RHEUMATOLOGY

Rheumatology 2012;51:460–467
doi:10.1093/rheumatology/ker271
Advance Access publication 15 November 2011

Original article

Scleroderma renal crisis: a retrospective multicentre study on 91 patients and 427 controls

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Abstract

Objective. Scleroderma renal crisis (SRC) is a severe manifestation of SSc, whose prognosis remains severe, despite treatment with angiotensin-converting-enzyme inhibitor and dialysis. This study was undertaken to describe SRC characteristics, prognosis and outcome, and evaluate the responsibility of CSs in its occurrence.

Methods. Analysis concerned 91 SSc patients with SRC who were compared with 427 non-SRC–SSc patients taken as controls.

Results. Among the 91 SRC patients, 71 (78.0%) had high blood pressure, 53 (58.2%) hypertensive encephalopathy and 51 (56.0%) thrombotic microangiopathy; 64 (70.3%) had received CSs before or concomitantly with SRC *vs* 156 (36.5%) non-SRC–SSc patients ($P < 0.001$). Treated SRC patients also received more prednisone 29.3 (28.4) *vs* 3.6 (9.9) mg than controls ($P < 0.001$). SRC clinical outcomes were poor: 49 (53.8%) patients required dialysis, which was definitive for 38. Thirty-seven (40.7%) SRC patients died *vs* 10.8% of the controls ($P < 0.001$). Death was most frequent among dialysed patients who never recovered renal function (22 *vs* 2) and 13 never-dialysed SRC patients died.

Conclusions. Although SRC prognosis has improved markedly, SRC remains a severe manifestation of SSc, despite treatment with angiotensin-converting enzyme inhibitor and dialysis. CSs contributed significantly to SRC occurrence.

Key words: systemic sclerosis, renal crisis, angiotensin-converting enzyme inhibitor, steroids.

CLINICAL SCIENCE

Introduction

SSc is a CTD involving multiple organs and characterized by excessive collagen deposition, autoimmunity, vascular hyperreactivity and obliterative microvascular phenomena [1]. Vascular injury manifests as RP, digital ischaemia, pulmonary arterial hypertension and scleroderma renal crisis (SRC) [2].

Before the late 1970s, SRC was observed in 12–18% of SSc patients and was a major cause of death [3]. Currently, interstitial lung disease and pulmonary arterial hypertension are the two main causes of SSc-related deaths, with SRC developing in 5% of the patients, mainly those with dcSSc [4–6].

Routine use of angiotensin-converting enzyme inhibitors (ACEIs) has dramatically improved outcome, with a 12-month mortality decline from 76 to <15% in the USA [7]. Despite improved prognosis, SRC remains a severe manifestation of SSc, and functional outcome and survival remain poor: 65% at 5 years [4, 8, 9]. In this multicentre, retrospective study, we analysed the clinical and biological characteristics, triggering factors, prognoses and

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Submitted 25 January 2011; revised version accepted 30 June 2011.

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treatments of SRC and, more specifically, tried to determine the responsibility of CSs in the occurrence of SRC.

Patients and methods

Patient selection

To be eligible for the study, SSc patients had to fulfil the ACR criteria [10] and/or the Leroy and Medsger [11] criteria. Patients were categorized as having one of two clinical forms [11]: lcSSC or dcSSc. Patients with sine scleroderma were not included in the study. SCR patients were defined as having rapidly progressive renal insufficiency with no other explanation. This study was conducted in compliance with the protocol Good Clinical Practices and Declaration of Helsinski principles. In accordance with French law, a formal approval from an ethics committee is not required for this kind of project.

The 91 SRC patients were collected retrospectively by physicians participating in the organized referral centre network founded by the Plan National Maladies Rares [12], a nationwide programme to treat rare diseases organized under the auspices of the French Ministry of Health. Patients without SRC came from our referral centre's database, which included 583 patients: 434 forms from non-SRC–SSc patients contained all the data required for analyses. Seven patients with renal manifestations unrelated to SRC [13] were excluded: two with tubulointerstitial nephritis, two with membranous GN, one with extracapillary GN and two with unclassified nephropathy. Finally, 427 SSc patients' files were retained as controls for this study. SSc patients with SRC and controls were diagnosed and followed during the same period.

