# Gastric Involvement in Systemic Sclerosis: A Prospective Study

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**OBJECTIVES:** This study aims to assess the prevalence of gastric electrical activity dysfunction with cutaneous electrogastrography (EGG), disturbances of gastric emptying function using radiopaque pellets, and gastric endoscopic abnormalities in patients with systemic sclerosis (SSc). We also investigate for an association between EGG and gastric-emptying data with clinical manifestations and esophageal motor disturbances.

**METHODS:** Fasting and postprandial gastric electrical activity was studied in 22 consecutive patients with SSc (17 with and 5 without clinical gastric manifestations) and 22 ageand sex-matched healthy subjects. Gastric emptying of radiopaque pellets and gastroscopy were also performed in SSc patients.

**RESULTS:** The prevalence of EGG disturbances was as high as 81.82% in SSc patients. SSc patients exhibited, compared with controls, higher median percentage of dominant frequency in bradygastria during the fasting period and lower median values for postprandial electrical power and postprandial to fasting ratio for electrical power. Gastric emptying of radiopaque pellets was delayed in 11 SSc patients, and gastroscopy demonstrated "watermelon stomach" in 3 SSc patients. No correlation was found between the severity of gastric impairment and clinical presentation, SSc duration and subsets, and esophageal manometric impairment.

**CONCLUSIONS:** Our study underlines the high frequency of gastric dysfunction in SSc patients. It suggests the usefulness of EGG in SSc in noninvasively detecting disorders of gastric electrical activity at an early stage and symptomatic patients with gastroparesis (because there was a correlation between values of postprandial to fasting ratio for electrical power of < 1 on EGG and delayed gastric emptying). Gastric-emptying evaluation of radiopaque pellets may further be a helpful method to depict symptomatic SSc patients with gastroparesis. Finally, our series confirms that watermelon stomach diagnosis should be excluded in SSc patients presenting with gastrointestinal hemorrhage or with anemia related to iron deficiency. (Am J Gastroenterol 2001;96: 77–83. © 2001 by Am. Coll. of Gastroenterology)

# INTRODUCTION

Systemic sclerosis (SSc) is a systemic inflammatory disorder affecting the skin and other organs, particularly the gastrointestinal tract, where lesions have led to motor activity impairment (1–5). Esophageal and anorectal motility abnormalities are frequent in SSc patients (70 to 95%) and have been extensively described (1–13). Gastric involvement is less recognized, although it may be responsible for dyspeptic manifestations, gastroparesis, deterioration of gastroesophageal reflux, or gastric hemorrhage related to antral vascular ectasia or the phenomenon known as *watermelon stomach* in SSc patients (1–4, 7–9, 11, 13–18).

To date, the diagnosis of gastric involvement in SSc has required invasive techniques, and systematic studies of gastric involvement are therefore rare (8, 10, 19). Cutaneous electrogastrography (EGG; 20-23) and gastric-emptying evaluation of radiopaque pellets may be both accurate and noninvasive tests for testing gastric impairment in SSc patients. This prompted us to conduct a prospective study in 22 consecutive patients with SSc, without prior selection of patients on clinical presentation, to 1) assess both the prevalence and the characteristics of gastric electrical activity disturbances with cutaneous EGG; 2) determine the frequency of the gastroscopic abnormalities and of disorders of gastric-emptying function, using radiopaque pellets; and 3) evaluate whether the findings of EGG and gastric emptying function are associated with gastric clinical manifestations, SSc duration and subsets, and esophageal motor disturbances.

# **MATERIALS AND METHODS**

## Patient and Control Population

Twenty-two consecutive patients, seen at the University of Rouen medical center between January 1998 and February 1999, with a definite diagnosis of SSc were included in the study. They consisted of 2 men and 20 women with a median age of 61.5 yr (range: 33–87 yr); the median duration of the disease, considered to have existed from the onset date of Raynaud's phenomenon, was 6 yr (range: 1–24 yr).

Nine patients fulfilled all the American College of Rheumatology diagnostic and therapeutic criteria for SSc (24). The 13 remaining patients who did not fulfill all the American College of Rheumatology criteria had the complete CREST variant (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias). Patients were grouped according to the criteria of Leroy *et al.* (25); 4 patients (18.18%) had diffuse cutaneous SSc (dcSSc), and 18 (81.82%) had limited cutaneous SSc (lcSSc).

