

## Clinical Study

# Esophageal Involvement in Scleroderma: Clinical, Endoscopic, and Manometric Features

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*Aim.* To evaluate characteristics of esophageal involvement in scleroderma. *Methods.* The study was prospective and concerned 194 patients with a definite systemic sclerosis. Gastroesophageal endoscopy and esophageal manometry were performed in all the cases. *Results.* Symptoms were present in 118 cases (60.8%); they were signs of GERD or dysphagia, respectively, in 94 (48.4%) and 91 patients (46.9%). Reflux esophagitis was found in 73 cases (37.6%); it was mild or moderate in 47 cases (24.2%) and severe or complicated in the remaining cases. Manometry revealed a lower esophageal sphincter incompetence and esophageal motor disorders, respectively, in 118 (60.8%) and 157 cases (80.9%). Presence of these late was not related to age, duration, or skin extension of the disease, but with clinical complaint and/or mucosal damage. *Conclusion.* Esophageal involvement is frequent during scleroderma. Manometry is the most sensible examination and could be a screening procedure.

## 1. Introduction

Involvement of esophagus is common in systemic sclerosis (SSc) [1, 2]. It consists mainly of esophageal motor disorders (EMDs) that are responsible for all clinical manifestations as well as gastroesophageal reflux disease (GERD) and its complications [2–4]. The factors which affect occurrence of esophageal involvement in SSc are discussed [5–7].

## 2. Aim

The aim of this study was to evaluate clinical, endoscopic, and manometric features of esophageal involvement in patients with scleroderma through a large cohort of patients with SSc.

## 3. Patients and Methods

The recruitment was prospective, at a single center, and concerned 194 consecutive patients with SSc diagnosed according to the American College of Rheumatology criteria [8], over a period of 20 years (April 1988–December 2008). Mixed connective tissue disease and forms associated with diabetes mellitus were excluded.

The patient's mean age was  $40.4 \pm 13.5$  years (11–73 years), gender was female in 170 cases (87.6%), and average duration of the disease was  $6.8 \pm 7.5$  years (6 months–32 years). According to LeRoy's classification of generalized scleroderma [9], a limited cutaneous form was observed in 158 cases (81.4%) and a diffuse form in 36 cases (18.5%).

All the patients underwent a standardized medical card, an upper gastrointestinal endoscopy, and a standard esophageal manometry during the same visit, before initiating any antisecretory treatment.

Data collected included patient's age, gender, clinical characteristic of the disease (duration, skin extension), and presence or absence of symptoms of GERD (heartburn and/or acid regurgitation) and/or dysphagia. Each symptom was graded on a scale from 0 to 3 by intensity (0 = absent, 1 = mild, could be ignored by the patient, 2 = moderate, could not be ignored, but had no effect on daily life activities, 3 = severe or incapacitating, affecting daily life activities) and by frequency (0 = absent or less than one per month; 1 = less than 1 per week; 2 = several times per week; 3 = every day) [10]. Symptoms were then categorized as mild for a total score less than, or equal to six, moderate for a total score of seven to twelve and severe for a total score greater than

TABLE 1: Factors linked with the presence or absence of esophageal symptoms.

	Esophageal symptoms		P
	Presence (n = 118)	Absence (n = 76)	
Limited/diffuse form	91/27	67/9	0.05
Duration of the disease (years)	7.2 ± 7	5 ± 7.8	0.22
Reflux esophagitis	60 (50.8%)	13 (17.1%)	<0.001
EMDs	109 (92.3%)	48 (63.1%)	<0.001

EMDs: esophageal motor disorders.

TABLE 2: Factors linked with presence or not of reflux esophagitis.

	Reflux esophagitis		P
	Presence (n = 73)	Absence (n = 121)	
Limited /diffuse form	58/15	100/21	0.57
Duration of the disease (years)	6.9 ± 6.9	6.6 ± 7.6	0.57
Esophageal symptoms	60 (82.2%)	58 (47.9%)	<0.001
EMDs	70 (95.9%)	87 (71.9%)	<0.001

EMDs: esophageal motor disorders.

twelve, or when one symptom was considered incapacitating every day (score = 9).

