Esophageal Scintigraphy with a Semisolid Meal to Evaluate Esophageal Dysmotility in Systemic Sclerosis and Raynaud's Phenomenon

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Esophageal transit scintigraphy seems to be a valid methodology to assess impaired esophageal motility in early stages of disease. The purpose of this study was to discriminate patients with primary Raynaud's phenomenon (RP) and patients with systemic sclerosis (SSc) from healthy subjects by esophageal scintigraphy with a semisolid meal. **Methods:** We studied 32 patients with primary RP, 18 with SSc and 13 healthy subjects. Dysphagia, acid regurgitation and heartburn were scored. After an overnight fast, all subjects underwent esophageal scintigraphy, using a semisolid orally ingested bolus (10 mL apple puree) labeled with ^{99m}Tc-sulfur colloid. Esophageal transit and emptying time and integral value were evaluated with the subjects in the upright (sitting) and supine positions. Transit time was defined as the time from the entry of 50% of radioactivity into the upper esophagus until the clearance of 50% of the bolus from the whole esophagus. Emptying time was defined as the time from the entry of 50% of radioactivity into the upper esophagus, until the clearance of 100% of the bolus from the whole esophagus. Integral value was defined as the total counts under the time-activity curve normalized to the maximum. **Results:** Esophageal transit and emptying time and integral value, evaluated in both positions, were significantly higher in patients with SSc than in healthy subjects and than in patients with RP. Moreover, patients with RP had all three parameters, assessed in supine position, significantly longer compared to healthy subjects. Clinical scores regarding dysphagia, acid regurgitation and heartburn were not significantly different between patients with RP and SSc. **Conclusion:** Esophageal transit and emptying time and integral value appear to be able to discriminate patients with primary RP from patients with SSc and patients with RP from healthy subjects, suggesting an early mild esophageal dysfunction in RP.

Key Words: esophageal scintigraphy; Raynaud's phenomenon; systemic sclerosis; esophageal motility

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Raynaud's phenomenon (RP) is characterized by episodic digital ischemia, manifested clinically by the sequential development of digital blanching, cyanosis and rubor of the fingers or toes after cold exposure and subsequent rewarming. RP is usually classified as either primary or secondary. Primary RP occurs as an isolated finding in an otherwise healthy subject, whereas secondary RP is caused by an associated disease. The most common cause of secondary RP is a connective tissue disease; about 90% of patients with systemic sclerosis (SSc) have RP (*1*). In SSc, a chronic systemic disease of unknown cause, characterized by fibroblast proliferation and collagen deposition, esophageal involvement is frequently observed in about 75% of patients, range 69%–92%, depending on whether there is limited or diffuse cutaneous disease involvement.

Typical symptoms of reflux esophagitis and dysphagia have been reported. Manometric and electrophysiological studies showed evidence of a neuropathy of the enteric nervous system in the early stages of the disease, resulting in disturbances of the digestive and interdigestive peristalsis and therefore leading to gastroparesis, bacterial overgrowth of the small intestine or constipation. In late SSc, collagen deposition and atrophy of the smooth muscle layer of the bowel wall cause loss of sphincter function in the lower esophageal sphincter or the anal sphincter and marked atony of the intestine (*2,3*). Most of these patients have RP.

Radionuclide esophageal transit study has been shown to be as effective as esophageal manometry, the current gold standard technique, in screening patients with esophageal motility disorders (*4*) and in detecting impaired esophageal motility in patients with SSc (*5*). Table 1 shows the high sensitivity of radionuclide studies in the diagnosis of esophageal dysfunction in patients with SSc (*5–15*). It has been reported that esophageal impairment in SSc might be the result of an alteration of the autonomic nervous system, causing a Raynaud's-like vascular alteration in the gastrointestinal tract, preceding sclerotic changes in the muscle (*16*). In agreement with this hypothesis, esophageal blood flow seemed to be reduced in patients with RP (*17*). Thus, we hypothesized that patients with primary RP, whether asymptomatic or complaining of mild gastroesophageal symptoms such as heartburn, regurgitation and dysphagia, might have impaired esophageal motility function.