All 22 patients had had a previous standardized evaluation of organ involvement, resulting in a disease score (range: 0–18) for each patient (26); higher SSc scores are known to be associated with increased severity of the disease. The median disease score in our patients was 3 (range: 1–8). Twenty patients had manometric evidence of esophageal involvement related to SSc. The patients were classified according to Hurwitz's (27) criteria for the degree of esophageal involvement on manometry; that is, 2 had normal esophageal motility (stage I); 3 had uncoordinated peristalsis with normal-pressure wave amplitude (stage II); 4 had uncoordinated peristalsis with low-pressure wave amplitude (stage III); and 13 had absence of peristalsis with decreased low-esophageal sphincter pressure (stage IV).

Seventeen of the 22 patients (77.27%) had digestive symptoms consistent with gastric impairment: epigastric pain (n = 4), epigastric fullness (n = 7), epigastric discomfort (n = 10), nausea (n = 3), and vomiting (n = 2).

EGG findings in SSc patients were compared with those in 22 age- and sex-matched healthy subjects [2 men and 20 women, with a median age of 55 yr (range: 25–61 yr)]. For each patient, we attempted to select a same-sex control subject whose age was within 5 yr of the patient's age. None of the SSc patients or controls had a previous history of rheumatic, liver or digestive surgery, cholecystectomy, or vagotomy.

The study was approved by the local Medical Research Ethics Committee. Written informed consent was obtained from all patients and controls before the study.

## Cutaneous Electrogastrography

RECORDING SYSTEM. Cutaneous EGG was performed with a 96-kb portable apparatus (Synectics Medical AB, Stockholm, Sweden). All recordings were carried out using sampling frequencies of 4 Hz and with both values of highand low-pass filters of 0.01 and 0.526 Hz, respectively; filtration of recorded signals allowed elimination of both pulmonary and cardiac signals. EGG data from transducers were digitized and then stored on the hard disk of an IBM PC computer. These findings were analyzed by a commercially available and validated software program (Synectics Medical AB).

STUDY DESIGN. Medication that might affect gastric motility (cisapride, metoclopramide, anticholinergics, calcium channel antagonists, macrolide antibiotics) was discontinued  $\geq$ 72 h before EGG. After a 12-h overnight fast, two bipolar silver chloride surface electrodes (Red Dot, 2271, 3M, Ontario, Canada) were positioned, under ultrasound control, on the skin directly overlying the gastric antrum, which provides a characteristic signal detection. A third skin surface electrode was placed, to form an equilateral triangle, and served as a reference lead. Gastric electrical activity was continuously recorded for 3 h: one in the fasting state and two after ingestion of a standard meal consisting of 20% protein, 50% carbohydrate, and 30% fat (750 kcal, *i.e.*, beefsteak, 100 g; french beans, 150 g; mashed potatoes, 150 g; orange juice, 20 cl; processed cheese, 15 g; butter, 15 g; and two rusks).

ANALYSIS OF THE TRACINGS. Both visual and computerized analyses of gastric electrical activity were performed by two of the authors (I.M. and P.D.), who are experienced in EGG chart assessment. One of the authors (P.D.) was blinded to the patients' clinical symptoms and test results. The following EGG parameters were assessed in fasting and postprandial periods: 1) dominant frequency [cycles per minute (cpm); normal values: 2 to 4 cpm]; 2) percentage of dominant frequency in bradygastria (bradygastria was defined as a frequency <2 cpm); 3) percentage of dominant frequency in tachygastria (tachygastria was defined as a frequency >4 cpm); 4) percentage of dominant frequency in normogastria (range: 2-4 cpm); 5) electrical power (amplitude of antral electrical activity); and 6) postprandial to fasting ratio for electrical power (normal values >1).

After analysis, EGG disorders were classified as normal, mild, or severe impairment. Patients were considered to have mild EGG impairment when they exhibited abnormalities of gastric electrical activity during fasting period (low values of dominant frequency, high percentages of bradygastria or tachygastria, or low values of electrical power). Patients were considered to have severe EGG impairment when they presented with disturbances of gastric electrical activity either during both fasting and postprandial periods (low values of dominant frequency, high percentage of bradygastria or tachygastria, or low values of electrical power) or during the postprandial period (low values of dominant frequency, higher percentage of bradygastria or tachygastria, or postprandial to fasting ratio for electrical power <1).

#### Gastric-Emptying Evaluation of Radiopaque Pellets

Medication that might affect gastric motility was discontinued  $\geq$ 72 h before gastric-emptying evaluation of radiopaque pellets. After a 12-h overnight fast, SSc patients ingested 10 radiopaque pellets with one bun and 240 ml of liquid (7-Up soda), as previously described (28). These radiopaque pellets were prepared from a Levin tube and cut in 5-mm pieces. All subjects underwent abdominal radiographs, which were performed at 0, 1, 2, 3, 4, 5, and 6 h after the ingestion of the standard meal.

