SEVERE ORGAN INVOLVEMENT IN SYSTEMIC SCLEROSIS WITH DIFFUSE SCLERODERMA

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Objective. To determine the natural history and timing of severe involvement of the kidney, heart, lung, gastrointestinal (GI) tract, and skin in patients with systemic sclerosis (SSc) and diffuse cutaneous involvement.

Methods. This study used the Pittsburgh Scleroderma Databank and included patients with diffuse scleroderma who were seen between January 1, 1972 and December 31, 1995. Patients had frequent follow-ups, and a 95% accountability for these patients was maintained. Severe organ involvement was defined as the presence of any of the following: 1) in the kidney, scleroderma “renal crisis”; 2) in the heart, cardiomyopathy, symptomatic pericarditis, or an arrhythmia requiring treatment; 3) in the lung, pulmonary fibrosis on chest radiograph and a forced vital capacity of <55% of predicted; 4) in the GI tract, malabsorption, repeated episodes of pseudoobstruction, or severe problems requiring hyperalimentation; and 5) in the skin, a modified Rodnan skin score >40. The timing from disease onset to survival for each case of severe organ involvement was determined.

Results. Of the 953 patients with diffuse scleroderma, kidney involvement developed in 177 (19%), heart involvement in 143 (15%), lung involvement in 151 (16%), GI tract involvement in 74 (8%), and skin involvement in 233 (24%). Severe skin and kidney involvement occurred during the first 3 years in 70% of those who ever developed these problems throughout a mean of 10 years of followup. Severe heart, lung, and GI tract involvement developed during the first 3 years in 45–55% of those who were ever affected. The survival of patients with severe organ involvement was poor. The 9-year cumulative survival rate of all patients with severe organ involvement was 38%, compared with 72% in patients without such involvement ($P < 0.0001$).

Conclusion. This study demonstrates that severe organ involvement in SSc patients with diffuse scleroderma most often occurs early in the course of the disease. Survival for patients with severe organ involvement is markedly reduced. Patients should therefore be monitored very closely during the first 3 years of disease for signs and symptoms that may signal the subsequent development of severe organ damage. Potential disease-modifying therapies must be initiated early to modify the natural history of SSc and to improve survival. Patients who survive the first few years without developing severe organ involvement are less likely to develop such life-threatening involvement later in the disease course.

Early literature described systemic sclerosis (SSc) as a progressive disease, hence the initial designation as “progressive systemic sclerosis” (1). Many of the first reported cases had severe cutaneous and internal organ involvement, which progressed relentlessly. However, since the more recent recognition that there are subsets of SSc which are milder and are not progressive, the term “progressive” has been dropped (2). Prior to 1991, when the term “regressive scleroderma” was described (3), spontaneous improvement in cutaneous manifestations had not been recognized. Additional case studies and clinical trials have documented that cutaneous involvement may improve spontaneously, even in untreated patients (4,5).

It was once thought that the risk of severe internal organ system involvement in patients with diffuse scleroderma increased linearly, in parallel with disease duration. However, studies of individual organ systems have shown that this is not the case. Renal crisis
occurs most often during the first 4 years (6), and volume loss in patients with severe pulmonary fibrosis is greatest during the first 2 years (7). There is great variability in the disease course of patients with diffuse scleroderma. In these two instances, complications occur very early in the course of disease. The present study was designed to examine the timing and natural history of the development of new, severe involvement in patients with the diffuse scleroderma.

**PATIENTS AND METHODS**

This study included all consecutive patients with SSc and diffuse scleroderma, as defined by LeRoy et al (2), who were evaluated at the University of Pittsburgh between January 1, 1972 and December 31, 1995. These patients have been followed up prospectively. All had a standardized initial evaluation, which included a scleroderma-specific medical history and a physical examination, a search for organ system abnormalities, and laboratory and serologic studies (4). Since 1986, patients have also completed a Health Assessment Questionnaire (HAQ) modified for use in scleroderma patients, which includes visual analog scales for scleroderma organ severity (8).

