doi.org/10.1097/01.tp.0000543384.74406.cb

[13] Pham, P.-T., Everly, M. and Faravardeh, A., *et al.* (2015) Management of Patients with a Failed Kidney Transplant: Dialysis Reinitiation, Immunosuppression Weaning, and Transplantectomy. *World Journal of Nephrology*, **4**, 148-159. https://doi.org/10.5527/wjn.v4.i2.148

[14] Pham, P.-T. and Pham, P.-C. (2011) Immunosuppressive Management of Dialysis Patients with Recently Failed Transplants. *Seminars in Dialysis*, **24**, 307-331. https://doi.org/10.1111/j.1525-139X.2011.00864.x

[15] Fiorentino, M., Gallo, P., Giliberti, M., *et al.* (2020) Management of Patients with a Failed Kidney Transplant: What Should We Do? *Clinical Kidney Journal*, **14**, 98-106. https://doi.org/10.1093/ckj/sfaa094

[16] Augustine, J.J., Woodside, K.J., Padiyar, A., Sanchez, E.Q., Hricik, D.E. and Schulak, J.A. (2012) Independent of Nephrectomy, Weaning Immunosuppression Leads to Late Sensitization after Kidney Transplant Failure. *Transplantation*, **94**, 738-743. https://doi.org/10.1097/TP.0b013e3182612921

[17] Vasilios, K., Gjorgjimajkoska, O., Sharples, L.D., *et al.* (2014) Impact of Donor Mismatches at Individual HLA-A, -B, -C, -DR, and -DQ Loci on the Development of HLA-Specific Antibodies in Patients Listed for Repeat Renal Transplantation. *Kidney International*, **86**, 1039-1048. https://doi.org/10.1038/ki.2014.106

[18] Martin, K., *et al.* (2021) Prolonged Immunosuppression Does not Improve Risk of Sensitization or Likelihood of Retransplantation after Kidney Transplant Graft Failure. *Transplant International*, **34**, 2353-2362. https://doi.org/10.1111/tri.13998

[19] Knoll, G., Campbell, P., Chassé, M., *et al.* (2022) Immunosuppressant Medication Use in Patients with Kidney Allograft Failure: A Prospective Multicenter Canadian Cohort Study. *Journal of the American Society of Nephrology*, **33**, 1182-1192. https://doi.org/10.1681/ASN.2021121642

[20] United States Renal Data System (2016) 2016 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Disease, Bethesda.

[21] Johnston, O., Rose, C., Landsberg, D., *et al.* (2007) Nephrectomy after Transplant Failure: Current Practice and Outcomes. *American Journal of Transplantation*, **7**, 1961-1967. https://doi.org/10.1111/j.1600-6143.2007.01884.x

[22] Molnar, M.Z., Ichii, H., Lineen, J., *et al.* (2013) Timing of Return to Dialysis in Patients with Failing Kidney Transplants. *Seminars in Dialysis*, **26**, 667-674. https://doi.org/10.1111/sdi.12129

[23] Gómez-Dos-Santos, V., Lorca-Álvaro, J., Hevia-Palacios, V., *et al.* (2020) The Failing Kidney Transplant Allograft. Transplant Nephrectomy: Current State-of-the-Art. *Current Urology Reports*, **21**, Article No. 4. https://doi.org/10.1007/s11934-020-0957-6

[24] Leal, R., Pardinhas, C., Martinho, A., Sá, H.O., Figueiredo, A. and Alves, R. (2022) Challenges in the Management of the Patient with a Failing Kidney Graft: A Narrative Review. *Journal of Clinical Medicine*, **11**, Article 6108. https://doi.org/10.3390/jcm11206108

[25] Lorenzo, V., Díaz, F., Perez, L., *et al.* (1993) Ablation of Irreversibly Rejected Renal Allograft by Embolization with Absolute Ethanol: A New Clinical Application. *American Journal of Kidney Diseases*, **22**, 592-595. https://doi.org/10.1016/S0272-6386(12)80934-6

[26] Takase, H.M., Contti, M.M., Nga, H.S., *et al.* (2018) Nephrectomy versus Embolization of Non-Functioning Renal Graft: A Systematic Review with a Proportional Meta-Analysis. *Annals of Transplantation*, **23**, 207-217. https://doi.org/10.12659/AOT.907700