	Gro	Group		
Parameter	SSc Patients (n = 22)	Control Subjects $(n = 22)$	р	
Interdigestive electrogastrographic parameters				
Dominant frequency (cpm)	2.81 (0.23-3.28)	2.81 (0.47-3.28)	0.181	
% of dominant frequency in bradygastria	33.50 (0.00-89.30)	1.80 (0.00-17.90)	< 0.0001	
% of dominant frequency in tachygastria	2.15 (0.00-20.00)	0.00 (0.00–15.10)	0.228	
% of dominant frequency in normogastria	62.85 (10.70–98.20)	96.95 (78.60-100.00)	< 0.0001	
Electrical power (amplitude of antral activity)	52.40 (3.39–619.63)	127.90 (9.15–339.53)	0.213	
Postprandial electrogastrographic parameters				
Dominant frequency (cpm)	3.05 (1.64-3.52)	3.05 (0.23-3.28)	0.559	
% of dominant frequency in bradygastria	20.95 (0.00-50.00)	15.50 (0.00-35.00)	0.115	
% of dominant frequency in tachygastria	1.50 (0.00-12.30)	1.75 (0.00–9.80)	0.341	
% of dominant frequency in normogastria	77.05 (41.30–100.00)	82.50 (65.00-100.00)	0.176	
Electrical power (amplitude of antral activity)	113.09 (20.00–6623.56)	269.06 (16.89-2294.88)	0.100	
Postprandial to fasting ratio of electrical power	1.89 (0.49–116.75)	3.30 (0.16–17.03)	0.0008	

**Table 1.** Characteristics of Electrogastrographic Parameters in Patients With SSc and in Healthy Controls During a 1-h Examination Under Fasting Condition and a 2-h Examination in the Postprandial Period

Values are the median (range). p values were determined by Mann-Whitney tests.

Time of gastric emptying was evaluated by counting the number of radiopaque pellets remaining in the stomach on the consecutive abdominal radiographs. Time of gastric emptying was considered normal when no radiopaque pellets remained within the stomach 6 h after the ingestion of the standard meal, as shown elsewhere (28). Analyses of gastric emptying of radiopaque pellets were carried out by two authors (I.M. and P.D.), and one of us (P.D.) was blinded to the patients' clinical symptoms and test findings.

#### Gastric Endoscopy

Gastroscopy was performed to disclose mucosal abnormalities associated with SSc, especially the phenomenon known as watermelon stomach. The endoscopic pattern of watermelon stomach was characterized by both parallel and longitudinal red folds within the distal antrum, radiating to the pylorus; antral biopsies revealed capillary ectasia with focal intravascular thrombi and fibromuscular hyperplasia in the lamina propria.

#### Statistical Analysis

Statistical analyses were performed by Fisher exact test for binary outcomes and by the Mann-Whitney test for continuous outcomes. Comparison of continuous outcomes between subgroups of patients with SSc was made by the Kruskal-Wallis test when the number of patient subgroups was >3.

# RESULTS

### Electrogastrography Results

In this prospective study, the prevalence of EGG evidence of gastric involvement was 81.82% in patients with SSc. Only four patients exhibited no EGG abnormalities.

FASTING PERIOD. In the healthy control group, EGG demonstrated normal recordings in all patients, with median

values of dominant frequency 2.81 cpm. The characteristics of EGG parameters in controls are given in Table 1.

During the 1-h fasting recording period, SSc patients exhibited abnormalities of gastric electrical rhythm: bradygastria in 14 patients (63.64%) and tachygastria in 2 patients (9.09%). Median percentage of dominant frequency in bradygastria was significantly higher in SSc patients than in controls (33.50% *vs* 1.80%), whereas median percentage of dominant frequency in normogastria was lower in SSc patients (62.85% *vs* 96.95%). Electrical power tended to be lower in SSc patients (52.41 *vs* 127.90). The characteristics of EGG recordings in the SSc patients are shown in Table 1.

POSTPRANDIAL PERIOD. In the healthy control group, three subjects exhibited bradygastria. No patient had disturbances of electrical power. The characteristics of the post-prandial EGG parameters in controls are given in Table 1.

Ten SSc patients (45.45%) experienced bradygastria in the 2-h–fed pattern-recording period. In these 10 patients, 7 (70%) concomitantly exhibited high percentages of brady-gastria during the fasting period; the standard meal subsequently failed to induce an increase of gastric electrical rhythm in two of them (n = 2/7).

Electrical power tended to be lower in SSc patients than in controls (113.09 *vs* 269.06); 5 SSc patients had no increase of electrical power in the postprandial period. Median postprandial to fasting ratio for electrical power was lower in SSc patients (1.89 *vs* 3.30). The characteristics of EGG recordings in the SSc patients are shown in Table 1.