The aim of this study was to evaluate esophageal transit

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TABLE 1
Esophageal Scintigraphy in Patients with Systemic Sclerosis

Authors	Year	Population	Meal	Dose	Position	Parameters	Sensitivity
Tolin et al. (*6*)	1979	5 SSc	L (15 mL)	150 μCi (^{99m}Tc-SC)	Supine, anterior	Percent emptying	100% (5/5)
Russel et al. (*7*)	1981	15 d/m+ 15 d/m−	L (10 mL)	250 μCi (^{99m}Tc-SC)	Supine, anterior	Total transit time	100% (15/15) 64%
Maddern et al. (*8*)	1984	12 SSc	S (10 g)	150 μCi (^{99m}Tc-SC)	Upright, anterior	Total transit time	58% (7/12)
Davidson et al. (*9*)	1985	15 SSc	L (10 mL)	300 μCi (^{99m}Tc-SC)	Upright, supine, anterior	Total transit time	87% (13/15)
Carette et al. (*10*)	1985	23 SSc	L (10 mL)	250 μCi (^{99m}Tc-SC)	Supine, anterior	Total transit time	91% (20/22)
Drane et al. (*11*)	1986	11 SSc	L (10 mL)	100–300 μCi (^{99m}Tc-SC)	Supine, anterior	Total transit time	100% (11/11)
						Percent emptying	100% (11/11)
Akesson et al. (*12*)	1987	60 SSc	SS (15 mL)	650 μCi (^{99m}Tc-SC)	Upright, supine, posterior	Total transit time	87% (52/60)
Klein et al. (*5*)	1992	17 SSc	L (15 mL)	300 μCi (^{99m}Tc-SC)	Supine, posterior	Percent emptying	82% 83% specificity 82% accuracy
Edenbrandt et al. (*13*)	1995	45 SSc	SS (10 mL)	110 μCi (^{99m}Tc-SC) × 6 swallows	Prone, posterior	Percent emptying Total transit time	
Kaye et al. (*14*)	1996	301 SSc	SS (10 mL)	250 μCi (^{99m}Tc-SC)	Upright, supine, posterior	Total transit time	82% (246/301)
Parkman et al. (*15*)	1997	4 SSc	L (15 mL)	150 μCi (^{99m}Tc-SC)	Supine, anterior	Percent empyting	75% (3/4)

Total transit time = transit time for all, or nearly all, of the administered radioactivity to traverse the esophagus (*25*).

Percent emptying = any measure of the amount of the total administered radioactivity that remains in (or, conversely, is emptied from) the esophagus after the completion of one or more swallows (*25*).

SSc = systemic sclerosis; L = liquid; SC = sulfur colloid; d = dysphagia; m+ = abnormal esophageal manometry; m− = normal esophageal motility; S = solid; SS = semisolid.

time (ETT) and emptying time (EET) by a noninvasive method such as esophageal scintigraphy with a semisolid meal in patients with SSc, in patients with primary RP and in healthy subjects.

MATERIALS AND METHODS

Study Population

We studied three groups of subjects, profiled in Tables 2 and 3.

Group I. Thirty-two patients (2 men and 30 women, mean age ± SD: 46 ± 13 y, range 20–77 y) had primary RP (mean time 7 y; range 2–30 y). Thirty-one percent (10/32) of patients had anticentromere antibodies (ACAs). The homogeneous form of antinuclear antibodies (ANAs) was present in 28% (9/32), and in 6% (2/32) the speckled form was present.

Group II. Eighteen patients (2 men and 16 women; mean age ± SD: 54 ± 13 y; range 23–70 y) had definite SSc, fulfilling the criteria of the American Rheumatism Association (*18*). Nine patients had limited cutaneous SSc (lcSSc), and 9 had the diffuse cutaneous form (dcSSc). All patients reported RP for a mean time of 13 y (range 1–30 y). The mean interval between the onset of RP and development of SSc was 5 y (range 1–11 y). Seventy-eight percent (7/9) of patients with lcSSc had ACAs. In dcSSc, 7 out of 9 patients (78%) had antitopoisomerase antibodies (ex-Scl 70), 5 out of 9 (56%) had homogeneous ANAs (ANA homog), 5 out of 9 (56%) had nucleolar ANAs (ANA nucleol) and 1 out of 9 (11%) had speckled ANAs (ANA speckl).

Group III. Thirteen healthy volunteers (1 man and 12 women, mean age ± SD: 49 ± 11 y; range 24–74 y) had no symptoms or history of esophageal disease, central nervous system disorders, peripheral neuropathy, diabetes mellitus, systemic disorders known to be associated with esophageal dysfunction or recent ingestion of medication known to alter esophageal function. Each subject was interviewed to ascertain the presence or absence of gastroesophageal symptoms such as dysphagia, acid regurgitation and heartburn and the administration of any drug influencing the gastroesophageal tract.

