Videofluorography swallow study in patients with systemic sclerosis: correlation with clinical and radiological features

P. Fraticelli[1], A.M. Pisani[2], D. Benfaremo[3], L. De Marino[4], D. Campioni[4], N. Carboni[4], C. Fischetti[3], L. Manfredi[1], A. Gabrielli[1,3], A. Giovagnoni[2,4]

[1]Clinica Medica, Dipartimento di Medicina Interna, and [2]SOD Radiologia Pediatrica e Specialistica, Dipartimento di Scienze Radiologiche, AOU Ospedali Riuniti di Ancona; [3]Dipartimento di Scienze Cliniche e Molecolari, and [4]Dipartimento di Scienze Cliniche e Specialistiche, Università Politecnica delle Marche, Ancona, Italy.

*Paolo Fraticelli, MD**
*Anna M. Pisani, MD**
Devis Benfaremo, MD
Luigi De Marino, MD
Daniele Campioni, MD
Nicola Carboni, MD
Colomba Fischetti, MD
Lucia Manfredi, MD
*Armando Gabrielli, MD***
*Andrea Giovagnoni, MD***

**These authors share first authorship;*
**These authors share senior authorship.*

Please address correspondence to:
Prof. Armando Gabrielli,
Clinica Medica, Dipartimento di Scienze Cliniche e Molecolari, Università Politecnica delle Marche, Via Tronto 10/A, 60126 Ancona, Italy.
E-mail: a.gabrielli@staff.univpm.it

Received on July 10, 2019; accepted in revised form on September 12, 2019.

Clin Exp Rheumatol 2019; 37 (Suppl. 119): S108-S114.

Key words: systemic sclerosis, cineradiography, oesophageal motility disorders, deglutition disorders

Competing interests: none declared.

ABSTRACT

Objective. *The aim of our study was to assess the role of videofluorography (VFG) in the evaluation of swallowing and oesophageal peristalsis in patients with systemic sclerosis (SSc).*

Methods. *From June 2014 to September 2017, 55 consecutive SSc patients, defined according to the 2013 ACR/EULAR classification criteria, underwent VFG study using a remote-controlled digital device. In order to evaluate possible abnormalities, 18 dynamic parameters were chosen, dividing the act of swallowing into three phases: oral, pharyngeal and oesophageal phases. The following dynamic radiological findings were considered: veil motility in phonation, leakage, drooling, salivation and presence of residues in the oral cavity, pharyngeal residues, penetration, aspiration, altered motility of the upper oesophageal sphincter, efficacy of primary peristaltic contractions, oesophageal clearance capacity, reflux, oesophagitis and motility of the lower oesophageal sphincter.*

Results. *The VFG study was well tolerated in all patients. Dysfunctions of oesophageal motility were common and included abnormal motility of UES (12.7%) and LES (76.4%), inadequate primary peristalsis (52.7%), abnormal secondary peristalsis (29.1%) and non-peristaltic contractions (40%). A defective oesophageal clearance was observed in 69.4% of patients. Moreover, most patients presented signs of oesophageal reflux (63.6%), oesophagitis (81.8%) and hiatal hernia (80%). Pharyngeal abnormalities were less common and involved up to 50% of patients. Oesophageal dysfunction and defective clearance were associated with dcSSc and pulmonary involvement.*

Conclusion. *The VFG study is a useful technique for the morphological and functional evaluation of swallowing in SSc patients.*

Introduction

Systemic sclerosis (SSc) is an autoimmune disorder characterised by vasculopathy, immunologic dysregulation, excessive collagen deposition with progressive fibrosis involving the skin as well as several internal organs (1).

The gastrointestinal (GI) tract is the second most common organ system involved in SSc (2, 3). Common GI symptoms in SSc patients include oesophageal reflux, dysphagia, constipation, abdominal pain, diarrhoea, foecal incontinence, and weight loss (4).

Motility disorders resulting from atrophy and fibrosis of smooth muscle are highly prevalent in SSc. The oesophagus is involved in 75–90% of cases (5), especially in the middle and distal tract. Motor dysfunctions lie at the basis of the manometric variations of the lower oesophageal sphincter (LES) with consequent onset of gastro-oesophageal reflux disease (GERD) and irritation of the oesophageal mucosa, producing a triad of symptoms typically characterised by dysphagia, usually for solid foods, dyspepsia and retrosternal pyrosis (50–90% of cases) (6).

Although oesophageal manometry, endoscopy and pH monitoring are considered the reference methods to identify motility abnormalities, GERD and mucosal lesions (5), some studies failed to show a direct correlation between the clinical symptoms and the alterations detected by these techniques (5). Moreover, none of these methods is able to provide direct information regarding the oral and pharyngeal phases of swallowing.