#### Gastric-Emptying Findings of Radiopaque Pellets

Gastric-emptying evaluation of radiopaque pellets was delayed in 11 SSc patients (50%); abdominal radiographs showed radiopaque pellets remaining within the stomach, 6 h after the ingestion of the standard meal.

	Gastric Emptying of		
Electrogastrographic Findings	Normal $(n = 11)$	$\begin{array}{l} \text{Delayed} \\ (n = 11) \end{array}$	р
Interdigestive electrogastrographic parameters			
Dominant frequency (cpm)	1.02 (0.23-3.28)	3.05 (0.23-3.28)	0.051
% of dominant frequency in bradygastria	36.80 (2.00-89.30)	31.60 (0.00-75.60)	0.669
% of dominant frequency in tachygastria	0.00 (0.00-20.00)	2.20 (0.00-17.50)	0.945
% of dominant frequency in normogastria	63.20 (10.70-90.90)	62.50 (21.20-98.20)	0.576
Electrical power (amplitude of antral activity)	53.86 (3.39–416.87)	50.95 (14.74-619.63)	0.818
Postprandial electrogastrographic parameters			
Dominant frequency (cpm)	2.81 (2.1-3.52)	3.28 (1.64–3.52)	0.973
% of dominant frequency in bradygastria	19.30 (0.00-46.90)	28.80 (0.00-45.30)	0.599
% of dominant frequency in tachygastria	1.70 (0.00-12.30)	1.30 (0.00-4.30)	0.468
% of dominant frequency in normogastria	78.00 (49.40–100.00)	70.70 (41.30-100.00)	0.622
Electrical power (amplitude of antral activity)	124.00 (20.00–1445.51)	109.61 (26.28–6623.56)	0.869

Table 2. Characteristics of	of Electrogastrographic Parameters as	a Function of Findings From	Gastric Emptying of Radiopaque Pellets

Values are the median (range). p values were determined by Mann-Whitney tests.

#### Gastroscopy Data

Gastroscopy demonstrated a characteristic pattern of watermelon stomach in three lcSSc patients (13.64%). Clinical manifestations associated with watermelon stomach were hemorrhage (n = 1) and asthenia (n = 2) secondary to anemia (due to chronic iron deficiency).

## Comparison of Electrogastrographic and Gastric Emptying of Radiopaque Pellets Findings

EGG parameters were similar in patients with normal (n = 11) and delayed (n = 11) gastric emptying of radiopaque pellets. The results are shown in Table 2. However, 4 of 5 SSc patients (80%), with values of postprandial to fasting ratio for electrical power of <1, exhibited delayed gastric emptying of radiopaque pellets.

# Predictive Factors of Gastric Impairment

COMPARISON OF CLINICAL DIGESTIVE MANIFES-TATIONS AND DATA OF EGG AND GASTRIC-EMP-TYING EVALUATION. As shown in Table 3, we failed to find a relationship between the presence of gastric symptoms and the severity of both EGG findings (as classified as severe, mild, or normal) and data of gastric emptying of radiopaque pellets.

PREDICTIVE FACTORS OF SEVERE EGG IMPAIR-MENT. There were no significant differences between patients with severe, mild, and normal electrogastrographic findings with respect to median SSc duration (7 vs 6 vs 5.5 yr; p = 0.814) and activity score (3 vs 5 vs 5; p = 0.545).

The prevalence of abnormal EGG tended to be higher in lcSSc patients compared with those of dcSSc patients (88.89 vs 50%; p = 0.089). Moreover, as shown in Table 4, the degree of EGG dysfunction also tended to be higher in lcSSc patients than in dcSSc patients.

Finally, EGG parameters were similar in patients with severe (stages III/IV; n = 17) and mild (stages I/II; n = 5) esophageal manometric dysfunction (p = 0.527). Severe EGG abnormalities were further found in two patients with normal esophageal manometry.

PREDICTIVE FACTORS OF ABNORMAL GASTRIC EMPTYING OF RADIOPAQUE PELLETS. Patients with normal and delayed gastric emptying had similar median SSc duration (5 vs 7 yr; p = 0.222) and activity score (5 vs 3; p = 0.330).

LcSSc patients had more often delayed gastric emptying of radiopaque pellets than did dcSSc patients [61.11% (11/ 18) *vs* 0% (0/4); p = 0.09].

Finally, the prevalence of delayed gastric emptying was similar in patients with stages III/IV and stages I/II esophageal dysfunction (47.06% vs 60%; p = 0.647). Delayed gastric emptying was observed in two patients with normal esophageal manometry.

