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Impact of Therapeutic Plasma Exchange and Rituximab for Prevention of Idiopathic Focal Segmental Glomerulosclerosis Recurrence Post–Kidney Transplantation

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Background. Focal segmental glomerulosclerosis (FSGS) recurs after kidney transplantation (KT) in 30%–50% of recipients. Recurrence is associated with early graft loss in up to 60% of cases. This study aimed to assess the efficacy of therapeutic plasma exchange (TPE) combined with rituximab (RTX) in preventing early FSGS recurrence within 1 y post-KT. **Methods.** This single-center, retrospective cohort study included patients receiving KT for idiopathic FSGS between June 2013 and August 2021. In May 2016, a preventative FSGS protocol was implemented where KT recipients with idiopathic FSGS received perioperative sessions of TPE followed by a dose of RTX with or without IVIG. The incidence of recurrent FSGS within the first year posttransplantation was assessed between the FSGS protocol cohort versus the historical group of patients who did not undergo prophylactic treatment. **Results.** A total of 65 patients received KT for idiopathic FSGS during the study period. Forty patients were included in the FSGS protocol cohort and 25 in the control cohort. When assessing clinical recurrence with proteinuria, there were significantly fewer cases in the FSGS protocol cohort versus the control cohort, 1 versus 5 patients (3% versus 20%, $P = 0.03$). There were no instances of death-censored graft loss at 1 y in the protocol cohort versus 2 cases in the control cohort (0% versus 8%, $P = 0.14$). **Conclusions.** TPE combined with RTX may prevent early FSGS recurrence without significant rates of infection.

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Focal segmental glomerulosclerosis (FSGS) is a nephrotic syndrome with cardinal features of proteinuria and progressive glomerular scarring paired with podocyte foot process effacement on biopsy.[1,2] Clinical presentation of FSGS includes sudden onset of proteinuria, hypoalbuminemia, hypercholesterolemia, and edema.[3] FSGS is further categorized as primary versus secondary based on the mechanism of podocyte injury. Primary or idiopathic FSGS is characterized as an immunologic-mediated injury via circulating factors resulting in primary podocytopathy.[4] Recent data published revealed the possible roles antinephrin antibodies play among the circulating factors in FSGS.[5] The mechanism of urokinase receptor signaling in the podocytes is hypothesized to precipitate foot process effacement and urinary protein loss.[6] In contrast, secondary FSGS is described as segmental scars attributed to drug exposure, viral infection, genetic mutation,

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or adaptive changes, such as structural and functional adaptations.[7] Secondary FSGS commonly does not reoccur posttransplant once the offending disease is treated or the drug is removed.

Idiopathic FSGS has an estimated prevalence of 4% in the United States and an incidence of 7 per 1 million people, yet accounts for 40% of cases of nephrotic syndrome in adults.[1,8] The Kidney Disease Improving Global Outcomes guidelines highlight empiric treatment of FSGS, which includes high-dose corticosteroids, calcineurin inhibitors, or alkylating agents with low-level evidence from small trials and case reports with obscure outcomes.[9] Due to low response rates to current treatment modalities, FSGS often results in end-stage renal disease requiring dialysis or transplantation.[10] The incidence of FSGS recurrence after kidney transplantation (KT) has been reported to range from 30% to 60% and is associated with up to 60% graft loss early after transplant, commonly within the first couple of months.[11-15] Those with FSGS recurrence are reported to have up to a 5-fold increased risk of graft loss compared with those without recurrence.[12] Factors such as younger age, non-Black race, high speed of disease progression, and higher degrees of proteinuria pretransplant are associated with a greater risk of disease recurrence.[1,15,16]

There is limited literature available proposing the use of therapeutic plasma exchange (TPE) and/or rituximab (RTX) for the prevention or treatment of recurrent FSGS after KT.[17-24] The hypothesized mechanism of TPE is the removal of circulating permeability factors in podocytopathy, with reports of early TPE use before recurrence suggesting beneficial results.[25-27] RTX is a chimeric monoclonal antibody against the CD20 antigen of B lymphocytes and has been studied as monotherapy or in combination with TPE. Aside from its immunomodulatory effects, RTX may also prevent the actin cytoskeleton disruption of the podocytes.[28] TPE and RTX regimens show significant variations with inconsistent efficacy, with published protocols differing in the choice, frequency, and timing of preemptive therapies. Thus, transplant centers have adopted center-specific protocols for FSGS patients. The purpose of this study was to assess the efficacy of a preemptive TPE and RTX treatment protocol for the prevention of early graft loss due to FSGS recurrence post–renal transplant.

