Overview on Sclerodermal Renal Crisis

Mahdi Ali M. Alyami1*, Jalawi Talal A. Alotaibi1, Shahad Saad A. Aljoaid1, Tariq Bander F. Alanazi1, Waleed Farhan D. Alshammari1, Nuwayr Hamdan D. Albalawi1, Reema Abdulrahman A. Alanazi1, Abrar Ali M. Aldhameen2, Mufihi Abdullah S. Albalawi1, Mona Khalid M. Alqubali3, Marawn Fahad H. Altemani3 and Abeer Abdulrhman. Basmih4

1Tabuk University, KSA.  
2Imam Abdulrahman Bin Faisal University, Dammam, KSA.  
3King Salman Armed Force Hospital, Tabuk, KSA.  
4AlNoor specialist Hospital, Makkah, Saudi Arabia.

Authors’ contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i36B31954  
Editor(s):  
(1) Dr. Wenbin Zeng, Central South University, China.  
Reviewers:  
(1) Daniel Xavier Xibillé Friedman, Hospital General de Cuernavaca, Mexico.  
(2) Ariesanti Tri Handayani, Udayana University, Indonesia.  
(3) T. Ruba, Sethu Institute of Technology, India.  
Complete Peer review History: https://www.sdiarticle4.com/review-history/70145

Received 01 May 2021  
Accepted 06 July 2021  
Published 12 July 2021

ABSTRACT

Usually, malignant high blood pressure and severe renal damage are main characters in SSC. SRCs is a relatively rare condition, found in approximately 5% of all SSc patients. This study was carried out to summarize the contemporary evidence regarding the causes, risk factors, manifestations, management and prognosis of Sclerodermal Renal Crisis. a simple review was carried out, searching databases PubMed, Google Scholar, and EBSCO. The authors extracted the needed data and stated that SRCs continues to be a rare diagnosis affecting up to six percent of SSc patients, but has a high morbidity and death influence. SRCs presentation is varied, with hypertension, normal BP and renal insufficiency. Medics should be minded by potential SRCs presentations. Early detection and initiation of aggressive ACEi antihypertensive medication in ED could enhance patient outcomes and around 60% of SRCs patients need dialysis.

Keywords: Scleroderma; systemic sclerosis; renal crisis.

*Corresponding author: E-mail: 371005232@stu.ut.edu.sa;
1. INTRODUCTION

Scleroderma, additionally called systemic sclerosis (SSc), is a rare, lifestyles-threatening, autoimmune-mediated, substantial inflammatory connective tissue disease which comes as a complication of systemic sclerosis [1,2] causing fibrotic changes in the skin and vasculature, ultimately affecting major organ systems [3,4].

SSc pathology is an unregulated buildup of collagen and extensive vasculopathy that is branded by vascular wall thickening and lumen restriction. Although the specific pathophysiology of SSc remains elusive, the formation of autoantibodies, lymphocytes and fibroblasts, vascular proliferation, obliterating microvascular disease or connective tissue fibrosis are probably the major components of SSc [5]. The typical age of onset of SSc is between the ages of 30 and 60, and it influences ladies four times as frequently as men. [4,6]. Although equally hereditary and ecological considerations, in particular distinctive cell and humour immunity, are considered to be related, the true aetiology of SSc remains undetected.

Usually, malignant high blood pressure and severe renal damage are main characters in SSc [7]. The clinical range of Sclerodermal Renal Crisis (SRCs), on the other side, is vast from full-blown diseases that show new arterial accelerated hypertension and speedily advancing oliguric renal failure, modest blood pressure and renal dysfunction increases and sometimes normotensive occurrences. Hypertension without uremia, urine irregularities and/or mild uremia is, on the other hand, caused by other causes (e.g. co-morbidities such as diabetes and nephrotoxic drug exposure) in SSc [2,8].

SRC must not be disorganized with these conditions. SRC is found to be comparatively infrequent, as it is found in about 5% of all SSc cases [7]. Cases having fast-moving wordy skin SSc (11%) are more commonly found than those with limited skin SSc (4%); [9]. SRC may also be classified as hypertensive or normotensive types constituting approximately 90% and 10% of SRC case [10,11]. The SRC is the major cause of death in SSc historically [12]. However, the fatality rates reduced considerably with the advent of angiotensin conversion inhibitors [13,14].

