ARTICLE ORIGINAL

Esophageal motor abnormalities on high-resolution manometry in patients with scleroderma

Troubles moteurs œsophagiens à la manométrie à haute résolution chez les patients ayant une sclérodermie

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RÉSUMÉ

Introduction: La sclérodermie systémique (SS) est une maladie auto-immune qui peut entrainer des troubles moteurs œsophagiens. Les anomalies manométriques typiques incluent l'hypotonie du sphincter inférieur de l'œsophage (SIO), l'absence de contractilité et la motricité œsophagienne inefficace.

Objectifs: Les objectifs de l'étude étaient d'identifier les anomalies de la motricité œsophagienne chez les patients ayant une SS en utilisant la manométrie à haute résolution et de déterminer les facteurs cliniques et endoscopiques associés à ces troubles moteurs.

Méthodes : Les patients suivis pour SS ayant bénéficié d'une manométrie œsophagienne à haute résolution entre décembre 2016 et Aout 2020 ont été inclus à l'étude. Les données démographiques ainsi que la fréquence des symptômes ont été obtenues à travers un questionnaire. Les troubles moteurs œsophagiens ont été identifiés selon la classification de Chicago v3.0.

Résultats : Un total de 49 patients a été inclus à l'étude. L'âge médian était de 56 ±13,4 ans. A la manométrie à haute résolution, l'absence de contractilité (n= 24 ; 49%) et la motricité œsophagienne inefficace (n=14 ; 28,6%) étaient les troubles moteurs les plus fréquents. Un cas d'obstruction de la jonction oeso-gastrique (OJG) a été observé chez une patiente. Une hypotonie du SIO a été notée chez 18 patients (36,7%). L'absence de contractilité était associée à la présence de régurgitations (p=0,013) et d'œsophagite érosive (p=0,003).

Conclusion : L'absence de contractilité et la motricité œsophagienne inefficace étaient les troubles moteurs œsophagiens les plus fréquents. Les patients ayant une absence de contractilité présentent plus fréquemment des régurgitations et avaient plus souvent une œsophagite érosive.

Mots-clés : troubles moteurs œsophagiens ; maladies auto-immunes ; sphincter œsophagien ; pyrosis ; œsophagite

SUMMARY

Background: Systemic sclerosis (SS) is an autoimmune disorder that may result in diverse esophageal motor disorders. Typical manometric disorders include decreased lower esophageal sphincter (LES) pressure, absent contractility and ineffective peristalsis.

Aims: The aims of the study were to assess esophageal motor abnormalities in SS patients using high resolution manometry and to evaluate clinical and endoscopic features that are associated with manometric findings.

Methods: Patients with SS who underwent esophageal high-resolution manometry (HRM) between December 2016 and August 2020 were enrolled in the study. Data regarding demographics and symptom frequency were obtained through a questionnaire. Chicago classification criteria (V3.0.) were used for defining esophageal dysmotility.

Results: A total of 49 patients were enrolled in the study. Median age was 56 ±13.4 years. High-resolution manometry showed that absent contractility (n= 24; 49%) and ineffective motility (n=14; 28.6%) were the most frequent motor abnormalities. One case of esophageal gastric junction (EGJ) outflow obstruction was observed in a female patient. A hypotensive LES was observed in 18 patients (36.7%). Absent contractility was associated with regurgitations (=0.013), and erosive esophagitis (p=0.003).

Conclusion: Absent contractility and ineffective motility were the most common esophageal contractile patterns among our patients. Patients with absent contractility experienced more frequently regurgitations and had more often erosive esophagitis.

Key-words: Esophageal Motility Disorders; Autoimmune Diseases; Esophageal Sphincter; Heartburn; Esophagitis

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INTRODUCTION

Systemic sclerosis (SS) (scleroderma) is a rare chronic autoimmune multisystem disease characterized by skin thickening and vascular abnormalities (1). Gastrointestinal (GI) involvement is the third most frequent manifestation of SS behind skin changes and Raynaud's phenomenon and occurs in up to 90% of patients (2). Although the entire GI tract may be affected, the esophageal involvement concerns almost 70% of SS patients. Symptoms may include heartburn, dysphagia, atypical chest pain, nausea, vomiting, and regurgitations (3). The mechanism by which SS affects the GI tract is not completely understood but initial vascular damage with subsequent collagen deposition resulting in thickening and fibrosis in the GI smooth muscle has been suggested (4). Esophageal muscle dysfunction may also result from neuronal degeneration leading to smooth muscle atrophy and loss of motor function mainly in the distal esophageal body (5). Until recently, classic manometry has been the gold standard method for the diagnosis of esophageal dysmotility. The typical manometric disorders include decreased lower esophageal sphincter (LES) pressure and absent contractility or ineffective peristalsis of the distal esophagus (6). With the advent of high-resolution manometry and esophageal pressure topography, this method has been preferred for the study of esophageal dysmotility in SS patients. The aims of the study were to assess esophageal motor abnormalities in SS patients using HRM and to evaluate the associations between clinical and endoscopic features of GI involvement and HRM patterns in such patients.