Videofluorography (VFG) is the reference examination for the morphodynamical study of swallowing and is also a reliable technique for identifying oesophageal motor alterations, GERD and hiatus hernia (7-9).

The aim of our study was to assess the role of VFG in the evaluation of swal-

lowing and oesophageal peristalsis in patients with SSc.

Materials and methods

Study population

From June 2014 to September 2017, 55 consecutive SSc patients, defined according to the 2013 ACR/EULAR classification criteria (10), were enrolled in the study. Subjects were further classified as limited or diffuse cutaneous involvement (lcSSc and dcSSc, respectively), according to modified LeRoy criteria (11). Duration of disease, the presence of autoantibodies, gastrointestinal symptoms, the presence of SSc-related interstitial lung disease (SSc-ILD) and oesophageal dilatation on chest CT were also recorded for all patients.

Gastrointestinal symptoms (retrosternal pain and dysphagia) were assessed as either present or absent.

Computed tomography

All patients underwent chest CT scan (CT Light Speed VCT 64 multislices, GE®), using high-resolution (HRCT) protocol (1,25 mm slice thickness, gap 7 mm, level 600 to 700 HU, width 1000–1500 HU) for the evaluation of SSc-ILD (12) and volumetric acquisition (2,5 mm slice thickness, gap 2,5 mm, level 20–50 HU, width 300–500 HU) to evaluate oesophageal coronal diameter (considering internal limits of inner oesophageal mucosa) and thickness at three points: at the level of carina, below aortic arch at the pulmonary venous confluence and at 1 cm above the right dome of diaphragm (13).

SSc-ILD and oesophageal dilatation were evaluated by an experienced radiologist, blinded to other clinical parameters. The lung parenchymal abnormalities were assessed according to the Warrick score. A score >7 was used to define the presence of a significant SSc-ILD (14)(15). Dilatation was considered present when the widest oesophageal diameter was ≥11 mm (16).

Videofluorography study

All patients underwent VFG study in the Radiology Unit of Ospedali Riuniti di Ancona Umberto I - G.M. Lancisi - G. Salesi, using a remote-controlled digital device (Diagnost 97® Philips) with 38 cm Triview image intensifier, 0.6 - to 1.3 - mm focal spot range, 8 images / second with 1024 * 1024 matrix, maximum tube voltage of 150 kVp in fluorography and 120 kVp in fluoroscopy.

The images and the dynamic sequences were transferred to the RIS/PACS system (Centricity PACS Radiology RA1000 Workstation, GE Healthcare®) of our Diagnostic Imaging Service for digital archiving of the static images (jpeg format) and video recordings (avi format), and for possible post-processing.

The VFG study consists of a static and a dynamic phase. Particular attention is paid to some important technical factors in the execution of the survey: the patient's head, in the absence of forced positions, perfectly aligned both in the anterior-posterior and lateral-lateral projection and careful collimation of the radiant beam to avoid unnecessary exposures, especially in the thyroid region and the orbital region for the lens.

In the static phase, the VFG study evaluates the cervical spine and the pre and paravertebral soft tissues, allowing the exclusion of organic pathologies. It is performed in a sitting position, upright, head in an indifferent position, paying attention to the alignment of the mandibular branches. The RX of the head is performed in latero-lateral projection (optionally in antero-posterior or oblique projection).

The dynamic phase includes an oropharyngeal and an oesophageal phase. The study of the oesophagus is distinguished in turn in a functional phase and a morphological phase.

In the precontrastographic phase of the fluoroscopy, phonation tests are performed to evaluate the velar motility. Subsequently, "empty" swallows of salivary boluses are performed.

The contrast phase is performed by using a suspension of BaSO4 (barium sulfate) 250% weight/volume with repeated individual boluses of 10–15 ml. The contrast medium is administered orally, inviting the patient to hold it in the oral cavity and to swallow it at the command of the operator.

The first bolus is used for oropharyngeal centering in latero-lateral projection, the second bolus is used for the lower centering (pharynx-hypopharynx-upper oesophageal sphincter), always in latero-lateral projection.

Subsequently, an anterior-posterior projection is made to swallow a 10-15 ml bolus with oropharyngeal centering. The second bolus of 10-15 ml is then swallowed with a pharyngo-oesophageal centering with a scopic observation until the passage into the gastric cavity. Then, a 10 ml dosed bolus is administered to the patient lying prone and the oesophageal phase of the swallowing is evaluated in depth.

The next step is the morphological study, where a double-contrast x-ray of the oesophagus is performed with the administration of effervescent oral powder followed by the ingestion of repeated barium boluses (radiograms on a radiographic cassette from 35 x 43 cm in anterior-posterior projection and in two projections semi-oblique).

In the last phase, a solid bolus (biscuit slice soaked in barium) is ingested with oro-pharyngeal and oesophageal evaluation in latero-lateral and antero-posterior projections.

