

Post-transplant Recurrence of Focal Segmental Glomerulosclerosis: Consensus Guidelines



Avisha Pandey¹, Amrit Khooblal¹, Christoph Licht², and Rupesh Raina^{1,3}
¹Department of Nephrology, Cleveland Clinic Akron General Medical Center, Akron, OH
²Division of Nephrology, The Hospital for Sick Children, Toronto, Ontario, Canada.
³Department of Nephrology, Akron Children’s Hospital, Akron, OH



Introduction

- Focal segmental glomerulosclerosis (FSGS) is a leading cause of steroid-resistant nephrotic syndrome in both the adult and pediatric population with an incidence ranging from 6% to 57%.¹⁻³
- FSGS is a descriptive term where “focal segments” of glomeruli show hyalinosis, sclerosis, and scarring.
- rFSGS is diagnosed when transplant recipients show nephrotic range proteinuria with hypoalbuminemia and/or edema.^{4,5}
 - Histological confirmation in the native kidney as well as the identification of the same disease in the kidney allograft is also required.
 - Since not all patients have undergone native kidney biopsies, the primary disease is sometimes unknown.
- FSGS may progress to end-stage kidney disease (ESKD), especially in patients who show non-response to standard therapies.
- FSGS may recur in the kidney allograft and is a notable cause of post-transplant morbidity and graft loss.

Methodology

- **Design:** This is a systematic review on the incidence and risk factors of rFSGS in in the adult and pediatric populations between January 1974 and October 2019.
- **Study Population:** Pediatric and adult patients with rFSGS.
- **Study Variables:** The transplant recipients’ age, sex, ethnicity of patient, type of donor, number of acute rejection episodes, and 5-year graft survival rates were extracted from the filtered studies.
- **Data Collection:** Recorded outcomes included the incidence of rFSGS, episodes of acute rejection, and 5-year graft survival.

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Objectives

- What is the incidence of rFSGS?
- How does it vary among various demographic groups?

Results

Incidence of rFSGS among:

- All kidney transplant recipients was 15.46% (N=1028/6650)
- Adults was 10% (95% CI; range 3.7% to 34.8%).
- Children was 37.2% (range: 31.7% to 85.7%)²⁶⁻²⁹
 - Odds ratio for children vs. adults was 4.52 (95% CI: 1.82-11.28, P = 0.001)
- Caucasians was 19-41% compared to non-Caucasians was at 10-13%
 - Odds ratio for Caucasians vs. non-Caucasians was 1.48 (95% CI: 1.19 - 1.84; P <0.001)
- Males to females held an odds ratio of 1.1 (95% CI: 0.91 - 1.34; P = 0.97)
- Living donors was 22.90% compared to deceased donors was 21.85%.
 - Odds ratio for living donors vs. deceased donors was (1.39; 95% CI 1.17 - 1.66; P <0.001).

Survival rate for 5-year graft s of adult FSGS patients:

- With recurrence was 56.11% (95% CI: 50.09 to 62.00%; n=276; P = 0.53)
- Without recurrence 82.66% (95% CI: 79.76 to 85.30%; n=749; P = 0.81)
- Odds ratio of 5-year graft survival among those without rFSGS vs. with rFSGS was 4.24 (95% CI: 2.77 – 6.48; P <0.001).

Discussion

- Risk Factors of rFSGS:

Decreased risk	Non-contributory	Increased risk
Older age	Duration of dialysis	Younger age
African American race	Gender	Children
Slow progression to ESRD	Post-transplant immune therapy	Caucasian race
Mutations causing FSGS	Histology: Columbia classification	Rapid progression to ESKD
Hereditary FSGS	Living donor	Focal mesangial proliferation
		Pretransplant bilateral nephrectomy
		Elderly donor
		Initial steroid sensitivity

- LD kidneys are associated with improved graft outcomes compared to DD kidneys.
- FSGS can be induced by several autosomal recessive (nephrin, podocin, CD2AP, PLCε1 and MYO1E) or autosomal dominant mutations (α-actinin-4, TRPC6 and INF2).⁴⁴
 - Potential donors should be evaluated carefully for genetic kidney diseases and mutations.
- A rapid progression to ESKD (within 3 yrs from the FSGS diagnosis)^{21,32,62} or recurrence of illness in a prior kidney allograft increases the risk for rFSGS in subsequent allografts.^{5,57}
 - Patients with hereditary forms of FSGS generally have a lower risk of recurrence.⁶³
- Current treatment options include: plasmapheresis or immunoadsorption therapy, and immunosuppressive therapy with rituximab and cyclosporine, and management of concomitant modifiable risk factors.