Most patients with diffuse scleroderma who are seen in followup at the University of Pittsburgh undergo a complete scleroderma-related history and physical examination every 3–12 months, although laboratory tests are obtained only as clinically indicated. An annual followup includes mail or telephone contact to ascertain information on symptoms, medications, use of oxygen, dialysis, and hospitalizations. Physician, laboratory, and hospital records on all patients who have been identified as having symptoms of, as being hospitalized for, or as taking medications used in the treatment of severe involvement are obtained as indicated, with the patient’s informed consent. This careful attention to followup information has allowed us to obtain the necessary comprehensive data to understand the long-term outcomes in this disease. We have an ongoing quality assurance program for the database, and for the present study, we also chose 30 patients at random (5%) and specifically determined the presence or absence of severe organ system involvement.

The primary cause of death is determined by the patient’s history, hospital and primary physician’s records, and the family’s description of the events surrounding the death, independently of what, if any, severe organ involvement group the patient was in. We also make clinical judgments on difficult-to-measure organ system problems, such as malabsorption, congestive heart failure, and intestinal pseudoobstruction.

The following definitions of severe organ involvement were used.

1. Kidney: malignant arterial hypertension and/or rapidly progressive renal failure and/or microangiopathic hemolytic anemia (MAH). Patients with new-onset hypertension without increases in serum creatinine levels or MAH were not included, even if they were successfully treated with an angiotensin-converting enzyme (ACE) inhibitor.

2. Heart: cardiomyopathy with a decrease in left ventricular ejection fraction and symptoms of congestive heart failure, symptomatic pericarditis that included pericardial pain or cardiac decompensation from effusion, or an arrhythmia attributable to scleroderma heart disease requiring treatment (4). Patients who had an asymptomatic decrease in the ejection fraction, an asymptomatic pericardial effusion, or asymptomatic arrhythmias were not considered to have severe heart involvement Non–scleroderma-related heart problems and nonspecific asymptomatic changes on echocardiogram, electrocardiogram, or Holter monitor were not considered severe involvement.

3. Lung: pulmonary fibrosis on chest radiograph, with a forced vital capacity <55% of predicted. Isolated pulmonary hypertension occurs in only 1–2% of patients with diffuse scleroderma, and it has a different course from that of pulmonary fibrosis (for review, see ref. 9). Patients with diffuse scleroderma and isolated pulmonary hypertension were excluded from this study.

4. Gastrointestinal (GI) tract: malabsorption syndrome, repeated episodes of intestinal pseudoobstruction, or severe GI problems which require hyperalimentation. Diarrhea responsive to antibiotics without malnutrition, bloating after meals, and esophageal stricture are evidence of significant GI involvement but were not classified as severe unless they were associated with a 10% weight loss or hospitalization.

5. Skin: a modified Rodnan total skin score >40 of a maximum possible score of 51 (10). Patients who had an initial total skin score <40 and who did not have repeat skin evaluation in Pittsburgh were not included in the denominator of this part of the study.

To ensure that we identified all patients who fulfilled criteria for severe organ system involvement, we examined the medications the patients were taking, their blood pressure levels, blood test results, and radiography reports, as well as causes of death, reasons for hospitalizations, changes in weight, and changes in values on the scleroderma HAQ. Patients who developed severe organ involvement prior to their first Pittsburgh visit were included only if appropriate documentation from the available medical records was identified. We validated our methods of identifying severe organ involvement by randomly reviewing patients’ records and by phoning the patients and/or their physicians to determine whether we had correctly ascertained the severity of organ involvement.

The time to the development of severe organ involvement (endpoint) was calculated from the time of onset of the first symptom attributed to SSc (starting point). The time when a patient fulfilled criteria for a specific severe organ involvement was used as a conservative estimate of the time of onset of severe organ involvement, even if symptoms were present earlier.

Data analysis included standard descriptive statistics and survival analysis, whereby the new onset of a severe organ involvement was considered the end point. For each organ system involved, each patient was evaluated independently of other involved organ systems; thus, patients with more than one organ system involved were included in more than one organ system involvement group. Calculations of patient sur-
vival used the time at which they satisfied criteria for severe organ involvement as the starting point, even if they had symptoms attributable to this organ system earlier, and the time of death as the end point.