In order to evaluate possible abnormalities, 18 dynamic parameters were chosen, dividing the act of swallowing into three phases: oral, pharyngeal and oesophageal phases.

The oral and pharyngeal phases of the swallowing were studied with the patient in standing position and using 10-15 ml liquid barium boluses in the frontal and lateral projections. For the oral phase, the following dynamic radiological findings were considered: veil motility in phonation, leakage, drooling (bolus loss from the oral cavity), salivation and presence of residues in the oral cavity. For the pharyngeal phase, consideration was given to: pharyngeal residues, penetration, aspiration, altered motility of the upper oesophageal sphincter (UES). Leakage refers to the occurrence of posterior bolus loss prior to elicitation of the reflex of swallowing, revealing inability to hold the bolus in the mouth. Drooling, on the other hand, is the anterior loss of the bolus from the oral cavity. Penetration is the entry of the bolus into the larynx during swallowing, without it being sucked up, *i.e.* without exceeding the glottal

rhyme. Aspiration is defined as the entry of the bolus into the trachea through the glottal rhyme before, during and after swallowing.

The oesophageal phase of the swallowing was examined by having at least five individual swallows performed in the prone position, each with 10-15 ml of liquid barium.

Primary peristalsis was assessed by examining five individual swallows and considering the relationship between swallowing acts and complete peristaltic contraction waves propagating along the entire oesophagus. The efficacy of primary peristaltic contractions was evaluated by means of a semiquantitative scoring system considering the form and velocity of propagation of the tail of the barium column along the entire oesophagus.

The clearance capacity was assessed on the basis of the residual barium bolus persisting in the oesophagus after each swallowing. Three different degrees of barium bolus clearance capacity have been identified: more than 60%, 35 to 60%, less than 35%.

Gastroesophageal (GE) reflux was defined as any bolus that initially passes across the LES but travels cephalad back across the LES. The score of the GE reflux was determinated by the level of the oesophagus reached by the bolus in 3 categories: mild at the third distal part, moderate at the middle part, and severe in the proximal part.

Oesophagitis was defined if there was one of the following findings on oesophagram (17):

- thickened or irregular mucosal folds;
- thick fold bridging gastroesophageal junction;
- ulcers and erosions;
- strictures.

Ethical approval

The study was conducted in accordance with the Declaration of Helsinki in its fifth edition (2000). Written informed consent was obtained from all patients.

Statistical analysis

Clinical and demographic characteristics were summarised by mean and standard deviation for quantitative variables and by absolute and percentage frequencies for qualitative variables. Comparison between groups were evaluated by means of unpaired Student t-test and Chi square test, as appropriate. Furthermore, univariate and multivariate regression analyses were performed to identify the factors associated with oesophageal dysfunction. Data were analysed with the SPSS software. A p-value <0.05 was considered statistically significant.

Table I. Baseline characteristics of scleroderma patients.

	n=55
Age (years)	59 ± 12
Sex (F)	49 (89%)
Subset of disease (lcSSc/dcSSc)	36/19
Mean duration of disease (years)	8.6 ± 6.8
Presence of comorbidities or overlap	16 (29.1)
Autoantibodies	
ANA	49 (89.1)
Anti-centromere	18 (32.7)
Anti-topoisomerase I	21 (38.1)
Other autoantibodies	3 (5.4%)
Presence of ILD on chest HRCT	41 (74.5)
Presence of oesophageal dilatation on HRCT	21 (38.2)
Presence of GI symptoms	49 (89.1)
Dysphagia	45
Reflux	49

Data are presented as mean ± SD or number (%) as appropriate.

Table II. Alterations of oral, pharyngeal and oesophageal phases of swallowing on videofluorography and comparison between limited and diffuse cutaneous subsets in patients with systemic sclerosis.

	VFG alterations	All patients (n=55)	lcSSc (n=36)	dcSSc (n=19)	p
Oral phase	Inadequate velar elevation	2 (3.6)	0 (0)	2 (10.5)	0.047*
	Leakage	8 (14.5)	5 (13.8)	3 (15.7)	0.81
	Drooling	0	–	–	–
	Reduced salivary flow	21 (38.2)	16 (44.4)	5 (26.3)	0.18
	Oral after-swallow residual	2 (3.6)	1 (2.7)	1 (5.2)	0.64
Pharyngeal phase	Pharyngeal after-swallow residual	27 (49.1)	17 (47.2)	10 (52.6)	0.70
	Penetration in the laryngeal aditus	29 (52.7)	20 (55.5)	9 (47.3)	0.56
	Post-swallowing aspiration	12 (21.8)	7 (19.4)	5 (26.3)	0.81
Oesophageal phase	Abnormal UES motility	7 (12.7)	5 (13.8)	2 (5.5)	0.25
	Inadequate primary peristalsis	29 (52.7)	13 (36.1)	16 (84.2)	0.001*
	Abnormal secondary peristalsis	16 (29.1)	10 (27.7)	6 (31.5)	0.76
	Non-peristaltic contractions	22 (40)	16 (44.4)	6 (31.5)	0.35
	Deficit of oesophageal clearance	38 (69.4)	22 (61.1)	16 (84.2)	0.02*
	Abnormal LES motility	42 (76.4)	26 (72.2)	16 (84.2)	0.43
	Hiatal hernia	44 (80)	32 (88.8)	12 (63.1)	0.02*
	Gastroesophageal reflux	35 (63.6)	22 (61.1)	13 (68.4)	0.65
	Oesophagitis	45 (81.8)	28 (77.7)	17 (89.4)	0.28
	Oesophageal stenosis	0	–	–	–