Data collected for the study

For cases and controls, the following data were collected: age; sex; race; age at SSc diagnosis and SRC onset; time from SSc diagnosis; SSc form (diffuse or limited, as defined above); telangiectasias; RP; history of digital ulcers; arthralgias; calcinosis; sicca syndrome; scleredema; pericarditis; myopathy, assessed as proximal muscle weakness and elevated creatine kinase (CK); heart involvement (i.e. left congestive heart failure, echocardiographically determined left-ventricular ejection fraction $<60\%$); interstitial lung disease (diagnosed based on thoracic high-resolution CT scan that included $\geqslant 1$ isolated ground-glass opacities, honeycombing and/or bronchiolectasis); restrictive syndrome, as assessed by pulmonary function tests (total lung capacity or forced vital capacity $<75\%$ of predicted values); pulmonary artery hypertension, defined as a mean pulmonary artery pressure $\geqslant 25$ mmHg, with normal pulmonary artery wedge pressure (<15 mmHg) measured during right heart catheterization; test results for ANAs, ACAs, anti-topoisomerase-1 antibodies (Abs) and ANCAs; and a history of SSc treatments. Few patients were tested for anti-RNA polymerase 3: results were included in the manuscript.

For SRC patients, additional parameters were recorded: arterial blood pressure (BP), especially when it rapidly occurred; maximal serum creatinine; estimated glomerular filtration rate (eGFR) computed using the modification of diet in renal disease equation [14]; white blood cell counts; platelet count; haemoglobin level; schizocytosis on blood smear ($>1\%$) or evidence of haemolysis, assessed by plasma haptoglobin and lactate dehydrogenase levels; haematuria; proteinuria; thrombotic microangiopathy, defined as thrombocytopenia $<100\,000/\text{mm}^3$, or elevated reticulocyte counts.

The normotensive SRC form was defined as a 50% increase of serum creatinine at baseline or serum creatinine $>20\%$ above the upper normal limit and one of the following five features: dipstick proteinuria $>2+$, dipstick haematuria $>2+$ or >10 red blood cells/high-power field; thrombocytopenia $<100\,000/\text{mm}^3$; haemolysis, defined as anaemia not due to other causes and either schizocytes or other red blood cell fragments seen on blood smear; high reticulocyte count, or renal biopsy findings consistent with SRC [15].

During follow-up, we collected data on renal function, dialysis (absent, temporary and permanent) and death. Causes of death were classified as SSc-related or not. Detailed medications prescribed before SRC, when it started and during follow-up, were also collected. When the patient was lost to follow-up, demographic data were obtained from the French death registry in which every French citizen's date and place of birth and death are recorded; the cause of death is not reported for ethical reasons.

Statistical analyses

Categorical variables are reported as numbers and/or percentages and were compared using a χ^2 or, when appropriate, Fisher's exact test. Quantitative variables are reported as means (S.D.) or medians (range) and were compared using Student's *t*-test. For all statistical analyses, $P \leqslant 0.05$ defined statistical significance. For univariate analysis, SRC patients' characteristics described above were compared with those of controls. Variables associated with SRC occurrence in that analysis with $P \leqslant 0.20$ were entered into a multivariate logistic-regression model [disease form (diffuse or limited), steroid treatment, calcinosis, RP, digital ulcers, cardiac insufficiency, pericarditis, myalgias and myopathy, arthralgias, interstitial pneumonia].

Survival was assessed by life-table analysis using the Kaplan–Meier method [16]. Survival time was calculated from the date of SRC diagnosis and ended at the censoring date or the time of death. We evaluated the mortality or dialysis-free survival rate as a function of the 10 demographic, clinical and laboratory parameters assessed at SRC diagnosis, and Cox proportional hazards models [17] were fitted to examine the individual and combined effects of those variables. The impact of continuous variables was analysed as continuous covariates and indicator covariates after stratification according to quartiles or the median values of their distributions. These variables were then used as a function of their linear or non-linear association with survival and, when used as categorical covariates, according to the threshold that defined the

group at highest risk. To explore the risk of SRC onset associated with prior exposure to CSs, their administration (prescription, dose and time before SRC occurrence) was compared between SRC patients and the non-SRC–SSc controls.

