Systemic Sclerosis Gastrointestinal Manifestations: Practical Tools for its Assessment and Management

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Disclosure

• I have no financial disclosures or commercial relationships.
Overview

• Review how gastrointestinal tract symptoms are assessed in Systemic Sclerosis (SSc).

• Highlight common gastrointestinal tract conditions in SSc.
  • Gastroesophageal reflux disease (GERD)
  • Gastroparesis
  • Food Allergy and Intolerance

• Discuss special management considerations for SSc-related gastrointestinal conditions.
Systemic Sclerosis Gastrointestinal Tract (SSc-related GIT)

Importance:

• The GIT is the most commonly involved internal organ in SSc.
• GIT involvement is the presenting feature in 10% of SSc patients.
• GIT involvement occurs during disease course in up to 95% of SSc patients.

Challenges:

• SSc –related GIT clinical presentation and disease course varies.
• Symptoms often precede laboratory or anatomical abnormalities.
• Absence of symptoms does not exclude esophageal dysfunction.
Prevalence by Organ Involvement

Symptom Assessment:
- Questionnaires
- Categorical Severity
- Objective GIT testing

Testing:
- Laboratory
- Direct tissue visualization
- Motility
- Imaging


Small Oral Aperture; Sicca; Dental issues
Reflux; Dysmotility, Stricture; Barrett’s; Adenocarcinoma
Gastroparesis; ulcer; GAVE
Pseudo-obstruction; SIBO; Diverticuli; Megacolon
Fecal incontinence; rectal prolapse
## Gastro-esophageal Symptoms: Assessment by Questionnaire

<table>
<thead>
<tr>
<th>Upper Tract Symptoms</th>
<th>Patient Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>GERD-Q*</td>
<td>6 Questions</td>
</tr>
<tr>
<td>UCLA SCTC GIT 2.0</td>
<td>8 Questions</td>
</tr>
<tr>
<td>NIH PROMIS*</td>
<td>8-13 Questions</td>
</tr>
<tr>
<td>- Reflux</td>
<td>7 Questions</td>
</tr>
<tr>
<td>- Disruptive Swallowing</td>
<td>3-4 Questions</td>
</tr>
<tr>
<td>- Nausea and Vomiting</td>
<td></td>
</tr>
</tbody>
</table>

*link calculates scores: [http://www.soapnote.org/digestive-system/gerdq](http://www.soapnote.org/digestive-system/gerdq); [http://www.healthmeasures.net](http://www.healthmeasures.net)

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### The UCLA SCTC GIT 2.0 Questionnaire

#### Table 1. The GerdQ questionnaire

The following symptoms should be assessed over the previous week.

<table>
<thead>
<tr>
<th>Question</th>
<th>(Check one response for each symptom: No Days, 1-2 Days, 3-4 Days, 5-7 Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In the <strong>past 1 week</strong>, how often did you ...</td>
<td></td>
</tr>
<tr>
<td>1. ... have difficulty swallowing solid food?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>2. ... have an unpleasant stinging or burning sensation in your chest (heartburn)?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>3. ... have a sensation of bitter or sour fluid coming up from your stomach into your mouth (acid reflux)?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>4. ... have heartburn on eating ‘acidic’ foods such as Tomatoes &amp; Oranges?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>5. ... regurgitate (throw up or bring up small amounts of previously eaten food)?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>6. ... sleep in a ‘raised’ or an ‘L shaped’ position?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>7. ... feel like vomiting or throwing up?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
<tr>
<td>8. ... vomit or throw up?</td>
<td>![No Days] ![1-2 Days] ![3-4 Days] ![5-7 Days]</td>
</tr>
</tbody>
</table>
GERD has 4 specific symptom clusters:
1) Liquid and food sensation
2) Painful sensations
3) Belching and hiccups
4) Head and neck sensations
12
GISX28
How often did you feel like there was a lump in your throat?

☐ 1
Never → If Never, you are finished.

