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Original Article

Clinical characteristics of juvenile systemic sclerosis in Korea: 31-year single-center study

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Objective: To evaluate the clinical and laboratory characteristics, therapeutic drugs, and prognosis of juvenile systemic sclerosis (JSSc) at a single center in Korea.

Methods: This study was a retrospective analysis of patients with JSSc aged <16 years at disease onset and who were treated at our hospital between January 1992 and April 2023. All patients met the Pediatric Rheumatology European Society/American College of Rheumatology/European League against Rheumatism provisional classification criteria for JSSc, and those with localized scleroderma (morphea) were excluded.

Results: Among the 13 patients, proximal skin sclerosis (100%), Raynaud's phenomenon (RP) (84.6%), and sclerodactyly (69.2%) were present at the time of diagnosis. The most common symptom before diagnosis was RP, which was present in 10 patients (76.9%), whereas proximal skin sclerosis was observed in only five patients (38.5%). Thirteen patients had positive anti-nuclear antibody (ANA). At the time of diagnosis, five individuals had findings suggestive of interstitial lung disease (ILD) on a pulmonary function test (PFT) or chest computed tomography (CT), two of whom were asymptomatic. During follow-up, three patients developed ILD, one developed renal dysfunction, one developed heart disease, and none died.

Conclusion: This study was the first descriptive analysis of clinical features of JSSc in South Korea. Clinical suspicion is essential for diagnosing JSSc in patients with RP, especially if ANA is positive; however, proximal skin sclerosis, which is crucial for diagnosing JSSc, was unrecognized in the early phase of the disease. PFT should be considered even if a patient is asymptomatic or has normal chest CT.

Keywords: Juvenile systemic scleroderma, Raynaud disease, Anti-nuclear antibody, Interstitial lung diseases

INTRODUCTION

Juvenile systemic sclerosis (JSSc) is an autoimmune, chronic, multisystem connective tissue disease characterized by progressive skin and internal organs fibrosis. Based on the provisional classification criteria for JSSc proposed by the Pediatric Rheumatology European Society/American College of Rheumatology/European League against Rheumatism (PRES/ACR/EULAR) in 2007, a diagnosis of JSSc was established when at least two of the following criteria were present before the age of 16 years: sclerodermatous skin involvement proximal to the metacarpophalangeal joints and involvement of two or more of the following 20 organ-based criteria (skin, vascular, gastrointestinal [GI], renal, cardiac, respiratory, neurological, and musculoskeletal symptoms or specific autoantibody positivity) [1].

In children, the incidence of systemic sclerosis was <10% of all cases [2,3]. Systemic sclerosis in the Asian population is considered an orphan disease, for which the prevalence rate is not well established.

In addition, the exact etiology and pathogenesis of JSSc are

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not fully understood. However, similar to adult systemic sclerosis, it is thought to be related to autoantibodies that affect the immune system, endothelium, and fibroblasts, leading to dysregulation of internal organs. Aberrations in disease-specific autoantibody circulation and immune cell abnormalities involving T and B lymphocytes and mast cells are thought to cause progressive deposition of fibrotic collagen and extracellular matrix in the skin and internal organs, leading to clinical symptoms [4,5].

The average age of onset of JSSc is 8 to 10.5 years, and it is characterized by an insidious course. Diagnosis is often delayed, ranging from 0.7 to 2.8 years, and 20% of patients experience a delay of >2 years [6]. Approximately 70% of patients with JSSc experience Raynaud's phenomenon (RP) as the first symptom; in some cases, RP can precede other manifestations of the disease by several years [7-10].

Currently, there are no established treatment guidelines for JSSc and reliance on research findings in adult patients remains because of insufficient evidence to support immunosuppressive therapy [11,12]. As it is a challenging disease to cure, the goal is to manage symptoms and minimize progression to permanent organ damage.

Here, we aimed to improve our understanding of the clinical features of JSSc in Korean children by conducting a comprehensive analysis of data from pediatric patients treated at a tertiary medical institution in South Korea.

