

# Kidney Disease Other than Renal Crisis in Patients with Diffuse Scleroderma

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**ABSTRACT. Objective.** To determine the frequency and severity of kidney abnormalities in patients with diffuse scleroderma.

**Methods.** All patients with diffuse scleroderma seen at the University of Pittsburgh between 1972 and 1993 were included in the study. Kidney function tests were routinely obtained as part of the Pittsburgh Scleroderma Outcome Study. Additional kidney tests were obtained as part of the 1992 biannual outcome assessment. Patients who had kidney abnormalities including a serum creatinine > 1.2 mg/dl or proteinuria prior to 1993 were identified. The clinical setting and longterm outcome of kidney disease were evaluated.

**Results.** Renal crisis occurred in 129/675 (19.5%) patients. Kidney function abnormalities or proteinuria were present in 173 (26%); 48% had no abnormalities. Most patients had other explanations for the abnormality. Only 12 (2%) of the 675 patients with diffuse scleroderma had no explanation for the elevated creatinine level. Most patients with proteinuria had toxicity from D-penicillamine. No explanations for proteinuria were found in 16 (2%) of this cohort. Thus, a total of only 28 (4%) of these 675 patients had an unknown cause for their kidney dysfunction or proteinuria. None of these patients, who were followed for a mean of 10 years after onset of scleroderma, have developed chronic renal insufficiency that progressed to dialysis.

**Conclusion.** Patients with diffuse scleroderma without renal crisis rarely have significant increases in serum creatinine or proteinuria that cannot be explained by other etiologies. These patients with scleroderma should be carefully evaluated for non-scleroderma causes of kidney disease. (J Rheumatol 2005; 32:649–55)

*Key Indexing Terms:*

SCLERODERMA  
KIDNEY DISEASE

SYSTEMIC SCLEROSIS  
PROTEINURIA

RENAL CRISIS  
INCREASED CREATININE

Scleroderma renal crisis with malignant hypertension and rapidly progressive renal failure is a major complication of systemic sclerosis (SSc). It occurs in approximately 20% of patients with diffuse scleroderma<sup>1</sup>. Cannon reported that kidney disease was present in 50% of patients with scleroderma<sup>2</sup>. Abnormalities included in Cannon's study were hypertension, abnormal kidney function, or proteinuria<sup>2</sup>. However, there was no specific information about the type or etiology of these abnormalities. Using sensitive measures of renal function, others have found abnormal glomerular filtration<sup>3</sup> and decreased blood flow by Doppler studies<sup>4</sup>. Pathology studies<sup>5,6</sup> show arterial involvement of renal ves-

sels in most diffuse scleroderma patients. However, the clinical significance and longterm outcomes of these abnormalities are not known.

Chronic kidney disease other than renal crisis is not well described although most physicians assume that it occurs. In a prior study, kidney abnormalities such as proteinuria, hypertension, or abnormal serum creatinine did not predict future renal crisis<sup>7</sup>. It has been presumed that such abnormalities reflect the vasculopathy that occurs pathologically in patients with scleroderma even in the absence of renal crisis. We looked at the natural history of major kidney abnormalities in a large cohort of patients with SSc and diffuse scleroderma to determine the frequency, type, and natural history of easily detected kidney abnormalities and to determine if there is clinically distinct kidney disease in scleroderma separate from renal crisis. We did not attempt to determine the frequency of subtle renal function abnormalities.

## MATERIALS AND METHODS

Consecutive patients with diffuse scleroderma, as described by Leroy, who were seen at the University of Pittsburgh between January 1, 1972 and January 1, 1993 were included in this study. All patients had diffuse skin thickening at some point in their illness. Patients had similar baseline kidney function data, including blood urea nitrogen (BUN), serum creatinine, creatinine clearance; urine studies including urinalysis and 24 h urine pro-