Results

SRC– *vs* non-SRC–SSc patients

Analyses concerned 91 SRC patients (48 had previously been reported [6]) and 427 controls. Their demographics are detailed in Table 1. SRC occurred more frequently in women, usually during the 3 years [mean (S.D.), 3.2 (8.1) years] following SSc diagnosis. dcSSc was more frequent in patients with SRC than in the group without [78 (85.7%) *vs* 145 (34%); $P < 0.001$]. Between-group comparisons of clinical symptoms showed significant differences for symptoms detailed in Table 1, with some between-group differences directly related to SRC presence or its absence in controls.

Among autoantibodies tested, the frequencies of those directed against the centromere were significantly higher for controls. Anti-RNA polymerase 3 Abs were more frequent in patients with SRC than without. In SRC patients with anti-RNA polymerase 3 Abs, four had diffuse and one limited SSc. In patients without SRC, six had diffuse and four limited SSc.

SRC characteristics are summarized in Table 2. Pertinently, high BP was the only manifestation in 85.7% of these patients. Hypertensive encephalopathy was found in 54 (59.3%) and 51 (56.0%) had thrombotic microangiopathy. Some patients had other symptoms, such as haemolysis. Renal biopsies obtained for 41 SRC patients at its diagnosis or shortly thereafter confirmed the diagnosis.

Notably, more SRC patients had received CSs before or concomitantly with SRC onset: 64 (70.3%) *vs* 156 (36.5%) controls ($P < 0.001$); and treated SRC patients received more steroids 29.3 (28.4) *vs* 3.6 (9.9) mg for controls ($P < 0.001$). Despite the small numbers of patients, a difference was also observed regarding other drugs: ciclosporin or tacrolimus (FK-506) (prescribed for the disease and not for transplantation; 4 patients *vs* 0 controls) and D-penicillamine (18.7 *vs* 7.3%, $P < 0.001$). ACEIs were prescribed to 83 (91.2%) out of 91 patients to treat SRC and 18 (19.8%) received angiotensin-2 receptor antagonists (ARA-2). Twenty-three (25.3%) patients had received ACEI before SRC onset. Seven patients received neither ACEI and/or ARA-2; three of them died during the month following SRC diagnosis: one was in end-stage renal disease and permanently dialysed, and the two others had never been dialysed. Fifty-one (56.0%) patients received both drugs together. Among controls, 82 (19.2%) received ACEI. Nine (39.1%) out of 23 patients who were under ACEI before the occurrence of SRC died *vs* 28 (41.2%) out of 68 who were not (NS). Fourteen (60.1%) out of 23 patients who were treated with ACEI before SRC were dialysed *vs* 35 (51.5%) out of 68 who were not non-significant (NS).

Clinical characteristics of patients who were dialysed and those who were not, were comparable for the majority of symptoms. The differences were as follows: arterial hypertension was present in 38 (76%) out of 41 patients who were dialysed and in 40 (97.6%) out of 41 who were not. Anti-topoisomerase 1 antibodies were also present more frequently in patients with dialysis: 22 (44%) out of 50 *vs* 6 (14.6%) out of 50 in the other group.

Clinical SRC outcome was poor. Forty-nine (53.8%) patients required dialysis, which was subsequently stopped for 11 patients, and the 38 others required chronic dialysis or died. Severe renal damage (mean GFR, 37 ml/min/1.73 m^2) persisted in dialysis-free survivors.

Thirty-seven (40.7%) SRC patients died, compared with 46 (10.8%) controls ($P < 0.001$). Twenty-four of the SRC patients who died were on dialysis or had been dialysed. Deaths were most frequent among dialysed patients who failed to recover renal function (22 *vs* 2). Thirteen never-dialysed SRC patients died. SRC patients' causes of deaths are summarized in Table 3.

Overall survival is reported in Fig. 1A. Figure 1B shows survival according to SRC presence or absence. Respective 1-, 2-, 5- and 10-year survival rates for SRC patients were 70.9, 66.6, 60 and 41.9%. Their median survival since SRC diagnosis was 99 months. Their 1-, 2- and 5-year dialysis-free survival rates were 55.3, 44.4 and 33.7%, respectively. Figure 1C shows that outcome was better for hypertensive (73.8%) than normotensive SRC patients (58%). Over the long term, this difference disappeared: 48.6% of normotensive *vs* 40.9% of hypertensive SRC patients survived (NS).