METHODS

The study was performed in accordance with the Declaration of Helsinki of the World Medical Association and was approved by the local ethics committee. All patients gave their informed consent prior to inclusion in the study.

Patients :

Patients with SS referred from Internal Medicine and Rheumatology departments for esophageal manometry between December 2016 and August 2020 were enrolled in the study. The diagnosis of SS was based on criteria from American College of Rheumatology (7). Patients were asked to complete a standardized demographic and symptom questionnaire prior to esophageal manometry to characterize the frequency of symptoms. Prior to esophageal manometry, all patients underwent upper gastrointestinal endoscopy to rule out contraindications to manometry including upper esophageal obstruction or to search for causes for their symptoms such as peptic esophagitis or hiatal hernia (8).

High-resolution manometry:

HRM was completed after an overnight fast using a solid-state system (MMS, Medical Measurement Systems, The Netherlands) with 36 circumferential sensors at 1 cm intervals. After calibration at 0 mmHg using externally applied pressure, the esophageal manometry assembly was passed trans-nasally under topical anesthesia and placed in the site that allowed to identify areas of both sphincters with approximately 3 intragastric sensors. Thereafter, the patients were placed in the supine position and were asked to swallow 5 mL of water 10 times at intervals of 20-30 seconds. Dedicated software (MMS, Medical Measurement Systems, The Netherlands) was used to interpret HRM studies.

Basal upper gastro-esophageal sphincter (UES) and lower esophageal sphincter (LES) pressures were recorded for 1 minute at the beginning of the exam.

The normal values of UES were: min: 33 mmHg; max: 180 mmHg and of LES were: min: 10 mmHg; max: 45 mmHg according to the software used.

The integrated relaxation pressure (IRP), distal contractile integral (DCI), and distal latency (DL) were calculated. A defective LES relaxation was defined by an IRP >21 mmHg. Motility disorders were defined according to Chicago Classification v 3.0(9).

Statistical analysis:

Statistical Package for Social Science (SPSS) software version 21.0 (IBM Corp., Armonk. New York, USA) was used for analysis of data. Data were summarized as mean and percentage. Categorical variables were compared using Fisher's exact tests and continuous variables were compared using Mann-Whitney test. Odds Ratios (OR) and 95% confidence intervals (CIs) were calculated.

A Spearman's correlation coefficient was calculated to investigate correlation between continuous variables. A $p < 0.05$ was considered .statistically significant.

RESULTS

A total of 49 patients were enrolled in the study. The patient group was primarily female (n= 44; 89.8%) with median age of 56 ±13.4 years. Dysphagia and heartburn were the leading causes of referral (n=27; 55.1%). Upper endoscopy was normal in almost half of the patients (n=26; 53 %) (Table 1).

Table 1. Demographics, symptoms and endoscopic findings of patient population

	N= 49
Demographics	
Age (years)	56 ±13.4
Female (%)	44(89.8)
Symptoms	
No symptoms (%)	9 (18.4)
Dysphagia (%)	27 (55.1)
Heartburn (%)	27 (55.1)
Regurgitations (%)	11 (22.4)
Chest pain (%)	1 (2)
Coughing (%)	1 (2)
ENT symptoms (%)	12 (24.5)
Endoscopy	
No anomalies (%)	32 (65.3)
Erosive esophagitis (%)	13 (26.5)
Hiatal hernia (%)	4 (8.2)

For age, data are expressed as median ± standard deviation
For sex, symptoms and endoscopy, data are expressed as number of cases (%).
ENT, ear, nose, throat;

HRM showed that absent contractility (n= 24; 49%) (Figure 1) was the most frequent motor abnormality, followed by ineffective motility (n=14; 28.6%) (Figure 2). The median basal LES pressure was 13 ±13 mmHg. A hypotensive LES was observed in 18 patients (36.7%) in which HRM revealed absent contractility (n=12; 66.7%), ineffective motility (n=4; 22.2%), fragmented peristalsis (n=1; 5.6%) and no motility disorders (n=1; 5.6%). The median basal UES pressure was 96 ± 62.4 mmHg. Most of patients had normotensive UES (n= 38; 77.6%) (Table 2).

