Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR

ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2021 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2022 for this activity.
MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 30, 2021
Post-ERCP Pancreatitis: Past, Present and Future
Mohammad Yaghoobi, MD, FACG
August 5, 2021 at Noon Eastern

Week 31, 2021
Screening for Barrett’s Esophagus: Beyond Upper Endoscopy
Prasad G. Iyer, MD, MS, FACG
August 12, 2021 at Noon Eastern

Visit gi.org/ACGVGR to Register
Disclosures:

Speaker:
C. Prakash Gyawali, MD, MRCP, FACG
Consulting: Medtronic, Diversatek, Ironwood, Takeda, IsoThrive, Quintiles

Moderator:
Amit Patel, MD, FACG
Dr. Patel, faculty for this educational event, has no relevant financial relationship(s) with ineligible companies to disclose.

*All of the relevant financial relationships listed for these individuals have been mitigated*

ACG 2020 Clinical Guidelines
Clinical Use of Esophageal Physiologic Testing

C. Prakash Gyawali, M.D.
Professor of Medicine
Division of Gastroenterology

Washington University in St. Louis
Objectives

1. Describe indications for currently available esophageal physiologic tests
2. Understand performance characteristics of esophageal physiologic tests

Initial Approach: History & Questionnaire

Evaluation starts with a good clinical history

Patient-reported symptom questionnaires may aid evaluation of patients with esophageal symptoms, but symptom questionnaires alone should not be used to diagnose specific esophageal conditions

References:

Jones R et al. APT 2009;30:1030-8
Bolier EA et al. Dis Esophagus 2015;28:105-20
Taft T et al. NGM 2016;28:1854-60
UES and LES visible in the same window
Real time visualization of catheter position
Curled catheter can be identified and rectified
Three dimensional assessment of esophageal peristalsis
Intuitive depiction of motor function
Patterns of abnormal motility can be easily recognized
Software tools can be used to assess sphincter function
Vigor and timing of peristalsis can be assessed
Location of LES can be quickly identified for pH probe placement

HRM vs. Conventional Manometry
Improved diagnostic yield for achalasia compared to conventional manometry
Superior inter-rater agreement for motor diagnoses compared to conventional manometry
Learners favor HRM over conventional manometry

Roman S et al, Am J Gastroenterol 2016;111:372-80
Carlson DA et al, Am J Gastroenterol 2015;110:967-77
Soudagar AS et al, Gut 2012;61:798-803

HRM is recommended over conventional manometry

When to request a high-resolution manometry
Transit symptoms (dysphagia, regurgitation) not explained on EGD and/or barium swallow
Suspected esophageal motor disorder
As part of pH monitoring
Unexplained esophageal symptoms
Post fundoplication dysphagia
Dysphagia localized to upper esophageal sphincter
Adjunctive HRM Measures

Utilization of supplementary/provocative maneuvers with HRM improves the diagnostic yield of esophageal motility disorders in patients with obstructive esophageal symptoms.

Chicago Classification 4.0

10 wet swallows (supine/upright)

- Abnormal median IRP
- Alternate position swallows RDC/MRS
  - Abnormal IRP persists RDC/MRS
  - Abnormal BE or FLIP
  - NO EGJOO

Disorders of EGJ Function
- Achalasia type 1: All swallows fail, no PEP
- Achalasia type 2: All swallows fail, 20% PEP
- Achalasia type 3: 20% premature swallows
  - Alternate position swallows RDC/MRS
  - Abnormal IRP persists RDC/MRS
  - Abnormal BE or FLIP

Disorders of Peristalsis
- Absent contractility
- DES
- Hypercontractile
- IEM
- NO DISORDER OF PERISTALSIS
  - Consider meal challenges if appropriate

Yadlapati R et al, CCv4.0, Neurogastroenterol Motil 2021
Barium Swallow

**When to Order Barium Studies**
- Transit symptoms (dysphagia, regurgitation) without conclusive diagnosis after endoscopy, HRM
- Follow up of symptomatic achalasia patients after therapy
- Evaluation of esophago-gastric junction anatomy
- Evaluation and management of complex strictures

**Performance characteristics of barium esophagram for detection of esophageal dysmotility**
- Sensitivity: 0.69
- Specificity: 0.50

**Timed Upright Barium Swallow**

**Standardized, upright, timed barium esophagram protocol should be used when barium studies are performed for obstructive symptoms**
- Barium pill swallow provides additional value
- Barium swallows can provide information on esophageal clearance vs bolus retention