Factors predicting SRC and outcome

According to our univariate analysis, factors significantly associated with SRC were digital ulcers, arthralgias, scleredema ($P < 0.0001$), pericarditis, high BP, myopathy and heart involvement ($P < 0.0001$). SRC patients had ANAs without any recognized specificity as frequently as non-SRC–SSc controls, respectively: 76 (87.4%) out of 87 *vs* 392 (91.8%) out of 427. Compared with non-SRC–SSc patients, multivariate analyses retained (Table 1) as significantly associated with SRC: dcSSc [85.7 *vs* 34%; adjusted odds ratio (aOR) 14.65 (4.12–52.16), $P < 0.001$], arthralgias [72.2 *vs* 55.7%; aOR 4.20 (1.27–13.85), $P = 0.018$], cardiac involvement [46.1 *vs* 26.3%; aOR 13.1 (4.157–41.35), $P < 0.0001$], myopathy [28.9 *vs* 49.6%; aOR 0.09 (0.03–0.27), $P = 0.0001$] and CS exposure [70.3 *vs* 36.5%; aOR 4.98 (1.52–16.30), $P = 0.0079$].

The absence of high BP in SRC patients was associated with a poorer outcome: 13 (14%) patients had been normotensive at SRC diagnosis. Among them, 8 (61.5%) had oligoanuria *vs* 24.3% of hypertensive patients ($P = 0.02$), 77% had pericarditis *vs* 31% in the latter ($P = 0.004$), and 11 (84.6%) required chronic haemodialysis *vs* 39 (50.6%) controls ($P = 0.032$). None of the normotensive patients recovered normal renal function and remained on dialysis; eight of them died. The number of patients exposed to ACEI before SRC onset was similar for both subgroups

Table 1 Demographics, clinical symptoms and biologic findings of SSc patients with and without SRC

Clinical symptoms	SRC	No SRC	Total	Univariate analysis, *P*	Multivariate analysis	
					P	aOR (95% CI)
Patients, *n*	91 (17.6)	427 (82.4)	518			
Male/female ratio	22/69	74/353	96/422			
Mean age at SSc diagnosis, mean (S.D.), years	50 (15)	55 (16)		0.14		
SSc onset-to-SRC interval, mean (S.D.), years	3.2 (8.1)	–	–			
Mean age at SRC onset, mean (S.D.), years	53 (15)	–	–			
Limited SSc	13 (14.2)	282 (66.0)	295 (56.9)			
Diffuse SSc	78 (85.7)	145 (34)	223 (43)	0.001	0.001	14.65 (4.12, 52.16)
Epidemiological factors and drugs						
Menopause	35 (50.7)	162 (45.9)	197 (38)	0.93		
CSs	64 (70.3)	156 (36.5)	220 (42.4)	<0.001	0.0079	4.98 (1.52, 16.30)
Oral CS at SRC onset	51 (56.0)	156 (36.5)	207 (40)	0.001		
Maximum CS dose,[a] mean (S.D.), mg	29.3 (28.4)	3.6 (9.9)		<0.001		
CS preceding SRC	47 (53)	–	–			
CS prescribed <3 months	19 (20.9)	–	–			
Oral CS-to-SRC interval, mean (S.D.), months	10 (15)					
IV CS	14 (15.4)	6 (1.4)	20 (3.86)	<0.001		
IV CS before SRC	14 (15.4)	–	–			
ACEI	83 (91.2)	–	–			
		82 (20.6)	165 (31.8)			
ACEI before SRC/anytime for controls	23 (25.3)	82/427(19.2)		0.19		
Ciclosporin	2 (2.2)	0	2 (0.4)	0.03		
D-Pen	17 (18.7)	31 (7.3)	48 (9.2)	0.001		
FK 506	2 (2.2)	0	2 (0.4)	0.03		
Clinical symptoms						
Telangiectasias	37 (40.7)	203 (47.5)	240 (46.3)	0.022	0.09	
Calcinosis	13 (14.3)	61 (14.3)	74 (14.3)	0.82		
RP	81 (89.0)	414 (97)	515 (99.4)	0.001	0.0096	0.03 (0.002, 0.43)
Digital ulcers	37 (40.7)	84 (19.7)	121 (23.3)	0.001	0.51	
High BP	78 (85.7)	18 (4.2)	91 (17.6)	0.027	0.10	
Renal insufficiency	91 (100)	–	–			
Creatininaemia, mean (S.D.)	452 (279)	75 (28)	–			
Cardiac insufficiency[b]	42 (46.2)	12 (2.8)	54 (10.4)	0.0001	0.0039	6.71 (1.84, 24.43)
Pulmonary hypertension[c]	4 (4.4)	35 (8.2)	39 (7.5)	0.212		
Pericarditis	35 (38.5)	37 (8.7)	72 (13.9)	0.001	0.02	4.05 (1.21, 13.56)
GI involvement (except oesophagus)	39 (42.9)	84 (19.7)	123 (23.7)	0.15		
Myalgias and myopathy	26/90 (28.9)	212 (49.6)	238 (46)	0.0001	0.0001	0.09 (0.03, 0.27)
Interstitial pneumonia	4 (4.4)	190 (44.5)	194 (37.4)	0.0101	0.9	
Arthralgias	65/90 (72.2)	238 (55.7)	303 (58.5)	0.0190	0.0186	4.20 (1.27, 13.85)
Sicca syndrome	31 (34.1)	141 (33.0)	172 (33.2)	0.85		
Immunology						
ANAs	76/87 (87.4)	392 (91.8)	468 (90.3)	0.19		
ACAs	3/87 (3.4)	121 (28.3)	124 (24)	0.001	0.67	
Anti-topoisomerase I (Scl 70)	27/87 (31.0)	131 (30.7)	158 (30.5)	0.95		
ANCAs	1/58 (1.7)	2/110 (1.8)	3/168 (1.8)	0.97		
Anti-RNA polymerase 3	5/18 (27.7)	10/155 (6.4)	15/173 (8.6)	0.028		
aPLs	6/66 (9.1)	45/225 (20)	51/291 (17.5)	0.06		
Outcome						
Mean follow-up, mean (S.D.), months	45.8 (61)	79 (90)				
Alive	54 (59.3)	381 (89.2)	435 (83.9)			
Deaths	37 (40.7)	46 (10.8)	83 (16.0)	<0.001		