MATERIALS AND METHODS

This retrospective study was conducted at a tertiary care referral center in South Korea. All patients meeting the 2007 PRES/ACR/EULAR provisional classification criteria for JSSc from January 1992 to April 2023 were included. All patients were aged <16 years at the onset of initial symptoms. Patients with localized scleroderma or morphea were excluded.

Electronic medical records were reviewed, and clinical features, including sex, age of onset, initial symptoms, age at diagnosis, type of disease, physical examination findings, laboratory test results, imaging studies, pulmonary function tests (PFTs), electrocardiography, echocardiography, and treatment medications during the course of the disease, were collected and analyzed. The presence of telangiectasia, RP, digital tip ulcers, sclerodactyly, proximal scleroderma, arthritis, and dyspnea was assessed at each follow-up visit from the first visit.

Laboratory data, including total white blood cell count, hemoglobin level, platelet count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), creatine kinase, aldolase, and urine protein/creatinine, were analyzed.

Anti-nuclear antibodies (ANAs) were detected by an indirect immunofluorescence assay using Hep-2 cells as substrates at a dilution of 1:40. An ANA titer of 1:40 for ANA is considered low and may be considered borderline or weakly positive, whereas a titer of 1:80 or higher was generally considered positive. In addition, the presence of autoantibodies was assessed, including anti-Scl-70, anti-RNP, rheumatoid factor (RF) and anti-Ro/La.

Imaging studies, including musculoskeletal magnetic resonance imaging, bone scan, chest computed tomography (CT), and pathology results of skin biopsies, were collected.

A diagnosis of interstitial lung disease (ILD) was made if the forced vital capacity (FVC) was <80% of the predicted value on spirometry or if high-resolution CT (HRCT) showed findings consistent with ILD. Pulmonary arterial hypertension (PAH) was diagnosed based on clinical symptoms and electrocardiographic evidence of right ventricular enlargement. GI involvement was identified by the presence of symptoms suggestive of reflux esophagitis, such as heartburn, regurgitation, or dysphagia. In some cases, patients underwent endoscopy or a video fluoroscopic swallowing study (VFSS) to confirm the presence of GI disease.

Therapeutic medications, such as corticosteroids, immunosuppressants (methotrexate [MTX], mycophenolate mofetil [MMF], and cyclophosphamide [CPM]), and vasodilators (calcium channel blockers [CCB]) were also reviewed. During drug therapy, we assessed the improvement or resolution of the above clinical symptoms, changes in pulmonary function, presence of proteinuria, and abnormalities in cardiac function.

Continuous data were presented as medians (minimum~maximum). Categorical variables were presented as absolute and relative frequencies. This study was approved by the Institutional Review Board (IRB) of the Seoul National University Hospital (IRB no. 2305-125-1434).

RESULTS

Thirteen patients were included in this cohort study; eight were female (61.5%) and six had overlap type SSc (46.2%). All patients fulfilled the provisional classification. Patient charac-

teristics are summarized in Table 1. The mean age of first symptoms onset in overlap type (4.5 years) was younger than diffuse cutaneous type (dcSSc) (12.5 years) and limited cutaneous type (lcSSc) (12.0 years); and the time to diagnosis (1.1 years) was shorter than dcSSc (1.5 years) and lcSSc (2.0 years).

Table 2 presents data on the frequency of clinical features over time. RP was the most common initial symptom in 10 patients (76.9%), followed by proximal skin sclerosis in 5 patients (38.5%) and arthritis in 1 patient (7.7%). At the time of diagnosis, proximal skin sclerosis was present in 100% of patients, as it is included in the diagnostic criteria, RP in 11 (84.6%), sclerodactyly in 9 (69.2%), digital tip ulcer, ILD, and arthritis in 5 (38.5%). Five patients had a mild restrictive pattern of ILD on PFTs or chest CT, of whom three had dyspnea on exertion and one of three had a chronic cough at the time of diagnosis. But the other two had no subjective dyspnea despite abnormal findings. Three patients with normal CT findings had FVC less than 80% on PFT and thus diagnosed with ILD.