However, 1-year results are still poor: more than 30% deaths and 25% of the patients still depend on dialysis [15]. Research to develop new therapies and enhance SRC results is urgently needed. Apart from heterogeneity and rareness, the absence of a gold standards and criteria for classification are key hurdles for SRC research. To date, most SRC research have applied ad hoc criteria, which have significantly differed between investigations. In a literature survey, 40 original SRC definitions were uncovered, including somewhat heterogeneous ones [16].

To date, only one study has partially verified SRC criterion [15]. In order to define categorization criteria for SRC, the Scleroderma Clinical Trials Consortium (SCTC) SRC Working group was established.

The aim of this phase was to produce a core collection of elements in order to define SRC by means of a consensus technique. In order to create and validate SRC Classification Criteria, future investigations using data-driven methodologies will be required [16].

1.1 Aim of the Study

This study was conducted to summarize the current evidence regarding the causes, risk factors, manifestations, management and prognosis of Sclerodermal Renal Crisis.

2. METHODOLOGY

A simple review was carried out, searching databases PubMed, Google Scholar, and EBSCO using the following terms in different combinations: Scleroderma, systemic sclerosis, Renal Crisis, causes, risk factors, manifestations, management and prognosis of Sclerodermal Renal Crisis with other key words. We included all full texts [randomized controlled trials, observational, review articles and experimental studies] in making up of this study. The authors extracted the needed data. Inclusion criteria included all relevant studies with similar objectives as our study. Time and language restrictions were made to 20 years and English language. Exclusion criteria included all studies irrelevant to our topic and papers published 20 years ago or more. No software has been utilized to analyze the data. These data were reviewed by the group members to determine the initial findings, and the modalities of the management. Double revision of each member’s outcomes was applied.
3. SYSTEMIC SCLEROSIS

Systemic sclerosis (SSc) is a systemic autoimmune disease (SSc) which is characterised by vasculopathy, inflammation and fibrosis in the skin and internal organs. The type of autoantibody discovered in SSc patients can damage any organ. Two types of SSc are possible: limited skin SSc with elbow and knee thickening and diffuse SSc (dcSSc) with varying skin involvement, respectively. SSc occurs primarily in women, with 7–489 cases per million population and an incidence of 0.6–122 cases per million population per year, with variations between geographical regions [17,18].

The internal organ involvement of SSc can result morbidity and death, such as lung fibrosis, PAH, gastrointestinal dysfunction and various malignancies and sclerodermal renal crisis (SRC), a rare yet life threatening event. SSc is also a consequence of disease and mortality. Renal vasculopathy is prevalent in SSc patients, is usually asymptomatic, but isolated proteinuria and/or hypertension might be associated with it [19,20]. None of these symptoms, however, indicate the development of the SRC [21,22].

4. HISTORY AND PROGNOSIS OF SCLERODERMA RENAL CRISIS (SRC)

In previous cases, up to 15% of systemic sclerosis patients (SSc) experienced a renal scleroderma (SRC) crisis [23,24,25,26]. SRC was found to occur. Downward frequencies have still been seen in recent years [27,28]. SRC is a patient medical emergency and a clinician's difficulty. In the past there has been a dramatic drop in the high mortality and morbidity rate, particularly outside specialist centres since the 1970s [28,29,30].

The reason may be firstly: reduced usage of high dosage systemic corticosteroids for patients with SSc, secondly: improves knowledge of SRC, and at the same time increases the research interest in this rare disorder, because of the development of angiotensin transforming enzyme inhibitors (ACEI).

Another factor may be that patients who are at danger of having this life-threatening organ manifestation may receive more intensive healthcare and earlier identification. The SSc patients who had a renal crisis had 5-year survival improved by <10 to 65 percent with the introduction of ACEI7, Steen and Medsger reported in 2007. This transformation can have been stimulated by patient registries, national and worldwide networking paired with increased awareness of the disease.