Comparison between dcSSc and lcSSc subsets were performed using the Chi square test.
UES: upper oesophageal sphincter; LES: lower oesophageal sphincter.

Results

Baseline characteristics of SSc patients are summarised in Table I. The mean age was 59±12 years, the mean disease duration 8.6±6.8 years, and 89% were women. Age and disease duration did not differ between lcSSc and dcSSc patients. A higher proportion of patients with dcSSc had ILD (94.7% *vs*. 63.8%, p=0.01) and oesophageal dilatation (73.6% *vs*. 19.4%, p<0.001) compared to lcSSc patients.

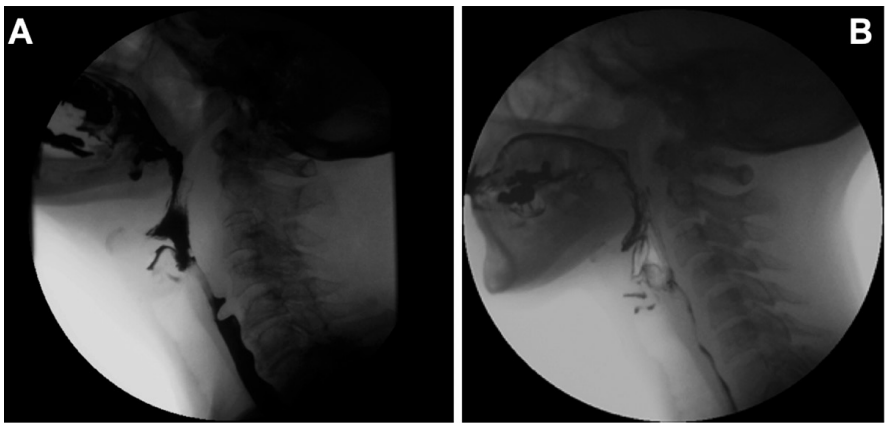

Fig. 1. This LL projection shows penetration and premature closure of upper oesophageal sphincter (panel A) and pre and intra-swallow aspiration (panel B).