**8 oz of thin barium in upright position**
- Normal: no retention of barium in the esophagus
- Abnormal: >5 cm barium column in 1 min
  - >2 cm barium column in 5 min

Functional Lumen Imaging Probe

- Placed trans-orally during sedated upper endoscopy
- Positioned with 2-3 channels beyond the waist identified as the EGJ
- Step-wise volumetric distension from 20 to 70 ml

Diameter 6.3 mm
Cross sectional area: 30 mm²
Distensibility index: 1.1

Placed trans-orally during sedated upper endoscopy
Positioned with 2-3 channels beyond the waist identified as the EGJ
Step-wise volumetric distension from 20 to 70 ml

Diameter 10.6 mm
Cross sectional area: 88 mm²
Distensibility index: 5.8

Carlson D et al, Gastroenterology 2016
Carlson D et al, AJG 2021 (in press)

Comparison of FLIP metrics (EGJ-DI, diameter) and HRM metrics (IRP) to gold standard of esophageal emptying on timed upright barium swallow and/or barium pill swallow in patients with dysphagia

<table>
<thead>
<tr>
<th></th>
<th>sIRP 15</th>
<th>uIRP 10</th>
<th>DI 7</th>
<th>Diameter</th>
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<tbody>
<tr>
<td>sens</td>
<td>0.79</td>
<td>0.82</td>
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<tr>
<td>spec</td>
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<td>0.55</td>
<td>0.76</td>
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<td>AUC</td>
<td>0.79</td>
<td>0.79</td>
<td>0.84</td>
<td>0.88</td>
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</tbody>
</table>

FLIP 2.0: Panometry

When to order a FLIP study
Transit symptoms (dysphagia, regurgitation) not explained on EGD, HRM and/or barium swallow
Suspected esophageal motor disorder

FLIP complements HRM for diagnosis of esophageal motility disorders
- Patients in whom manometry cannot be completed
- Measurement of EGJ cross-sectional area or distensibility during and following achalasia treatment
- Measurement of cross-sectional area or distensibility to assess fibrostenotic remodeling in EoE

Carlson D et al, Am J Gastroenterol 2016;111:1726; DDW 2018
Dysphagia ± chest pain and bland regurgitation
GERD symptoms not responsive to PPI therapy

Upper endoscopy

- Normal
- Esophageal dilation, EGJ resistance retained food, diverticulum

Definitive therapy

HRM

PROVOCATIVE MANEUVERS

- TIMED UPRIGHT BARIUM RADIOGRAPH
- SECOND OPINION ENDOSCOPY
- FUNCTIONAL LUMEN IMAGING PROBE

Dilate, Botulinum toxin

Observe, Behavioral therapy

Reflex Symptoms: Definitions Are Important!

**Refractory Heartburn**

Heartburn not responding to stable PPI therapy over 12 weeks

Implication: symptoms may or may not be from reflux

**Refractory GERD**

Symptoms caused by reflux of gastric content not responding to stable PPI therapy over 12 weeks

Implication: symptoms are from inadequate management of reflux

Unproven GERD

Proven GERD

No GERD

Sifrim D, Zeribib F. Gut 2012;61:1340-54
Empiric PPI Therapy for Typical GERD

Primary care referral: 347 pts

GERDQ blinded

Stratification

GERDQ blinded

GERDQ

Rx

86.5%

Esophageal symptoms
NNT for PPI response
Heartburn: 2
Regurgitation: 5.6
Chest pain: 4-7

GERDQ

80.1%

Similar symptom relief

Rx

GERDQ

GERDQ

Baseline

4 weeks

8 weeks

Up-front esophageal testing, preferably with pH-impedance monitoring off PPI and HRM, has value over laryngoscopy and empiric PPI trials for the evaluation of extra-esophageal symptoms when GERD is suspected

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Approach: Reflux Pathway

Unproven GERD

Reflux suspected

Esophageal
- heartburn
- regurgitation
- chest pain

Alarm symptoms
- Lack of PPI response

Extraesophageal
- cough
- hoarseness
- sore throat

Obstructive/atypical pathway

UPPER GI ENDOSCOPY

To evaluate for conclusive reflux evidence
To evaluate for confounding diagnoses

Proven GERD

Obstructive/atypical pathway

Alarm symptoms
- Lack of PPI response

UPPER GI ENDOSCOPY

To evaluate for conclusive reflux evidence
To evaluate for confounding diagnoses

Yield of Endoscopy

Endoscopy has high specificity but low sensitivity for findings of conclusive GERD