Instant identification and direct beginning of ACEi therapy in patients with renal crisis can contribute to improving the output of these individuals [31,32]. In the case of patients with SRC independently, whether or not renal replacement therapy is needed, the Scleroderma Study Group established guidelines for diagnosis and treatment with SRC and urged that ACEi medication be continued [33]. Fortunately after renal crisis, renal recovery may still occur until 3 years after SRC (usually 12–18 months) developments [34].

Event cases of kidney crisis were described as of SSc centres on wholly regions by the International Scleroderma Renal Crisis Survey. They demonstrated a greater risk of death for those treated with ACEi prior to SRC inception14. It led to discussion whether or not ACEi could hide the earliest clinical indications of an SRC, therefore leading to poor results [35,36]. In addition, the survey found that cases having the wordy type of SSc, early start, and graduated disease have a higher chance of SRC development (characteristically within the first 3–5 yrs after the onset of non-Raynaud signs19). Also individuals with tendon rubber / significant articular contractures [37], positive anti-nucleoprotein (ATA) [37,38], polymerase anti-RNA (RNAP) antibodies and current exposures to corticosteroids [39,40].

The introduction of an ACEi enhances the SRC’s prediction considerably with an existing one-year survival of 70% to 82%, which is reduced for those patients with ongoing dialysis to 50-70% for five years [33]. Patients that have no dialysis and need only temporary dialysis have great results with a survival of 90% in 5 years [33]. However, the result of this treatment is highly effective. In the last 30 years of such initiatives, there has unfortunately been no obvious trend towards progress. Male sex, older age, lower BP at diagnosis, and the development of congestive heart failure are the risk factors for the mortality of these patients [41,42].

Many of these patients need close hemodynamic monitoring in the critical care environment solely.

5. CORTICOSTEROIDS AND THE RISK OF SCLERODERMA RENAL CRISIS

A variety of risk variables predict the emergence of SRC, including SSc < 4 years, diffuse, rapidly
progressive skin thickening, palpable tendon-rubbing, and new anaemia or heart failure. The use of glucocorticoids at particularly high dosages (e.g. prednisone > 15 mg per day), which has dose-related impacts on the chance to develop SRC, is another significant risk factor for SRC. Glucocorticoids cause salt and volume retention, hypertension onset and deterioration, and an increased risk of SRC in patients' subsets. Corticosteroids (CS) and their putative function in SSc precipitation of SRC since 1951 have been concerned [43]. The possible link was later substantiated by other case reports [44,45] and retrospective studies [46,47].

The new continued use of 15 mg/day usage of prednisone was related with a four-fold increase in SRC onset (odds ratio 4.37, 95 per cent confidence interval 2.03–9.43) [47]. A case-control study conducted with 110 Pittsburg SSc patients who acquired SRC between 1982 and 1993 involved a new usage of prednisone [48]. On the other hand, CS was no independent risk factor for SRC in early Diffuse Cutaneous Systemic Sclerosis (dcSSc) [49]. However, the SRC only occurred in patients with extensive skin involvement, with substantial joint contractures, in the subgroup analysis low doses of prednisone (median 7.4 mg/day). The results therefore remain contradictory and unsatisfactory, and prospective data investigations are required to elucidate the role of CS in inducing SRCs [46,50].

6. HISTORY AND PHYSICAL EXAMINATION

SRC's diagnosis is based on typical findings for high-risk SSc patients and focusses particularly on the development of quickly increasing hypertension and renal failure.

Patients with renal disease typically do not have hypertension before the acute onset and blood pressure (BP) increases fast. Oliguria or uremic symptoms may occur in patients. Vascular blockage and tissue ischemia in serious SRCs can lead to autopsy-visible renal infarcts and subcapsular hemorrhage [51].

SSc should therefore be considered in any patient with malignant hypertension. A recent onset of Raynaud's phenomenon, acute start-ups, weight loss, polyarthritides, pinch extremities, carpal tunnel syndrome, and tendon friction rubs are the clinical symptoms that aid identify patient with SSc in this connection [52,53]. After several months of initial symptoms, the skin thickening, which becomes a diverse type of SSc generally occurs. Nevertheless, in individuals without evidence of skin thickening or other indications of SSc, it is important to emphasise that SRC can occur [54,55].