Upper gastrointestinal endoscopy was used to identify and stage reflux esophagitis according to the Los Angeles classification [11]. Manometry was performed with a four-channel infusion probe (distilled water infusion rate: 0.5 mL/mm). The procedure was used after discontinuation of medication that might affect esophageal motility at least 72 h before exam and following a 12-hour fast. Normal manometric values were established in our laboratory using a control population of 24 healthy subjects matched for age and gender (gender ratio of 0.2, mean age of 41.7 ± 10.7 years, age range: 29–60 years).

Student's *t*-test,  $\chi^2$ , and a reduced standard deviation (SD) test were used as appropriate to compare means and percentages. The level of significance was  $P < 0.05$ .

#### 4. Results

Esophageal symptoms were found in 118 patients (60.8%) with GERD symptoms observed in 94 cases (48.4%) and dysphagia in 91 cases (46.9%). Both type of symptoms were present in 67 cases (34.5%). The clinical complaint was considered mild in 74 cases (38.1%), moderate in 27 cases (13.9%), and severe in 17 cases (8.7%).

Reflux esophagitis was found in 73 cases (37.6%). It was mild or moderate (stage A or B LA) in 47 cases (24.2%), severe (stage C or D LA) in 7 cases (3.6%), and complicated by stenosis and/or Barrett esophagus in 19 cases (9.8%). No case of esophageal ulcer or adenocarcinoma was observed.

Manometry was disrupted in 167 cases (86%). There was a hypotensive lower esophageal sphincter (LES) pressure in 118 patients (60.8%) and EMDs in 157 cases (80.9%); both disorders were present in 108 cases (55.6%). A hypotensive upper esophageal sphincter pressure was present in 14 patients (7.2%). EMDs were severe, of aperistalsis type,

in 118 cases (60.8%), and a low pressure wave amplitude was observed in 36 cases (18.5%) and an uncoordinated peristalsis in 25 cases (12.9%). EMDs were extended to lower two-thirds of the esophagus in 137 cases (70.6%).

Presence of esophageal symptoms was not related with duration of the SSc, but it was significantly more frequent in diffuse form of the disease and in those with esophageal mucosal lesions and/or EMDs (Table 1).

Presence of reflux esophagitis was not linked with subtype or duration of the disease, but it was statistically more frequent in the symptomatic population and was also more observed in forms with EMDs. Nevertheless, it remained silent in 13 cases (17.8%) (Table 2).

EMDs were common in all forms of the disease, regardless of age, gender, degree of skin involvement, or duration of the disease. However, they were significantly more often present in cases with clinical complaints and/or reflux esophagitis, but they remained asymptomatic in 48 cases (30.5%) (Table 3).

#### 5. Discussion

Overall incidence of esophageal symptoms during SSc has been estimated to be between 42% and 79% [2, 3, 12–16]. The complaint is related to signs of reflux in 14–71% of patients and dysphagia in 24–82% of cases [2, 5, 15, 17, 18], both symptoms being present in 29%–66% of cases [15, 19]. In our series, overall incidence of symptoms was 61%, signs of reflux and dysphagia were, respectively, near 48% and 47%; both were present in more than 34% of cases. Presence of esophageal complaint was not related to the duration of the disease in the literature [5, 7] and in this work. Their relationship with the subtype of SSc is more controversial. Thus, for Akesson and Wollheim [5], Koshino et al. [6], and Bassotti et al. [17], presence of symptoms was not related to the subtype of SSc, but in our series, they were significantly

TABLE 3: Parameters linked with presence or not of EMDs.

	Esophageal motor disorders		P
	Presence (n = 157)	Absence (n = 37)	
Mean age (years)	40.7 ± 13.5	39.4 ± 13.5	0.59
Male/female	18/139	6/31	0.6
Limited/diffuse form	125/32	33/4	0.17
Duration of the disease (years)	6.8 ± 7.2	6.2 ± 7.9	0.65
Esophageal symptoms	109 (69.4%)	9 (24.3%)	<0.001
Reflux esophagitis	70 (44.6%)	3 (8%)	<0.001

more frequent in diffuse form of the disease. Esophageal complaint was also more frequent and more severe in case of presence of reflux esophagitis in our experience as well as in literature [15, 20].

Even if, for most authors, there is no correlation between presence of esophageal symptoms and presence of EMDs [13, 21], a link was, however, established between their severity and presence of EMDs [6, 7, 22]. In this study, symptoms were significantly more frequent in presence of esophageal dysmotility and are, therefore, a simple warning sign that should prompt search of EMDs by manometry.