**RESULTS**

There were 953 patients with diffuse scleroderma whose mean disease duration from the first symptom attributable to SSc until the last followup contact was 9.8 years. Eighty percent were female, and 94% were Caucasian. All patients fulfilled the American College of Rheumatology criteria for SSc (11). Thirty percent had the onset of symptoms after age 50 years, 68% had <2 years of symptoms at the time of their first visit, 42% had Raynaud’s phenomenon as their first symptom, and 48% were residents of the Pittsburgh referral area. As of May 1997, we knew the vital status on 95% of these patients. Adequate patient, physical, and laboratory information to ascertain the presence of cardiac, renal, and GI severe organ involvement was available on 91% of the patients. Results of more than 2 skin score examinations and pulmonary function tests were available on 65% and 80% of these patients, respectively.

We randomly contacted 50 patients and their physicians to validate the accuracy of our database information. We correctly identified the presence or absence of 97% of a potential 250 cases of severe organ system involvement (5 organ systems per person) in these 50 patients. The ones we did not identify included 5 patients who developed severe skin thickening after their last Pittsburgh skin evaluation. One patient each had malabsorption and congestive heart failure that had not previously been identified.

Figure 1 demonstrates the overall frequency of severe organ involvement during the observation period in the 953 patients with diffuse scleroderma. The most frequent severe involvement was skin thickening in 233 patients (24%). There were 177 patients (19%) who developed renal crisis, 143 (15%) who developed severe heart disease, and 151 (16%) who had severe pulmonary fibrosis. The least frequent severe organ involvement was the GI tract, affecting 74 patients (8%). An additional 84 patients with esophageal stricture, severe reflux esophagitis, or diarrhea responding to antibiotics were not included in the severe organ involvement groups.

Many of the patients with severe skin thickening also had severe kidney (n = 55, 24%), heart (n = 56, 24%) or lung (n = 35, 15%) involvement. There were patients with renal crisis who also had heart involvement (n = 47), even though we attempted to separate and exclude heart involvement secondary to renal crisis (e.g., transient congestive heart failure due to malignant hypertension). It was uncommon for patients to have severe kidney disease along with either severe lung or GI disease (n = 20 and n = 25, respectively). One hundred forty-eight of the SSc patients with diffuse scleroderma had severe skin involvement without other severe internal organ damage. Fortunately, a majority (n = 656, or 69%) of these 953 patients with diffuse scleroderma have not developed severe involvement of any of the 4 internal organ systems concerned.

Figures 2 and 3 show the timing of the development of the different severe organ involvements during 3 time periods, 0–3 years, 3–6 years, and 6–9 years after the onset of SSc. These intervals were chosen primarily to have 3 equal time periods during followup. Figure 2 shows the cumulative percentage of all patients with diffuse scleroderma who developed involvement of each of the organ systems. The most frequent was severe skin involvement, where 18% of those with diffuse scleroderma developed severe skin thickening by 3 years after the onset of symptoms. This increased to 27% at 9 years. The least frequent, GI tract involvement, only occurred in 4% of patients by 3 years and 8% by 9 years. In the subset of patients with early disease (<2 years of symptoms at initial visit), there were no differences in the frequency of individual severe organ involvements compared with the entire group with diffuse scleroderma (data not shown).
Figure 3 shows the cumulative acquisition of severe organ involvement among all patients (100%) who ever developed such organ involvement. For example, 80% of all patients who ever developed severe skin thickening did so by 3 years and 92% by 9 years. In the remaining 8%, severe skin involvement first occurred after year 9.

For all organ systems, the first 3 years from disease onset was the time period in which the highest proportion of new organ system involvement occurred ($P < 0.01$). More than 70% of severe skin and kidney involvement occurred during the first 3 years. Thereafter, additional patients who developed severe involvement of these 2 organs did so at a rate that was evenly divided throughout the next 6 years. For the other 3 organ systems, 45–55% of severe involvement occurred during the first 3 years, which was twice the rate of acquisition in the later 2 time periods.