Esophageal symptoms were scored as follows: 0 = less than one episode a month, 1 = at least once monthly, 2 = at least once weekly, 3 = daily. Informed consent was obtained from all subjects, and the study was approved by the Ethic Committee of S. Paolo Hospital of Milan.

Esophageal Scintigraphy

Esophageal scintigraphy was performed using the method developed by Åkesson et al. (*12*). All subjects were examined after 4 h of fasting. A semisolid radioactive meal was prepared mixing ^{99m}Tc-sulfur colloid with 50 mL of apple puree (25 Kcal) to achieve an activity concentration of 1 MBq/mL. Labeling efficiency of the apple puree with ^{99m}Tc sulfur colloid was 78%, and the radiolabel remained "fixed" on the semisolid meal, maintaining a standard viscosity for the next 4 h. Imaging was performed using a large-field-of-view gamma camera (ADAC; ADAC Laboratories, Milpitas, CA) fitted with a parallel-hole collimator. The gamma camera was connected to a SUN computer (ADAC). The camera head was oriented vertically and the subject seated erect on a stool with his/her back to the camera in posterior projection. The field of view covered an area including the throat and upper abdomen. The positions of the jugular and xiphoid were demarcated using ^{57}Co markers. A practice nonradioactive run preceded the study. The computer was set to acquire a dynamic study in a 64 × 64 matrix

TABLE 2
Clinical and Investigational Features of Patients with Raynaud's Phenomenon

Patient no.	Age (y)	RP (y)	Symptoms‡			Serology	Drugs
			Dysphagia	Acid regurgitation	Heartburn		
1	25	2	1	2	1		
2	40	1	3	0	0	ANA homogeneous	
3	45	5	0	3	0		
4*	43	2	3	0	1	ANA speckled	
5†	20	3	2	3	2		
6	32	2	2	0	2		
7	43	1	0	0	0		
8†	56	15	2	3	1		
9	42	1	3	0	0		
10*	52	24	3	3	1		Domperidone
11†	59	2	2	2	1		Sucralfate
12†	23	1	0	1	1		
13	45	10	1	1	1		
14	58	1	2	1	2		
15*	77	20	2	1	1		
16†	27	9	0	0	0		
17*	43	7	2	1	2		
18†	67	10	3	1	0	ACA	
19†	52	2	3	3	0		Sucralfate
20†	59	2	2	2	2	ACA	
21†	62	15	3	3	3	ACA	Sucralfate
22†	49	3	0	1	0	ACA	
23†	49	30	3	3	3	ANA speckled	
24	49	10	1	0	0		
25†	29	4	0	0	0	ANA homogeneous	
26*	49	3	0	0	0		Sucralfate
27†	34	4	0	1	1		Sucralfate, domperidone
28†	40	8	1	0	0		
29†	60	10	0	0	0		Sucralfate
30†	49	9	2	3	0	ANA homogeneous	
31*	54	2	0	2	0	ACA	Sucralfate
32†	38	3	0	0	0	ACA	

*Supine esophageal emptying time longer than 300 s.
†Supine esophageal emptying time between 68 and 300 s.
‡Symptoms were scored as follows: 0 = less than one episode a month; 1 = at least once monthly; 2 = at least once weekly; 3 = daily.
RP = Raynaud's phenomenon; ANA = antinuclear antibody; ACA = anticentromere.

comprising 0.5-s frames for 30 s followed by 15-s frames for the succeeding 6.0 min. The radioactive meal (dose 10 MBq in 10 mL volume) was placed in the mouth of the subject, who then refrained from swallowing until prompted. The computer was activated for study acquisition. The subject was asked to perform a single swallow and to abstain from further swallowing for the duration of the acquisition period. If during the dynamic acquisition there was evidence of pieces of radiolabeled bolus, a sign of possible additional swallows, the study was repeated after assessment of absence of activity in the whole esophagus. After completion of the study a drink of water was given to the subject to remove any residual activity in the esophagus. This was confirmed by visual assessment on the video of the gamma camera. The procedure was then repeated with the subject lying supine on the imaging table with the camera underneath. Patients were asked about the presence of dysphagia, heartburn and regurgitation during the study in the upright and in the supine position. Reflux of gastric contents during the scintigraphic procedure was not analyzed due to the short time period of the study and the small volume of the semisolid meal.