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tein, as well as demographic, clinical, laboratory, and serologic studies as part of our standard scleroderma evaluation<sup>8</sup>. Half of these patients were seen regularly at the University of Pittsburgh. As part of our prospective, longitudinal, natural history outcome study in systemic sclerosis, patients complete a questionnaire biannually. This questionnaire includes information relating to symptoms, organ system outcomes including kidney problems, dialysis, medications, hospitalizations, and disability. The cause of death is carefully determined from all available information. With informed consent, the patient's physicians and hospitals are contacted to obtain hospital discharge summaries and laboratory data. During the 1991-1992 questionnaires patients were requested to send us a repeat BUN, serum creatinine, and urine protein. We followed the natural history of the disease and specifically tried to determine the frequency and outcome of kidney disease using standard kidney laboratory tests. We chose not to perform serial creatinine clearances or other supersensitive measures of kidney function since the identification of subtle asymptomatic abnormalities was not our intent.

Patients were divided into specific subgroups as described below based on the most abnormal findings as of 1993. In the 2000 outcome study additional outcome data, including hospitalizations, causes of death, patient's report of dialysis or kidney problems, and available laboratory studies were obtained. From this assessment, we determined outcomes (not necessarily serum creatinines) on 93% of patients in this cohort. We have previously validated our ability to identify severe organ abnormalities<sup>9</sup> and thus, it is unlikely that patients had significant chronic renal insufficiency that we were not aware of. However, minor abnormalities in kidney function could be present in patients without recent laboratory tests.

The specific patient subsets and the definitions that we used are as follows: (1) Renal crisis: new onset malignant hypertension and/or rapidly progressive renal failure; (2) Hypertension: preexisting or new hypertension (140/90 on 2 occasions) requiring anti-hypertensive medication without evidence of an increased serum creatinine or urine abnormalities at the onset of hypertension; (3) Renal abnormalities: kidney dysfunction, BUN > 25 mg/dl, serum creatinine > 1.2 mg/dl, 3 or 4+ proteinuria on 2 occasions on dipstick, or > 250 mg/24 h<sup>2</sup>; and (4) No abnormalities: patients who had none of the above as of 1993.

We next carefully reviewed the records of patients in the subset with renal abnormalities to determine the clinical settings and outcomes associated with these abnormalities. In patients with kidney abnormalities we defined possible explanations into the following categories: (1) Prerenal: patients who had an elevated BUN or serum creatinine from conditions that were likely due to prerenal problems, such as heart failure, dehydration from infection, or gastrointestinal problems, etc.; (2) Time of death: patients with an elevated BUN/creatinine that occurred at the time of death from any cause other than renal crisis; (3) Transient: patients with an elevated BUN/creatinine that was present without a definite cause and returned to normal within the next year; (4) Unknown: patients with an elevated BUN/creatinine that remained abnormal and did not have an obvious cause; (5) Proteinuria: caused by drugs such as D-penicillamine (D-Pen), from other causes, or an unknown cause.

The survival of patients with kidney abnormalities other than renal crisis was compared to the survival of patients who had no renal problems. Descriptive statistics including survival analysis was performed using Medlog, our data management and analysis program.

## RESULTS

Between 1972 and 1993, 675 new patients with diffuse scleroderma were seen at the University of Pittsburgh Scleroderma Clinic. During the mean followup of 8.5 years, these patients had a mean of 7.5 measurements of blood pressure, 4.3 of serum creatinine, and 4.3 urinalyses. Ninety percent of patients had more than 2 determinations of one of these measurements and 78% of living patients had a serum

creatinine in 1993. There was a mean of 5.8 years between the first and last set of tests in these patients. Renal crisis occurred in 129 (19.5%) patients, 79 (12%) patients had isolated hypertension unassociated with renal crisis, 173 (26%) patients had kidney abnormalities including elevated BUN/creatinine as described above or proteinuria unassociated with renal crisis, and 322 (48%) patients did not have any of these abnormalities prior to 1993. Thirty-four patients (5%) had more than one abnormality (Figure 1).

**Renal crisis.** The description of the course and longterm outcome of patients in this cohort with renal crisis has been recently summarized<sup>10</sup>. Fifty-five percent of these patients with renal crisis had a good outcome in that they did not initially require dialysis or only had temporary dialysis. The survival of these patients was similar to the patients with diffuse scleroderma without any renal crisis<sup>10</sup>. In these 129 patients with renal crisis, only 8% had a prior history of hypertension. Three patients had proteinuria from D-Pen toxicity but none had an increased serum creatinine prior to the onset of renal crisis.