In patients with early disease, the frequency of severe skin, renal, and cardiac involvement was significantly greater than in the whole patient group. For skin, 70% had severe involvement by 3 years in the whole group, but 80% of the early disease group who ever had severe skin involvement had it by 3 years. Likewise for renal, 74% of the whole group, but 88% of the early disease group, and for cardiac, 56% of the whole group, but 75% of the early disease group, developed severe organ involvement by 3 years ($P < 0.001$). There were no differences for pulmonary or severe GI tract disease. Rarely, patients developed severe organ involvement after 9 years of symptoms. Thus, we conclude that the majority of patients with SSc and diffuse scleroderma who develop severe organ involvement do so early in the course of their disease.

Figure 4 shows the cumulative survival, using the time of documentation of severe organ system involvement as the starting point. Not surprisingly, the outcome for patients with severe organ involvement was ex-
tremely poor. Patients with severe skin involvement had
the best outcome of the 5 severely affected organ
systems. From the time the patients developed a total
skin score >40, which was a mean of 2.5 years after SSc
onset, they had a 9-year cumulative survival rate of 54%.
Patients with both severe skin and severe heart involve-
ment had a worse prognosis than patients whose heart
was the only severely involved organ. Patients with
severe skin involvement along with severe involvement
of one of the other organ systems had survival rates
similar to those of patients with the severe organ in-
volvement without severe skin thickening.

In the 148 patients who had only severe skin
involvement without additional severe organ damage,
the survival was 72% at 9 years. The outcome for
patients with 2 severely involved organ systems (exclud-
ing skin) was similar to that of patients with only 1
severely involved organ system, although in many situa-
tions, the groups were quite small. When patients diag-
nosed with renal crisis before the availability of ACE
inhibitors were excluded from the analysis, the 9-year
survival of patients with severe renal involvement was
68%, rather than the 40% shown in Figure 4. Not
surprisingly, severe disease of the heart, lung, and GI
tract all had a poor prognosis, with 9-year cumulative
survival rates ranging from 15% to 40%. The cumulative
survival rate from the first diagnosis of scleroderma by
any physician for those patients without any severe
organ involvement was 72% at 9 years, compared with
38% for those who had any severe organ involvement
\( P < 0.0001 \).

During followup, 352 of the 953 patients (37%)
died. Renal crisis was the most frequent SSc-related
cause of death, although fewer kidney-related deaths
have occurred since the routine use of ACE inhibitors
for renal crisis. Death from severe scleroderma involve-
ment of the heart, lung, and GI tract occurred with equal
frequency in this population. In this series, 38% of
deaths were attributed to non–scleroderma-related ill-
nesses, including cancer and coronary artery disease.

Table 1 summarizes the distribution of deaths
according to the time from disease onset until the time
of death. Renal- and cardiac-related deaths occurred
with greater frequency in the first 5 years compared with
the subsequent 5 years. Pulmonary-related deaths oc-
curred significantly more frequently in the second 5
years compared with the first 5 years (16% versus 6%;
\( P < 0.01 \)). Non–scleroderma-related causes of death
were significantly more frequent than scleroderma-
related causes in the later time period (42% versus 33%;
\( P < 0.01 \)).

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Years 0–5 (n = 148)</th>
<th>Years 5–10 (n = 204)</th>
<th>Odds ratio; ( P ) (95% CI)</th>
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<tbody>
<tr>
<td>Renal-related</td>
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<tr>
<td>Renal</td>
<td>45 (30)</td>
<td>17 (8)</td>
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<tr>
<td>Cardiac</td>
<td>20 (14)</td>
<td>20 (10)</td>
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<tr>
<td>Pulmonary</td>
<td>9 (6)</td>
<td>32 (16)</td>
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<tr>
<td>Gastrointestinal</td>
<td>13 (9)</td>
<td>21 (10)</td>
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<tr>
<td>Multiple systems</td>
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<td>12 (6)</td>
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<tr>
<td>Total</td>
<td>99 (67)</td>
<td>102 (51)</td>
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</tr>
<tr>
<td>Non–scleroderma-related</td>
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<tr>
<td>Cancer</td>
<td>10 (7)</td>
<td>27 (13)</td>
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<tr>
<td>Coronary artery disease</td>
<td>8 (5)</td>
<td>12 (6)</td>
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<tr>
<td>Infection</td>
<td>9 (6)</td>
<td>12 (6)</td>
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<tr>
<td>Other nonscleroderma</td>
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<tr>
<td>Total</td>
<td>49 (33)</td>
<td>85 (42)</td>
<td>1.74; &lt;0.01 (1.08–2.81)</td>
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* Values are the number (%) of patients. 95% CI = 95% confidence interval.