Values are expressed as *n* (%), unless stated otherwise. [a]When SRC occurred. [b]Unrelated to pulmonary artery hypertension or interstitial pneumonia. [c]Mainly evaluated by echocardiography. NS: non-significant; GI: gastrointestinal.

Table 2 Clinical characteristics and complementary investigations of SSc patients with SCR

Characteristic	Value
Age at SCR onset	53 (15)
SSc onset-to-SRC interval, year	3.3 (8.2)
Mean follow-up, months	41.7 (47.9)
SSc duration <1 year	53 (58.2)
SSc duration <3 years	72 (79.1)
Clinical characteristics	
Arterial hypertension	78 (85.7)
Mean systolic BP, mean (S.D.), mmHg	184 (39)
Mean diastolic BP, mean (S.D.), mmHg	107 (23)
Hypertensive encephalopathy	53 (58.2)
Renal insufficiency	91 (100)
Mean creatininaemia at SRC onset, mean (S.D.), μmol/l	452 (270)
Creatinine clearance, ml/min	
Before SRC, mean (S.D.)	73.6 (32.1)
At SRC onset, mean (S.D.)	18 (16.3)
For dialysis-free survivors, mean (S.D.)	37 (21.4)
Oligoanuria	26 (28.6)
Dialysis	49 (53.8)
Definitive	36 (39.6)
Temporary	13 (14.2)
Thrombotic microangiopathy	51 (56.0)
Haemolysis (LDH and/or low haptoglobin)	56 (61.5)
Elevated ESR or CRP	50 (54.9)
Proteinuria	50/73 (68.5)
Haematuria	27/65 (41.5)
Mean platelet count/mm^3, mean (S.D.)	162 (139)
Mean haemoglobin, mean (S.D.), g/dl	9.6 (2.1)
SSc treatment	
Immunosuppressants	33 (36.3)
CYC	21 (23.1)
MTX	13 (14.3)
AZA	1 (1.1)
MMF	7 (7.7)
Death after SRC diagnosis	
Within 6 months	19 (20.9)
6–12 months later	18 (19.8)

Values are expressed as *n* (%), unless stated otherwise. Creatinine clearance was computed with the modification of diet in renal disease formula. LDH: lactate dehydrogenase.