☐ 2
Rarely

☐ 3
Sometimes

☐ 4
Often

☐ 5
Very often

13
GISX30
How much did having a lump in your throat bother you?

☐ 1
Not at all

☐ 2
A little bit

☐ 3
Somewhat

☐ 4
Quite a bit
Practical Aspect of Using Questionnaires

Goal is for symptom identification.

Minimal patient time burden.

With no cost, can guide care decisions.

Not clear if improves patient satisfaction.¹

¹Almario. Am J Gastroenterol. 2016
Assessing Heartburn and Difficulty Swallowing

90% prevalence of esophageal symptoms in SSc patients.

Heartburn
- Is the patient adhering to behavioral interventions?
- Is the patient on treatment?
- Is the patient considering surgical intervention?

Difficult swallowing
- Liquids?
- Solids?
- Regurgitation?
## GERD Management Considerations

### Behavioral
- Smaller meals
- No eating 4 hours before bedtime
- Elevate head of the bed
- Avoid esophageal irritants
- Avoid tight fitting clothes
- Avoid alcohol and tobacco

### Invasive
- Medications
  - Coating
    - Sulfacrate/carafate
  - Acid suppression
  - Acid neutralization
  - Pro-motility

Procedure:
- Partial Nissen
Current Management Strategies for GERD

• Rely on empiric trials of acid suppression as both therapeutic and diagnostic tools.

• The PPI test:
  • Patients are started on a single-dose proton pump inhibitor (PPI).
  • Patients that fail single-dose PPI are increased to twice daily.
  • Sensitivity 80% for GERD diagnosis
  • Specificity 74% for GERD diagnosis
  • Not studied in patients with complex symptoms.
  • Long-term management has not been adequately studied.
Proton Pump Inhibitor Acid Suppression

Proton Pump Inhibitors
- Omeprazole (Prilosec, Zegrid)
- Lansoprazole (Prevacid)
- Dexlansoprazole (Dexilant)
- Esomeprazole (Nexium)
- Pantoprazole (Protonix)
- Rabeprazole (Acidphex)

Cautions
- Gastric acid is important for breakdown of food and release of micronutrients.
- High dose and/or long-term use, increased risk of bone fractures.
- Small bacterial overgrowth.

Indications
- Symptomatic GERD
- Peptic ulcer disease
- As part of Helicobacter pylori eradication therapy
- Barrett’s esophagus
- Eosinophilic esophagitis
- Laryngopharyngeal reflux causing laryngitis and chronic cough
Histamine (H2) Blockers Acid Suppression

**H2 Blockers**
- Ranitidine (Zantac)
- Famotidine (Pepcid)

**Cautions**
- Many drug interactions, including calcium channel blockers.

**Indications**
- Peptic ulcer disease
- GERD
Acid neutralization with Antacids

Other Antacids:
- CaCO₃ \((H^+ \text{ binds w/ } CO_3^{2-})\)
- Mg(OH)₂ \((H^+ \text{ binds w/ } OH^-)\)
- Al(OH)₃ \((H^+ \text{ binds w/ } OH^-)\)

NOTE:
- Mg has laxative effects (laxatives w/ Mg are used prior to endoscopy)
- Al causes constipation
- Antacids combining Al & Mg are used to lower stomach acid w/o producing undesirable constipation or diarrhea

Adapted from Lüllmann H et al. (2003)
Radiographic Assessment: Barium Swallow

Swallow evaluation with speech language pathologist
• Ordered for concern for aspiration.

Upper GI series or sine esophagram
• Single contrast provides information on stricture.
• Double contrast provides information on mucosal abnormalities:
  • Erosive esophagitis, hiatal hernia, cancer, and abnormal motility.