DISCUSSION

Classic descriptions of scleroderma suggest that
the disease is relentless, with new problems developing progressivly throughout the course of the illness (1). There seemed to be little hope for any stabilization.
Accordingly, early studies of survival showed a dismal
outcome, with 10-year cumulative survival rates seldom
better than 50%. The Multicenter Scleroderma Criteria
Cooperative Study, which established criteria for the
classification of scleroderma, suggested that not all
patients had that type of progressive disease and recom-

dended that the adjective “progressive” be dropped
(11).

A recent survival study examined the patients
who were in the above criteria study, all of whom had <2
years of symptoms at the time of study entry (12). As of
1987, the cumulative survival rate of these patients was
80% at 2 years, 50% at 8.5 years, and 30% at 12 years.
The authors found that survival declined linearly
throughout a 12-year followup period. Although both
limited cutaneous and diffuse scleroderma patients were
included, those with limited scleroderma were underrep-

resented since they seldom present within 2 years of
disease onset. Also, the methods used to separate these
subsets were not clearly defined, and it was impossible to
determine the separate survival rates for these 2 subsets.
The earliest comprehensive survival study, from
the 1970s, showed that the presence of any organ system
involvement, particularly heart, lung, and kidneys, was
associated with a worse prognosis than the absence of organ abnormalities (13). Since that study included even mild abnormalities, it was impossible to determine the prognosis for a patient with severe involvement. Altman et al (12) and Lee et al (14) found similar results in their SSc survival studies. Neither of those investigations distinguished the severity of internal organ damage and its effect on outcome, which is a more clinically relevant issue.

To better understand the natural history of this disease and to determine the best time for therapeutic intervention, we carefully evaluated the time at which severe organ involvement was first recognized. We focused on severe organ involvement, since previous studies have examined the presence of moderate organ involvement (12,13). Since Altman’s study patients had early disease and since the 5-year cumulative survival for patients with kidney or heart involvement was very poor, those investigators believed that damage to these organs occurred early (12). However, disease duration was not found in their regression analyses to be a factor affecting survival. As expected, Lee noted that patients dying of causes unrelated to scleroderma were older and had had their disease longer (14). In studies of specific organ systems, it has been shown that organ damage occurs early. Renal crisis occurs within the first 4 years of disease in 80% of patients who develop this complication (6,15). The greatest loss of lung volume in patients with severe pulmonary fibrosis occurs in the first 2 years of disease, even though patients are often asymptomatic (7).

In the present study, we have shown that severe organ damage occurs within the first 3 years of disease onset in 70–80% of SSc patients who ever develop severe kidney and skin involvement. This was even higher when we used an early disease subset of patients with <2 years of disease. Thus, patients should be monitored very closely for the new onset of hypertension and renal crisis during the early years of their illness.

Additionally, this finding helps us to understand the natural course of the cutaneous changes. Patients can be reassured that progression to severe skin thickening seldom occurs after they have had symptoms for 5 or 6 years (10% of patients). Evidence of severe damage also occurred in other organs early in the illness, although less dramatically than for the skin and kidney. The likelihood of developing severe changes in any organ is decreased after 6 years of symptoms compared with the first 6 years. However, severe organ involvement did occur in 10% of patients after 6 years, and since this study did not address the presence of moderate organ involvement, patients in the later years of disease are still at some risk for significant organ system involvement. The progression from initial symptoms of organ involvement until classification as severe disease often occurred silently early in the disease. It is necessary to search for agents which can alter these early changes and, hopefully, with aggressive therapy, minimize or prevent disease progression or, even better, reverse clinically detected abnormalities.

Although these data have been collected prospectively, there are inherent biases in this type of study. The referral bias, the inability to include patients who die before they have the opportunity to come to our center, and the likelihood of having more severely ill patients need to be considered carefully. We have made every effort to minimize these concerns and, for this reason, have not emphasized the overall frequencies of organ involvement. However, the time to severe organ involvement and the survival once this organ involvement has occurred should not be significantly affected by these biases.