Table 3 Causes of death in SSc patients with SRC

Cause of death	*n*
Related to SSc without renal crisis	9
Heart failure	4
Gastrointestinal tract involvement	3
Interstitial lung disease	1
Cardiac arrhythmia	1
Related to SRC and its treatment	12
Cardiogenic shock	3
Tamponade	1
Cardiac arrest during dialysis	1
Multiorgan failure	1
Ischaemic enterocolitis	1
Septic shock	3
Drug-induced epidermolysis	1
Dialysis withdrawal	1
Miscellaneous	16
Cardiac arrest	1
Anti-coagulant overdose	1
Stroke	1
Cholesterol embolism	1
Pharyngeal carcinoma	1
Unknown	11

($P = 0.7$ and $P = 1$). Median survival was 12.7 *vs* 99.2 months for the hypertensive group.

Discussion

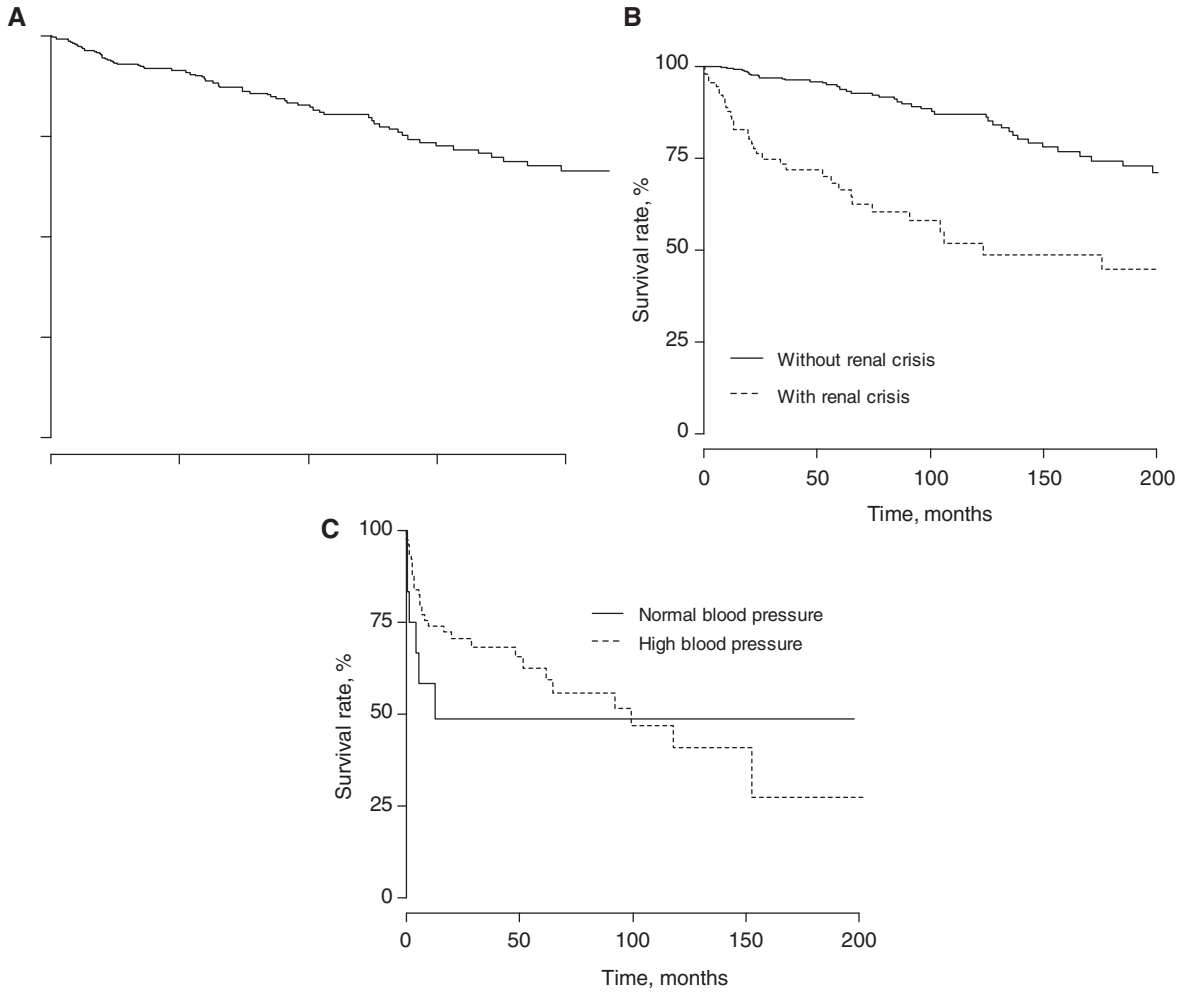
Herein we described our 91 SSc patients who developed SRC and 427 non-SRC–SSc patients, with the objectives of analysing clinical, biological and immunological characteristics, and SRC outcomes, and attempting to identify factors predicting or favouring its occurrence.