Table 3. Gastric Clinical Manifestations as a Function of Electrogastrographic and Gastric-Emptying Findings

			Gastric Symptoms				
Finding	No. of Patients	None	Epigastric Pain	Epigastric Fullness	Epigastric Discomfort	Nausea	Vomiting
Severe electrogastrographic impairment	9	5	4	1	2	1	1
Mild electrogastrographic impairment	9	0	6	2	6	2	1
Normal electrogastrography	4	0	3	4	3	0	0
Delayed gastric emptying of radiopaque pellets	11	3	7	4	4	2	1
Normal gastric emptying of radiopaque pellets	11	2	6	3	7	1	1

	SSc		
	dc	lc	
Electrogastrographic Findings	(n = 4)	(n = 18)	р
Interdigestive electrogastrographic parameters			
Dominant frequency (cpm)	2.93 (1.41-3.28)	2.81 (0.23-3.28)	0.227
% of dominant frequency in bradygastria	24.05 (2.00-62.50)	33.05 (0.00-89.30)	0.609
% of dominant frequency in tachygastria	5.00 (0.00-20.00)	2.15 (0.00-17.50)	0.623
% of dominant frequency in normogastria	75.60 (17.50-88.70)	56.70 (10.70-98.20)	0.609
Electrical power (amplitude of antral activity)	151.33 (29.59–416.87)	50.04 (3.39-619.63)	0.173
Postprandial electrogastrographic parameters			
Dominant frequency (cpm)	3.40 (2.81-3.52)	3.05 (1.64-3.52)	0.09
% of dominant frequency in bradygastria	8.4 (5.00-22.20)	29.05 (0.00-50.00)	0.147
% of dominant frequency in tachygastria	3.85 (0.00-12.30)	0.65 (0.00-4.30)	0.179
% of dominant frequency in normogastria	82.45 (76.10-95.00)	70.35 (41.30–100.00)	0.201
Electrical power (amplitude of antral activity)	197.62 (90.90–1445.51)	109.19 (20.00–6623.56)	0.173

Table 4.	Characteristics	of Electrogastrographic	Parameters as a	Function of SSc Subsets
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Values are the median (range). p values were determined by Mann-Whitney tests.

### DISCUSSION

Gastric involvement occurs in as high as 10 to 75% of SSc patients (1-9, 11-13, 29-32). It is still recognized to be associated with high morbidity, as gastroparesis may lead to the following (1-4, 9-11): 1) inability to ingest sufficient calories, resulting in malnutrition and at later stages, in cachexia and electrolyte disturbances; and 2) gastroesophageal reflux exacerbation. Early management of gastric motor disorders is therefore particularly important in SSc. However, to date, all tests previously used to detect gastric involvement in SSc patients were either nonsensitive (barium meal), poorly tolerated (manometry), or caused radiation exposure (scintigraphy), and both noninvasive and sensitive methods to detect gastric impairment remain to be established. It has been well documented that there is a pacemaker potential arising from the stomach, resulting in a cyclical variation in gastric electrical activity (20, 21, 23, 33, 34): 1) basic electrical rhythm, characterized by a regular frequency (3–4 cpm), occurring in the fasting period; and 2) electrical response activity in the postprandial period. The rate of gastric emptying of solids may be proportional to this antral electrical response activity. Because the antrum seems to be the site for the occurrence of gastric electrical activity, the recording of antral electrical activity, using cutaneous EGG, may provide a helpful noninvasive test in the diagnosis of gastric impairment (21, 23, 34) at an early stage in SSc patients.

Our prospective series is, to our knowledge, the first to evaluate SSc patients who were not selected according to their clinical digestive presentation. We observed a high frequency (81.82%) of EGG disturbances. We therefore conclude that gastric impairment in SSc is somewhat more prevalent than has previously been reported. Our data are at variance with that reported by Pfaffenbach *et al.* (35), who failed to find electrical disturbances on EGG in 17 SSc patients. However, one could argue that because of the shorter duration of the total recording, those authors (35) could have underestimated the frequency of gastric dysfunction.

In the present series, the EGG data demonstrated that SSc patients presented numerous alterations of gastric electrical rhythm. During the fasting state, SSc patients exhibited a high prevalence of bradygastria (63.64%); 10 SSc patients (45.45%) also had a concomitant high frequency of bradygastria in the postprandial period. These data are particularly relevant; other authors have noted a relationship between the presence of electrical rhythm disturbances and digestive symptoms (i.e., nausea/vomiting) in patients, with return to normal gastric electrical activity being associated with improvement of symptoms (20-23). Our findings are consistent with those of previously published series, as our three SSc patients with nausea/vomiting had bradygastria on EGG; bradygastria may have contributed to less effective contractions and gastroduodenal coordination in these patients. Marycz et al. (36) have also reported that bradygastria was more frequent in SSc patients with antral hypomotility than in those without.