Image Processing and Data Analysis

The study was processed using a standard software program designed for the analysis of dynamic scintigraphy. Regions of interest were outlined for the mouth, whole esophagus and stomach. Time-activity curves were created. Three parameters were calculated:

Transit Time. Defined as the time from the entry of 50% of radioactivity into the upper esophagus until the clearance of 50% of the bolus from the whole esophagus.

Emptying Time. Defined as the time from the entry of 50% of radioactivity into the upper esophagus until the clearance of 100% of the bolus from the whole esophagus.

Integral Value. Defined as the total counts beneath the curve normalized to the maximum value. Radionuclide stagnation was defined as an esophageal emptying time longer than 300 s.

Statistical Analysis

Data are given as mean ± SD. Statistical analysis was performed using Kruskal-Wallis nonparametric analysis of variance and the Wilcoxon two-sample test. Correlations were assessed with

TABLE 3
Clinical and Investigational Features of Patients with Systemic Sclerosis

Patient no.	Age (y)	RP (y)	Diagnosis	SSc (y)	Symptoms* D	R	H	Serology	Drugs
1†	39	16	lcSSc	4	1	2	1	ACA	
2†	56	15	lcSSc	2	3	0	3	ACA	
3†	59	21	lcSSc	11	3	3	2	ACA	
4†	51	1	lcSSc	1	3	2	0		
5†	62	6	lcSSc	5	2	2	2	ACA	Domperidone
6†	65	3	lcSSc	3	2	2	0	ACA	
7†	60	10	dcSSc	2	3	3	3	ANA homog + nucleol, Scl 70	Domperidone, sucralfate, omeprazole
8†	31	1	dcSSc	1	0	1	3	Scl 70	Rantidine
9†	60	20	dcSSc	3	3	3	2	ACA	Omeprazole
10†	62	30	dcSSc	10	3	2	0	ANA homog, Scl 70	Domperidone, sucralfate, omeprazole
11‡	54	3	dcSSc	1	2	0	0	ANA homog + nucleol, Scl 70	
12†	36	12	dcSSc	10	0	0	3	ANA homog + nucleol, Scl 70	Ranitidine
13†	69	30	dcSSc	9	3	3	2	ANA speckl	Ranitidine, sucralfate
14†	70	20	lcSSc	15	2	3	0		
15‡	23	3	dcSSc	1	1	0	0	ANA nucleol, Scl 70	
16†	50	6	dcSSc	1	0	1	3	ANA homog + nucleol, Scl 70	Sucralfate, domperidone
17‡	59	4	lcSSc	1	2	2	0	ACA	
18†	60	30	lcSSc	5	3	3	3	ACA	

*Symptoms were scored as follows: 0 = less than one episode a month; 1 = at least once monthly; 2 = at least once weekly; 3 = daily.
† = supine esophageal emptying time longer than 300 s.
‡ = supine esophageal emptying time between 68 and 300 s.
RP = Raynaud's phenomenon; D = dysphagia; R = acid regurgitation; H = heartburn; lcSSc = limited systemic sclerosis; dcSSc = diffuse systemic sclerosis.
Abbreviations for antinuclear antibodies (ANA) are: ACA = anticentromere; homog = homogeneous; nucleol = nucleolar; Scl 70 = antitopo-isomerase-I; speckl = speckled.

the Spearman rank correlation procedure. A P value of <0.05 was considered significant.

RESULTS

Patients with RP, patients with SSc and healthy controls were matched for age. There were no statistical differences among the three groups. No significant difference was found between patients with lcSSc and those with dcSSc form with regard to esophageal function parameters and the symptoms score.

The percentage of patients with symptoms was not significantly different between the group of patients with primary RP and the patients with SSc. Dysphagia was present in 66% (21/32) of patients with primary RP and in 83% (15/18) of patients with SSc, acid regurgitation in 63% (20/32) and in 78% (14/18), and heartburn in 50% (16/32) and in 56% (10/18), respectively. If we consider only severe symptoms (score 2.3), 53% (17/32) of primary RP patients complained of dysphagia compared with 78% (14/18) of SSc patients (P = ns). Thirty-eight percent (12/32) of primary RP patients had acid regurgitation compared with 67% (12/18) of SSc patients (P = ns). Twenty-two percent (7/32) of primary RP patients had heartburn compared with 56% (10/18) of SSc patients ($P = 0.05$).