MATERIALS AND METHODS

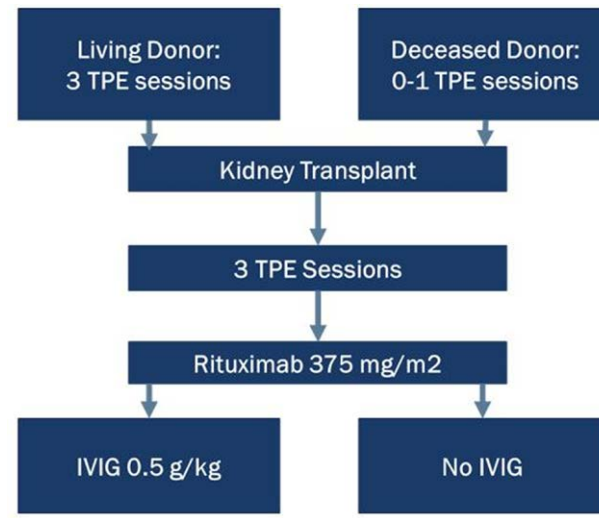
Study Design, Patient Selection, and Data Collection

This was a single-center, retrospective study of index KT patients transplanted at Houston Methodist J.C. Walter Jr. Transplant Center. All adult patients aged 18 y or older who received a KT with an indication of idiopathic FSGS between June 1, 2013, and August 31, 2021, were included in this study. The diagnosis for idiopathic FSGS pretransplant was determined on the basis of native biopsy-confirmed FSGS with podocyte foot effacement by electron microscopy and confirmed diagnosis from the transplant nephrologist. Patients who received multiorgan transplants, those with confirmed secondary FSGS, and those without native biopsies were excluded.

The FSGS protocol was implemented in May 2016, where any patients undergoing kidney transplants for the indication of idiopathic FSGS received preemptive plasmapheresis and RTX. Per the protocol, living donor recipients received 3 sessions of TPE in the week before transplantation, whereas deceased donor recipients received 1 session of TPE, if time permitted, before transplantation. Posttransplant, all recipients received 3 sessions of TPE followed by RTX at a dosage of 375 mg/m^2 with or without IVIG 0.5 g/kg, based on the presence of hypogammaglobulinemia (Figure 1). The choice of replacement fluid (5% albumin with/without fresh frozen plasma) for TPE is determined by the physician based on the patients' coagulation labs, mainly driven by the fibrinogen. The total volume exchanged varied from 2 to 4 L of plasma for replacement fluid. Urinary protein-creatinine (UPC) ratios were monitored daily during the index admission and at all follow-up visits after kidney transplant. All recipients under the FSGS protocol underwent protocol biopsy at 1 and 6 mo post-KT to screen for FSGS recurrence. To determine the effect of this protocol on FSGS recurrence within the first year posttransplantation, a historical control was used comprising kidney transplant recipients with a diagnosis of idiopathic FSGS transplanted at this center immediately before the introduction of the FSGS protocol. The historical control group did not receive any preemptive therapies for FSGS recurrence, nor did they undergo any protocol biopsies. Patients were grouped according to those who received the FSGS protocol with TPE, RTX, ±IVIG, and those who did not.

Patients were induced with rabbit antithymocyte globulin if their calculated panel-reactive antibody (cPRA) was >20%, had a previous renal allograft lost due to immunologic reasons, African American race, or positive donor-specific antibody at time of transplant. All others received basiliximab induction. All recipients received maintenance immunosuppression consisting of tacrolimus, mycophenolate mofetil, and 3 d of methylprednisolone followed by a prednisone taper. Target tacrolimus trough levels during the first month of transplant were 8–10 ng/mL and 7–9 ng/mL for months 2 and 3, respectively, 6–8 ng/mL for months 4–12, and then 4–8 ng/mL thereafter.

Patient electronic medical records (Epic Systems Corporation, Verona, Wisconsin) were reviewed to collect



Abbreviations: IVIG, intravenous immune globulin; TPE, therapeutic plasma exchange

FIGURE 1. FSGS protocol breakdown. FSGS, focal segmental glomerulosclerosis; TPE, therapeutic plasma exchange.