In our study population, 2 patients (15.4%) experienced GI problems during disease follow-up. Three of the 13 patients underwent gastroscopy: one for abdominal pain, acidic belching with meals, and epigastric pain, one for dyspepsia and vomiting, and one for evaluation of asymptomatic GI tract invasion. Only one patient was confirmed to have gastroesophageal reflux disease by gastroscopy, and the other two were normal. Another child was asymptomatic but underwent VFSS to evaluate GI tract involvement and showed no evidence of oropharyngeal dysphagia.

Table 1. Demographic data of patients

Patient characteristic	Total (N=13)	Clinical subtypes of systemic sclerosis		
		Overlap (N=6)	DcSSc (N=4)	LcSSc (N=3)
Female	8 (61.5)	2 (33.3)	3 (75.0)	3 (100)
Age of symptom onset (yr)	10.0 (2~13)	4.5 (2~12)	12.5 (4~13)	12.0 (5~13)
Age at diagnosis (yr)	11 (3~16)	7.5 (3~12)	13 (6~15)	15 (7~17)
Duration from symptom onset to diagnosis (yr)	2.0 (0.4~5)	1.1 (0.4~5)	1.5 (0.5~2)	2.0 (2~5)
Total follow-up period (yr)	7.3 (1.2~28.8)	2 (1.8~8.2)	7.3 (1.2~28.8)	14.2 (10.3~18.6)

Values are presented as number (%) or median (range). N: the total number of patients with available data, DcSSc: diffuse cutaneous systemic sclerosis, LcSSc: limited cutaneous systemic sclerosis.

Table 2. Frequency of clinical features at symptom onset, diagnosis, and during follow-up

	Clinical features*	At symptom onset	At diagnosis	Newly developed during the course	Entire period		
					Overlap (N=6)	DcSSc (N=4)	LcSSc (N=3)
Cutaneous	Proximal skin sclerosis	5 (38.5)	13 (100.0)	0 (0)	6	4	3
	Sclerodactyly	0 (0)	9 (69.2)	0 (0)	5	3	1
Peripheral	Raynaud's phenomenon	10 (76.9)	11 (84.6)	0 (0)	5	3	3
	Telangiectasia	0 (0)	2 (15.4)	0 (0)	1	1	0
	Digital tip ulcer	0 (0)	5 (38.5)	2 (15.4)	2	4	1
Cardiac	Arrhythmias	0 (0)	0 (0)	1 (7.7)	0	1	0
Renal	Proteinuria	0 (0)	0 (0)	1 (7.7)	1	0	0
Respiratory	Interstitial lung disease*	0 (0)	5 (38.5)†	2 (15.4)	3	4	0
	Pulmonary arterial hypertension	0 (0)	1 (7.7)	1 (7.7)	1	1	0
Musculo-skeletal	Arthritis	1 (7.7)	5 (38.5)	1 (7.7)	6	0	0
Gastrointestinal	Dysphagia/GERD	0 (0)	0 (0)	2 (15.4)‡	0	2	0

Values are presented as number (%). N: the total number of patients with available data, DcSSc: diffuse cutaneous systemic sclerosis, LcSSc: limited cutaneous systemic sclerosis, GERD: gastroesophageal reflux disease, *Interstitial lung diseases included cases confirmed by chest CT or restrictive pattern findings in pulmonary function tests. †Three patients had dyspnea of exertion, one of whom complained of a chronic cough. The other two patients had no respiratory symptoms. ‡Two patients underwent gastroscopy for periumbilical pain, acid belching with meals, epigastric discomfort, or vomiting, and only one patient had confirmed gastroesophageal reflux disease.