**Hypertension.** Hypertension, defined as blood pressure greater than 140/90 on 2 occasions requiring anti-hypertension medication, was seen in 79 (12%) of these patients (Table 1). This is similar to the frequency of hypertension in the general population. In 40 patients, hypertension developed a mean of 6.8 years prior to the onset of scleroderma symptoms. None of the patients had an abnormal serum creatinine or urinalysis at the time of their initial visit. These patients were older at onset of their scleroderma, their mean peak blood pressure was 168/99, and their peak serum creatinine was 1.3 mg/dl. The mean last recorded serum creatinine was 1.0 mg/dl 12.7 years after onset of hypertension.

Thirty-nine patients developed hypertension a mean of 4.7 years after the onset of scleroderma symptoms. Their mean peak blood pressure was 162/100 and mean serum creatinine in 1993 was 1.2 mg/dl. Sixty-one percent of these patients had received corticosteroids shortly before the onset of hypertension. None had an elevated serum creatinine, proteinuria, or microangiopathic hemolytic anemia at the time they were first diagnosed with hypertension. However, many of the patients were treated with an angiotensin converting enzyme (ACE) inhibitor, making it difficult to determine if they actually had a mild or an aborted case of renal crisis. The last serum creatinine in these patients was 0.9 mg/dl, 4.8 years after the first documented elevated blood pressure. Since 1993 two of these hypertensive patients (one from the subgroup with hypertension before scleroderma and the other from the subgroup with hypertension after scleroderma onset) developed typical renal crisis more than 3 years after their initial onset of hypertension.

**Renal abnormalities.** There were 173 patients without renal crisis who had an elevated BUN, serum creatinine, or proteinuria at some point during this study (Table 1). We were able to explain the likely etiology of these abnormalities in

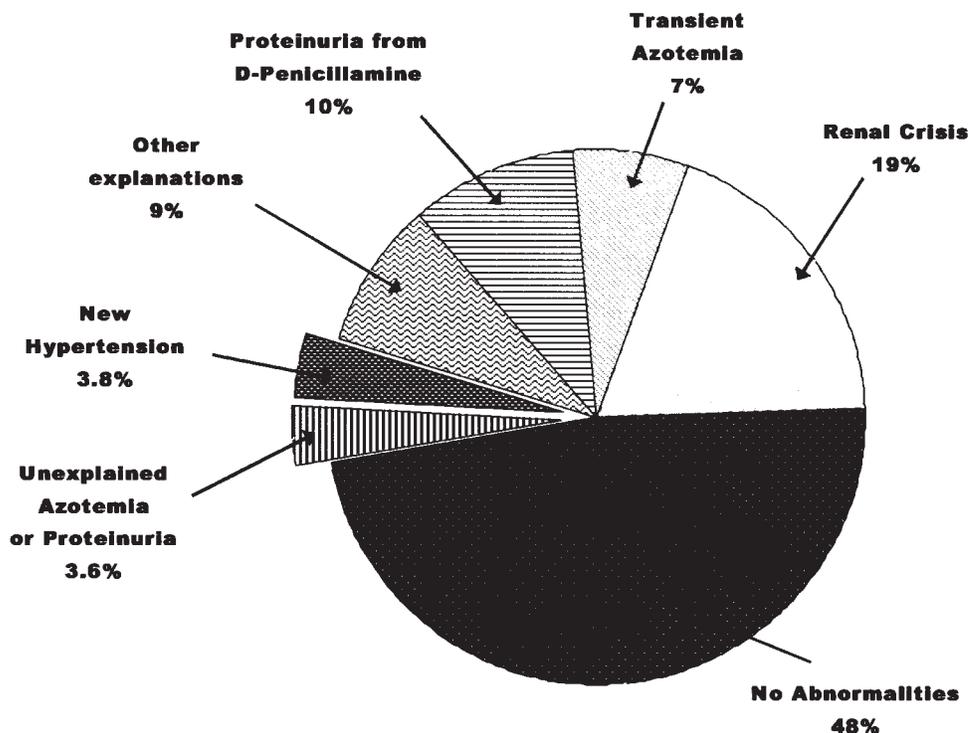


Figure 1. The etiologies of renal disease in diffuse cutaneous scleroderma.