baseline demographics, including age at FSGS diagnosis and transplantation, sex, ethnicity, comorbidities at the time of transplant, and type and time on dialysis. The primary endpoint was the incidence of clinical FSGS recurrence within the first year posttransplantation. Disease recurrence was defined as nephrotic-range proteinuria ≥3 g/24 h and a renal biopsy showing podocyte foot process effacement. Secondary endpoints included FSGS recurrence at the following time points: 1, 3, and 6 mo (with a 7-d window allowing for protocol biopsy scheduling). Additional endpoints included the incidence of biopsy-proven FSGS recurrence without proteinuria, infections, length of index hospitalization stay, incidence of biopsy-proven acute rejection (BPAR) at 1 y, and incidence of death-censored graft loss (return to chronic dialysis or retransplantation) at 1 y, and incidence of mortality at 1 y. Adverse events within 2 wk of TPE and within 3 mo of RTX were reported. Additional data points included type of donor (living versus deceased), cPRA, induction therapy, maintenance immunosuppression, use of ACEi or angiotensin receptor blockers, development of posttransplant infections, and any posttransplant renal biopsies. Data were acquired and analyzed after obtaining approval from the Institutional Review Board at the Houston Methodist Hospital (IRB ID: PRO00032488).

Statistical Analyses

Continuous data were presented as median (interquartile range [IQR]) and analyzed with the Mann-Whitney *U* test. Categorical data were presented as proportions represented in percentages (%) and analyzed with chi-square or Fisher exact test as appropriate. Recurrence of FSGS and graft loss were analyzed using the Kaplan-Meier analysis with log-rank tests. Reported *P* values of <0.05 were considered statistically significant. Statistical analysis was performed using SPSS software version 25 (IBM SPSS Statistics, IBM Corporation, Armonk, NY).

RESULTS

A total of 1807 patients received kidney transplants at Houston Methodist Hospital from June 2013 to August 2021. Of this population, 100 patients received kidney transplants for the indication of FSGS during that time frame. Thirty-five patients did not meet the inclusion criteria and were excluded from this analysis (Figure 2). A total of 65 patients were included for analysis. This study sample was divided into the FSGS protocol cohort and the control cohort. Of the study patients, 25 patients were included in the historical control group and 40 patients were included in the FSGS protocol group. Baseline characteristics are presented in Table 1. There were no statistically significant differences in baseline characteristics or demographics, although there was a clinically higher percentage of deceased donors performed in the control cohort versus the FSGS protocol cohort (56% versus 33%, $P = 0.06$, respectively). Of the living donor KT of the FSGS protocol group, 22 patients (81%) received the complete 3 TPE sessions, 4 patients (15%) received only 1 session of TPE, and 1 patient (4%) did not receive any sessions of TPE before transplant. Among the deceased donor KT of the protocol group, only 6 patients (46%) received a session of TPE before transplant. Thirty-two patients within this cohort (80%) received all 3 sessions of TPE posttransplant. A total of 8 patients did not receive the full 3 sessions of TPE posttransplant, mainly due to physician preference early after protocol implementation. One patient completed 2 sessions of TPE posttransplant with fresh frozen plasma as replacement fluid, but the last session was deferred due to a hemoglobin drop and received a blood transfusion with no other complications. There were no other instances of bleeding complications in these patients. Thirty-8 of 40 patients (95%) in the FSGS protocol group received RTX. The 2 other patients did not complete the RTX infusion. One patient had an anaphylactic reaction to RTX and the second patient did not receive RTX due to physician preference.

Clinical FSGS Recurrence at 1 y Posttransplant

The FSGS protocol cohort had significantly fewer patients with clinical FSGS recurrence at 1 y compared with the historical cohort, with 1 versus 5 patients (3% versus 20%, $P = 0.03$, respectively; Figure 3).

Protocol Biopsy FSGS Recurrence Without Proteinuria

Within the FSGS protocol cohort, 4 patients (11%) were found to have early subclinical FSGS recurrence on the protocol biopsy, none of whom had significant changes in serum creatinine (defined as at least 1.5 times baseline serum creatinine) or nephrotic range proteinuria at time of recurrence.

Characteristics of Patients With Biopsy-proven FSGS Recurrence

In total, 5 versus 6 patients (13% versus 24%, $P = 0.25$) were found to have biopsy-proven recurrent FSGS (with or without proteinuria) in the FSGS protocol cohort versus control cohort, respectively. The median time (IQR) to recurrence posttransplant was 36 (36–43) versus 88 d (9–156) in the FSGS protocol cohort versus the control cohort ($P = 0.93$). The median UPC ratio (IQR) at the time of FSGS recurrence in the FSGS protocol cohort versus control cohort was 0.2 g/24 h (0.1–0.2) versus 11 g/24 h (5–20; $P = 0.07$, respectively).