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Reflux Monitoring

- Higher sensitivity for detection of reflux episodes
- Higher potential for reflux-symptom association
- Acid reflux episodes become non-acid with PPI therapy

When to order ambulatory reflux monitoring:
- Esophageal symptoms persisting despite PPI
- Prior to antireflux surgery or invasive GERD therapy
- Persisting symptoms despite antireflux surgery
- Symptoms following LES disruption, e.g., myotomy, POEM
- Investigation of belching and regurgitation syndromes

Abnormal pH Patterns

- Reflux episodes
- Reflux-symptom correlation
Esophageal acid exposure (% time pH<4.0)

Upper limit of normal

GERD with esophagitis (mean)

GERD without esophagitis (mean)

Wireless pH monitoring

**p=0.002-0.014

*p=0.026-0.05

Abnormal acid exposure time (AET) is a predictor of symptom improvement following GERD management, including antireflux surgery
Clinical Value of Prolonged pH Monitoring

Symptom Response to Antireflux Therapy

NERD: 77%
FH: 45%

Diagnosis may shift to non-erosive reflux disease when prolonged pH monitoring is utilized.

Newer Metrics: Markers of Longitudinal Injury

Impedance signature of a bolus passing across a pair of sensors

Baseline impedance

Pearson’s $r = -0.5$

25 20 15 10 5 0

Ambulatory reflux monitoring is superior to history, questionnaires, PPI trial and inconclusive endoscopy for the diagnosis of pathologic GERD

Ambulatory reflux monitoring is performed off PPI in patients without prior conclusive evidence for GERD

*Factors that increase confidence for presence of pathologic reflux when evidence is otherwise borderline or inconclusive

ENDOSCOPY  pH or pH-IMPEDEANCE  HRM

CONCLUSIVE EVIDENCE FOR PATHOLOGIC REFLUX

LA grades C&D esophagitis
Long segment Barrett’s mucosa
Peptic esophageal stricture

AET>6%

EVIDENCE AGAINST PATHOLOGIC REFLUX

Reflux episodes<40

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Subsequent Approach

**Unproven GERD**
- Reflux suspected
  - **Esophageal**
    - heartburn
    - regurgitation
    - chest pain
  - **Extraesophageal**
    - cough
    - hoarseness
    - sore throat

**UPPER GI ENDOSCOPY**
- To evaluate for conclusive reflux evidence
- To evaluate for confounding diagnoses

**Alarm symptoms**
- Lack of PPI response
- Negative or equivocal evidence

**AMBULATORY REFLUX MONITORING**
- To evaluate for conclusive reflux evidence

**ADJUNCTIVE METRICS**
- baseline impedance, PSPW, mucosal integrity, HRM

**Proven GERD**
- Conclusive evidence

**No GERD**
- Negative evidence

**GERD likely**
- Positive evidence

**GERD less likely**
- Negative evidence

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**Wireless pH vs. pH-Impedance Testing**

**Wireless pH (off PPI)**
- Catheter intolerance
- Infrequent symptoms, needing reflux-symptom association
- High clinical suspicion of GERD with negative 24-hour reflux monitoring
- Very low clinical suspicion of GERD

**pH-impedance (off PPI, rarely on PPI)**
- Refractory typical or atypical symptoms in patients with proven GERD (on PPI)
- Respiratory symptoms or cough in patients with pulmonary disease (off PPI)
- Repetitive belching in patients with and without reflux symptoms (off PPI)
- Suspicion of rumination syndrome (off PPI)
- Persistent reflux or increased belching following antireflux procedures (off PPI)

**Either option (off PPI)**
- High pre-test likelihood of GERD, prior to invasive antireflux procedures
- Investigation of persisting reflux symptoms despite empiric PPI trial

Sifrim D, Gyawali CP. Am J Gastroenterol 2020;115:1150-1152
Using Pre-Test Probability of Reflux

**Typical Symptoms**
- heartburn

**Extra-Esophageal Symptoms**
- cough
- hoarseness
- asthma
- No response to BID PPI

**HAs-BEER tool**
- Heartburn=1
- Asthma=1
- BMI>25=1
- Cough=0
- Hoarseness=0

**HAs-BEER tool score of 3:**
- 97.8% sensitivity for AET>5.5%
- 92% positive predictive value

**HAs-BEER tool score of ≤2:**
- 80% negative predictive value

- pH monitoring off PPI
- Prolonged wireless pH monitoring

- pH-impedance monitoring on PPI

- Reflux episodes, non-acid reflux

<10% of atypical symptoms

Reflux Episodes Predict GERD Response

**Satisfaction with therapy**
- 35 reflux episodes
  - sensitivity 0.64
  - specificity 0.67
  - AUC 0.76

**GERD HRQL**
- 35 reflux episodes
  - sensitivity 0.64
  - specificity 0.59
  - AUC 0.71

>80 reflux episodes pre-crossover to MSA predicted improvement from MSA

Randomized Study
Comparing BID PPI to MSA
Refractory regurgitation
123 patients
- age 46.9±1.2 yr
- 43% female