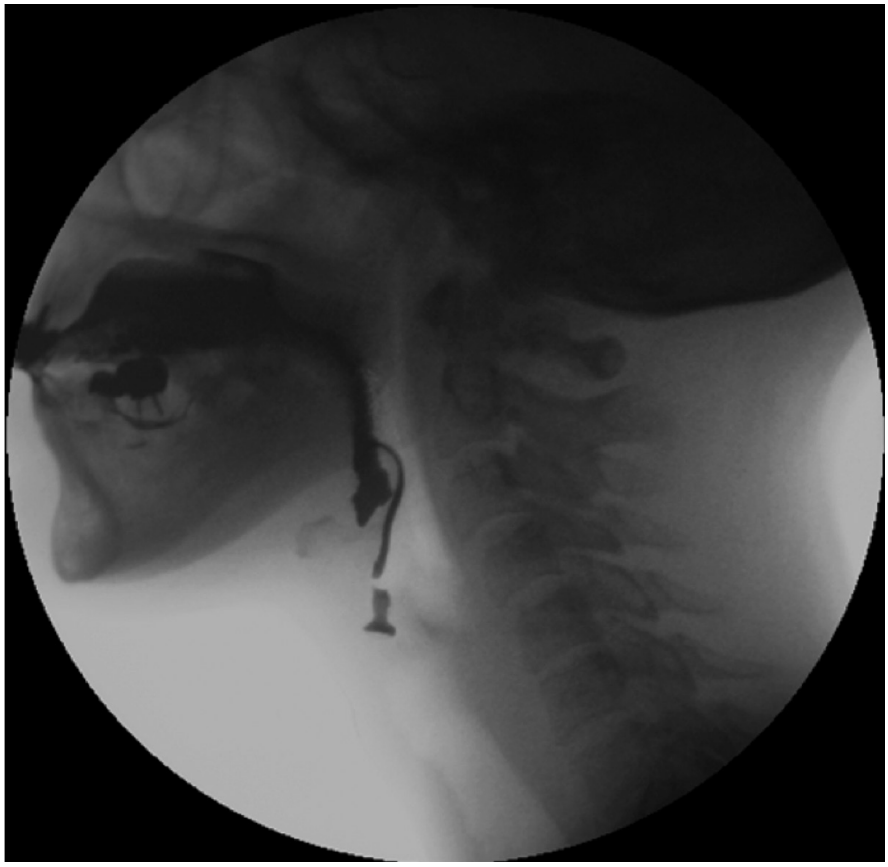

Fig. 2. This LL projection shows signs of penetration and delayed swallowing reflex.

Videofluorographic study of swallowing was well tolerated in all patients.

All patients presented the alteration of at least one phase of swallowing (oral, pharyngeal or oesophageal).

Abnormalities of the oral phase involved few patients. A reduced salivary flow was seen in 21 (38.2%) patients, leakage in 8 (14.5%) patients, whereas only a total of 4 patients presented inadequate velar elevation (2 pts, 3.6%) or oral after-swallow residual (2 pts, 3.6%). No patient presented drooling.

The pharyngeal phase presented alterations in a higher proportion of subjects. The abnormalities included penetration in the laryngeal aditus in 29 (52.7%) patients (Fig. 1A and 2), after-swallow residuals in 27 (49.1%) patients, and post-swallowing aspiration in 12 (21.8%) patients (Fig. 1B).

Among the 31 patients with the most common pharyngeal abnormalities (*i.e.* penetration and aspiration), all but two of them (93.5%) had evidence of either a defective oesophageal clearance or reflux disease. Of the two patients that showed laryngeal penetration without significant oesophageal disease, one had also leakage and the other one had evidence of reduced salivary flow.

Abnormalities of the oesophageal phase were common. Most patients presented signs of oesophageal reflux (63.6%), oesophagitis (81.8%) and hiatal hernia (80%). No patient presented oesophageal stenosis. Dysfunctions of oesophageal motility were also common and included abnormal motility of UES (12.7%) and LES (76.4%), inadequate primary peristalsis (52.7%)(Fig.3), abnormal secondary peristalsis (29.1%) and non-peristaltic contractions (40%). A defective oesophageal clearance was observed in 69.4% of SSc patients.

We found no differences between dcSSc and lcSSc patients in the prevalence of alterations in the oral and pharyngeal phases of swallowing, except for a minimal statistically significant difference in the velar elevation (2 dcSSc vs no lcSSc patient, p=0.047).

More strikingly, concerning the oesophageal phase, a higher number of dcSSc patients presented an abnormal primary peristalsis (84.2% *vs*. 36.1%, p=0.001) and a clearance deficit (84.2% *vs*. 61.1%, p=.02). Conversely, a higher number of lcSSc patients had hiatal hernia (88.8% *vs*. 63.1%, p=0.02) (Table II).

Furthermore, a higher proportion of subjects with a dysfunctional primary peristalsis and with a clearance deficit had SSc-ILD than patients with normal oesophageal findings (93.1% *vs*. 53.8% and 89.4% *vs*. 41.1%, respectively, p=0.001 for both comparisons).

The results of the regression analysis are presented in Table III. In the univariate model, the presence of anti-topoisomerase antibodies (OR 3.57, 95%CI 1.11–11.4, p=0.03), of oesophageal dilation on chest CT scan (OR 55.5, 95%CI 6.48–476, p<0.001), of SSc-related ILD on chest CT (OR 11.5, 95%CI 2.27–59.1, p=0.003) and the dcSSc subset (OR 9.43, 95%CI 2.31–38.6, p=0.002) resulted predic-