During the follow-up period, one to two patients had new organ involvement for each organ. There were no deaths or neurological involvement in this cohort. The number of patients with each clinical feature by subtype over the entire period is summarized in Table 2.

Among the blood tests, CRP, AST, and ALT levels were measured at diagnosis in all patients (Table 3) and most were within normal limits. ESR was performed at diagnosis in 13 patients and was elevated in 6 patients, with a mean value of 9 mm/h and a range of 2~29 mm/h (normal range: 0~9 mm/h).

As shown in Table 3, several autoantibodies were tested and all 13 children tested positive for ANA. Anti-Scl-70 antibody (ab) (also known as antitopoisomerase 1) was positive in 7 (53.8%) of the 13 patients tested, and anti-RNP Ab was positive in 2 (18.2%) of the 11 patients tested. Autoantibody tests, including RF, anti-cyclic citrullinated peptides (anti-CCP) Ab,

Table 3. Laboratory findings

Result	Patient	Normal range
At diagnosis (chemistry)		
WBC (×10^3/μL)	7.04 (4.7~10.27) (n=13)	4.5~13.0
Hb (g/dL)	12.5 (10.4~14.6) (n=13)	12~16
Platelet (×10^3/μL)	1.95 (0.8~17) (n=12)	130~400
Eosinophil (%)	1.95 (0.8~17) (n=12)	1~5
CRP (mg/dL)	0.03 (0.01~0.58) (n=13)	0~0.5
ESR (mm/h)	9 (2~29) (n=10)	0~9
AST (OT) (IU/L)	21 (15~32) (n=13)	1~40
ALT (PT) (IU/L)	13 (6~31) (n=13)	1~40
CPK (CK) (IU/L)	121 (57~232) (n=5)	20~270
Aldolase (U/L)	9.55 (6.5~20.2) (n=4)	0~7.6
At diagnosis (autoantibodies)		
ANA	13/13 (100)	
SSc-selective autoantibodies		
Scl-70 ab	7/13 (53.8)	
RNP ab	2/11 (18.2)	
Other autoantibodies		
Anti-SSA/Ro ab, Anti-SSB/La ab	1/9 (11.1)	
RF, Anti-CCP, Anti-ds DNA, Anti-Sm ab, Anti-centromere ab, ANCA, ASCA	All negative	
Autoantibody by subtype		
Scl-70 ab		
Overlap	2/6 (33.3)	
Diffuse	3/4 (75.0)	
Limited	2/3 (66.7)	
RNP ab		
Overlap	1/6 (16.7)	
Diffuse	1/3 (33.3)	
Limited	0/2 (0)	
During follow-up (chemistry)		
CPK (CK) (IU/L)	131.5 (63~343)	20~270
Aldolase (U/L)	10.3 (7.1~20.2)	0~7.6

Values are presented as median (minimum~maximum) or n/N (%), where N is the total number of patients with available data. WBC: white blood cell, Hb: Hemoglobin, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, AST: aspartate transaminase, ALT: alanine transferase, CPK: creatine phosphokinase, ANA: anti-nuclear antibody, Scl-70: anti-topoisomerase I, RNP ab: anti-ribonucleoprotein antibody, Anti-SSA: Antibodies against Sjögren's syndrome–related antigen A, Anti-SSB: Antibodies against Sjögren's syndrome–related antigen B, RF: rheumatoid factor, Anti-CCP: anti-cyclic citrullinated peptide, Anti-ds DNA: anti-double stranded deoxyribonucleic acid, Anti-Sm: anti-Smith, ANCA: anti-neutrophil cytoplasmic antibody, ASCA: anti-saccharomyces cerevisiae antibodies.

anti-double stranded DNA (anti-dsDNA) Ab, anti-Smith (anti-Sm) Ab, anti-centromere antibodies (ACA), anti-neutrophil cytoplasmic antibodies (ANCA), and anti-saccharomyces cerevisiae antibodies (ASCA) were performed, but all were negative.

