"SS" answering litter

No	Reviewer one (I.D.05863472)	Answers	Remarks
(1)	General comments: 1. The title "The Journey of a Patient with Scleroderma from Renal Failure up to Kidney Transplantation" is not to the contents mentioned above.	In fact, many specialties have been contributing in the practice of SS management, e.g., Rheumatology, dermatology, etc.…, however, the practicing nephrologist often see the Scleroderma patient in one of the three major clinical stages coincident with his sub-specialties, i.e., Clinical nephrology (SRC), Dialysis (SS patient with ESRD), and kidney transplantation, and those currently were the major partitions of this article.	
	2. The presentation is too long in chapter "Abstract".	Contracted (100 word have been removed) as follows: *The increased awareness of systemic sclerosis (SS) and its pathogenetic background made the management of this disease more amenable than previously thought. However, scleroderma renal crisis (SRC) is a rarely seen as an associated disorder that may involve 2-15% of SS patients. Patients presented with earlier, rapidly progressing, diffuse cutaneous SS disease, mostly in the first 3-5 y after non-Raynaud clinical manifestations, are more vulnerable to develop SRC. SRC comprises a collection of acute, mostly symptomatic rise in blood pressure (BP), elevation in serum creatinine concentrations, oliguria and thrombotic microangiopathy (TMA) in almost 50% of cases. The advent of the antihypertensive ACE inhibitors (ACEi) in 1980 was associated with significant improvement in SRC prognosis. In a scleroderma patient maintained on regular dialysis; every effort should be exerted to declare any possible evidence of renal recovery. A given period of almost two years has been suggested prior to proceeding in a kidney transplant. Of note, SS patients on dialysis have the highest opportunity of renal recovery and withdrawal from dialysis as compared to other causes of end-stage renal disease (ESRD). Kidney transplant (KTx) that is the best well-known therapeutic option for ESRD patients can also be offered to SS patients. Compared to other primary renal diseases, SS-related ESRD was considered for a long period of poor patient and allograft survivals. Pulmonary involvement in an SS patient is considered a strong post-transplant independent risk factor of death. Recurrence of SRC after transplantation has been observed in some patients. However, an excellent post-transplant patient and graft outcome have been recently reported. Consequently, the absence of extrarenal manifestations in an SS-induced ESRD patient can be accepted as a robust indicator for a successful kidney transplant.*	
	3.Too much basic treatment guidelines in main text.	Concise guidelines related to each stage of SS journey have to be outlined and provided to the readers to delineate the various therapeutic options	
	4. There are repetitions and irrelative contents between different paragraphs, such as Recurrence of SRC and Post-transplantation care, treatment of ACEi.	[1] Recurrence of SRC: mentioned only two times, first to denote its liability of development, on the other hand, in the second time mentioned, the paragraph of "Recurrence of SRC" has been greatly contracted. ***Recurrence of SRC and the reported bias:*** *In Bertrand D et al, study, 3 patients with suspected recurrent SRC (8.3%), one recurrent case was complicated by graft loss. All the recurrent cases were on CNI, steroids and ACEi therapy. In follow up biopsies, no subclinical vascular alteration has been observed. Of note, only 6 cases with recurrent SRC have been reported in the literature. An estimated proportion of 1.9 % has been reported in the literature with recurrent SRC-induced allograft loss [37]. Whilst UNOS may under-estimate the actual rate of SRC recurrence, published series may over-estimate SRC recurrence, considering the publication bias of recording serious cases with worst outcome. In addition, two potential diagnoses must be differentiated from the recurrent SCR: firstly, acute/chronic AMR and, secondly: CNI toxicity [55]. Consequently, it is difficult to conclude a definite diagnosis particularly with the retrospective nature of the current reports. The SRC prediction in the non-transplant cohort is quite certain [61-64]. Recognition of RNA polymerase III could be a helpful screening technique in the setting of high-risk patients of recurrence [35, 37 and 65].* [2] Post-transplantation care: Mentioned ONE time and it is crucial to	

		declare the post-transplant impact of both the type of immunosuppressive agents as well as various medical care medications on the native disease progress. [3] Treatment with ACEi: repetition removed.	
	5. Chapter “Conclusions” have to be improved.	**Conclusion** (*amended*): Systemic sclerosis is a multisystem disorder that can be clinically encountered in several stages. In contrary to the reported poor survival of systemic sclerosis patients maintained on renal replacement therapy in comparison to other groups, these patients may show the highest likelihood of renal recovery permitting their withdrawal from dialysis. Recent data in the literature are in favor of better outcome of SS patients receiving a kidney transplant as compared to the previous results. Furthermore, these results were comparable to KTRs in other groups of patients. A particular insight, however, should be focused on the extrarenal manifestations of this disease, especially those related to the pulmonary involvement, an independent risk factor of death in this cohort. Furthermore, the post-transplant cardiac and gastrointestinal involvement should be closely monitored as they may getting worse. In view of the comparable patients and allograft survival rates that have been observed in transplanted SS patients with other groups, further work-up should be tailored to identify which type of an SS patient may benefit more from an offered transplant.	
	6. The authors quoted sufficient clinical articles, but have to use some papers in recent years, after analyzed and summarized, to highlight the novelty and foresight of the disease.	*The following recent references have been included in this article:* **2016**: **4** ref.: No. 9,11, 56 and 57. **2017**: **2** ref.: No. 22, 37. **2018**: **one** ref.: No. 36 **2019**: **three** ref.: No.16, 18 and 50. - Moreover, additional very recent reference, **2020,** has been added, Stochmal A, et al,[30]	
	7.The manuscript could be adopted for publication in this journal after necessary modifications.	Thank you, Sir.	