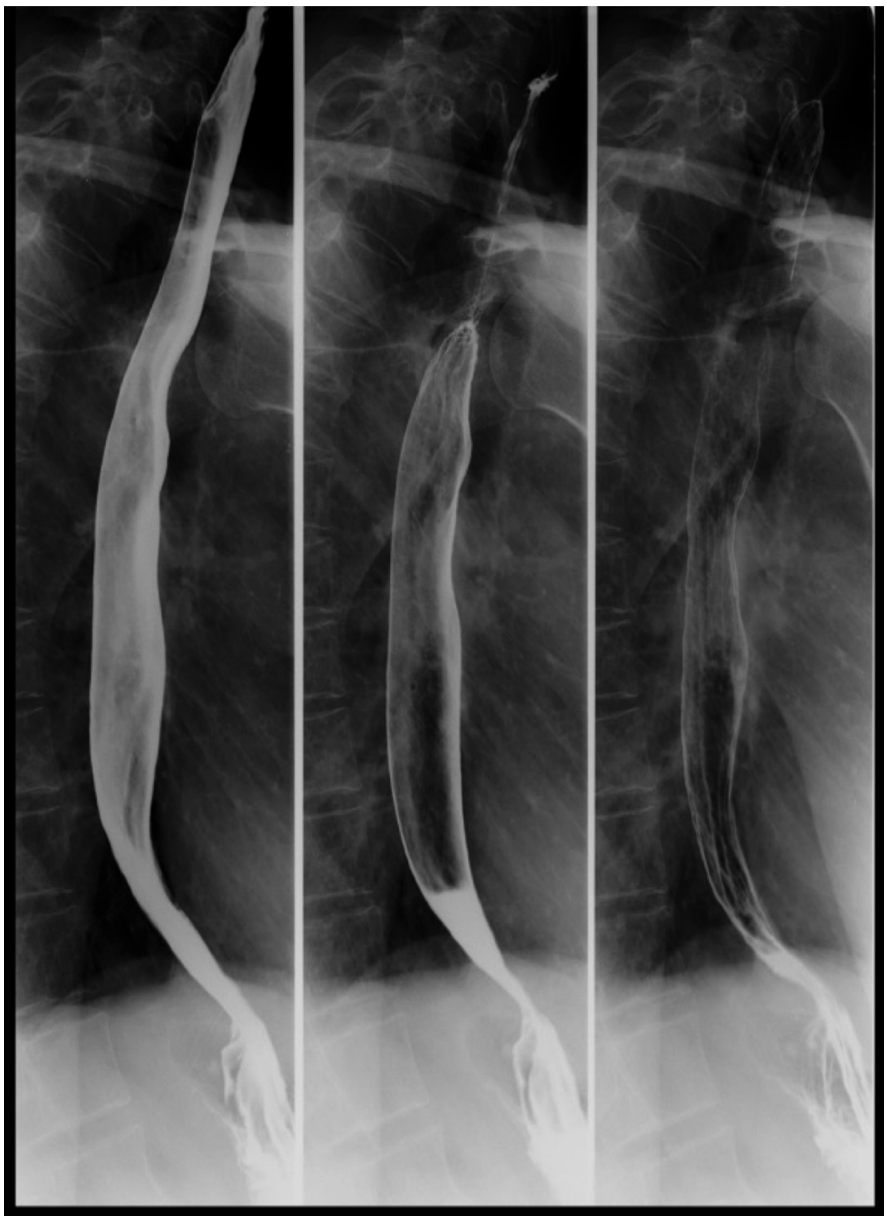

Fig. 3. This oblique projection shows reduced validity of primary peristalsis.

Table III. Univariate and multivariate analysis models predicting the presence of inadequate primary esophageal peristalsis in scleroderma patients.

	Univariate analysis			Multivariate analysis		
Variable	OR	95%CI	*p*	OR	95%CI	*p*
Disease duration	1.01	0.93-1.09	0.08			
Comorbidities	0.41	0.12-1.38	0.15			
Anti-centromere positivity	0.30	0.09-0.99	*0.04**			
Anti-topoisomerase I positivity	3.57	1.11-11.4	*0.03**	0.66	0.10-4.22	0.66
Oesophageal dilatation on CT	55.5	6.48-476	*<0.001**	51.5	4.07-652.7	*0.002**
ILD on CT	11.5	2.27-59.1	*0.003**	13.2	1.12-154.7	*0.04**
Subset of disease (dcSSc)	9.43	2.31-38.6	*0.002**	2.55	0.31-20.9	*0.*38

Data were analysed trough binary logistic regression using the presence of inadequate primary oesophageal peristalsis as dependent variable.
CT: chest computed tomography; ILD: interstitial lung disease; dcSSc: diffuse cutaneous systemic sclerosis.

tors of inadequate primary peristalsis on VFG. However, in the multivariate model only the presence of oesophageal dilatation and the presence of ILD on chest CT were significantly associated to abnormal primary peristalsis (OR 51.5, 95%CI 4.07–652.7, p=0.002 and OR 13.2, 95%CI 1.12-154.7, p=0.04, respectively).

Discussion

In scleroderma, the involvement of GI tract is often overlooked, though it represents the most affected organ system after the skin (4, 18). SSc-related GI manifestations may occur from the mouth to the anus, with the oesophagus being involved in almost 90% of the cases, followed by intestinal tract, stomach, oral cavity and anus (4).

Different pathophysiological mechanisms have been proposed to explain oesophageal abnormalities in SSc, including autonomic dysfunction (19), but all of them eventually lead to atrophy and fibrosis of the smooth muscle of the lower two thirds of the oesophagus (4).