Table 1. Demographic features in patients with and without renal abnormalities.

Features at Initial Evaluation	Renal Abnormalities n = 173			
	Isolated Hypertension n = 79 (12%)	Increased BUN/Creatinine n = 105 (16%)	Proteinuria n = 91 (13%)	No Abnormalities n = 322 (48%)
Sex, % males	27	35	24	21
Age, yrs	42	42	42	44
Disease duration, yrs	3.6	3.8	2.8	3.9
Frequency of studies				
Patients with > 2 creatinine tests, %	92	72	86	61
Number of creatinine tests performed, mean	4	6	4	3
Time between creatinine tests, yrs	3.0	5.2	5.3	2.9
1 or more 24-h urine creatinine tests, %	75	59	89	50

86% of these patients. Table 2 summarizes the clinical information in the 105 patients who had kidney dysfunction with an elevated BUN or serum creatinine. Using the above definitions we were able to explain a likely etiology for these abnormalities in all but 12 patients.

*Prerenal.* Potential prerenal causes explained the increased BUN/creatinine in 22 patients. Twelve had severe congestive heart failure: 5 had scleroderma heart disease, 3 had right heart failure secondary to pulmonary fibrosis, and 4 had non-scleroderma heart disease. Four patients had severe small intestinal dysmotility with vomiting, malabsorption,

pseudoobstruction, dehydration, and/or hyperalimentation. Six patients had increased serum creatinine/BUN secondary to effects from medications, including nephrotic syndrome associated with D-Pen toxicity, diuretics, and nonsteroidal antiinflammatory drugs (NSAID). The mean peak creatinine in the prerenal group was 1.8 mg/dl. The highest creatinine occurred in a man with nephrotic syndrome secondary to taking D-Pen. His peak serum creatinine was 6 mg/dl, which returned to 1.4 mg/dl within one year. Chronic or progressive renal insufficiency did not occur in any of these patients. The last mean serum creatinine in these patients as

Table 2. Features associated with patients who developed an increased BUN or creatinine unassociated with renal crisis.

Features (mean values)	Prerenal n = 22	Transient n = 49	Time of Death n = 22	Unknown n = 12
First abnormal creatinine, mg/dl	1.4	1.3	1.8	1.4
Peak creatinine	1.8	1.4	1.8	1.7
Last creatinine	1.6	1.0	1.8	1.5
Disease duration at time of first abnormal creatinine, yrs	3.7	6.4	4.7	2.4
Time between creatinine tests, yrs	3.2	4.5	0.2	5.4
Possible contributing features*				
Scleroderma heart disease	5	3	9	0
Pulmonary fibrosis	3	3	4	0
Gastrointestinal disease	4	3	3	0
Other non-scleroderma causes				
Cancer	1	0	3	0
Infection	1	3	3	0
Atherosclerotic heart disease	3	3	0	0
Drug (possible)	6	19	13	9
NSAID	1	4	2	5
Diuretic	2	16	11	3
D-penicillamine	2	2	3	3
ACE-inhibitors	1	2	3	4

\* Number of patients with features that may contribute to kidney abnormalities.

of 1993, 3.2 years after the first abnormal creatinine, was 1.6 mg/dl. Between 1993 and 2000, 2 of these 22 patients developed renal crisis late in their illness, 8 and 11 years after disease onset. Their serum creatinine levels remained between 1.2 and 1.4 until the time of their renal crisis. Two other patients had a slower progression of renal insufficiency. One had severe hypertension for 10 years prior to the onset of scleroderma. She died of heart failure at the age of 68 with a serum creatinine of 3.7 mg/dl. The other patient, who had severe gastrointestinal disease with multiple episodes of pseudoobstruction and 3 years of hyperalimentation, died of sepsis with a serum creatinine of 4.6 mg/dl. Neither required dialysis.