7. MANAGEMENT OF SCLERODERMA RENAL CRISIS

Untreated, it is possible for SRC to develop to renal disease (ESRD) near the end of the stage over a period of 1 to 2 months, usually with death within one year [56]. While it is still challenging to diagnose and start therapy early in SRC, it is vital to recognise the SRC promptly. The cornerstone of SRI treatment is effective, rapid control of BP, which in roughly 70 per cent of patients has been shown to improve or stabilise renal function and to improve survival to about 80 per cent in one year [41]. The success of antihypertensive medication is nevertheless dependent on its commencement in advance of irreversible renal damage [42].

It is recommended that BP be methodically reduced, as a rapid decline causes renal perfusion to diminish and increased risk of acute tubules necrosis. The ultimate objective is to achieve the patient with 72 hours of pre-SRC BP [33].

An ACEi is the ideal SRC antihypertensive agent. Determined renal perfusion, after a hyperplasia of the juxtaglomerular system and enhanced renin release are included in the pathogenesis. Hyperreninemia generates further hypoperfusion and vasoconstriction that perpetuates the initial offense [57].

An ACEi interrupts this viscous cycle by altering the system of renin–angiotensin–aldosterone. Those drugs have not been well assessed in this context and their efficacy is not established, but angiotensin receptor blocker (ARBs) should theoretically be proof of efficacy in SRC [58,59]. However, given scant evidence of hypertension hypertension is not responsive to ACEi, consensus advocates that these actors be a potential secondline agent [60]. The role of direct renin inhibitors is shown not. The most generally known nifedipin blocker (CCBs) for the treatment of dcSs, including Rayneaud disease, in more than 90 percent of dcSSc patients, is dihydropyridine calcium channel blockers.
Approximately 60 percent of patients with SRC require dialysis despite adequate ACEi treatment. Electrostotic ESRD treatment caused to SRC [57,41,61,62] is advised as either hemodialysis or continuous peritoneal dialysis. There is minimal experience with kidney transplantation in SRC patients, partly because the severity of the external signs of SSc is occasionally prevented. In patients on dialysis who do not recover function of the kidney within 2 years, expert agreement has been that renal transplants should be included in this survey, although this is controversial and some professionals dispute in emergent kidney transplants for patients with new ES. Early consultation with a nephrologist is encouraged for all cases of SRC.

8. CONCLUSION
SRCs continues to be a rare diagnosis affecting up to six percent of SSc patients, but has a high morbidity and death influence. SRCs presentation is varied, with hypertension, normal BP and renal insufficiency. Medics should be minded by potential SRCs presentations. Early detection and initiation of aggressive ACEi antihypertensive medication in ED could enhance patient outcomes and around 60% of SRC patients need dialysis.

CONSENT
It is not applicable.

ETHICAL APPROVAL
It is not applicable.

CONFLICT OF INTEREST
The products used for this research are commonly and predominantly use products in our area of research and country.

There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge.