In this paper, we reported the findings of VFG examination when used to evaluate abnormalities of the upper GI tract in SSc patients. Our work confirms that VFG swallowing study, despite the technological development in diagnostic imaging, remains the benchmark exam for the morphodynamical evaluation of the upper digestive tract, in particular of the oesophagus, in patients diagnosed with SSc. In fact, this technique allows to highlight functional typical alterations in the various phases of swallowing, and to correlate them with the anatomical-morphological findings (20).

As is known in literature, we observed that the most frequent alterations of swallowing in patients with SSc concern the oesophageal phase. Patients with SSc display altered oesophageal motility, particularly involving the LES, inadequate primary peristalsis and deficit of oesophageal clearance. In our cohort, these alterations most often involve patients with dcSSc than lcSSc, as well as patients with established SSc-ILD, as it is already known with regard to oesophageal dilatation on CT (16).

Basing on several studies, oesophageal

dysfunction has repeatedly been implicated in the pathogenesis of SSc-ILD. It has been postulated that continuous microaspiration of gastric content may contribute to the onset of pulmonary parenchymal lesions in ILD (21, 22), although none of the studies has actually demonstrated a causal relationship between oesophageal abnormalities and ILD (23). In fact, even if a correlation between functional and radiological lung parameters and oesophageal abnormalities exists, oesophageal dilatation does not predict worsening and progression of ILD in SSc patients (4, 24). Alternatively, some authors suggested that the tractional effects of pulmonary fibrosis may contribute, together with the primary involvement of the muscular layer, to oesophageal dilatation, leading to reflux and aspiration (23). Nevertheless, it is known that in lcSSc without significant lung involvement the oesophageal dilatation can be as frequent as in dcSSc with diffuse lung fibrosis.

In our study, we could not find an association between GERD or laryngeal aspiration, as assessed by VFG, and SSc-ILD. This may be due to the small sample size, the intrinsic limitations of the VFG method to detect smaller aspirations or reflect the lack of correlation between these two disease manifestations.

The alterations observed in the pharyngeal phase, that occur in about half of SSc patients, include pharyngeal after-swallow residuals, laryngeal penetration and post-swallowing aspiration. Our study further confirms that primary swallowing alterations are not a hallmark of SSc-related GI involvement, reflecting the fact that fibrosis and atrophy do not usually involve the striated muscle in SSc. These abnormalities are more likely to be the consequence of oesophageal alterations rather than the manifestation of a primary swallowing alteration, as it has already been reported (20). In fact, almost all of the patients with pharyngeal dysfunction showed signs of altered oesophageal clearance or reflux disease.

Finally, in our patients hyposcialia is the most frequent complication of the oral phase of swallowing, and it appears to be more common in patients with limited cutaneous skin involvement, though the difference is not statistically significant. Of note, lcSSc frequently overlaps with other autoimmune diseases that involve salivary glands such as Sjögren's syndrome. The reduction of salivary flow not only affects the correct formation of the bolus, but also the subsequent oesophageal phase. In particular, hyposcialia may significantly hamper the formation and the oral processing of the solid bolus, causing a meaningful increase of the residues in the vallecular and in the piriform sinuses during the pharyngeal phase. Furthermore, in the oesophageal phase hyposcialia may reduce the progression of the solid bolus and reduce its clearance, often requiring the administration of water boluses for a complete transit of the same in the oesophagus.

Our study has several limitations, including a small sample size that reflects the difficult enrollment of SSc patients, and the fact that the VFG examinations were performed with a different latency with respect to the onset of the disease.

As future objective, we are planning to repeat VFG examinations in the same cohort at scheduled time frames in order to evaluate the longitudinal trajectory of swallowing alterations in patients with SSc, as well as the responsiveness to clinical change of this technique.

In conclusion, our study suggests that the VFG study is a reliable technique for the morphological and functional evaluation of the swallowing phases in SSc patients. In fact, VFG not only provides evidence of oesophageal kinetic abnormalities, but it is also a valid indicator of morphological alterations such as hiatus hernia and GERD. Moreover, providing information regarding the oral and pharyngeal phases of swallowing, VFG is useful to evaluate dysphagia and other upper GI symptoms reported by SSc patients.

VFG should be considered among the useful investigational methods for the evaluation of upper GI involvement in SSc patients.

Acknowledgements

The authors would like to acknowledge all the subjects that participated in this study.