*Time of death.* There were 22 patients who had an elevated BUN/creatinine only present at the time of death. The mean maximum serum creatinine in this group was 1.8 mg/dl, and all patients died during that hospitalization, 9 from scleroderma heart disease, 4 from pulmonary fibrosis, 3 had severe gastrointestinal dysfunction, 3 had sepsis, and 3 had cancer.

*Transient.* The largest group of patients with an elevated BUN/serum creatinine was the transiently increased group. Forty-nine patients, 47% of the patients with kidney dysfunction, had a transiently increased mean BUN or serum creatinine of 24 mg/dl and 1.4 mg/dl 6.0 years after disease onset. Acute gastrointestinal problems (3 patients), pulmonary fibrosis (3 patients), cardiac failure (6 patients), drug reactions (3 patients), and infections (3 patients) were identified as possible contributing causes in 18 patients. Another 16 patients were receiving NSAID, diuretics, or

cyclosporine, which could potentially have caused the increased BUN/creatinine. There was no other obvious illness or medication that contributed to the abnormal values in the other 11 patients. The serum creatinine returned to 1.2 mg/dl or less in all patients within 1 year of the abnormal value. Their last mean recorded serum creatinine as of 1993 was 1.0 mg/dl, 4.5 years after the first abnormal one. As of 2000, none of these patients had developed chronic renal disease although one patient who died of atherosclerotic heart disease had an increased serum creatinine.

*Unknown.* Of the 675 patients with diffuse scleroderma, there were only 12 patients (2%) who developed a persistently increased serum creatinine independent of renal crisis or any other illness or medication that could easily explain the renal dysfunction. Six of the patients had a history of hypertension for 2 to 15 years prior to the onset of scleroderma symptoms. The first elevated serum creatinine occurred 5.4 years after onset of disease. None of the 12 patients developed chronic renal failure, and 2.5 mg/dl was the highest serum creatinine in any of these patients. The last mean serum creatinine was 1.7 mg/dl, 5.4 years after the first abnormal creatinine. Seven of the 12 patients were still alive as of our 2000 followup (5 died of non-renal scleroderma problems). None of them had scleroderma renal crisis, were on ACE-inhibitors, or had a history of any significant renal problems although we did not have actual serum creatinine values for most.

*Proteinuria.* There were 91 patients who had proteinuria between 1972 and 1993 (Table 3). The vast majority, 67 patients (74%), developed proteinuria from D-Pen toxicity.

Table 3. Clinical features of patients with proteinuria.

Features At Time of Proteinuria	D-penicillamine Toxicity (n = 67)	Other Causes (n = 8)	Unknown (n = 16)
Greatest 24-h urine, g	2.7	1.0	0.4
Red blood cells > 5, %	24	25	44
Creatinine, mg/dl	0.9	1.1	0.8
Hypertension, % diastolic BP > 100 mm Hg	7	50	6
Disease duration, yrs	3.0	6.6	3.4
Number with proteinuria that resolved in 1 yr (%)	55/87 (82)	2/8 (25)	0
Mean duration of proteinuria at resolution, yrs	0.6	1.4	—

The mean 24 h urine protein was 2.7 g/24 h (range 0.5 to 13 g protein/24 h), which developed a mean of 2.8 years after onset of disease and 1.2 years after onset of D-Pen treatment. In patients who had proteinuria related to D-Pen toxicity, 51% had hypoalbuminemia or more than 2+ peripheral edema and 7 patients had a transiently elevated serum creatinine associated with this complication. Proteinuria decreased to less than 300 mg/24 h within one year in all but 12 of these patients. Six with persistent proteinuria from D-Pen toxicity for more than a year underwent a renal biopsy. All showed minimal change or a mild membranous nephropathy. Some patients had intimal proliferation of the interlobular arteries, but none had changes severe enough to be consistent with renal crisis. There were 8 other patients who had proteinuria felt to be secondary to other causes including severe congestive heart failure, urinary tract infection, hematuria from cyclophosphamide, and bladder cancer.