Practical Considerations:
• Not useful for making a diagnosis of GERD.
• Time: ~15 minutes to 1 hour
• Cost: ~$305 (with speech therapy $516)
Esophagogastroduodenoscopy (EGD)

Diagnostic:
- Esophagitis:
  - Infectious
  - Pill-induced
  - GERD-related
  - Barrett’s
  - Eosinophilic
- GAVE
- Celiac

Therapeutic
- Stricture dilation

Practical Considerations:
- Preparation: ~12 hours
- Time: ~ 2 hours (with recovery)
- Cost: $1,170 to $2,400

Alternative wireless capsule
- Indicated for identification of occult bleeding in small bowel.
- Contraindications:
  - Stricture
  - Gastroparesis
- Time: ~30 hours
- Cost: ~$1,400
GERD Monitoring

pH-monitoring in SSc:
- Assessing symptom relationship to reflux
- Assessing efficacy of therapy
- Indicated before surgical referral

Catheter-based:
- Assessing if reflux reaching pharynx
- Composite score:
  - % time pH < 4
  - # of reflux episodes
  - # of episodes > 5 minutes
- Time: 24-48 hours
- Cost: $225-1500

pH-Impedance
- Assessing non-acid reflux
- Time: ~24 hours
- Cost: $450

Wireless:
- Cannot assess pharyngeal reflux
- Time: 48-96 hours
- Cost: $1,000
GERD Surgical Options

Patients with Normal Motility

- Nissen Laproscopic Fundoplication
- Toupet Partial Fundoplication
Motility assessment: Manometry

- Indicated if reflux testing normal
- Practical Considerations:
  Time: ~30-40 minutes
  Costs: ~$500-1500
Nausea, Vomiting and Abdominal Distention

Abdominal Imaging: Pseudo-obstruction

- Indicated if acute mechanical obstruction suspected.
- Practical consideration:
  - Outpatient: Abdominal radiograph
  - Inpatient: CT without contrast
- Outcomes:\(^1\):
  - 70% resolution
  - 9% surgical resection
  - 16% mortality

Motility testing: Gastric Emptying Study\(^2\)

- Intestinal dysmotility occurs in 40-90%.
- Indicated if gastroparesis suspected.
- Obtain prior to initiation of pro-kinetics\(^3\).
- Practical considerations:
  - Time: ~5 hours
  - Cost: $2800

## Gastroparesis Management

### Behavioral
- High-fiber foods can make gastroparesis worse
  - Oranges, broccoli, apple with the skin on, wheat, beans, nuts, kale, and red cabbage.
- Fatty foods can make gastroparesis worse
  - Butter, cheese, processed meats, canned goods, and any fried meat.
- Minimize exacerbating medications:
  - Narcotic
  - Tricyclic antidepressants
  - Calcium channel blockers
  - Clonidine
  - Dopamine agonists
  - Lithium
  - Nicotine
  - Progesterone

### Treatment Options
- Metoclopromide (Reglan®)
- Erythromycin (low dosages, not antibiotic dosing levels)
- Domperidone (Motilium®, now only under special FDA protocols)
- Tegaserod (Zelnorm®, Zelmac®, now only available under special FDA protocols)

**Mechanism:**
- Speeds up stomach emptying and movement of the upper intestines.
- Caution: Cardiac toxicity

**Treatment of nausea**

Botulinum toxin injections are not recommended
Surgical Options: Gastroparesis

**Gastric Electrical Stimulation**
- Battery-operated device is implanted into the abdomen
- Sends electrical pulses to the muscles of the abdomen to increase gastric emptying

**Feeding Tube**
- Usually inserted directly into the small intestine through the abdomen
Assessing Abdominal Pain and Distention

Is small intestinal bacterial overgrowth (SIBO) suspected¹?

• Effects 50% of SSc patients.