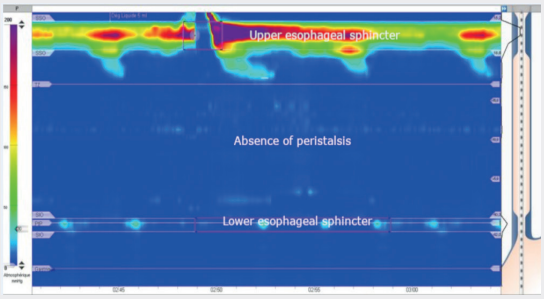

Figure 1. Absent contractility
Absent peristalsis with normal integrated relaxation pressure (IRP) (8.2 mmHg).

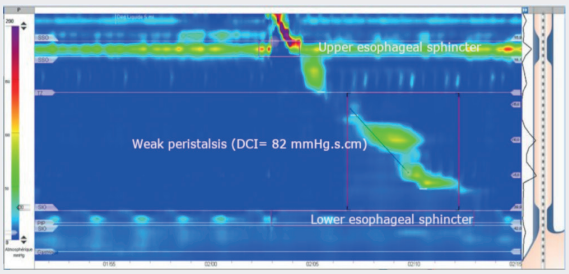

Figure 2. Ineffective motility
Weak peristalsis (DCI < 100 mm Hg.s.cm) with normal integrated relaxation pressure (IRP) (9 mmHg).
DCI: distal contractile integral

Table 2. Manometric features and esophageal motility abnormalities

Parameter	
UES resting pressure (mmHg)	96 ± 62.5
LES resting pressure (mmHg)	13 ± 13
Distal Contractile Integrale (mmHg·s·cm)	194 ±611.4
Hypotensive UES (%)	4 (8.2)
Hypertensive UES (%)	7 (14.3)
Hypotensive LES (%)	18 (36.7)
Hypertensive LES (%)	2 (4.1)
Absent contractility (%)	24 (49)
Ineffective motility (%)	14 (28.6)
Fragmented peristalsis (%)	1 (2)
Achalasia (%)	0 (0)
EGJ outflow obstruction (%)	1 (2)
Normal motility (%)	9 (18.4)

Data are expressed as median ± standard deviation or the number of cases (%).
UES, upper esophageal sphincter; LES, lower esophageal sphincter; EGJ,

esophageal gastric junction.

One case of esophageal gastric junction (EGJ) outflow obstruction was observed in a 57-year-old female patient (Figure 3). She had heartburn for which she started on proton pump inhibitors (PPIs) with partial symptom relief. Shortly thereafter, she started having dysphagia. Upper endoscopy was normal. HRM showed an elevated median IRP (22 mmHg) and a preserved esophageal body peristalsis in 100% of swallows. Median DCI was 2108 mmHg and median LES resting pressure was 55.8 mmHg.

Demographic, clinical and endoscopic findings were compared between patients with and without absent contractility. This manometric pattern was associated with regurgitations (p=0.013), and erosive esophagitis (p=0.003) (Table 3). There was no association between ineffective motility and demographic, clinical and endoscopic features. All asymptomatic patients (n=9) had motor abnormalities: ineffective motility (n=4), absent contractility (n=4) and fragmented peristalsis (n=1).

Table 3. Factors associated with absent contractility

	Absent contractility		P value
	Yes (N=24)	No (N=25)	
Female sex (%)	50	50	1.000
Age, median (years)	51.2	55.4	0.332
Dysphagia (%)	55.6	44.4	0.308
Heartburn (%)	48.1	51.9	0.897
Regurgitations (%)	81.8	18.2	0.013*
Coughing (%)	100	0	0.490
ENT symptoms (%)	41.7	58.3	0.560
Erosive esophagitis (%)	90	10	0.003*
Hiatal hernia (%)	66.7	33.3	0.595

Data are expressed as median ±standard deviation or number of cases (%)
ENT, ear, nose throat;
*p<0.05