REFERENCES
1. Denton CP, Khanhanna D. Systemic sclerosis. Lancet. 2017;390:1685–99.
2. Steen VD, Syzd A, Johnson JP, Greenberg A, Medsger TA. Kidney disease other than renal crisis in patients with diffuse scleroderma. J Rheumatol. 2005;32:649–55.
3. Pope J, Harding S, Khimdas S, Bonner A, Canadian Scleroderma Research G, Baron M. Agreement with guidelines from a large database for management of systemic sclerosis: Results from the Canadian Scleroderma Research Group. J Rheumatol. 2012;39(3):524–531.
4. Sapadin AN, Fleischmajer R. Treatment of scleroderma. Arch Dermatol. 2002;138(1):99–105.
5. Abraham DJ, Krieg T, Distler J, Distler O. Overview of pathogenesis of systemic sclerosis. Rheumatology (Oxford). 2009;48(Suppl 3):ii3–7.
6. Penn H, Howie AJ, Kingdon EJ, Bunn CC, Stratton RJ, Black CM, Burns A, Denton CP. Scleroderma renal crisis: Patient characteristics and long-term outcomes. QJM 2007;100(8):485–494.
7. Mouthon L, Bérezné A, Bussone G, Noël LH, Villiger PM, Guillemin L. Scleroderma renal crisis: A rare but severe complication of systemic sclerosis. Clin Rev Allergy Immunol. 2011;40:84–91.
8. Caron M, Hudson M, Baron M, Nessim S, Steele R. Longitudinal study of renal function in systemic sclerosis. J Rheumatol. 2012;39:1829–34.
9. Nihytanov A, Schreiber BE, Ong VH, Rosenberg D, Moinzadeh P, Coghlan JG, et al. Prediction of pulmonary complications and long-term survival in systemic sclerosis. Arthritis Rheumatol 2014;66:1625–35.
10. Steen VD, Mayes MD, Merkel PA. Assessment of kidney involvement. Clin Exp Rheumatol. 2003;21:S29–31.
11. Steen VD. Scleroderma and renal crisis. Rheum Dis Clin North Am. 2003;29:315–33. Generation of a Core Set of Items for Src Criteria | 971
12. Traub YM, Shapiro AP, Rodnan GP, Medsger TA, McDonald RH, Steen VD, et al. Hypertension and renal failure
(scleroderma renal crisis) in progressive systemic sclerosis. Medicine (Baltimore). 1983;62:335–52.

13. Guillevin L, Berezne A, Seror R, Teixeira L, Pourrat J, Mahr A, et al. Scleroderma renal crisis: A retrospective multicentre study on 91 patients and 427 controls. Rheumatology (Oxford). 2012;51:460–7.

14. Teixeira L, Mouthon L, Mahr A, Berezné A, Agard C, Mehrenberger M, et al. Mortality and risk factors of scleroderma renal crisis: A French retrospective study of 50 patients. Ann Rheum Dis. 2008;67:110–6.

15. Hudson M, Baron M, Tatibouet S, Furst DE, Khanna D, Hummers L, et al. Exposure to ACE inhibitors prior to the onset of scleroderma renal crisis—results from the international scleroderma renal crisis survey. Semin Arthritis Rheum. 2014;43:666–72.

16. Hoa S, Stern EP, Denton CP, Hudson M, Baron M, Frech T, et al. Towards developing criteria for scleroderma renal crisis: A scoping review. Autoimmun Rev. 2017;16:407–15.

17. Mayes MD et al. Prevalence, incidence, survival, and disease characteristics of systemic sclerosis in a large US population. Arthritis Rheum. 2003;48:2246–2255.

18. Barnes J, Mayes MD. Epidemiology of systemic sclerosis: Incidence, prevalence, survival, risk factors, malignancy, and environmental triggers. Curr. Opin. Rheumatol. 2012;24:165–170.

19. Steen VD, Syzd A, Johnson JP, Greenberg A, Medsger TA Jr. Kidney disease other than renal crisis in patients with diffuse scleroderma. J. Rheumatol. 2005;32:649–655.

20. Denton CP. Renal manifestations of systemic sclerosis—clinical features and outcome assessment. Rheumatology. 2008;47(Suppl. 5):v54–v56.

21. Clements PJ et al. Abnormalities of renal physiology in systemic sclerosis. A prospective study with 10 year followup. Arthritis Rheum. 1994;37:67–74.

22. Caron M et al. Longitudinal study of renal function in systemic sclerosis. J. Rheumatol. 2012;39:1829–1834.

23. Steen VD. Scleroderma renal crisis. Rheum Dis Clin North Am. 2003;29:315-33.

24. Bose N, Chiesa-Vottero A, Chatterjee S. Scleroderma renal crisis. Semin Arthritis Rheum. 2015;44:687-94.

25. Muangchan C. Canadian Scleroderma Research Group, Baron M, Pope J. The 15% rule in scleroderma: the frequency of severe organ complications in systemic sclerosis. A systematic review. J Rheumatol. 2013;40:1545-56.

26. Tangri V, Hewson C, Baron M, Bonner A, Fritzler M, Pope JE. Associations with organ involvement and autoantibodies in systemic sclerosis: results from the Canadian Scleroderma Research Group (CSRG). OJRA. 2013;3:113-8.