Treatment of Recurrent FSGS

The patient with clinical recurrence in the FSGS cohort received additional sessions of TPE and RTX (Table 2); he was also initiated on corticotropin 80 unit/mL injectable gel and losartan for persistent proteinuria. The patient's renal function improved as serum creatinine was down to a new baseline of 1 mg/dL 2 wk post-treatment. Of the FSGS cohort, 2 of 4 patients with recurrent FSGS on protocol biopsy without proteinuria or graft dysfunction (or subclinical FSGS) were further treated with additional sessions of TPE and RTX (Table 2). Their graft function remained stable throughout treatment.

Within the control cohort, 5 of 6 patients received treatment with multiple sessions of TPE and RTX. The remaining patient did not receive further treatment for FSGS recurrence in the setting of clinical instability. Two of 5 who received treatment did not respond, resulting in graft loss within 1 y posttransplant.

Early Graft Loss

Sixty-one patients completed 1 y follow-up at the time of study completion. The overall serum creatinine and UPC ratio trends were similar between the 2 cohorts as shown in Table 3.

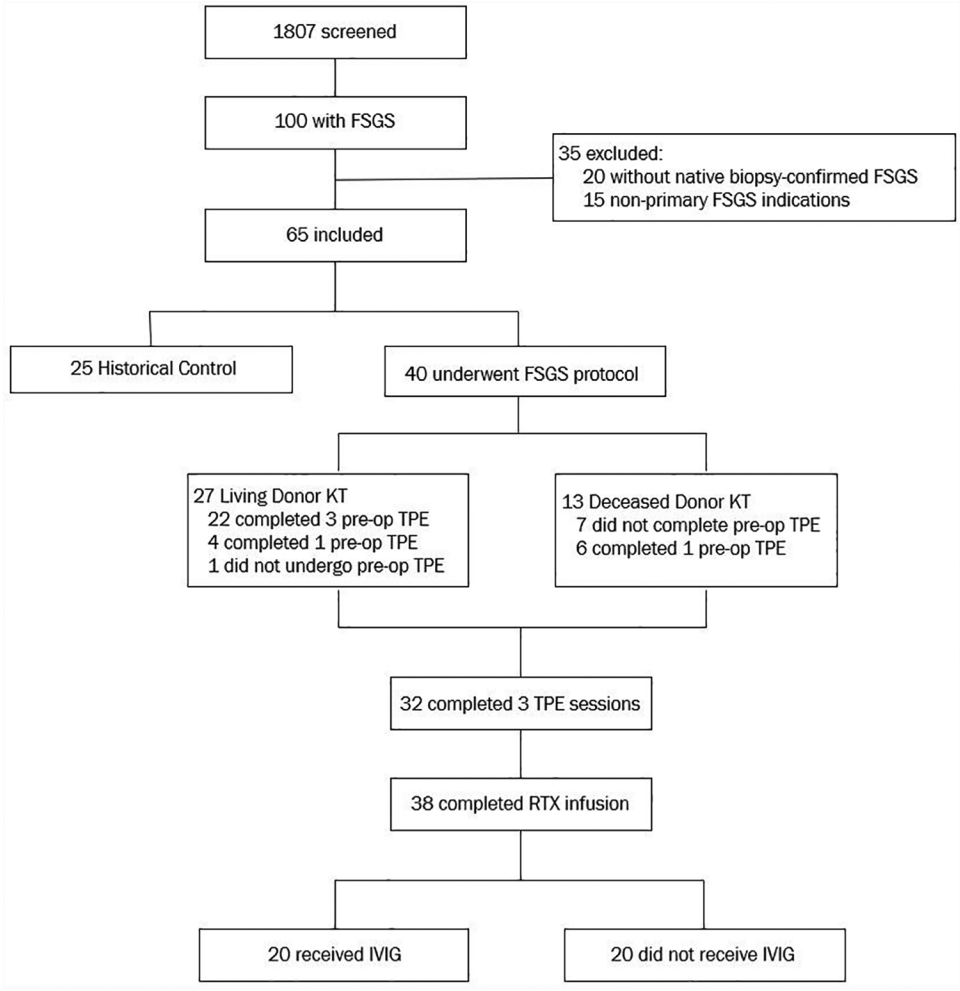


FIGURE 2. Consort diagram. FSGS, focal segmental glomerulosclerosis; KT, kidney transplantation; RTX, rituximab; TPE, therapeutic plasma exchange.