In the 16 patients who had unexplained proteinuria, one had prior hypertension and 7 had more than 5 red blood cells. One patient had a renal biopsy that showed a mesangial glomerulonephritis that was not felt to be related to her scleroderma. The mean 24 h urine protein level in these 16 patients was 400 mg 3.4 years after disease onset. No patient with proteinuria of unknown cause had an elevated creatinine or developed renal crisis, renal insufficiency, or nephrotic syndrome between 1993 and 2000.

*No abnormalities.* There were 322 patients who prior to 1993 had 6.7 years of disease and had no abnormalities described above. Seven of the 322 (2%) had late onset renal crisis (range 5-14 years of disease) between 1993 and 2000. One hundred and six patients died prior to 1993 or between 1993 and 2000 without evidence of kidney dysfunction. One hundred and ninety-eight patients completed the 2000 Outcome Questionnaire. The status of 11 patients was not known as of 2000. Serum creatinine levels were available after 1993 in 110 patients completing the 2000 Outcome Questionnaire. Eight of these 110 had abnormal creatinine levels shortly before they died of other severe scleroderma organ involvement, excluding renal crisis: 7 had proteinuria

from D-Pen toxicity and 7 had transient increases in serum creatinine between 1993-2000.

*Survival.* Not only do these patients rarely go on to develop renal insufficiency, but their survival is also very good. Survival was determined from the time of first visit in the renal abnormalities subgroups (excluding those in the terminal group and the patients with renal crisis) and was compared to those without these abnormalities. Patients in the prerenal, transient, unknown, and proteinuria subgroups were combined because there was no significant difference between the subgroups. The 5-year survival was 75% for the renal abnormality group and 80% for the group with no renal abnormality (p = 0.126).

## DISCUSSION

Scleroderma renal crisis is a major complication in patients with SSc with diffuse cutaneous scleroderma. Early studies, particularly Cannon's classic study of renal involvement found that 45-60% of patients with scleroderma had hypertension, proteinuria, or azotemia<sup>2</sup>. Historically, renal crisis occurs in about 20% of patients with diffuse scleroderma but there has been little description of kidney disease unrelated to renal crisis. Pathologic vascular changes, diminished creatinine clearance, abnormal measures of blood flow, and other abnormal measures of renal function are present in a large number of patients without renal crisis, but these findings are not predictive of renal crisis<sup>3,4</sup>. In our study, creatinine clearance in patients without renal crisis was less than 75 ml/h in 43% of the 359 patients with available data. These patients had the same outcomes as those with a normal creatinine clearance. There was no difference in the development of future renal crisis, future development of renal insufficiency, or survival between these groups. We focused on the longterm prevalence of clinically apparent kidney disease other than renal crisis rather than subclinical abnormalities.

We found that 52% of 675 patients with diffuse scleroderma developed renal crisis or hypertension, kidney dysfunction, and/or proteinuria unrelated to renal crisis during an average of 8.5 years of disease. This corroborates findings from Cannon's earlier study. We did not find any evidence of a chronic renal disease independent of renal crisis. Because ours was a prospective, observational study, not all patients had repeat testing at designated intervals. However, as part of an ongoing survey, we maintain a 93% accountability of these patients, obtain medical records from hospitalizations and intermittently from primary physicians, and document our ability to identify severe organ disease. Although it is likely that there are additional patients who have mildly elevated creatinine levels for various reasons, it is unlikely that, using our aggressive followup measures, we have missed a significant number of patients who had chronic renal insufficiency.

In contrast we found only 81 (8%) of the 979 patients

with limited scleroderma who ever had a serum creatinine greater than 2.0 mg/dl. Disease duration in these patients was 20 years at time of last serum creatinine measurement. There was a mean of 8.7 creatinine tests performed in this group and 60% had more than 2 creatinine measures available. A similar classification of these 81 patients found that 16 had elevated serum creatinine related to a prerenal cause, primarily right heart failure from pulmonary hypertension. In 16 others it was increased at the time of death from other causes. There were 17 patients with renal crisis (2% of the 979 patients with limited scleroderma). None of these 17 patients ever developed diffuse skin thickening but at the time of renal crisis they had symptoms similar to most of the typical patients with diffuse renal crisis. Seven of the 17 had symptoms for less than 1 year, 2 had anti-topoisomerase antibody, and 4 had anti RNA-polymerase III. Only 1 patient with classic renal crisis had an anti-centromere antibody.