The second main EGG finding, in the present series, was lower median values of electrical power (decreased amplitude of electrical activity) in SSc patients, compared with the case of healthy controls, during fasting and postprandial periods. Moreover, increase of electrical power was less significant in SSc patients postprandially, postprandial to fasting ratio of electrical power being lower in SSc patients than in controls (1.89 vs 3.30). Because higher increase in electrical power ( $\geq 3$  to 4 times) in the postprandial compared with the fasting period has been reported to be associated with stronger gastric contractions in healthy subjects (20-22, 33, 34), our findings indicate a decrease of gastric contractile activity in SSc patients. Interestingly, EGG values of postprandial to fasting power ratio <1 have been noted to be correlated with gastric hypomotility (21). Our results are in accordance with those reported in the literature, as four of our five SSc patients (80%) who did not experience increase of gastric electrical power postprandially (with values of postprandial to fasting power ratio < 1) had concomitant delayed gastric emptying of radiopaque pellets. Marycz *et al.* (36) have also noted previously a relationship between decreased postprandial electrical power on EGG and antral hypomotility in two SSc patients. We therefore suggest that absent increase of postprandial electrical power could result in postprandial gastric hypomotility in SSc patients.

The radiological evaluation of radiopaque markers' gastric emptying is a simple and convenient method for the detection of gastroparesis in clinical practice (28, 37, 38). In the present series, we have observed that 50% of SSc patients had delayed gastric emptying of radiopaque pellets. As shown by Feldman et al. (37), the gastric emptying of radiopaque indigestible markers probably involves the phase III of the migrating motor complex (MMC); because of their size (>2 mm), which prohibits their passage through the pylorus, the markers cannot be emptied during the postprandial period and would be subject to the reestablishment of the interdigestive motility pattern, in which phase III MMC plays the role of a "gastric housekeeper" (1, 38). The radiological marker test may therefore evaluate the delay of the return of the interdigestive motility pattern (i.e., phase III MMC) after a meal (1, 38). We suggest that gastricemptying evaluation of radiopaque pellets may also be a helpful method to detect symptomatic SSc patients, who have delayed gastric emptying of solids and abnormal phase III MMC.

The pathological mechanisms of gastric dysmotility in SSc remain unknown, although it has been postulated that gastric impairment may result from progressive histological lesions, similar to those found in the skin (3). Sjögren (3) has proposed the following steps for the occurrence of sclerodermatous gastric involvement: vascular damage (grade 0), neurogenic impairment (grade 1), and myogenic dysfunction (grade 2), with the replacement of normal smooth muscle by collagenous fibrosis and atrophy of muscle fibers. In the present series, we observed patterns of neurogenic dysfunction (abnormal gastric electrical activity on EGG) in 81.82% of SSc patients, whereas 50% of SSc patients had patterns of myogenic impairment (delayed gastric emptying of radiopaque pellets). Our data suggest that neurogenic abnormalities precede myogenic disturbances within the stomach of SSc patients and further indicate that gastric myogenic disorders may occur earlier during the course of SSc than has previously been noted.

Another practical finding, in this instance, is that 3 of 22 SSc patients had watermelon stomach. In a series of 45 patients with watermelon stomach, Gostout *et al.* (15) have also noted that 13.33% of patients had an associated SSc. Our findings therefore confirm that watermelon stomach may represent a component of vascular alterations in SSc (1–3, 14–18). Interestingly, our three patients with watermelon stomach had lcSSc, indicating that it may be a digestive manifestation of lcSSc. Because systemic manifes-

tations may precede cutaneous impairment in SSc, when watermelon stomach is diagnosed, an evaluation for SSc (including clinical examination, antinuclear antibodies, nailfold capillaroscopy) should therefore be carried out systematically. Finally, our findings highlight that diagnosis of watermelon stomach should be also excluded in SSc patients presenting with gastrointestinal hemorrhage and/or anemia due to iron deficiency. Duchini *et al.* (14), in 22 SSc patients with gastrointestinal hemorrhage, also disclosed watermelon stomach in 9.09% of cases.