Prevalence of reflux esophagitis has averaged between 30% and 40%. In fact, it is variously reported between 3.2% and 60% [15, 16, 18, 20, 23, 24]. The highest rates were reported by Zamost et al. [20] and Hendel [23] and are probably due to the fact that these patients on a large catch of anti-inflammatory drugs. The lowest, prevalence (3.2%), reported by Poirier in a surgical series concerned forms complicated by stenosis [13]. In an autopsy series of 58 patients with SSc, D'Angelo found erosive esophagitis in 40% of cases [25].

Complicated forms of reflux esophagitis were also more frequent in patients with SSc than in the general population [18]. Reflux esophageal stenosis is reported in 3–40% of cases depending on the series [13, 15, 26–28], while Barrett esophagus in 6.8–37% [13, 15, 26–28] or even 71% of cases [29] and, more rarely, ulcer of esophagus [16]. Adenocarcinoma of esophagus would be also more frequent in SSc, its rate reaches 7% for Katzka et al. [26] and Recht et al. [30] but, Segel relates only one case in a large series of 680 patients with SSc followed for 11 years [31]. In our series, reflux esophagitis was observed in nearly 38% of cases and was complicated by stenosis and/or Barrett esophagus in 10% of cases.

Esophageal dysmotility of SSc is characterized by a LES hypotonia and EMDs respecting the cervical segment of esophagus. In the recent series, overall frequency of manometric abnormalities is very high, 70%–96% [16, 19, 31–34]. LES hypotonia is present in more than 50% of cases and is, in general, associated with EMDs. These latter are noted in more than 60% of cases. There is a low pressure wave amplitude in 48%–81% of cases [1, 18], an uncoordinated peristalsis in 40%–91% [18, 34, 35], and an aperistalsis in 23%–52% [18, 32, 33] of patients.

Relationship between presence of EMDS and subtype of SSc is controversial. For some authors, there is no parallelism

between frequency or severity of EMDs and subtype of SSc [2, 32, 36–38]. For others, they would be more severe in diffuse form of scleroderma [5, 6, 39], yet in other works, EMDs are both more frequent and more severe in the diffuse SSc [14, 16, 17, 34]. In our series, degree of skin involvement did not significantly influence frequency or severity of manometric disorders.

Moment occurrence of EMDs would be very early. Indeed, they occur within one year after diagnosis of the disease in the work of Hostein et al. [21] and Hamel-Roy et al. [40], even at the stage of isolated Raynaud's phenomenon, before the onset of skin involvement [21, 38]. The subsequent evolution is more controversial. Frequency and severity of the disorder increase with disease duration [23, 32] for some authors, rather not for others [16, 19].

For most authors, presence of esophageal symptoms is not a good indicator of those of EMDs [2, 6, 14, 20, 35, 41]. Thus, in Lock's series, 25% of EMDs remained asymptomatic, and, conversely, 50% of symptomatic patients had a normal manometry [2]. The existence of symptoms had a negative predictive value of 50% and a positive predictive value of 62%. For this author, this means a weak association and justifies manometry in the assessment of any SSc. In other series, severe EMDs remained asymptomatic in 21%–40% of cases and the presence of symptomatic patients with normal manometry is also often reported [15, 17, 39]. For Sjögren, this discrepancy may be related to the existence of visceral autonomic neuropathy [4]. However, there seems to be a link between severity of symptoms and existence of esophageal dysmotility [6, 7, 41]. In our experience, although manometry was significantly more often and more severely impaired in patients with esophageal complaint, EMDS remained asymptomatic in 48 cases (30.5%).

EMDS are also a major predictor factor of occurrence of reflux esophagitis [4, 16, 17, 24, 37]. Peristalsis is never or rarely normal in this case as well for us than in published series [15, 20].

## 6. Conclusion

Esophagus involvement is very frequent during scleroderma. It occurs early and comprises a reflux esophagitis in more than one third of cases. Esophageal manometry is useful in all forms of the disease, more particularly in asymptomatic population and without endoscopic lesions. At an early stage, it allows detection of EMDs which are a strong marker of

the disease and at definite form of the disease, and it assesses risk of occurrence of reflux esophagitis. Then, manometry could be a screening procedure in scleroderma.

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