However, at 1 y posttransplant, there were no cases of graft loss in the FSGS protocol group compared with 2 cases in the control group (0% versus 8%; $P = 0.14$; Figure 4). The 2 cases of graft loss were due to recurrent FSGS in the control group; an additional patient in the control cohort had expired on postoperative day 21 due to a possible hematoma post-transplant with a functioning graft. Among the FSGS protocol group, 37 had functioning grafts at the 1 y mark, whereas 1 patient expired with a functioning graft at postoperative day 245 due to COVID-19 pneumonia-related complications. Two of 40 patients in the FSGS protocol cohort were lost to follow-up before 1 y post-KT.

Infectious Complications

There were no significant differences in rates of infections (cytomegalovirus [CMV] or BK virus) within 3 mo posttransplantation in the FSGS protocol cohort versus the control group, 2 versus 3 cases (5% versus 13%; $P = 0.36$, respectively). IgG levels were available in 25 patients (63%) before discharge, and the median (IQR) IgG level was 447 (385–616) mg/dL. Twenty patients (50%) received IVIG 0.5 g/kg on the day of discharge. The patients who received IVIG had zero cases of infection compared with patients who did not receive IVIG (2 cases, $P = 0.15$). There was a total of 4 patients in the FSGS protocol cohort with COVID-19 infection, one of which resulted in mortality within 1 y posttransplant. The historical cohort did not have any cases of COVID as the endpoints collected at 1 y posttransplant were before the start of the COVID-19 pandemic.

Biopsy-proven Acute Rejection

At 1 y, there were no differences in rates of BPAR between the FSGS protocol cohort and the control cohort, 4 versus 4 cases (10% versus 16%) respectively, ($P = 0.73$; Table 4). There were no clinical differences in immunologic baseline characteristics between the 2 cohorts (Table 1). The median (IQR) time to BPAR was 42 d (31–124) in the FSGS protocol cohort and 64 d (39–130) in the control cohort ($P = 0.15$).

DISCUSSION

The goal of this study was to assess the efficacy of TPE in combination with RTX for the prevention of FSGS recurrence and early graft loss in the KT population. In this study, we report a low rate of clinical FSGS recurrence with no death-censored graft loss in 1 y post-KT compared with historical control. The FSGS protocol was well tolerated with a low rate of significant infection.

TABLE 1.

Baseline characteristics

Characteristic	Protocol cohort (N = 40)	Pre-protocol control (N = 25)	*P*
Age at FSGS diagnosis, y, median (IQR)	28 (19–45)	33 (23–41)	0.56
Age at transplantation, y, median (IQR)	39 (29–52)	40 (35–43)	0.68
Sex, male, n (%)	25 (63)	19 (76)	0.26
Ethnicity, n (%)			
White	16 (40)	13 (52)	0.34
African American	14 (35)	10 (40)	0.68
Hispanic or Latino	6 (15)	0 (0)	0.07
Asian	2 (5)	2 (8)	0.64
Other	2 (5)	0 (0)	0.52
BMI at transplantation, kg/m^2, median (IQR)	27.0 (23.5–30.9)	30.0 (25.0–31.8)	0.54
Comorbidities, n (%)			
Hypertension	34 (85)	23 (92)	0.18
Diabetes mellitus	3 (8)	1 (4)	1.00
Type of dialysis, n (%)			
Intermittent hemodialysis	18 (45)	12 (48)	0.81
Peritoneal dialysis	9 (23)	8 (32)	0.40
Preemptive	13 (32)	5 (20)	0.27
Time on dialysis, y, median (IQR)	2.0 (1.0–3.0)	2.0 (1.0–6.5)	0.49
History of prior kidney transplant, n (%)			
Recurrence of FSGS	3 (8)	4 (16)	0.42
Chronic graft nephropathy	2 (5)	3 (8)	0.37
Recurrence of FSGS	1 (3)	1 (4)	1.00
cPRA peak, median (IQR)	18 (2–60)	29 (0–71)	0.43
PRA >20%, n (%)	20 (50)	15 (60)	0.43
HLA-A/-B/-DR mismatch, median (IQR)	5 (3–5)	4 (4–5)	0.93
Deceased donor, n (%)	13 (33)	14 (56)	0.06
Donor after circulatory death	2 (5)	2 (5)	0.64
Induction therapy, n (%)			
Antithymocyte globulin	24 (60)	17 (68)	0.52
Basiliximab	16 (40)	8 (32)	0.52
Delayed graft function, n (%)	5 (13)	0 (0)	0.15
CMV high risk (D^+/R^-) serostatus, n (%)	9 (23)	6 (24)	0.89
ACEi/ARB within 1 y posttransplant, n (%)	8 (20)	6 (24)	0.76

ACEi, angiotensin-converting-enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; CMV, cytomegalovirus; cPRA, calculated panel-reactive antibody; D, donor; FSGS, focal segmental glomerulosclerosis; IRQ, interquartile range; R, recipient.