ETT was significantly higher ($P < 0.005$) in primary RP patients compared to healthy subjects in the supine position only, as shown in Table 4. Moreover, ETT was significantly longer in SSc patients than in healthy subjects and in patients with primary RP in both positions (upright $P < 0.005$, supine $P < 0.005$ and upright $P < 0.01$, supine $P < 0.005$, respectively). There was no significant difference between

TABLE 4
Esophageal Transit Time, Empyting Time and Integral Value: Comparison Between Patients with Primary Raynaud's Phenomenon, Patients with Systemic Sclerosis and Healthy Subjects

	RP	SSc	Healthy subjects
Esophageal transit time (s)			
Upright	9.84 ± 5.90	19.6 ± 13.8*	7.00 ± 0.32
Supine	9.29 ± 2.21*	16.2 ± 8.06*	7.00 ± 0.39
Esophageal emptying time (s)			
Upright	106 ± 62.7*	269 ± 119*	43.1 ± 12.4
Supine	163 ± 126*	362 ± 67*	40.1 ± 14.8
Integral value (counts)			
Upright	47.9 ± 31.3*	261 ± 211*	22.7 ± 13.3
Supine	48.8 ± 56.9†	386 ± 262*	11.5 ± 5.9

Values are mean ± SD.
*$P < 0.005$.
†$P < 0.05$.
RP = Raynaud's phenomenon; SSc = systemic sclerosis.

TABLE 5
Esophageal Emptying Time in Upright and Supine Positions

Subjects	Upright <300 s	Supine >300 s
Raynaud's phenomenon	32/32 (100%)	6/32 (19%)
Systemic sclerosis	10/18 (56%)	15/18 (83%)

supine and upright position for all three groups. Moreover, 19/32 (59%) and 26/32 (81%) of primary RP patients, in upright and supine position respectively, had an ETT longer than 7.7 s (2 SD above the mean value of the control group). All SSc patients had ETTs longer than 7.7 s.

Table 4 shows much more significant differences in EET among SSc, primary RP and healthy subjects in both positions. In the upright and supine positions there was a significant difference between primary RP and healthy subjects ($P < 0.005$ and $P < 0.005$, respectively) and between SSc and healthy subjects ($P < 0.005$). EET was significantly longer in SSc patients compared to primary RP patients in the supine and upright positions ($P < 0.0001$). Only in SSc patients was the supine position average value significantly higher than the upright one ($P < 0.01$). In 21 of 32 primary RP patients (66%) and in all patients with SSc, the EET was longer than 68 s (2 SD above the mean value of healthy subjects). Moreover the supine emptying time was severely prolonged (>300 s) in 6/32 (19%) primary RP patients and in 15/18 (83%) SSc patients. All these subjects showed radionuclide stagnation in the lower esophagus (Table 5) in the absence of anatomical strictures found by endoscopy or barium esophagram.

The data for mean integral value (IV) are shown in Table 4. They were significantly greater in SSc patients than in healthy subjects (upright $P = 0.001$; supine $P = 0.0001$) and than in patients with primary RP (upright $P < 0.0001$; supine $P = 0.0001$). In both upright and supine positions the IV was significantly higher in RP-affected patients than in healthy subjects ($P < 0.05$). There was no significant difference between the supine and upright positions for the three groups of subjects.

Figure 1 shows a comparison between dynamic images, obtained respectively in an RP- and SSc-affected patient in supine positions. The SSc images clearly demonstrate a