Conclusion

- The risk of rFSGS was higher among children in comparison to adults, with younger age (6-10 years) of onset being an important determinant.
- The variability in the perceived incidence is attributable to confounding factors such as patients' race and donor graft characteristics.

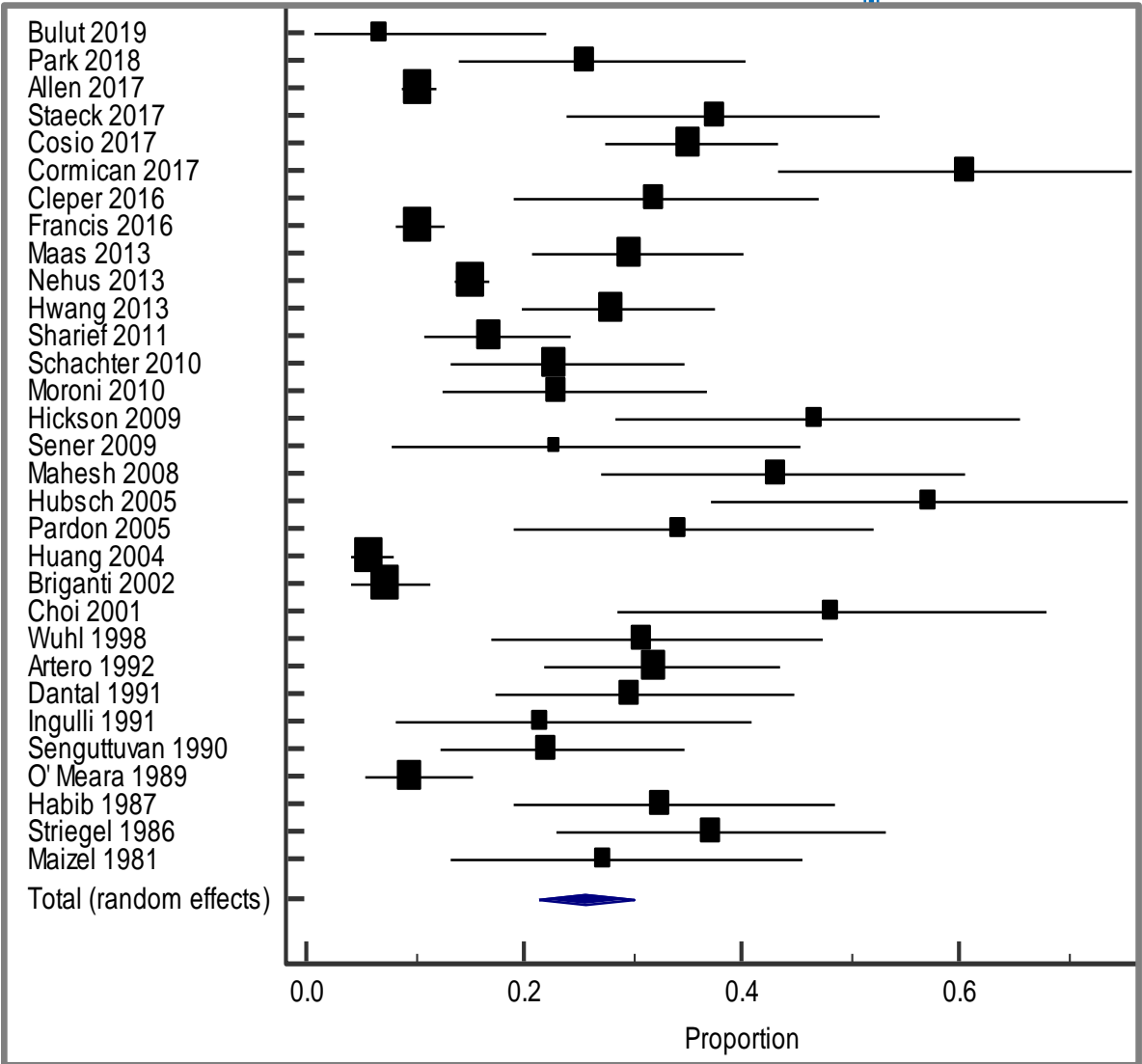


Figure 1: Forest plot of the meta-analysis of rFSGS incidence among kidney transplant recipients. The lower diamond in represents the pooled estimate.