MSA: magnetic sphincter augmentation device

Magnetic sphincter augmentation device

**Studies ‘on PPI’**

- **Healthy volunteers given BID PPI**
  - European heartburn-predominant cohort: n=43
  - North American regurgitation-predominant cohort: n=42
  - Median values in healthy volunteers:
    - median AET 0.0%
    - median reflux episodes 16
    - median 5 cm MNBI 2400 ohms

- **Patients with proven GERD treated with BID PPI**
  - European heartburn-predominant cohort: n=43
  - North American regurgitation-predominant cohort: n=42
  - pH-impedance monitoring on BID PPI

**GERD Evidence: Studies ‘on PPI’**

- **Response to Surgical Management**
  - Total 14 patients (32.6%)
  - 10 with AET>4%; 7 with episodes>80; 5 with MNBI<1500 ohms; 2 with episodes 40-80; 10 with RSA; 14 with PSPW index <50%

- **Overall 79%**
  - Heartburn 60%
  - Regurgitation 83%

- **Overall 85%**
  - Heartburn 60%
  - Regurgitation 93%

- **In patients with proven GERD, ambulatory reflux monitoring performed on PPI therapy can be useful in identifying persistent GERD that might benefit from surgical management**

**Parameters based on new thresholds**

- **Abnormal reflux burden and/or abnormal mucosal integrity**
  - Total 14 patients (32.6%)
  - 10 with AET>4%; 7 with episodes>80; 5 with MNBI<1500 ohms; 2 with episodes 40-80; 4 with RSA; 14 with PSPW index <50%

- **Overall 57.1% non-responders**
  - AET>4%
  - episodes>80

- **Overall 57.0% non-responders**
  - AET 0.5-4%

- **Overall 100% non-responders**
  - RSA

- **Overall 50% non-responders**
  - 10 with episodes 40-80; 8 with AET 0.5-4%; 2 with RSA; 13 with PSPW index <50%

- **Overall 50% non-responders**
  - 10 with episodes 40-80; 8 with AET 0.5-4%; 12 with RSA

**Hypervigilance**

- Total 1 patient (2.3%)
- 10 with AET>4%; 7 with episodes>80; 5 with MNBI<1500 ohms; 2 with episodes 40-80; 4 with RSA; 14 with PSPW index <50%

- **Overall 100% NR**
- 10 with episodes>80

- **Overall 50% NR**
- 14 with episodes<40

**Normal study**

- Total 2 patients (4.8%)
- 10 with episodes 40-80; 8 with AET 0.5-4%; 2 with RSA; 13 with PSPW index <50%

- **Overall 71.4% R**
- 10 with episodes>80

- **Overall 50% R**
- 10 with episodes<40

**Escalate reflux management**

- If other supportive features e.g. hiatus hernia

**Neuromodulators**

**RSA: reflux-symptom association**

Role of HRM in GERD

Predictors of post-fundoplication dysphagia

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Univariate</th>
<th>Multivariate</th>
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</thead>
<tbody>
<tr>
<td>n=157, 2.1 yr follow up</td>
<td>OR 95% CI</td>
<td>OR 95% CI</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.99 0.96, 1.02</td>
<td>0.97 0.92, 1.02</td>
</tr>
<tr>
<td>Gender (F)</td>
<td>2.10 0.75, 5.92</td>
<td>1.12 0.25, 4.95</td>
</tr>
<tr>
<td>Pre-fundoplication dysphagia</td>
<td>2.95 1.25, 6.98</td>
<td>1.15 0.34, 3.87</td>
</tr>
<tr>
<td>Early post-fundoplication dysphagia</td>
<td>3.10 1.23, 7.76</td>
<td>1.40 0.34, 5.83</td>
</tr>
<tr>
<td>Dysmotility on post-fundoplication barium swallow</td>
<td>2.17 0.89, 5.24</td>
<td>1.43 0.19, 10.67</td>
</tr>
<tr>
<td>Recurrent Hernia on barium swallow</td>
<td>3.37 0.36, 31.50</td>
<td></td>
</tr>
<tr>
<td>Absent contraction reserve</td>
<td>3.73 1.11, 12.56</td>
<td></td>
</tr>
</tbody>
</table>

In patients with persistent reflux symptoms, HRM rules out motor disorders, and assesses esophageal peristaltic performance.