The reported rate of FSGS recurrence after KT ranges from 30-60%, resulting in graft loss in 40%–60% in those with recurrence.[12-22] A large, multicenter study by Uffing et al[12] reported an FSGS recurrence rate of 32% with a median time to recurrence of 1.5 mo after KT. In those with recurrence, 39% of patients had graft loss, with a median time of 7 mo from recurrence to graft loss.

There is limited data addressing preemptive therapy of FSGS recurrence posttransplantation. Studies have assessed the isolated effects of TPE or RTX, but infrequently, the combination of both in a protocolized manner. A report by Gohh et al[18] assessed the use of preemptive TPE in preventing FSGS recurrence (defined as proteinuria of >3g/d confirmed with biopsy). After 10 sessions of perioperative TPE in patients with high risk for FSGS recurrence (retransplantation for FSGS recurrence and/or rapid progression to end-stage renal disease), 7 of 10 patients were free of recurrence at follow-up.[18] Several reports have investigated the use of perioperative RTX in the prevention of FSGS recurrence after KT. A large study by Fornoni et al[29] compared a prospective cohort that received a single dose of RTX 375 mg/m^2 within 24 h of KT to a retrospective untreated group, showing a reduction in the incidence of proteinuria high rates of graft survival at 12 mo post-KT.[29] Another prospective study by Alasfar et al[22] only treated patients at high risk (defined as having 2 or more risk factors) for FSGS recurrence with perioperative RTX with or without TPE. This study was unable to show a reduction in FSGS recurrence or graft loss. Overall, these studies show mixed reports of the benefits of preventative RTX or TPE in reducing rates of FSGS recurrence.[11-14]

The study reported herein is unique in that both TPE and RTX were used in a protocolized manner for the prevention of FSGS along with routine biopsies, resulting in a clinical recurrence rate of 3% (1/40 patients), an outcome that is superior to the historical control cohort 20% (5/25) which is consistent with reported rates of around 30%–60% without preemptive therapy.[12] In this study, recurrence of FSGS after KT was divided between clinical recurrence (biopsy-confirmed diagnosis accompanied with nephrotic-range proteinuria) and protocol biopsy-confirmed FSGS without proteinuria or graft disfunction. Unlike the historical control, the FSGS protocol cohort had completed routine protocol biopsies to detect early recurrence of FSGS. In fact, 4 of 5 patients were diagnosed with FSGS recurrence through routine protocol biopsies without significant change in serum creatinine or new onset proteinuria. There is a possibility that

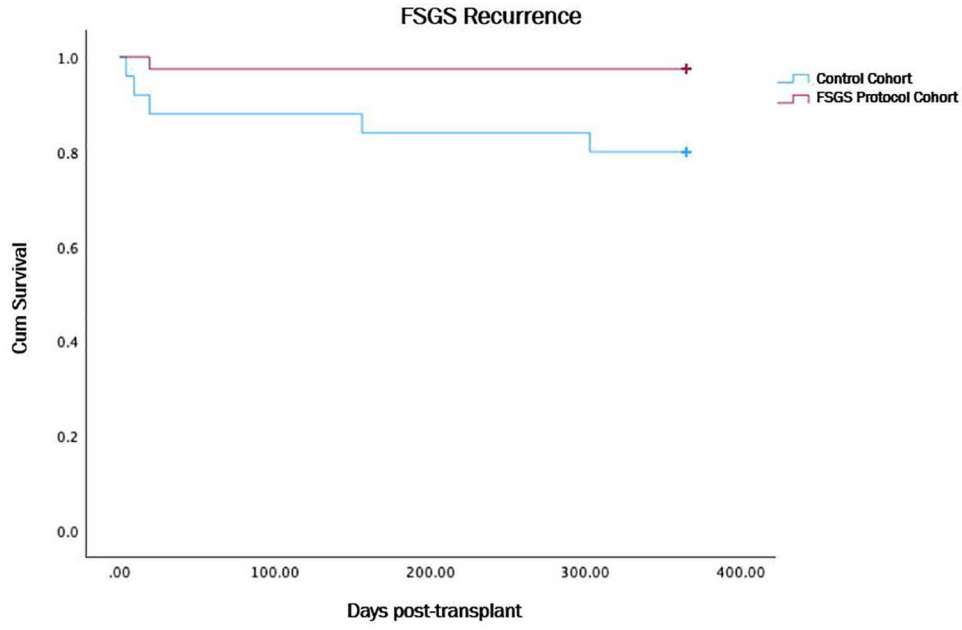


FIGURE 3. Kaplan-Meier curve assessing clinical FSGS recurrence. FSGS, focal segmental glomerulosclerosis.