Five of these 81 patients with limited scleroderma required hemodialysis for non-scleroderma kidney disease. The etiology of their kidney disease included renal artery stenosis, chronic hypertension dating from prior to onset of scleroderma, and 3 with biopsy-proven crescentic glomerulonephritis. Nine patients with limited scleroderma had an unknown cause for the creatinine greater than 4 mg/dl, and these patients have not required dialysis. Repeat creatinine tests and a detailed analysis of the etiology of the elevated creatinine levels were not performed. As this represents only 1% of the patients with limited scleroderma, it is very unlikely that a significant number of such patients develop chronic progressive renal failure from scleroderma.

Kidney disease other than renal crisis in scleroderma has not been well characterized. No specific etiology has been described and abnormalities are just ascribed to scleroderma. Less than 5% of these 675 patients with diffuse scleroderma had unexplained renal abnormalities over a mean of 12.5 years. Twelve had unexplained increases in serum creatinine and the mean last recorded serum creatinine was 1.5 mg/dl; 16 had unexplained proteinuria. Persistent kidney abnormalities from a chronic renal disease in patients with diffuse scleroderma were mild and nonprogressive.

In our entire scleroderma database, including patients prior to and after this study period, we have had only 2 patients with diffuse scleroderma who developed chronic renal failure and required dialysis independent of renal crisis. One had hypertensive nephropathy and was on dialysis before he developed scleroderma. The other had biopsy proven crescentic glomerulonephritis, which has been reported in patients with scleroderma. Initially, it was only seen in patients treated with D-Pen<sup>11</sup>, however, recently more than 30 cases of rapidly progressive glomerulonephritis have been reported in patients with scleroderma unrelated to D-Pen<sup>12,13</sup>. Most of them have been from Japan and have limited scleroderma, normal blood pressure, marked

proteinuria, and progressive renal insufficiency<sup>13</sup>. Almost all have had a myeloperoxidase antineutrophil cytoplasmic antibody, (ANCA). ANCA have also been seen in 4-10% of scleroderma patients without kidney abnormalities<sup>14</sup>. Thus, in patients with kidney abnormalities without typical renal crisis, it is important to consider other etiologies rather than assuming that the renal insufficiency is from scleroderma kidney disease independent of renal crisis.

Benign hypertension has also been reported as a manifestation of scleroderma. We have shown that increased blood pressure was not predictive of renal crisis<sup>7</sup>. Sixty-one percent of patients with new hypertension received steroids for scleroderma features shortly before they developed hypertension. This may have contributed to the development of the hypertension<sup>15</sup>. These patients had no other evidence of renal crisis, but since many of them were treated with an ACE-inhibitor, it is possible that they had a mild or aborted episode.

Our findings show an infrequent occurrence of kidney disease other than renal crisis in patients with diffuse scleroderma. Any patient with the new onset of kidney dysfunction without scleroderma renal crisis should be carefully evaluated for other causes of renal disease such as drug toxicities and non-scleroderma kidney problems. If an explanation is not easily identified, a renal biopsy should strongly be considered. Many scleroderma patients have underlying pathologic vascular changes in the kidney that may result in the more rapid development of renal insufficiency when they are seriously ill. Asymptomatic vascular changes are frequently present but do not seem to be associated with significant longterm renal dysfunction.

In summary, although half of our patients with diffuse disease have some renal abnormality in the first 10 years of their illness, only 4% had unexplainable abnormalities and only 2.4% had new hypertension independent of renal crisis. Slowly progressive chronic kidney failure other than renal crisis did not occur in our large cohort of patients with diffuse scleroderma. If kidney abnormalities are present, careful evaluation for other etiologies of kidney disease is necessary. Patients and physicians can be reassured that in diffuse disease, kidney abnormalities, other than those associated with renal crisis, are usually mild and non-progressive.

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