Prednisolone was the most prescribed first-line treatment for JSSc, given to 8 children (61.5%), followed by MTX (n=6, 46.2%). Five patients received MMF as second-line therapy if they did not respond to initial treatment, and two received CPM. Throughout the follow-up period, glucocorticoids (92.3%) were the most prescribed medications, followed by MTX (53.8%). For symptom control, CCBs were prescribed for severe RP in 12 children (92.3%), and 11 patients (84.6%) were treated with proton pump inhibitor or H_2-receptor blockers. The other therapeutic options are listed in Table 4.

DISCUSSION

JSSc is a rare disease worldwide [13]. The annual incidence in the United Kingdom and Ireland is 0.27 per 1,000,000 individuals, whereas the prevalence in the United States is 3 per 1,000,000 individuals [2,3]. Several studies have reported JSSc incidence of 0.3%~2.7% in Japan, and one study reported a prevalence of 9% in patients in a Southeast Asian SSc cohort with JSSc [14,15]. In Asia, there are only a few retrospective cohort studies with a small number of patients, which are insufficient to characterize clinical features of JSSc in Asian populations. This retrospective study was conducted at a pediatric hospital in South Korea. To our knowledge, this is the first single-center comprehensive study to describe JSSc in South Korea.

Large international JSSc cohort studies have shown a female predominance, although not as strong as in adult-onset SSc (aSSc), with a 4:1 female-to-male ratio and a frequency of female participants ranging from 76% to 84% [7,16]; in our study population, girls outnumbered boys by approximately 61.5%. Previously published studies have reported a mean age at onset of 8.1~12 years and a mean time from first symptoms to diagnosis of 1.9~4 years, with this study reporting 10 and 2 years, respectively [7,8,10].

In addition to meeting the classification criteria for systemic sclerosis, similar to aSSc, pediatric patients with JSSc can be further classified into three primary subtypes: dcSSc, lcSSc, and overlap SSc. These subtypes are associated with specific antibodies and share similar manifestations in the skin and organs. DcSSc is characterized by skin thickening beginning in the fingers and toes, rapidly progressing to the proximal skin beyond the elbows and knees; rapid involvement of internal organs, including the lungs, heart, and kidneys; and antibodies such as Scl-70 and RNA. In contrast, lcSSc involves skin changes limited to the distal fingers and toes that do not extend beyond the antecubital or popliteal fossa, slow internal organ involvement such as PAH or malabsorption, and antibodies to anticentromeres and anti-Th/To autoantibodies. Overlap type SSc may have features seen in both dcSSc and lcSSc as well as features of other connective tissue diseases, such as dermatomyositis or systemic lupus erythematosus [5,16]. Most overlaps in the juvenile-onset group exhibited features of polymyositis/dermatomyositis [17]. In this study, overlap type features were also common (6 of 13 [46.2%]), and the most common symptom in children with overlap type features was arthritis. Due to faster disease progression in the dcSSc subtype, lcSSc has been reported to take longer to di-

Table 4. Pharmacological treatment of patients with juvenile systemic sclerosis

Pharmacological treatment	Patient (N=13)
Immunosuppresant or immunomodulator	
1st therapy	
Prednisolone	8 (61.5)
Methotrexate	6 (46.2)
Tranilast	3 (23.1)
Hydroxychloroquine	1 (7.7)
Total period	
Prednisolone	12 (92.3)
Methotrexate	7 (53.8)
Tranilast	4 (30.8)
Hydroxychloroquine	2 (15.4)
Mycophenolate mofetil	6 (46.2)
Cyclophosphamide	2 (15.4)
Tocilizumab	2 (15.4)
Symptomatic medication	
CCB	12 (92.3)
Amlodipine	6 (46.2)
Diltiazem	1 (7.7)
Nifedipine	6 (46.2)
Proton pump inhibitor/H_2-receptor blocker	11 (84.6)
Sarpogrelate/beraprost	5 (38.5)
Celebrex/brexin/naxen	5 (38.5)
Sildenafil/bosentan	3 (23.1)
Enalapril	1 (7.7)

Values are presented as number (%). N: the total number of patients with available data, CCB: calcium channel blocker.

agnose than dcSSc [16]. In our study, patients with lcSSc took approximately 5 months longer to diagnosis than patients with dcSSc, with a median time from first symptom to diagnosis of 1.5 years for the dcSSc and 2 years for the lcSSc.