The most frequent causes of death in patients with diffuse scleroderma are directly related to a specific organ system involvement. Over the last 10–15 years, ACE inhibitors have been very effective in treating renal crisis. Improved survival from renal crisis has made pulmonary fibrosis the most common cause of death in SSc. This study has shown that during the first 5 years of disease, there are significantly more scleroderma-related deaths than non–scleroderma-related deaths (e.g., cancer and atherosclerosis). During the first 5 years of symptoms, 44% of deaths were cardiac or renal, compared with 18% after 5 years of symptoms. In contrast, there was a higher proportion of deaths from pulmonary fibrosis in the later 5-year time period than in the earlier 5-year span. This result is consistent with the observation that the greatest lung volume loss occurs early in the disease, when the patient is asymptomatic, but the patients die later from infections or minor progression that results in lung failure.

The reduced survival of patients with these severe organ involvements is not surprising. Death occurred in most of the patients within 3 years of the diagnosis of severe GI tract involvement, and only 15% of such patients were alive at 9 years. Since the criteria for severe GI tract involvement included pseudoobstruction, malabsorption syndrome, and hyperalimentation, all of which are very difficult to treat, a poor outcome would be expected. Milder GI tract disease, such as esophageal stricture or easily managed bacterial overgrowth, are not likely to have this poor outcome.

Patients with severe pulmonary fibrosis, renal
CRISIS, AND CARDIAC DISEASE EACH HAD A SIMILAR PROGNOSIS, WITH ~50% 5-YEAR CUMULATIVE SURVIVAL. IN RENAL CRISIS PATIENTS WHO ARE TREATED WITH ACE INHIBITORS, THERE HAS BEEN A DRAMATIC IMPROVEMENT IN SURVIVAL OF RENAL CRISIS, FROM <10% TO 70% AT 5 YEARS. RENAL CRISIS PATIENTS MANAGED MEDICALLY WHO DID NOT REQUIRE PERMANENT DIALYSIS HAD AS GOOD AN OUTCOME AS THOSE WHO HAD NEVER HAD RENAL CRISIS (80% 5-YEAR CUMULATIVE SURVIVAL) (16).

SOMETHING SURPRISING WAS THE FINDING THAT HALF THE PATIENTS WITH SEVERE CARDIAC INVOLVEMENT SURVIVED FOR >5 YEARS. IT IS POSSIBLE THAT A NUMBER OF OTHER LESS SEVERE HEART DISEASE ETIOLOGIES (E.G., ATHEROSCLEROSIS) CONTRIBUTED TO THE CARDIAC DYSFUNCTION. ALTERNATIVELY, MILD, NONPROGRESSIVE SCLERODERMA HEART DISEASE MAY BE EASY TO IDENTIFY AND TREAT USING MODERN TECHNOLOGY. PATIENTS WITH SYMPTOMATIC CARDIOMYOPATHY HAD THE WORST OUTCOME.

SEVERE SKIN THICKENING REMAINS A RISK FACTOR FOR A POOR OUTCOME IN SCLERODERMA, ALTHOUGH IN THIS STUDY, SUCH PATIENTS HAD THE BEST SURVIVAL OF ALL THE SEVERE ORGAN INVOLVEMENTS (54% AT 9 YEARS). GENERALLY, IT IS THOUGHT THAT THE TOTAL SKIN THICKNESS SCORE PARALLELS VISCERAL INVOLVEMENT, BUT A HIGH SKIN THICKNESS SCORE ALONE DOES NOT ITSELF PREDICT A POOR OUTCOME. THE PATIENTS WITH SEVERE SKIN THICKENING BUT WITHOUT OTHER SEVERE ORGAN DAMAGE HAD A SIGNIFICANTLY BETTER PROGNOSIS, WITH A CUMULATIVE SURVIVAL OF 72% AT 9 YEARS.