TABLE 2.

Characteristics of patients with clinical FSGS recurrence

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age at transplantation, y	21	48	43	36	26	25
Ethnicity	White	White	White	Black	White	White
History of prior transplants	Y	Y	N	N	N	N
Type of donor	DD	LD	DD	DCD	DD	LD
FSGS protocol received	Y	N	N	N	N	N
No. of preoperative TPE	1					
No. of postoperative TPE	3					
RTX	Y					
IVIG	N					
Biopsy-confirmed	Y	Y	Y	Y	Y	Y
UPC ratio at time of recurrence, g/24 h	32	19.5	5.3	4.5	33	17.2
Serum creatinine at time of recurrence, mg/dL	2.67	1.7	3.8	1.6	1.6	6.5
eGFR at time of recurrence, mL/min/1.73 m^2	32	32	17	49	52	10
Albumin at time of recurrence, g/dL	1.4	3.2	1.4	2.9	4.5	1.7
Time to FSGS recurrence, d	19	303	19	156	4	9
Treatment for recurrence	TPE RTX Losartan Corticotropin gel	TPE RTX Enalapril	TPE RTX	TPE RTX Lisinopril	TPE RTX	Not treated due to clinical instability
Graft loss at 1 y	N	N	Y	N	N	Y

DCD, donor after circulatory death; DD, deceased donor; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; LD, living donor; N, no; RTX, rituximab; TPE, therapeutic plasma exchange; UPC, urine protein-creatinine; Y, yes.

these patients had been diagnosed early enough on biopsy and further treated before progressing to nephrotic syndrome. Furthermore, there were no cases of death-censored graft loss (1 case of death with graft function) within the first year of transplant in the FSGS protocol cohort, which differs from previous studies with high rates of graft loss.

As RTX administration is linked with an increased risk of infectious complications, patients were assessed for CMV or BK infection within 3 mo of RTX treatment. The incidence of infections within the 3-mo period was similar between the FSGS protocol cohort and the historical cohort. Patients are also at risk of hypogammaglobulinemia due to the depletion of IgG from the multiple sessions of TPE, resulting in an increased risk of infection. We monitored IgG levels before discharge to assess for hypogammaglobulinemia and treated with IVIG as needed. A subanalysis to assess the effects of IVIG on infection showed that the cohort receiving IVIG had clinically fewer episodes of infection overall. These findings were similar to a study by Lanaret et al,[30] who found no difference in severe infections among patients who received

TABLE 3.

Posttransplant complications

Posttransplant complications	Protocol cohort (N = 39)	Control cohort (N = 24)	*P*
Incidence of infections within 3 mo of transplant, n (%)	2 (5)	3 (13)	0.36
CMV	1 (3)	2 (8)	0.55
BK	1 (3)	1 (4)	1.00
BPAR at 1 y, n (%)	4/37 (10)	4/24 (16)	0.73
ACR	2 (5)	2 (8)	0.63
AMR	0 (0)	0 (0)	NA
Mixed ACR/AMR	2 (5)	2 (8)	0.63
De novo DSAs at 1 y, n (%)	6/37 (16)	7/24 (29)	0.09

ACR, acute cellular rejection; AMR, antibody-mediated rejection; BPAR, biopsy-proven acute rejection; CMV, cytomegalovirus; DSA, donor specific antibody.