27. Nihtyanova SI, Tang EC, Coghlan JG, Wells AU, Black CM, Denton CP. Improved survival in systemic sclerosis is associated with better ascertainment of internal organ disease: A retrospective cohort study. QJM. 2010;103:109-15.

28. Shanmugam VK, Steen VD. Renal disease in scleroderma: An update on evaluation, risk stratification, pathogenesis and management. Curr Opin Rheumatol. 2012;24:669-76.

29. Steen VD, Medsger TA. Changes in causes of death in systemic sclerosis, 1972-2002. Ann Rheum Dis. 2007;66:940-4.

30. Tyndall AJ, Bannert B, Vonk M, Airò P, Cozzi F, Carreira PE, et al. Causes and risk factors for death in systemic sclerosis: a study from the EULAR Scleroderma Trials and Research (EUSTAR) database. Ann Rheum Dis. 2010;69:1809-15.

31. Turk M, Pope JE. The frequency of scleroderma renal crisis over time: A metaanalysis. J Rheumatol. 2016;43:1350-5.

32. Steen VD, Costantino JP, Shapiro AP, Medsger TA Jr. Outcome of renal crisis in systemic sclerosis: Relation to availability of angiotensin converting enzyme (ACE) inhibitors. Ann Intern Med. 1990;113:352-7.

33. Kowal-Bielecka O, Landewe R, Avouac J, Chwiesko S, Miniatí I, Czirjak L, Clements P, Denton C, Farge D, Fligelstone K, Foldvari I, Furst DE, Muller-Ladner U,
angiotensin converting enzyme (ACE) systemic sclerosis: relation to availability of
drug. Medsger TA Jr. Outcome of renal crisis in St Ann Intern Med. 133(8):600–628.

34. Lynch BM, Stern EP, Ong V, Harber M, Burns A, Denton CP. UK Scleroderma
Study Group (UKSSG) guidelines on the diagnosis and management of
scleroderma renal crisis. Clin Exp Rheumatol. 2016;34(Suppl 100):106-9.

35. Steen VD. Kidney involvement in systemic sclerosis. Presse Med. 2014;43:e305-14.

36. Teixeira L, Mouton L, Mahr A, Berezne A, Agard C, Mehrenberger M, et al. Group
Francais de Recherche sur le Sclerodermie (GFRS). Mortality and risk factors of scleroderma renal crisis: A
French retrospective study of 50 patients. Ann Rheum Dis. 2008;67:110-6.

37. Avouac J, Walker UA, Hachulla E, Riemekasten G, Cuomo G, Carreira PE, et al. EUSTAR collaborators. Joint and
tendon involvement predict disease progression in systemic sclerosis: A
EUSTAR prospective study. Ann Rheum Dis. 2016;75:103-9.

38. Iniesta Arandia N, Simeón-Aznar CP, Guillén Del Castillo A, Colunga Argüelles D, Rubio-Rivas M, Trapiella Martínez L, et al. RESCLE Investigators, Autoimmune Diseases Study Group (GEAS): Influence of antibody profile in clinical features and
prognosis in a cohort of Spanish patients with systemic sclerosis. Clin Exp
Rheumatol. 2017;35(Suppl 106):98-105.

39. Hudson M, Baron M, Tatibouet S, Furst DE, Khanna D. International Scleroderma
Renal Crisis Study Investigators. Exposure to ACE inhibitors prior to the onset of
scleroderma renal crisis-results from the International Scleroderma Renal Crisis
Survey. Semin Arthritis Rheum. 2014;43:666-72.

40. Denton CP, Khanna D. Systemic sclerosis. Lancet. 2017;390:1685-99.

41. Steen VD, Medsger TA Jr (2000) Long-term outcomes of scleroderma renal crisis.
Ann Intern Med. 133(8):600–603

42. Steen VD, Costantino JP, Shapiro AP, Medsger TA Jr. Outcome of renal crisis in
systemic sclerosis: relation to availability of angiotensin converting enzyme (ACE)
inhibitors. Ann Intern Med. 1990;113(5):352–357

43. Lunseth JH, Baker LA, Shifrin A. Chronic scleroderma with acute exacerbation
during corticosteroid therapy; report of a case with autopsy observations. AMA Arch
Intern Med. 1951;88(6):783–792.