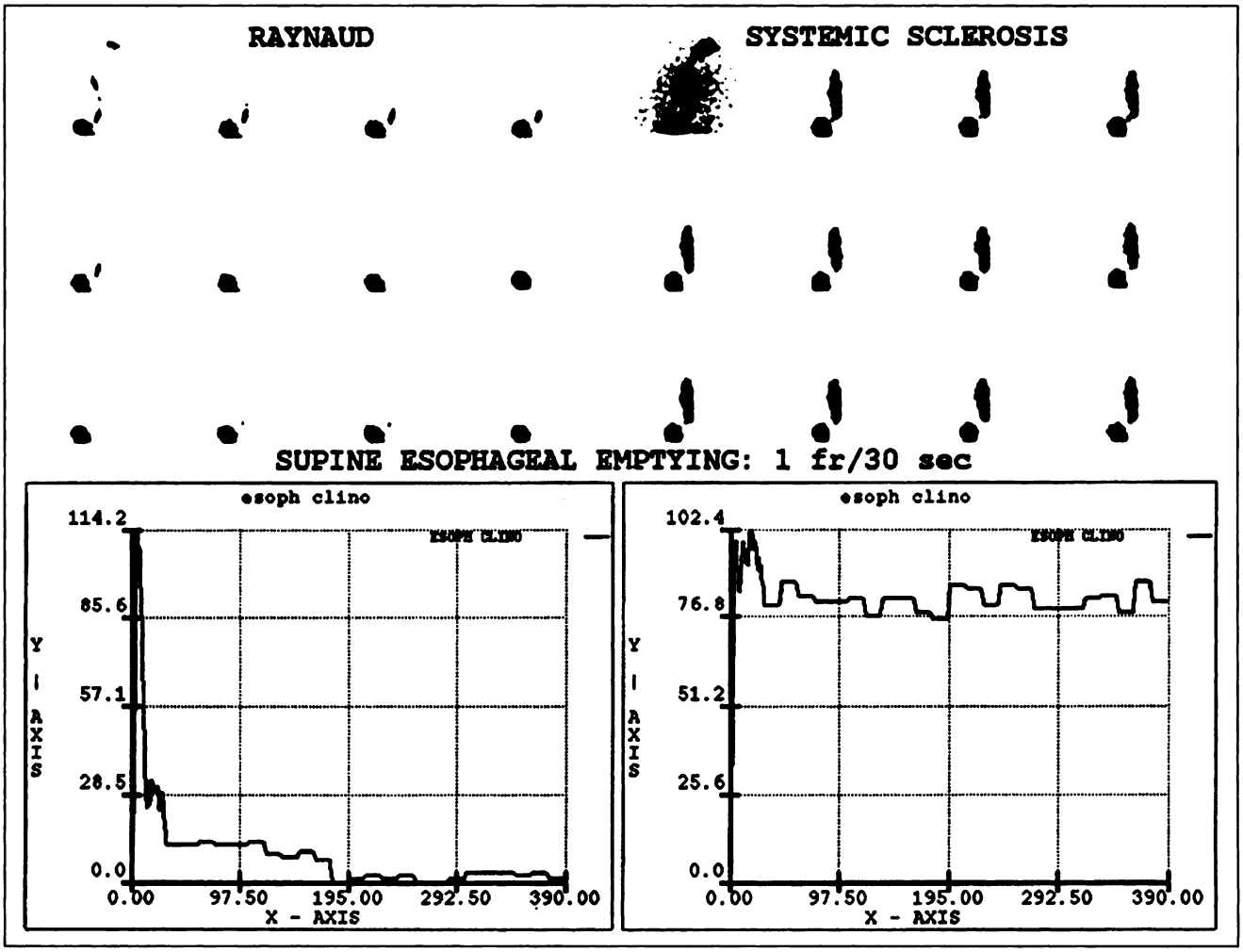

FIGURE 1. Scintigraphic dynamic images and time-activity curves in RP- and in SSc-affected patients, respectively. Y-axis expresses counts (cps); x-axis expresses time (s).