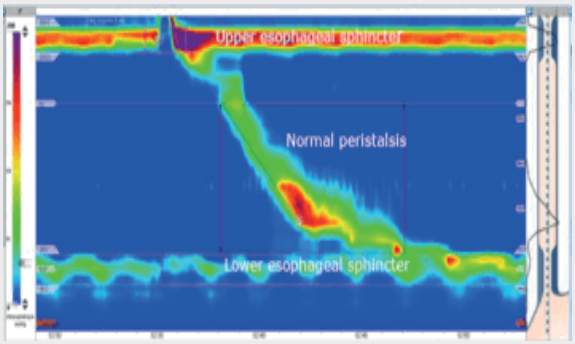

Figure 3. Esophageal gastric junction outflow obstruction

Synchronous peristaltic waves following a wet swallow with defective LES relaxation (integrated relaxation pressure (IRP) = 23 mmHg)

DISCUSSION

The current study showed that absent contractility and ineffective motility are the major dysmotility patterns in patients with SS. Absent contractility was significantly more common among patients with regurgitations and/or erosive esophagitis. One of the main strengths of this study is the use of Chicago classification (V3.0.) which is the latest classification system of esophageal motor disorders. Another strength point is that our study is the first at the national level to assess esophageal motor abnormalities using high resolution manometry. However, the main limitation of our study is the small population size which could be explained by the relatively recent introduction of this new technique (HRM) in our department.

As it has been previously mentioned, the relation between esophageal dysmotility and scleroderma is well established. In our study, motility disorders according to Chicago classification were noted in 81.6% of SS patients. The most frequent manometric alterations were absent contractility (49%) and ineffective motility (28.6%). Hypotensive LES was found in 36.7% of patients. Our study corroborates previous research showing that esophageal dysmotility in SS ranges from 53% to 90% and hypotensive LES and failed or weak peristalsis are the most common dysmotility patterns in such patients (6, 10-12). Other manometric abnormalities have been rarely reported in SS patients such as achalasia, esophagogastric junction (EGJ) outflow obstruction, hypercontractile esophagus

and distal esophageal spasm (11, 13). In our series, only esophagogastric junction (EGJ) outflow obstruction has been described in one patient. It is uncertain whether these rare abnormalities are due to SS or independent pathological mechanism.

It is worth mentioning that major previous studies on motility disorders in SS patients have been based on conventional manometry. Although HRM offers much improved spatial resolution than conventional manometry, the most frequent motility disorders detected by both techniques are roughly the same including aperistalsis, hypocontractility and hypotensive LES (13, 14). Nevertheless, thanks to standardized metrics of esophageal motility offered by HRM, new dysmotility patterns have emerged such as fragmented peristalsis or esophagogastric junction (EGJ) outflow obstruction which have been observed in 4% of our patients.

As far as consequences of motility disorders in SS patients, the resulting of decreased LES pressure and esophageal body hypomotility leads to gastroesophageal reflux disease (GERD) and its complications such as erosive esophagitis (15). In fact, in the current study, SS patients with absent contractility reported more frequently regurgitations (p=0.013) than patients without absent contractility. Moreover, erosive esophagitis (p=0.003) was more commonly encountered in patients with absent contractility than other patients. However, other symptoms such as heartburn, dysphagia and chest pain were not significantly associated with motility disorders in our patients. Our findings are in accordance with previous studies showing that usually esophageal symptoms are not predictive of motility disorders in SS patients since there is commonly a dissociation between symptoms and HRM findings (16, 17). Indeed, it has been shown that nearly 20- 40% of SS patients do not report symptoms despite known esophageal dysmotility (18). One explanation for this dissociation is that symptoms such as heartburn and dysphagia may be influenced by other factors such as therapeutic anti-reflux medications or other gastro-intestinal illnesses.

In the current study, Ear-Nose-Throat (ENT) symptoms were reported in 12 patients (24.5%) and coughing in one patient (2%). These symptoms may be due to GERD and had to be proven by 24h esophageal pH-metry. In such patients, failed or weak peristalsis may be associated with delayed esophageal acid clearance resulting in ENT or respiratory symptoms (19).

In conclusion, absent contractility and ineffective motility were the most common distal esophageal contractile patterns among our patients. Patients with absent contractility experienced more frequently regurgitations and had more often erosive esophagitis. There was a poor correlation between symptoms and motility patterns which could probably be explained by co-illnesses. Future studies with larger population size are needed to investigate symptoms and dysmotility patterns according to phenotypic findings in SS patients such as cutaneous manifestations, Raynaud's phenomenon and pulmonary fibrosis which could explain symptoms such as coughing or ENT symptoms.

***Les auteurs déclarent ne pas avoir de liens d'intérêts*.**

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