References

1. GABRIELLI A, AVVEDIMENTO EV, KRIEG T: Scleroderma. *N Engl J Med* 2009; 360: 1989-2003.
2. CARLSON DA, HINCHCLIFF M, PANDOLFINO JE: Advances in the evaluation and management of esophageal disease of systemic sclerosis. *Curr Rheumatol Rep* 2014; 17: 475.
3. ORLANDI M, BARSOTTI S, LEPRI G *et al*.: One year in review 2018: systemic sclerosis. *Clin Exp Rheumatol* 2018; 36 (Suppl. 113): S3-23.
4. SAVARINO E, FURNARI M, DE BORTOLI N *et al*.: Gastrointestinal involvement in systemic sclerosis. *Presse Med* 2014; 43: e279-91.
5. EBERT EC: Esophageal disease in scleroderma. *J Clin Gastroenterol* 2006; 40: 769-75.
6. NTOUMAZIOS SK, VOULGARI PV, POTSIS K, KOUTIS E, TSIFETAKI N, ASSIMAKOPOULOS DA: Esophageal Involvement in Scleroderma: Gastroesophageal Reflux, the Common Problem. *Semin Arthritis Rheum* 2006; 36: 173-81.
7. BARBIERA F, CONDELLO S, DE PALO A, TODARO D, MANDRACCHIA C, DE CICCO D: Role of videofluorography swallow study in management of dysphagia in neurologically compromised patients. *Radiol Med* 2006; 111: 818-27.
8. LO RE G, GALIA M, LA GRUTTA L *et al*.: Digital cineradiographic study of swallowing in patients with amyotrophic lateral sclerosis. *Radiol Med* 2007; 112: 1173-87.
9. MONTESI A, PESARESI A, CAVALLI ML, RIPA G, CANDELA M, GABRIELLI A: Oropharyngeal and esophageal function in scleroderma. *Dysphagia* 1991; 6: 219-23.
10. VAN DEN HOOGEN F, KHANNA D, FRANSEN J *et al*.: 2013 classification criteria for systemic sclerosis: an American college of rheumatology/European league against rheumatism collaborative initiative. *Ann Rheum Dis* 2013; 72: 1747 LP-1755.
11. LEROY EC, BLACK C, FLEISCHMAJER R *et al*.: Scleroderma (systemic sclerosis): classification, subsets and pathogenesis. *J Rheumatol* 1988; 15: 202-5.
12. SVERZELLATI N, ODONE A, SILVA M *et al*.: Structured reporting for fibrosing lung disease: a model shared by radiologist and pulmonologist. *Radiol Med* 2018; 123: 245-53.
13. PANDEY AK, WILCOX P, MAYO JR *et al*.: Oesophageal dilatation on high-resolution CT chest in systemic sclerosis: what does it signify? *J Med Imaging Radiat Oncol* 2011; 55: 551-5.
14. WARRICK JH, BHALLA M, SCHABEL SI, SILVER RM: High resolution computed tomography in early scleroderma lung disease. *J Rheumatol* 1991; 18: 1520-8.
15. BELLIA M, CANNIZZARO F, SCICHILONE N *et al*.: HRCT and scleroderma: semiquantitative evaluation of lung damage and functional abnormalities. *Radiol Med* 2009; 114: 190-203.
16. SALAFFI F, DI CARLO M, CAROTTI M, FRATICELLI P, GABRIELLI A, GIOVAGNONI A: Relationship between interstitial lung disease and oesophageal dilatation on chest high-resolution computed tomography in patients with systemic sclerosis: a cross-sectional

study. *Radiol Med* 2018; 123: 655-63.
17. LAUFER I: Double contrast gastrointestinal radiology with endoscopic correlation. Saunders Company, 1979.
18. BARSOTTI S, BRUNI C, ORLANDI M *et al*.: One year in review 2017: systemic sclerosis. *Clin Exp Rheumatol* 2017; 35 (Suppl. 106): S3-20.
19. GIGANTE A, MARGIOTTA D, NAVARINI L *et al*.: Parasympathetic activity increases with digital microvascular damage and vascular endothelial growth factor in systemic sclerosis. *Clin Exp Rheumatol* 2018; 36 (Suppl. 113): S24-27.
20. RUSSO S, LO RE G, GALIA M *et al*.: Videofluorography swallow study of patients with systemic sclerosis. *Radiol Med* 2009; 114: 948-59.
21. JOHANNSON KA, STRÂMBU I, RAVAGLIA C *et al*.: Antacid therapy in idiopathic pulmonary fibrosis: more questions than answers? *Lancet Respir Med* 2017; 5: 591-98.
22. JOHNSON DA, DRANE WE, CURRAN J *et al*.: Pulmonary disease in progressive systemic sclerosis: a complication of gastroesophageal reflux and occult aspiration? *Arch Intern Med* 1989; 149: 589-93.
23. STREK ME: Systemic sclerosis-associated interstitial lung disease: Role of the oesophagus in outcomes. *Respirology* 2018; 23: 885-86.
24. WINSTONE TA, HAGUE CJ, SOON J *et al*.: Oesophageal diameter is associated with severity but not progression of systemic sclerosis-associated interstitial lung disease. *Respirology* 2018; 23: 921-26.