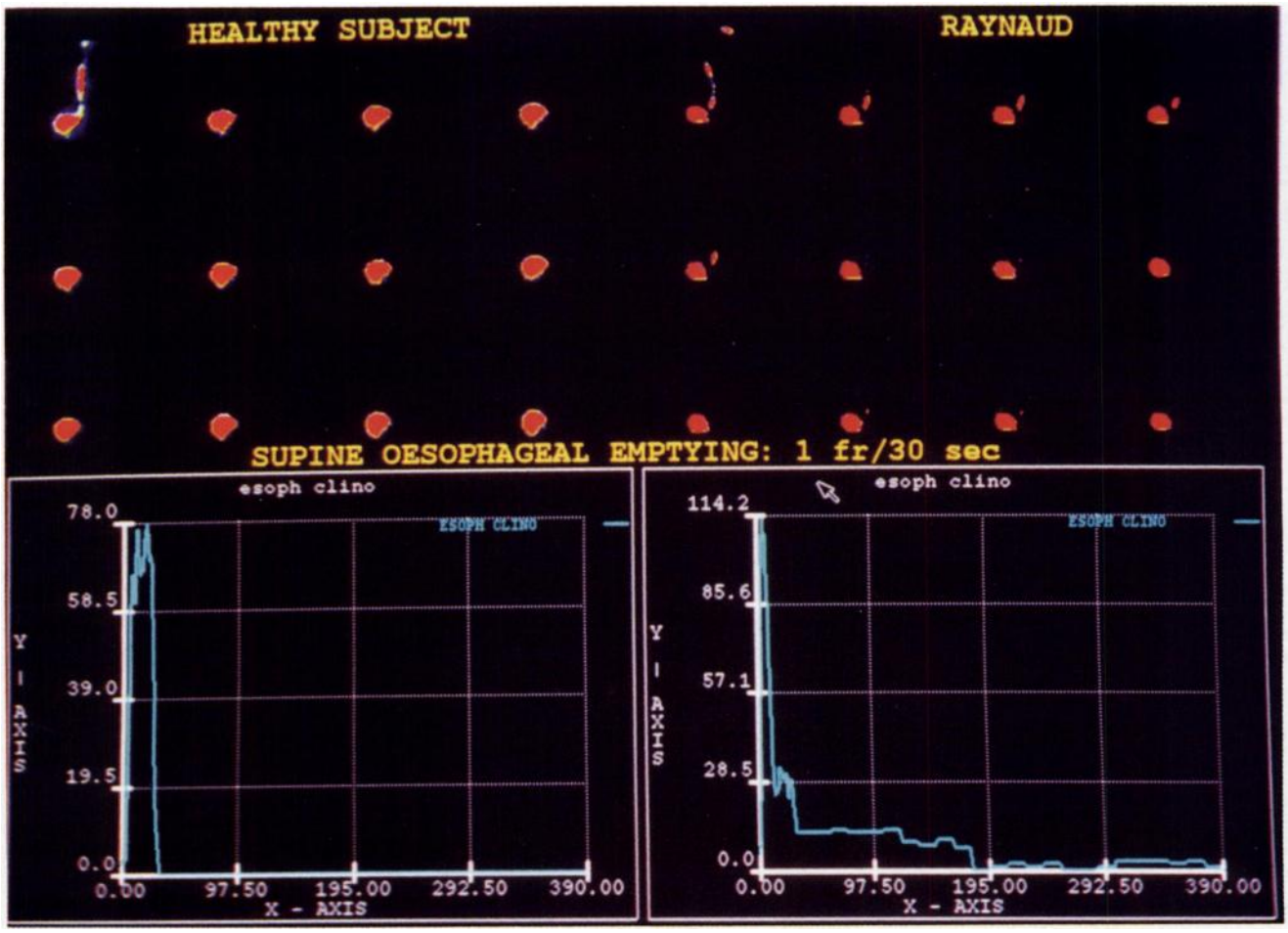

FIGURE 2. Scintigraphic dynamic images and time-activity curves in healthy subject and in RP-affected patients, respectively. Y-axis expresses counts (cps); x-axis expresses time (s).

significant stagnation of radioactivity into the esophageal body confirmed by time-activity curves. The RP images on the right side of Figure 2 show a small and temporary stagnation of labeled meal into the lower third of the esophagus in comparison to the healthy subject's images on the left.

The relationship between all three parameter values and the symptom score was not significant ($P > 0.05$). The mean ± SD symptom score of RP patients was 1.43 ± 1.45 for dysphagia, 1.25 ± 1.22 for acid regurgitation and 0.78 ± 0.96 for heartburn. A positive correlation was found ($r > 0.6$, $P < 0.05$) between the duration of disease in SSc-affected patients and transit time in upright position, and between duration of disease and integral value in orthostatism in the same group of patients. During the study, 4/32 patients with primary RP and 5/18 with SSc reported only dysphagia as esophageal symptoms.

DISCUSSION

Esophageal transit scintigraphy was introduced more than 20 y ago, but its exact role in the evaluation of patients with suspected esophageal motility diseases remains controversial. Opinions vary, but it seems at the very least to be useful clinically under the following conditions: (a) when esophageal manometry is unavailable or not tolerated, (b) when manometry is equivocal or negative but reasonable suspicion of disease remains and (c) when clinical management is aided by monitoring for serial changes or response to therapy (*19*).

One of the most interesting and intriguing fields of application is the assessment of esophageal involvement in SSc-affected patients (Table 1). It is known that about 75% of patients with SSc develop a significant esophageal involvement (*3*). Several authors (*5–15*) have demonstrated that radionuclide esophageal transit is a safe, noninvasive, highly sensitive method that might be used as an alternative to esophageal manometry in patients with SSc. As shown in Table 1, esophageal scintigraphy compared to esophageal manometry has a high sensitivity (range 82%–100%) using a liquid and semisolid radiolabeled bolus in the supine position. The low sensitivity found by Maddern et al. (*8*) might be due to the upright position, because gravity plays an important role in accelerating the esophageal clearance of a radioactive bolus. A similar case of low sensitivity (75%) was found by Parkman et al. (*15*) when studying only four patients affected by SSc.