Healthy controls
n=484

GERD patients
n=482

97.1% 61.8%

2.9% 25.9%

0 12.2%

HRM had sensitivity of 94.3% and specificity of 91.5% in detecting hiatus hernia using hernia size at surgery as gold standard compared to endoscopy (96.2%, 74.5%) and barium radiography (69.8%, 97.9%).

HRM complements EGD and barium studies in increasing diagnostic yield of hiatus hernia.

Rogers BD et al. Neurogastroenterol Motil 2020

Tolone et al, UEG Journal 2018
Barium Radiography

20 patients with reflux symptoms
50% had "reflux" on esophagram
Gold standard: pH impedance

Sensitivity 46%
Specificity 44%
PPV: 50%, NPV: 40%

Reflex observed during barium studies cannot be used as evidence supporting pathologic reflux

Refractory reflux symptoms cannot be used as evidence supporting pathologic reflux

Proven GERD

LA Grades C/D Esophagitis
Barrett's Esophagus >1 cm
Peptic Stricture
Acid Exposure Time >6%

Unproven GERD

Endoscopy
High resolution manometry
pH or pH impedance monitoring off PPI

No GERD evidence*

Gastroesophageal reflux disease (GERD)

Persistent symptoms

Proven GERD

Endoscopy
High resolution manometry
pH impedance monitoring on PPI**

Refractory GERD symptoms

Persistent Acid Reflux
Persistent Weakly-Acid Reflux

No ongoing GERD evidence*
Other Mimickers of Esophageal Symptoms

**Post prandial study:** monitoring for 30-90 min following a meal

![Graph showing rumination, reflux, supragastric belching, and normal categories]

- n=94 PPI non-responders
- ≥1 episode/hr
- >6 TLESR/hr
- >2 episodes/hr

Yadlapati R et al, Clin Gastroenterol Hepatol 2018;16:211

Supragastric Belching

**Inter-rater Comparison of Diagnosis of a Behavioral Disorder**

- Supragastric Belching, Rumination
- 3 raters, 22 pH-impedance and PP HRIM studies
- Inter-rater agreement was higher for pH-impedance monitoring
- Diagnostic yield was higher for post prandial HRIM
- Inter-rater agreement is higher when clinical context was provided

Delay K et al, Neurogastroenterol Motil 2021;e14106

**pH-impedance monitoring can be used for investigation of excessive belching**

**Post-prandial HRIM can be used for investigation of suspected rumination**
Atypical-Behavioral Pathway

ENDOSCOPY

to evaluate and treat mucosal and mechanical processes

HIGH RESOLUTION MANOMETRY, HIGH RESOLUTION IMPEDANCE MANOMETRY

to rule out obstructive disorders, major motor disorders, achalasia

PROVOCATIVE HRM:ATYPICAL/BEHAVIORAL

standardized test meal, post prandial monitoring

AMBULATORY REFLUX MONITORING

To evaluate for conclusive reflux evidence and behavioral syndromes

Proven GERD

GERD + Behavioral

Behavioral syndrome

Neither, Functional

Gyawali CP et al, ACG Guidelines, Am J Gastroenterol 2020;115:1412-1428

Evaluation of Esophageal Symptoms

Esophageal symptoms

Apply appropriate testing

Analyze and interpret test results

Symptom Improvement

Phenotype esophageal disorders

Lyon Consensus 1.0

Chicago Classification 4.0

Other criteria

Past investigation

Past treatment

Overlap between disorders

Choose appropriate management

Characterize symptoms

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Take Home Points

• Start with a good history, which can direct investigation
• EGD, HRM, barium esophagram and FLIP, usually performed in sequence, leads to a diagnosis of obstructive symptoms
• PPI trial is a reasonable starting point for typical reflux symptoms
• Up front esophageal testing is cost effective for atypical symptoms
• Concept of unproven vs. proven GERD determines reflux monitoring off vs. on PPI therapy; interpretation paradigms differ
• Behavioral syndromes are diagnosed using pH-impedance monitoring and post prandial HRIM
Questions?

Speaker: C. Prakash Gyawali, MD, MRCP, FACG

Moderator: Amit Patel, MD, FACG