Previous series (13) have noted that the frequency of gastric involvement increases with the duration of SSc and the age of SSc patients. In our experience, neither the patients' age nor duration and activity of SSc could be considered to be predictive of gastric impairment on EGG and gastric-emptying evaluation of radiopaque pellets. Our data confirm the results reported by Maddern et al. (10), who were also unable to find a correlation between SSc duration and scintigraphic delayed gastric emptying. Few authors (1, 4) have further shown that gastric involvement did not correlate with SSc subsets. Our series reveals that gastric dysfunction tends to be more frequent in lcSSc than in dcSSc patients on EGG (88.89% vs 50%) and gastric emptying of radiopaque pellets (61.11% vs 0%); all patients with watermelon stomach further had lcSSc. Finally, we have demonstrated that esophageal manometric dysfunction should not be considered a predictive factor of gastric disturbances; among the patients with EGG and radiological involvement, two had no esophageal abnormalities. Our results are at variance with those of other authors (19) who have noted a correlation between delayed esophageal and gastric emptying.

In conclusion, our study underlines the high frequency of gastric involvement in SSc patients. Our findings also suggest that EGG may be useful in noninvasively depicting the following: 1) disorders of gastric electrical activity at an early stage, notably in asymptomatic patients; however, it is questionable whether patients presenting with no clinical symptoms but exhibiting EGG disturbances require prokinetic therapy and 2) the subgroup of symptomatic SSc patients with gastroparesis, because we observed a correlation between EGG disturbances (*i.e.*, postprandial to fasting ratio for gastric electrical power of <1) and delayed gastric emptying of radiopaque markers. Moreover, our series demonstrates that gastric-emptying evaluation of radiopaque pellets may be a helpful method to detect symptomatic SSc patients with gastroparesis; gastric emptying of radiopaque pellets may also assist in the selection of SSc patients who may require manometry of the upper digestive tract because delayed gastric emptying of radiopaque markers may be associated with abnormalities of phase III MMC. Finally, our series confirms that watermelon stomach diagnosis should be excluded in SSc patients presenting with gastric hemorrhage and/or anemia related to iron deficiency.

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# REFERENCES

- Jiranek GC, Bredfelt JE. Organ involvement: Gut and hepatic manifestations. In: Clements PJ, Furst DE, eds. Systemic sclerosis. Baltimore, MD: Williams & Wilkins, 1996:453–82.
- Sjögren RW. Gastrointestinal motility disorders in scleroderma. Arthritis Rheum 1994;37:1265–82.
- Sjögren RW. Gastrointestinal features of scleroderma. Curr Opin Rheumatol 1996;8:569–75.
- Lock G, Holstege A, Lang B, Schölmerich J. Gastrointestinal manifestations of progressive systemic sclerosis. Am J Gastroenterol 1997;92:763–71.
- Marie I, Levesque H, Ducrotte P, et al. Manometry of the upper intestinal tract in patients with systemic sclerosis. A prospective study. Arthritis Rheum 1998;41:1874–83.
- Bortolotti M, Turba E, Tosti A, et al. Gastric emptying and interdigestive antroduodenal motility in patients with esophageal scleroderma. Am J Gastroenterol 1991;86:743–7.
- Cohen S, Laufer I, Snape WJ, Shiau YF, Levine GM, Jimenez S. The gastrointestinal manifestations of scleroderma: Pathogenesis and management. Gastroenterology 1980;79:155–66.
- Greydanus MP, Camilleri M. Abnormal postcibal antral and small bowel motility due to neuropathy or myopathy in systemic sclerosis. Gastroenterology 1989;96:110–5.
- Horowitz M, Maddern GJ, Maddox A, Wishart J, Chatterton BE, Shearman DJC. Effects of cisapride on gastric and esophageal emptying in progressive systemic sclerosis. Gastroenterology 1987;93:311–5.
- Maddern GJ, Horowitz M, Jamieson GG, Chatterton BE, Collins PJ, Roberts-Thomson P. Abnormalities of esophageal and gastric emptying in progressive systemic sclerosis. Gastroenterology 1984;87:922–6.
- Mittal BR, Wanchu A, Das BK, Ghosh PP, Sewatkar AB, Misra RN. Pattern of gastric emptying in patients with systemic sclerosis. Clin Nucl Med 1996;21:379–82.
- Poirier TJ, Rankin GB. Gastrointestinal manifestations of progressive systemic scleroderma based on a review of 364 cases. Am J Gastroenterol 1972;58:30–44.
- Rees WDW, Leigh RJ, Christofides ND, Bloom SR, Turnberg LA. Interdigestive motor activity in patients with systemic sclerosis. Gastroenterology 1982;83:575–80.
- Duchini A, Sessoms SL. Gastrointestinal hemorrhage in patients with systemic sclerosis and CREST syndrome. Am J Gastroenterol 1998;93:1453–6.
- Gostout CJ, Vigganio TR, Ahlquist DA, Wang KK, Larson MV, Balm R. The clinical and endoscopic spectrum of the watermelon stomach. J Clin Gastroenterol 1992;15:256–63.
- Manolios N, Eliades C, Duncombe V, Spencer D. Scleroderma and watermelon stomach. J Rheumatol 1996;23:776–8.
- Marie I, Cailleux N, Levesque H. Watermelon stomach and systemic sclerosis: localization of digestive system involvement? Arthritis Rheum 1996;39:1439.
- Watson M, Hally RJ, McCue PA, Varga J, Jimenez SA. Gastric antral vascular ectasia (watermelon stomach) in patients with systemic sclerosis. Arthritis Rheum 1996;39: 341–6.
- Wegener M, Adamek RJ, Wedmann B, Jergas M, Altmeyer P. Gastrointestinal transit through esophagus, stomach, small and large intestine in patients with progressive systemic sclerosis. Dig Dis Sci 1994;39:2209–15.
- 20. Chen J, McCallum RW. Electrogastrography: Measurement