SRC developed mainly (85.7%) in patients with dcSSc, while only 34% of controls had that form, as reported previously [4, 18]. SRC incidence and prevalence in SSc could not be assessed for the study population because recruitment was biased by the case-collection methodology. According to the literature, SRC frequency was ~19% (129 out of 675) of a cohort with diffuse SSc [13]. Although several clinical signs differed between patients with SRC and those without, the clinical characteristics of patients with diffuse SSc developing SRC were the same as those of controls. SRC patients had manifestations reflecting more prominent vascular disease (e.g. cardiac symptoms), but they could also be related to high BP.

Significantly more SRC patients had been treated with CSs in the weeks or months preceding the crisis: 70.3% of them *vs* 36.5% of controls. SRC patients had also received a significantly higher mean maximum CS dose than controls (29.3 *vs* 3.6 mg; $P < 0.001$). That dose was not the dose prescribed during the few days preceding SRC, but reflects more intensive therapy during the weeks preceding SRC. Steen *et al.* [19] observed that, during the 6 months preceding SRC onset or the first consultation, high-dose CSs (>15 mg/day of prednisone or its equivalent) were administered significantly more frequently to SRC patients (36%) than controls (12%) (OR 4.37) [19]. Our data support the crucial SRC-preventive role of avoiding CSs in patients at risk of developing this severe SSc complication.

Prolonged survival and improved renal function were attributed to the immediate and extensive use of ACEIs [20]. Nearly all our patients had been taking ACEIs. The previously published recommendations [7] should be applied and ACEIs should be prescribed very early during the course of SRC, with the dose being increased daily to achieve a systolic BP reduction of 10–20 mmHg per 24 h, even for patients with continued deterioration of renal function. Should maximal dose ACEIs fail to normalize

FIG. 1 Kaplan–Meier survival curves for SSc patients. (**A**) Overall survival of all 518 patients; (**B**) survival of SSc patients with SRC (91 patients) or without (427 patients); and (**C**) survival of hypertensive ($n = 78$) or normotensive SCR patients ($n = 13$).



BP, additional anti-hypertensive agents may be useful, including combinations of calcium-channel blockers, ARA-2 or other vasodilators. The preventive role of ACEIs does not seem obvious. Twenty-three (25.3%) patients were on an ACEI at SRC onset *vs* 82 (19.2%) controls. These observations suggest that ACEIs are not able to prevent SRC, but only more extensive ACEI use as a preventive measure would be able to resolve this issue.

Forty-nine (53.8%) SRC patients required haemodialysis, comparable with the 50% reported in the literature [21]. Dialysis was temporary for 13 (14.3%) patients, confirming that patients developing SRC might be able to recover renal function and come off dialysis. However, that outcome is rare for normotensive patients. In our study, after a mean follow-up of 41 months, 37 (40.7%) patients had died. Steen *et al*. [5, 7] reported dramatically lower mortality attributable to SRC, which might be the consequence of more effective treatments, including dialysis. It could also be hypothesized that extensive ACEI prescription for patients with early dcSSc might contribute to containing SRC occurrence, but our study does not provide any proof of that hypothesis because the number of patients treated with ACEIs before SRC was too small to allow any conclusion to be drawn. Normotensive SRC affected 20% of our patients, the majority of whom did not obtain functional improvement and their prognoses were poor. Indeed, our analyses identified diffuse SSc and CS use, among others, as being associated with poorer outcomes.