[27] Kaplan, B. and Meier-Kriesche, H.U. (2002) Death after Graft Loss: An Important Late Study Endpoint in Kidney Transplantation. *American Journal of Transplantation*, **2**, 970-974.https://doi.org/10.1034/j.1600-6143.2002.21015.x

[28] Sud, M., Tangri, N., Pintilie, M., Levey, A.S. and Naimark, D. (2014) Risk of End-Stage Renal Disease and Death after Cardiovascular Events in Chronic Kidney Disease. *Circulation*, **130**, 458-465. https://doi.org/10.1161/CIRCULATIONAHA.113.007106

[29] Laurin, L.P., Harrak, H., Elftouh, N., Ouimet, D., Vallée, M. and Lafrance, J.P. (2015) Outcomes of Infection-Related Hospitalization According to Dialysis Mod-

ality. *Clinical Journal of the American Society of Nephrology*, **10**, 817-824. https://doi.org/10.2215/CJN.09210914

[30] Brar, A., Markell, M., Stefanov, D.G., *et al.* (2017) Mortality after Renal Allograft Failure and Return to Dialysis. *American Journal of Nephrology*, **45**, 180-186. https://doi.org/10.1159/000455015

[31] British Transplantation Society (2014) Management of the Failing Kidney Transplant British Transplantation Society Guidelines. https://bts.org.uk/wp-content/uploads/2016/09/13_BTS_Failing_Graft-1.pdf

[32] Bunthof, K.L.W., Hazzan, M. and Hilbrands, L.B. (2018) Review: Management of Patients with Kidney Allograft Failure. *Transplantation Reviews*, **32**, 178-186. https://doi.org/10.1016/j.trre.2018.03.001

[33] Gill, J.S., Abichandani, R., Khan, S., Kausz, A.T. and Pereira, B.J. (2002) Opportunities to Improve the Care of Patients with Kidney Transplant Failure. *Kidney International*, **61**, 2193-2200. https://doi.org/10.1046/j.1523-1755.2002.00373.x

[34] Wanner, C. and Metzger, T. (2002) C-Reactive Protein a Marker for All-Cause and Cardiovascular Mortality in Haemodialysis Patients. *Nephrology Dialysis Transplantation*, **17**, 29-40. https://doi.org/10.1093/ndt/17.suppl_8.29

[35] Kabani, R., *et al.* (2014) Risk of Death Following Kidney Allograft Failure: A Systematic Review and Meta-Analysis of Cohort Studies. *Nephrology Dialysis Transplantation*, **29**, 1778-1786. https://doi.org/10.1093/ndt/gfu205

[36] Mourad, G., Minguet, J., Pernin, V., *et al.* (2014) Similar Patient Survival Following Kidney Allograft Failure Compared with Non-Transplanted Patients. *Kidney International*, **86**, 191-198. https://doi.org/10.1038/ki.2014.6

[37] Knoll, G., Muirhead, N., Trpeski, L., Zhu, N. and Badovinac, K. (2005) Patient Survival Following Renal Transplant Failure in Canada. *American Journal of Transplantation*, **5**, 1719-1724. https://doi.org/10.1111/j.1600-6143.2005.00921.x

[38] Perl, J., Zhang, J., Gillespie, B., Wikström, B., Fort, J., Hasegawa, T., Fuller, D.S., Pisoni, R.L., Robinson, B.M. and Tentori, F. (2012) Reduced Survival and Quality of Life Following Return to Dialysis after Transplant Failure: The Dialysis Outcomes and Practice Patterns Study. *Nephrology Dialysis Transplantation*, **27**, 4464-4472. https://doi.org/10.1093/ndt/gfs386

[39] Chan, M.R., Oza-Gajera, B., Chapla, K., *et al.* (2014) Initial Vascular Access Type in Patients with a Failed Renal Transplant. *Clinical Journal of the American Society of Nephrology*, **9**, 1225-1231. https://doi.org/10.2215/CJN.12461213

[40] SmakGregoor, P.J., Zietse, R., van Saase, J.L., *et al.* (2001) Immunosuppression Should Be Stopped in Patients with Renal Allograft Failure. *Clinical Transplantation*, **15**, 397-401. https://doi.org/10.1034/j.1399-0012.2001.150606.x