analysis and prospective applications. Med Biol Eng Comput 1991;29:339–50.

- Geldof H, Van Der Schee EJ, Van Blankenstein M, Grashuis JL. Electrogastrographic study of gastric myoelectrical activity in patients with unexplained nausea and vomiting. Gut 1986;27:799–808.
- Koch KL, Stern RM, Stewart WR, Vasey MW. Gastric emptying and gastric myoelectrical activity in patients with diabetic gastroparesis: Effect of long-term domperidone treatment. Am J Gastroenterol 1989;84:1069–75.
- 23. You CH, Lee KY, Chey WY, Menguy R. Electrogastrographic study of patients with unexplained nausea, bloating and vomiting. Gastroenterology 1980;79:311–4.
- Subcommittee for Scleroderma Criteria of the American Rheumatism Association Diagnostic and Therapeutic Criteria Committee. Preliminary criteria for the classification of systemic sclerosis (scleroderma). Arthritis Rheum 1980;23:581– 90.
- Leroy EC, Black C, Fleischmajer R, et al. Scleroderma (systemic sclerosis): Classification, subsets and pathogenesis. J Rheumatol 1988;15:202–5.
- Levesque H, Baudot N, Delpech B, et al. Clinical correlations and prognosis based on hyaluronic acid serum levels in patients with progressive systemic sclerosis. Br J Dermatol 1991; 124:423–8.
- Hurwitz AL, Duranceau A, Postlethwait RW. Esophageal dysfunction and Raynaud's phenomenon in patients with scleroderma. Dig Dis 1976;21:601–6.
- Bertrand J, Metman EH, Danquechin-Dorval E, et al. Etude du temps d'évacuation gastrique de repas normaux au moyen de granules radio-opaques. Applications cliniques et validation. Gastroenterol Clin Biol 1980;4:770–6.
- D'Angelo WA, Fries JF, Masi AT, Shulman LE. Pathologic observations in systemic sclerosis (scleroderma): A study of fifty-eight autopsy cases and fifty-eight matched controls. Am J Med 1969;46:428–40.
- Dull JS, Raufman JP, Zakai MD, Strashun A, Straus EW. Successful treatment of gastroparesis with erythromycin in a patient with progressive systemic sclerosis. Am J Med 1990; 89:528–30.
- Hoskins LC, Norris HT, Gottlieb LS, Zamcheck N. Functional and morphologic alterations of the gastrointestinal tract in progressive systemic sclerosis (scleroderma). Am J Med 1962; 33:459–70.
- Weston S, Thumshirn M, Wiste J, Camilleri M. Clinical and upper gastrointestinal motility features in systemic sclerosis and related disorders. Am J Gastroenterol 1998;93:1085–9.
- Mintchev MP, Kingma YJ, Bowes KL. Accuracy of cutaneous recordings of gastric electrical activity. Gastroenterology 1993;104:1273–80.
- Smout AJPM, Van Der Schee EJ, Grashuis JL. What is measured in electrogastrography? Dig Dis Sci 1980;25:179–87.
- Pfaffenbach B, Adamek RJ, Hagemann D, Wegener M. Gastric myoelectrical activity and gastric emptying in patients with progressive systemic sclerosis. Am J Gastroenterol 1996; 91:411–2.
- Marycz T, Muehldorfer SM, Gruschwitz MS, et al. Gastric involvement in progressive systemic sclerosis: electrogastrographic and sonographic findings. Eur J Gastroenterol Hepatol 1999;11:1151–6.
- Feldman M, Smith HJ, Simon TR. Gastric emptying of solid radiopaque markers: studies in healthy subjects and diabetic patients. Gastroenterology 1984;87:895–902.
- Poitras P, Picard M, Déry R, et al. Evaluation of gastric emptying function in clinical practice. Dig Dis Sci 1997;42: 2183–9.