44. Sharnoff J, Carideo H, Stein I. Cortisone-treated scleroderma. JAMA. 1951;145(16):1230–1232

45. Naniwa T, BAnno S, Takahashi N, Maeda S, Hayami Y, Ueda R. Normotensive
scleroderma renal crisis with diffuse alveolar damage after corticosteroid
therapy. Mod Rheumatol. 2005;15(2):134–138.

46. Steen VD Jr. Case-control study of corticosteroids and other drugs that either
precipitate or protect from the development of scleroderma renal crisis. Arthritis
Rheum. 1998;41(9):1613–1619

47. Penn H, Howie A, Kingdon E et al. Scleroderma renal crisis: patient characteristics and long-term outcomes. QJM. 2007;100(8):485–494.

48. Clements P, Furst D, Wong W, Mayes M, White B. Highdose versus low-dose D-
Penicillamine in early diffuse systemic sclerosis: analysis of a two-year, double-
blind, randomized, controlled clinical trial. Arthritis Rheum. 1999;42(6):1194–1203.

49. DeMarco P, Weisman M, Seibold J, Furst D, Wong W, Hurwitz E. Predictors and
outcomes of scleroderma renal crisis: the high-dose versus low-dose D-
Penicillamine in early diffuse systemic sclerosis trial. Arthritis Rheum. 2002;46(11):2983–2989.

50. Denton C. Renal manifestations of systemic sclerosis: clinical features and
outcome. Rheumatology. 2007;46(11):2983–2989.

51. Fisher ER, Rodnan GP. Pathologic observations concerning the kidney in
progressive systemic sclerosis. AMA Arch Pathol. 1958;65(1):29–39.

52. Steen VD, Medsger TA Jr. The palpable tendon friction rub: an important physical
examination finding in patients with systemic sclerosis. Arthritis Rheum. 1997;40(6):1146–1151.

53. Randone SB, Guiducci S, Cerinic MM. Musculoskeletal involvement in systemic
sclerosis. Best Pract Res Clin Rheumatol. 2008;22(2):339–350.

54. Molina JF, Anaya JM, Cabrera GE, Hoffman E, Espinoza LR. Systemic sclerosis sine scleroderma: an unusual
presentation in scleroderma renal crisis. J Rheumatol;1995;22(3):557–560.

55. Gonzalez EA, Schmulbach E, Bastani B. Scleroderma renal crisis with minimal skin involvement and no serologic evidence of systemic sclerosis. Am J Kidney Dis. 1994;23(2):317–319.

56. Traub YM, Shapiro AP, Rodnan GP, Medsger TA, McDonald RH, Jr, Steen VD, Osial TA Jr., Tolchin SF. Hypertension and renal failure (scleroderma renal crisis) in progressive systemic sclerosis. Review of a 25-year experience with 68 cases. Medicine (Baltimore). 1983;62(6):335–352.

57. Denton CP, Lapadula G, Mouthon L, Muller-Ladner U. Renal complications and scleroderma renal crisis. Rheumatology (Oxford). 2009;48Suppl3:iii32–35.

58. Caskey FJ, Thacker EJ, Johnston PA, Barnes JN. Failure of losartan to control blood pressure in scleroderma renal crisis. Lancet. 1997;349(9052):620.

59. Cheung WY, Gibson IW, Rush D, Jeffery J, Karpinski M. Late recurrence of scleroderma renal crisis in a renal transplant recipient despite angiotensin II blockade. Am J Kidney Dis. 2005;45(5):930–934.

60. Walker KM, Pope J. Participating members of the Scleroderma Clinical Trials C, Canadian Scleroderma Research G. Treatment of systemic sclerosis complications: what to use when first-line treatment fails—a consensus of systemic sclerosis experts. Semin Arthritis Rheum. 2012;42(1):42–55.

61. Robson M, Oreopoulos DG. Dialysis in scleroderma. Ann Intern Med. 1978;88(6):843.

62. Copley JB, Smith BJ. Continuous ambulatory peritoneal dialysis and scleroderma. Nephron. 1985;40(3):353–356.

© 2021 Alyami et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.