Our results confirmed that early mortality remained elevated, highlighting the need for new therapeutic strategies, in addition to immediate and extensive ACEI use. At present, it should be emphasized that immunosuppressants and/or biotherapies are unable to improve clinical manifestations of SSc with renal involvement, while they increase the risk of side effects [22].

Limitations of the study reflect the heterogeneity of recruitment: patients with SRC came from different French hospitals, but the control group came from our own centre. The recruitment period was long and therapeutic modifications could have influenced patients care. However, SSc treatments have not changed dramatically since the introduction of ACEIs to treat SRC and no new therapeutic approaches showed efficacy. In France, therapeutic decisions concerning SSc patients are made by specialists working in hospitals and never by general practitioners or rheumatologists in private practice. Therapeutic decisions comply with the recommendations published by the referral centre and published on the Haute Autorité de Santé web site (www.has-sante.fr). Consequently, this codification of care and treatments provides more homogeneity to the cohort of patients described herein.

Rheumatology key messages

- Renal crisis is a rare complication of scleroderma characterized by hypertension and oligo/anuric acute renal failure.
- The occurrence of renal crisis is more common in patients treated with glucocorticoids.
- SRC remains associated with severe morbidity and mortality despite treatment with ACEI and dialysis.

Acknowledgements

We thank the following physicians for their help: Kiet Tiev (Hôpital Saint-Antoine, Paris); Camille Francès, Stephane Barète, Selim Trad, Bertrand Wechsler and Jean-Charles Piette (Hôpital la Pitié–Salpêtrière, Paris); Fadi Fakhouri, Philippe Lesavre and Jean-Pierre Grünfeld (Hôpital Necker, Paris); Dominique Farge-Bancel, Michael Darmon and Elie Azoulay (Hôpital Saint-Louis, Paris); Françoise Mignon (Hôpital Bichat, Paris); Elisabeth Diot, Jean-Louis Guilmot (Hôpital Bretonneau, Tours); Hervé Levesque (Hôpital Bois-Guillaume, Rouen); David Launay, Eric Hachulla and Pierre-Yves Hatron (Hôpital Claude-Huriez, Lille); Patrick Jégo (Hôpital Sud, Rennes); Nicolas Artigues, Yann Ollivier and Philippe Letellier (Hôpital Côte de Nacre, Caen); Arnaud Cénac (Hôpital de la Cavale Blanche, Brest); Patrick Carpentier, (Hôpital André-Michallon, Grenoble); Claire Grange, Hugues Rousset, Denis Vital-Durand (Centre Hospitalier Lyon-Sud, Lyon); Isabelle Delevaux and Olivier Aumaître (Hôpital Gabriel-Montpied, Clermont-Ferrand); Eric Alamartine and Pascal Cathebras (Hôpital Sud, Saint-Etienne); Joël Constans, Christian Combe, Patrick Mercié and Maïté Longy-Boursier (Hôpital Saint-André, Bordeaux); and Christophe Jégo and Philippe Carli (Hôpital d'Instruction des Armées, Saint-Anne, Toulon). The authors also thank the following pathologists for analysing renal biopsies: Isabelle Brocheriou (Hôpital la Pitié–Salpêtrière, Paris); Francine Walker (Hôpital Bichat, Paris); Marie-Christine Copin (Hôpital Claude-Huriez, Lille); Nicole Pinel (Hôpital André-Michallon, Grenoble); Bernard Laurent, (Hôpital-Nord, Saint-Etienne); Frédérique Dijoud (Centre Hospitalier Lyon-Sud, Pierre Bénite); and Antoine Martin (Hôpital Avicenne, Bobigny). This work was presented, in part, at the 6th Annual Congress of the European League against Rheumatism (EULAR), 8–11 June 2005, Vienna, Austria, and at the 70th ACR/ARHP Annual Scientific Meeting, 10–15 November 2006, Washington, DC, USA.

Disclosure statement: L.G. has received honorarium for lectures from Actelion pharmaceuticals and has participated to Actelion Pharma advisory boards. L.M. has received grants/research support and is a consultant for Actelion, Pfizer, GSK and Lilly. All other authors have declared no conflicts of interest.

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