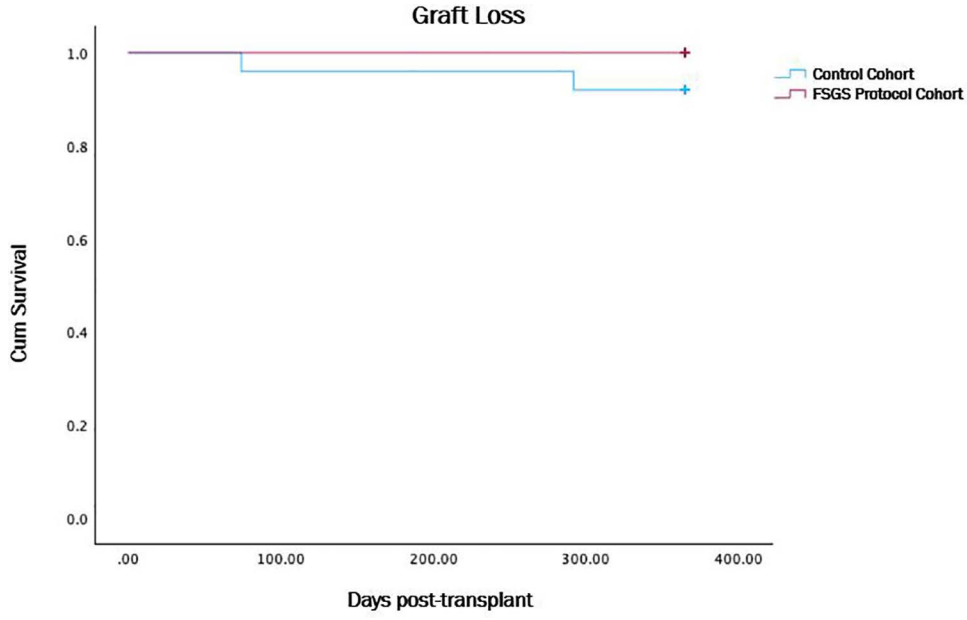


FIGURE 4. Kaplan-Meier curve assessing graft loss. FSGS, focal segmental glomerulosclerosis.

TABLE 4.

Renal function and UPC ratio trends

Laboratory values	Protocol cohort (N = 40)	Control cohort (N = 25)	*P*
Serum creatinine, mg/dL, median (IQR)			
1 mo	1.50 (1.18–1.80)	1.40 (1.30–1.80)	0.93
3 mo	1.44 (1.11–1.72)	1.40 (1.30–1.60)	0.86
6 mo	1.56 (1.26–1.79)	1.35 (1.20–1.53)	0.20
9 mo	1.45 (1.20–1.78)	1.40 (1.10–1.70)	0.77
12 mo	1.50 (1.16–1.73)	1.45 (1.18–1.73)	0.81
UPC ratio, g/24 h, median (IQR)			
1 mo	0.17 (0.11–0.27)	0.15 (0.11–0.31)	0.95
3 mo	0.12 (0.08–0.25)	0.12 (0.09–0.27)	0.90
6 mo	0.11 (0.09–0.21)	0.13 (0.09–0.25)	0.46
9 mo	0.11 (0.07–0.19)	0.12 (0.06–0.48)	0.71
12 mo	0.09 (0.08–0.22	0.10 (0.08–0.18)	0.25

IQR, interquartile range; UPC, urine protein-creatinine.

RTX, although hypogammaglobulinemia <5 g/L was associated with higher rates of infection. Similarly, Uffing et al[12] found that after adjusting for confounders, there was no difference in the incidence of BK or CMV viremia in those that received RTX.

Although overall rejection rates were similar, the median time to BPAR occurred earlier posttransplant in the FSGS cohort compared with the historical cohort. An early rejection episode could possibly be attributed to the removal of the induction immunosuppressive agent by TPE. There is

limited literature guiding appropriate timing of these agents in conjunction with TPE. West-Thielke et al[31] suggested that approximately 50%–60% of rabbit antithymocyte globulin would be cleared by TPE, and Okechukwu et al[32] reported approximately 65% of a standard 20 mg dose of basiliximab is removed during TPE. As per center protocol, all patients received induction POD 0, but subsequent doses were timed to be given after plasmapheresis to minimize drug removal.

Given the retrospective nature of this study, there were several limitations regarding data collection. Due to the difficult nature of diagnosing true idiopathic FSGS, this study defined diagnosis through pathological findings combined with a documenting transplant nephrologists' diagnosis, which could open the possibility for selection bias. Clinical decisions regarding FSGS therapy initiation, modification, or omission were based on physician discretion. Thus, many of the deceased donor KT recipients in this study did not receive a preoperative TPE session due to the timing of the organ offer and the unplanned nature of a deceased donor transplant. Genetic testing was not regularly available throughout the study period, and thus, genetic forms of FSGS could not be ruled out of this population. Also, there was no documentation of B-cell depletion available to assess the efficacy of RTX as this is not often used at our center. Going forward, this monitoring parameter can be incorporated into the FSGS protocol and future practice. Furthermore, the follow-up period for this study was 1 y post-transplant, which may not be adequate time to capture the complete risk of recurrent disease in this population.

In conclusion, this study has shown that protocolized use of perioperative TPE and RTX may prevent early disease recurrence of FSGS and subsequent graft loss after renal transplant. Additionally, the adjunctive use of IVIG potentially reduces the risk of infection post-RTX and TPE. Larger, prospective-controlled studies would be of benefit in confirming the long-term outcomes of FSGS recurrence and possible effects of long-term graft survival.

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