THE SURVIVAL OF PATIENTS WHO DEVELOPED EVIDENCE OF ANY 1 OF THE 5 SEVERE ORGAN INVOLVEMENTS DURING THE FIRST 5 YEARS OF THEIR ILLNESS WAS 50% AT 5 YEARS AND 38% AT 10 YEARS. THIS RESULT IS SIMILAR TO SURVIVAL RATES REPORTED IN EARLIER SERIES OF SSc PATIENTS (12–14). HOWEVER, PATIENTS WHO HAD NO EVIDENCE OF ANY SEVERE ORGAN INVOLVEMENT IN THE FIRST 5 YEARS OF THEIR ILLNESS HAD A DRAMATICALLY BETTER SURVIVAL, WITH A 10-YEAR SURVIVAL RATE OF 80% (P < 0.001).

THESE DATA SUPPORT THE FINDING THAT THE RISK OF DEVELOPING AND DYING OF SEVERE ORGAN INVOLVEMENT IN SSc IS GREATEST DURING THE FIRST 5 YEARS OF DISEASE. THEREAFTER, SURVIVAL WITH SSc IMPROVES FOR EACH SUCCESSIVE TIME PERIOD. SSc ORGAN DAMAGE MAY BE A CONTRIBUTING FACTOR TO NON-SSc CAUSES OF DEATH.

RISK FACTORS FOR THE DEVELOPMENT OF SEVERE ORGAN INVOLVEMENT HAVE BEEN EXAMINED IN A VARIETY OF STUDIES (17,18). AUTOANTIBODIES HAVE BEEN ESPECIALLY HELPFUL IN IDENTIFYING PATIENTS AT RISK FOR SEVERE ORGAN INVOLVEMENT. ANTI–TOPOISOMERASE I ANTIBODY IS STRONGLY ASSOCIATED WITH PULMONARY FIBROSIS AND ANTI–RNA POLYMERASE III WITH SEVERE SKIN INVOLVEMENT AND RENAL CRISIS (19,20). THALLIUM DEFECTS HAVE BEEN SHOWN TO BE ASSOCIATED WITH PRESENT AND FUTURE SSc CARDIAC DISEASE (21). UNFORTUNATELY, THERE ARE NO KNOWN RISK FACTORS ASSOCIATED WITH GI DISEASE. OTHER FEATURES WHICH HAVE BEEN ASSOCIATED WITH A POOR OUTCOME IN SCLERODERMA (I.E., OLDER PATIENTS, MALES, AFRICAN AMERICANS, AND INCREASED ERYTHROCYTE SEDIMENTATION RATE) ARE MORE NONSPECIFIC AND DO NOT DEMONSTRATE A PREDILECTION FOR ANY ONE TYPE OF ORGAN DAMAGE. THESE GROUPS HAVE A WORSE PROGNOSIS WITH WHATEVER ORGAN SYSTEM PROBLEMS THEY HAVE. IT WOULD BE VERY HELPFUL TO FIND ADDITIONAL SPECIFIC RISK FACTORS WHICH WOULD IDENTIFY PATIENTS WHO ARE LIKELY TO DEVELOP SPECIFIC ORGAN-SYSTEM DAMAGE. THE PATIENTS COULD THEN BE MONITORED MORE CLOSELY, AND THE PHYSICIANS WOULD HAVE THE OPPORTUNITY TO BEGIN AGGRESSIVE THERAPY EARLY.

IN SUMMARY, THIS STUDY CONFIRMS THAT SEVERE ORGAN INVOLVEMENT MOST OFTEN OCCURS EARLY IN THE COURSE OF SSc WITH DIFFUSE SCLERODERMA. PHYSICIANS AND PATIENTS SHOULD BE MORE ATTENTIVE TO THE POTENTIAL RISK FACTORS FOR ORGAN DAMAGE, PARTICULARLY VERY EARLY IN THE DISEASE, EVEN WHEN THE PATIENTS MAY NOT BE SYMPTOMATIC. TREATMENT SHOULD BE INITIATED AS SOON AS PROBLEMS ARE IDENTIFIED. FURTHER RESEARCH INTO EARLY TREATMENT AND RISK FACTORS IS NEEDED. THIS STUDY GIVES HOPE TO MANY PERSONS WITH SSc WHO PRESUME THAT ALL PATIENTS HAVE A DOWNHILL COURSE THROUGHOUT THEIR ILLNESS.

REFERENCES