Pulmonary disease is the most common form of visceral involvement. Pulmonary involvement in JSSc is reported to occur in approximately 35% to 55% of cases and includes ILD and PAH, which can be either primary due to vasculopathy or secondary to ILD [8,10,16]. Approximately one-third of the documented cohort of patients with JSSc is affected by ILD [7,13]. However, diagnosis is challenging in the early stages of ILD because there are no clinical symptoms, and it can only be confirmed by chest imaging or PFT. Therefore, screening for ILD is essential and previous studies have suggested PFT (including DLCO [diffusing capacity of the lungs for carbon monoxide], HRCT, and the 6-minute walk test as methods [11,16]. In our study, 5 patients (38.5%) had ILD confirmed by PFT or chest CT at the time of JSSc diagnosis and an additional 2 patients (15.4%) during follow-up. Three children with ILD at the initial JSSc diagnosis complained of dyspnea on exertion, one of whom also had a chronic cough. The other two patients had no respiratory symptoms. In a recent evaluation of an international pediatric cohort, both PFT and HRCT were performed in 67 patients with JSSc; 33 (49.3%) had evidence of ILD on CT, but 22 (66.7%) had normal PFT results (FVC >80%), suggesting a low sensitivity of PFT in screening for ILD in JSSc [5]. However, in our study, there were three patients with no obvious changes on chest CT but with a restrictive pattern on PFT, and not vice versa. All patients underwent PFT at the age of 6 years or older, and one patient who complained of subjective symptoms also showed a restrictive pattern on PFT but did not show any abnormality on chest CT.

In contrast, PAH is less common in pulmonary disease, occurring in <15% of all JSSc and aSSc cohorts [7,13], and in our study, only two patients (2/13, 15.4%) had PAH: one at diagnosis and one during follow-up.

Cardiac manifestations are the leading cause of mortality in JSSc, although uncommon (approximately 5%~15%) [7,16]. One patient developed arrhythmia during follow-up; however, no life-threatening events were reported.

There are some differences between JSSc and aSSc; for example, musculoskeletal involvement is more common (possibly due to the increased frequency of overlap type SSc) and scleroderma renal crisis is rare in JSSc [10,13,16]. Similar to previous publications, six patients (46.2%) had arthritis during the entire period, no renal crisis was reported, and one patient developed new-onset proteinuria during follow-up.

In previous studies, approximately 90% of patients with JSSc are ANA-positive [16,18], simillarly, 100% were ANA-positive in our study. Specific antibodies, except for ANA, are less common in children than in adults with SSc [13]. Sousa et al. [10] reported that the majority (94%) of patients were ANA-positive, while only 8 of 17 patients (47.1%) had anti-Scl-70 antibodies, and none had ACA antibodies. Similarly, we reported anti-Scl-70 antibody positivity in only 53.8% of patients and no children tested had positive RF, anti-CCP Ab, anti-dsDNA Ab, anti-Sm Ab, ACA, ANCA, and ASCA.

