



Timely renal transplantation for scleroderma end-stage kidney disease patients can improve outcomes and quality of life

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Indication for and timing of renal transplantation for systemic sclerosis (SSc) patients who require renal replacement therapy (RRT) as a result of scleroderma end-stage kidney disease (ESKD) is controversial. We recently published a review of scleroderma renal crisis (SRC) and renal involvement in SSc that included an examination of outcomes of RRT, and the role and timing of renal transplantation in SSc patients who become dialysis-dependent as result of ESKD (1). In our review of 10 articles published between 1990 and 2015 the vast majority of patients experienced SRC, with 1–5% of patients found to have ANCA-associated vasculitis or microangiopathic hemolytic anemia (1). These articles describe the onset and clinical course of SSc-associated renal failure, including issues with dialysis outcomes related to vascular access and poor tolerability of dialysis procedures—peritoneal and hemodialysis; four additional publications described results of renal transplantation in the context of a practice of delaying transplant until it was certain that renal function would not recover (2–5). This approach was thought to be supported by observations of research groups in USA, France and UK that up to 25% of SRC ESKD patients recovered renal function within a year on dialysis (6–9).

The article by Hruskova *et al.* published recently in the *American Journal of Kidney Disease* adds substantially to our evidence-base regarding ESKD outcomes in SSc, regardless of cause (10). Their systematic analysis of data in 19 European Renal Association-European Dialysis and

Transplant Association (ERA-EDTA) European Union (EU) registries for RRT in SSc end-stage ESKD provides clinicians with a comprehensive, evidence-based understanding of the incidence, prevalence and management of SSc patients who develop ESKD. RRT includes dialysis—hemo- and/or peritoneal—as well as renal transplantation (10). As reported in two other recent publications, one from France (11) and another from the US (12), they found that the incidence of SRC decreased by over 50% between 2002 and 2013, while the prevalence increased by about 10%, suggesting some success of RRT, as well as success in preventing SRC with rapid treatment of SSc-associated malignant hypertension with angiotensin-converting enzyme inhibitors.

Importantly, the authors' comparison of RRT outcomes in SRC patients with those of diabetics, as well as those with primary renal disease ESKD, highlights several key points (10):

- ❖ Higher initial mortality in older SRC patients despite dialysis;
- ❖ Recovery of renal function during first year was only 7.6% (more likely in young women);
- ❖ Perceived possibility of recovery resulted in longer time on dialysis before being offered transplantation, compared to the control groups—256 days compared to 112–163 days ($P < 0.001$);
- ❖ Median time to transplantation was longer—2.9 (Q1–3, 1.6–4.7) years for SRC patients compared to that for diabetics—1.6 (Q1–3, 0.8–1.9) years, and

for other renal diseases—1.6 (Q1–3, 0.5–3.6);

- ❖ A smaller proportion of SRC patients received a renal allograft compared to those in the other cohorts; 13.7% SSc patients compared to 18.7% for diabetics and 27.1% for the other kidney disease control groups, respectively (both $P < 0.001$ compared to SSc);
- ❖ Renal transplant outcomes were comparable to those of the other cohorts, acknowledging the possibility of selection bias; 5-year patient and graft survival after receiving a first kidney transplant, respectively, for patients with scleroderma [88.2% (95% CI, 75.3–94.6%) and 72.4% (95% CI, 55.0–84.0%)] and for the matched control group patients with diabetes [84.3% (95% CI, 80.5–87.4%) and 76.5% (95% CI, 72.2–80.3%)] and other primary kidney diseases [89.3% (95% CI, 86.0–91.8%) and 81.5% (95% CI, 77.6–84.8%)], matched on age group at kidney transplantation and sex.

Important strengths of this report include the detailed examination of 10+ years of systematically collected data from 11 EU countries with relevant comparisons among SSc patients, diabetics, and patients with primary renal diseases, though France, Italy, and Germany are not included. A recent publication from France, however, does support the findings of Hruskova *et al.* Bertrand *et al.* surveyed 20 French transplant centers and identified 34 patients receiving 36 renal allografts between 1987 and 2013. Patient and (death-censored) graft survival were considered excellent: 100/97.2%, 90.3/97.2%, and 82.5/92.8% at 1, 3 and 5 years, respectively (11).

In our view, the points made in the Hruskova *et al.* report, together with the results reported by the French, provide further evidence that outcomes and quality of life for SSc ESKD patients can be better optimized, as SSc patients remained on dialysis longer and successful transplantation was delayed. Renal transplant should be offered as soon as evaluation on an individualized basis documents that recovery of renal function is unlikely, and before complications associated with extended duration dialysis develop.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Woodworth TG, Suliman YA, Li W, et al. Scleroderma renal crisis and renal involvement in systemic sclerosis. *Nat Rev Nephrol* 2016;12:678-91.
2. Chang YJ, Spiera H. Renal transplantation in scleroderma. *Medicine (Baltimore)* 1999;78:382-5.
3. Pham PT, Pham PC, Danovitch GM, et al. Predictors and risk factors for recurrent scleroderma renal crisis in the kidney allograft: case report and review of the literature. *Am J Transplant* 2005;5:2565-9.
4. Gibney EM, Parikh CR, Jani A, et al. Kidney transplantation for systemic sclerosis improves survival and may modulate disease activity. *Am J Transplant* 2004;4:2027-31.
5. Siva B, McDonald SP, Hawley CM, et al. End-stage kidney disease due to scleroderma--outcomes in 127 consecutive ANZDATA registry cases. *Nephrol Dial Transplant* 2011;26:3165-71.
6. Penn H, Howie AJ, Kingdon EJ, et al. Scleroderma renal crisis: patient characteristics and long-term outcomes. *QJM* 2007;100:485-94.
7. Steen VD, Medsger TA Jr. Long-term outcomes of scleroderma renal crisis. *Ann Intern Med* 2000;133:600-3.
8. Denton CP, Lapadula G, Mouthon L, et al. Renal complications and scleroderma renal crisis. *Rheumatology (Oxford)* 2009;48 Suppl 3:iii32-5.
9. Guillevin L, Berezne A, Seror R, et al. Scleroderma renal crisis: a retrospective multicentre study on 91 patients and 427 controls. *Rheumatology (Oxford)* 2012;51:460-7.
10. Hruskova Z, Pippias M, Stel VS, et al. Characteristics and Outcomes of Patients With Systemic Sclerosis (Scleroderma) Requiring Renal Replacement Therapy in Europe: Results From the ERA-EDTA Registry. *Am J Kidney Dis* 2018. [Epub ahead of print].
11. Bertrand D, Dehay J, Ott J, et al. Kidney transplantation in patients with systemic sclerosis: a nationwide multicentre study. *Transpl Int* 2017;30:256-65.
12. Sexton DJ, Reule S, Foley RN. End-Stage Kidney Disease From Scleroderma in the United States, 1996 to 2012. *Kidney Int Rep* 2018;3:148-54.

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