In a study by Luggen et al. (*20*) it was concluded that 50%

of patients with suspected secondary RP will develop connective tissue disease over a period of 8.4 y. Nailfold capillary microscopy predicts the development of SSc or any definite connective tissue disease and should be included in the evaluation of all such patients. The aim of our study was to assess whether a well-tolerated and quick method, such as esophageal scintigraphy, could not only discriminate between SSc and primary RP patients but also demonstrate esophageal involvement in primary RP patients, symptomatic or not.

In this study, we used a semisolid meal (apple puree) that provided a standardized bolus and that is commercially available. Kim et al. (*21*) found transit in normal subjects to be progressively slower as the aqueous bolus became more viscous. Before commencing this study we verified in healthy subjects that the consistency of apple puree allowed us to clear the activity from the whole esophagus in a scintigraphy study lasting only 6.5 min. The acquisition methods are identical to those applied by previous authors (*12,14*), who evaluated transit times and condensed images, respectively. Kaye et al. (*14*) divided the parametric images into five grades taking into account both erect and supine scans. We assessed three quantitative indices obtained by the time-activity curves of the whole esophagus: transit times, emptying times and integral counts. Considering the possibility that there could be differences in the spatial distribution of lesions and dysmotility in SSc and RP, a calculation of parameters for the three segments might have been a more sensitive approach but would have worked to the detriment of reproducibility. Moreover, the transit time alone may be misleading when the labeled bolus leaves a portion in the esophagus.

In addition we used EET to try to distinguish those patients who had a normal transit time of a portion of radioactive meal and a stagnation of the rest of the meal in the lower esophagus. In fact, this parameter was revealed to be the most sensitive. The phenomenon of aberrant swallows and deglutitive inhibition with resultant misleading ineffectual emptying of the esophagus have been supported by some investigators (*10,22*) but not by others (*7,23,24*). This phenomenon creates a risk of false-positive results when using only the initial swallow. However, none of these 13 healthy subjects (26 studies) showed any residual of radioactive meal in the esophageal body. Evaluation of other thresholds such as 75% or 90% of esophageal emptying should not reduce the specificity of our method, considering the consistency of radioactivity stagnation that was found in the lower esophagus in these patients.

The originality of this study has been to compare not only SSc and healthy subjects but also primary RP-affected patients. The two patient populations were not so significantly different regarding the prevalence of symptoms. In fact only the frequency of severe heartburn (score 2.3) was higher in the SSc group compared to the RP group ($P = 0.05$). Dysphagia was equally distributed between the two groups, and, overall, in contrast with previous studies, there was not a significant correlation between symptoms and quantitative indices. This could be due to the limited population studied.

All three parameters, in particular in the supine position, discriminated well between SSc patients, RP patients and healthy subjects, confirming the presence of impaired peristalsis, previously demonstrated by other authors (*25*). Moreover, EETs in both positions were able to distinguish primary RP-affected patients from healthy individuals.

In 6 out of 32 RP patients (19%), supine EET was >300 s. Two of these patients had score 2 dysphagia, two patients had score 3 dysphagia and the last two patients had score 0. These patients did not show any anatomical abnormalities or strictures on endoscopy. Moreover, there was no positive correlation in RP patients between the symptom score and the presence of stagnation in the lower esophagus. The 6 patients with stagnation of radioactivity in the lower esophagus did not show a significant difference in the symptom score compared to the rest of patients affected by RP.

In agreement with previous studies, 85% of SSc patients had radioactivity stagnation in the lower esophageal third.

These preliminary data seem to have the following implications: (a) primary RP patients have an esophageal involvement that in a few cases may be severe and not deriving from anatomical abnormalities or from the presence of a gastroesophageal acid reflux. An important limit of this study is the lack of a comparison with manometry, which, being considered the most sensitive method to detect isolated lower esophageal sphincter dysfunction (*15*), might have demonstrated an early sphincter involvement. (b) Earlier esophageal involvement could have a prognostic value in identifying those patients in whom scleroderma disease will develop. Only long-term follow-up will determine the frequency with which the systemic syndrome develops in such patients. It appears reasonable to consider these patients to have a *forme fruste* of SSc.

CONCLUSION

ETT, EET and IV of the time-activity curve obtained by dynamic scintigraphic studies, particularly in the supine position, proved to be sensitive parameters to assess esophageal involvement in SSc patients. Both transit and emptying times in the supine position also seem to be useful in assessing esophageal dysfunction in primary RP-affected patients with mild or absent symptomatology, discriminating them from healthy subjects.

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