• Breath testing²:
  • Sensitivity ranges form 65-70%

• Laboratories:
  • Serum³: carotene, vitamin D-25OH, B12, iron.
  • Fecal calprotectin⁴

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**Small Intestinal Bacterial Overgrowth**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Behavioral</th>
<th>Therapeutics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>Minimize certain medications</td>
<td>Pro-motility drugs</td>
</tr>
<tr>
<td>Distention</td>
<td>Hormone replacement</td>
<td>Initiate or cycle antibiotics</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>PPI dose</td>
<td>Probiotic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nutrition</td>
</tr>
</tbody>
</table>
Food Allergies and Intolerance

• Food allergy is an urgent, severe reaction that can be identified by allergy testing.
  • Skin prick testing
  • Atopy patch testing
  • Blood RAST testing

• Food intolerance or sensitivity has less severe symptoms, but is very uncomfortable and can be associated with pain and distention.
  • Lactose
    • Lactose-free products.
  • Fructose
    • Limit fruit (including juices and dried), honey, high-fructose corn syrup, and alcohol.
Nutritional Considerations

- The physical ability to digest food including chewing, swallowing, absorption, and elimination.
- Appetite fluctuations
- Taste changes
- Food/drug interactions
- Skills and ability to comply with dietary lifestyle changes.

**FODMAP Diet:**
- Short-chain carbohydrates
- Poorly absorbed
- Osmotically active
- Rapidly fermented
- Result in symptoms of abdominal bloating and pain.

https://stanfordhealthcare.org/content/dam/SHC/for-patients-component/programs-services/clinical-nutrition-services/docs/pdf-lowfodmapdiet.pdf

http://www.med.monash.edu/cecs/gastro/fodmap/iphone-app.html
FODMAP Education

• Low FODMAP education consists of initially eliminating FODMAPs from the diet for 6-8 weeks.

• Following symptom resolution, gradual reintroduction of foods to determine individual tolerance.

• FODMAP dietary education should be provided by a trained dietician.
Prevalence of malnutrition in 18-25% of SSc patients.

Malnutrition occurs across BMI or dietary self-report.

Clinical assessment tools:
- Malnutrition universal screening tool
- Laboratory: Serum carotene, folate, pre-albumin.
Prevalence of colon and anorectal disorders

Colonic involvement is seen in up to 20-50% of SSc patients.

Anorectum is involved in 50-70%.

Fecal incontinence occurs in over 20%.

Digital rectal exam is first step in evaluation.

Colonoscopy:
- All fecal incontinence patients.
- All SSc patients > age 50.
- Diagnostic and therapeutic.

Cost:
Assessment of Incontinence

Gastroenterology/Colorectal Surgeon

- **Endo-sonography:**
  - Time: 45 minutes
  - Cost: $175

- **Manometry:**
  - Time: 60 minutes
  - Cost: $600-1500

- **Balloon Expulsion test:**
  - Cost: $275

Radiographic Assessment:

- **Scintigraphic Defecography:**
  - Time: ~3 hours
  - Cost: $500

- **Dynamic MRI:**
  - Time: ~1 hour
  - Cost: $750
Additional Considerations: Oral-Facial Assessment

• Increase incidence of Sjögren’s syndrome in SSc\(^1\).
  • Practical assessment: Documentation of dentition in clinical assessment for dental coverage.

• Sub-lingual frenulum changes\(^2\).
  • Practical assessment: Clinical assessment of sublingual frenulum may assist in speech therapy evaluation.

SSc-related GIT Management Care Team

Components
- Team based care with Rheumatology, Gastroenterology, Social Work.
- Care coordination for access to specialists.
- Outcome measures to guide research.

Domains
- Transdisciplinary approach.
- Scheduling based on complexity.
- Quantification of processes and outcomes.

Key Elements
- Close liaison amongst providers.
- Dedicated schedulers and medical assistants with iterative flexibility.
- System to identify clinical care gaps.

Allred D. J Med Pract. 2017
Prevalence and Practical Assessment Conclusions:

- It is essential to ask SSc patients questions in order to understand symptoms. Questionnaires allows both severity grading and proper test ordering.
- The ordering of a GIT test should be guided by burden on patient and cost. The role of symptom relief versus prevention not yet clear.
- Oral and nutritional assessment can support ancillary services for SSc patients. All SSc patients should be assessed for malnutrition risk.
- True prevalence and best practice for management for SSc-related GIT will only be possible with collaboration.
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