Compared to the adult form, JSSc is generally milder, with less frequent internal organ involvement, especially at the time of diagnosis [7]. However, there are reports of a specific group of patients who present with early and rapidly progressive disease; in these cases, the prognosis is poor, with a higher mortality rate [7,8]. Therefore, treatment guidelines different from those for adults are needed. To date, the treatment of JSSc remains empirical, as no large long-term studies are available. Clearly defined guidelines are lacking; however, recently, a Single Hub and Access point for pediatric Rheumatology in Europe (SHARE) published recommendations for the management of JSSc. Corticosteroid therapy should be initiated at the time of JSSc diagnosis to reduce inflammation, and monitoring for drug side effects (e.g., blood pressure and renal function tests) is necessary. Early initiation of MTX is suggested when there are skin lesions, arthritis, and vascular or GI involvement. If resistance to MTX treatment occurs, consideration should be given to adding or switching to MMF. CPM administration is thought to involve lung and cardiac involvement. Vasodilators are commonly used for RP, and CCBs are the most widely used vasodilators [11,12]. Our patients were treated similarly, mainly with immunosuppressive or immunomodulatory drugs, and their long-term prognosis remains unclear. In general, the long-term outcomes of JSSc are favorable than aSSc, as evidenced by the 10- and 20-year cumulative survival rates of 88% and 84%, respectively, from the initial physician diagnosis [10,13]. Our median follow-up was 7.3 years, and no patients died during the follow-up period.

Throughout the follow-up period, most patients experienced recurrent improvements and flare-ups of skin lesions or other affected organ function and their medications were modified

according to the SHARE recommendations described above. One patient with overlap type SSc, with proximal skin sclerosis, telangiectasia and arthritis, but no RP, improved and discontinued medication. Conversely, one patient with dcSSc, diagnosed at age 12 and treated for 20.8 years, has worsening ILD and is being treated with tocilizumab and considering lung transplantation.

Our study had several limitations. First, this was a retrospective study with a small sample size and was conducted at a single-center in South Korea. As this study was conducted in a tertiary hospital that receives referrals from other medical facilities, patients presented at different stages of the disease, making direct comparisons challenging.

Second, with retrospective nature of this study, analyzing progression in medical records may be inaccurate and information may be missing.

Finally, diagnosis criteria might not have been perfect. This study included patients diagnosed with JSSc according to the provisional classification criteria for JSSc proposed in 2007, which is based on the ACR adult systemic sclerosis criteria established in 1980. However, ACR and EULAR released a new set of adult systemic sclerosis classification criteria in 2013, which included some early disease features that were not previously included [16,19]. Thus, there might have been limitations and errors in diagnosing JSSc based on 2007 provisional criteria for JSSc, especially early in the disease course.

Despite the limitations above, this was the first descriptive analysis of patients with JSSc in South Korea. The findings were mostly consistent with the previous studies.

However, we revealed a discrepancy regarding respiratory involvement of JSSc. Previous studies found out low sensitivity of PFT and early CT changes even if patients are asymptomatic. In contrast, three asymptomatic patients in our study with no obvious changes on chest CT showed a restrictive pattern on PFT and one patient who complained of subjective respiratory symptoms also showed a restrictive pattern on PFT but did not show any abnormality on chest CT. Further studies are needed to discover whether this discrepancy is due to bias regarding small, single center nature of this study or distinct characteristics of South Korean population.

CONCLUSION

In the early phase of JSSc, diagnosis is difficult because of the insidious and subtle onset of skin changes. In our study population, proximal skin sclerosis, which is crucial for the diagnosis of JSSc, was not observed in the early phases of the disease. Considering the importance of timely diagnosis and treatment in the early phases of the disease, clinical suspicion is essential for the diagnosis of JSSc with RP, particularly when ANA are positive. Since all autoantibodies other than ANA were negative in 38% of the patients, JSSc cannot be excluded even if all autoantibodies other than ANA are normal in children with RP, and careful physical examination is required. PFT should be performed at the time of diagnosis, even if patients are asymptomatic or have normal chest CT findings. Since 43% of patients in our population had a restrictive pattern on PFT suggestive of ILD in the absence of symptoms or abnormal chest CT findings, PFT should be performed at the time of diagnosis.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

AUTHOR CONTRIBUTIONS

J.E.J. and S.H.K. designed the study, contributed to data acquisition and analysis, and drafted the manuscript. All the authors approved the final manuscript.

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