EIGHT different award types; INCREASED Junior Faculty FUNDING; NEW Health Equity Research Award; Med Resident and Student Awards

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Grant System Opens: September 7, 2021

Deadline: December 3, 2021

Read the Grant Flyer, FAQs, or visit the webpage for the full RFAs.

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EIGHT different award types; NEW Health Equity Research Award; Bridge Funding; GIQuIC Research funding; Med Resident and Student Awards

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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 32, 2021
Isolated GI Alpha-Gal Meat Allergy: What Clinicians Need to Know
Sarah K. McGill, MD, MSc
August 19, 2021 at Noon Eastern

Week 33, 2021
Hepatocellular Carcinoma: Epidemiology, Diagnosis and Treatment
Patricia Jones, MD, MSCR
August 26, 2021 at Noon Eastern

Visit gi.org/ACGVGR to Register

Disclosures:

Speaker:
Prasad G. Iyer, MD, MS, FACG
Research Funding: Exact Sciences, Pentax Medical. Consulting: Medtronic, Symple Surgical

Moderator:
Christina J. Tofani, MD
Dr. Tofani, 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
Screening for Barrett’s Esophagus: Beyond Upper Endoscopy

Prasad G. Iyer MD MSc
Professor of Medicine
Director, Esophageal Interest Group
Division of Gastroenterology and Hepatology
Mayo Clinic, Rochester, Minnesota

ACG Grand Rounds
2021

Objectives

• Understand **rationale and challenges** for BE/EAC screening
  • Context of **current recommendations** for BE screening

• Discuss progress in **non-endoscopic** BE screening

• Pitfalls and Next steps
Screening and (Surveillance) WHY?

EA Incidence, Mortality, Survival

Relative incidence of Esophageal AdenoCa/other malignancies

Relative disease specific mortality of Esophageal AdenoCa/other malignancies

Current BE-EAC Paradigm

RISK FACTORS
- Male gender
- Caucasian ethnicity
- Central obesity
- Smoking
- Family history

BARRETT’S ESOPHAGUS

DYSPLASIA LGD, HGD

ADENOCARCINOMA

Level 1 evidence
Endoscopic Rx of Dysplasia: Reduced Cancer Incidence

Shaheen NEJM 2009 BE-HGD

Phoa JAMA 2014 BE-LGD

Endoscopic Rx of Dysplasia
Reduced EAC risk
Excellent Outcomes of EET for HGD/IMCa
EET = Esophagectomy

**Meta Analysis**

**Overall 5-year survival**

<table>
<thead>
<tr>
<th>Study name</th>
<th>Risk ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pech 2011</td>
<td>0.97</td>
<td>0.86</td>
<td>1.10</td>
<td>.64</td>
</tr>
<tr>
<td>Prasad 2007</td>
<td>1.00</td>
<td>0.92</td>
<td>1.09</td>
<td>.99</td>
</tr>
<tr>
<td>Prasad 2009</td>
<td>1.03</td>
<td>0.87</td>
<td>1.21</td>
<td>.75</td>
</tr>
<tr>
<td>Wani 2014</td>
<td>0.31</td>
<td>0.19</td>
<td>0.51</td>
<td>.00</td>
</tr>
<tr>
<td>Schmidt 2014</td>
<td>0.86</td>
<td>0.69</td>
<td>1.07</td>
<td>.17</td>
</tr>
</tbody>
</table>

Rationale for Early Detection of BE and BE related Dysplasia and Neoplasia

Prevention: ↓ EA incidence

Treatment: ↑ EA free survival

American College of Gastroenterology
Challenges

BE screening: How?

- Expensive
- Not cost effective
- Invasive
- Endoscopist
- Sedation
- Unsuitable for widespread application
- 10% of those eligible screened

Median 30 day costs of BE screening (direct and indirect)

EGD $2022

Gastrointestinal Endoscopy 2017
Inaccurate Targeting of EGD for BE screening

- VA study
- More EGDs:
  - Females, < 50 years

- GERD centric screening recommendations
  - 40-50% of BE/EAC patients do not have frequent GERD

---

Missed Opportunity for Early Detection?

<table>
<thead>
<tr>
<th></th>
<th>EAC diagnosed in surveillance</th>
<th>EAC with BE at diagnosis</th>
<th>Early stage EAC with BE at diagnosis</th>
<th>Proportion of prevalent BE under surveillance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>11.8</td>
<td>56.6</td>
<td>91.3</td>
<td>33</td>
</tr>
</tbody>
</table>

Tan, APT 2020, Jung Iyer AJG 2010
Early Stage EAC: Small Proportion, No change

Solutions
BE screening: How?
Screening tests for BE

- uTNE
- Swallowed esophageal sampling devices + Biomarkers
- Swallowed esophageal imaging devices
- Exhaled VOCs

INVASIVENESS

U Transnasal Endoscopy

- Accurate (Sens and Spec > 90%)
- Well-tolerated, Safe,
- Comparable diagnostic yield, patient preference
- Can be done by non-physicians

uTNE: Lower costs

30 day median total costs of

uTNE can be done at 1/4th - 1/7th the cost of sEGD

Challenges to Widespread TNE use

Provider

- Increasing utilization of deep sedation
  - Unsedated procedures performed less frequently
  - Lack of training in unsedated procedures
- Perception of patient discomfort and lack of patient preference
- Shorter scope: missing pathology?
- $$$$
Potential Advantages of Minimally Invasive Non-endoscopic Screening Tools

DETECTION = SENSITIVITY X PARTICIPATION X ACCESS

RN administration: ↑ ACCESS
↑ PARTICIPATION
Lower Cost: Cost effective

Esophageal Cell Collection Devices + Biomarkers

Non-endoscopic Esophageal sampling (cytology)

Biomarkers
- Protein markers (TFF3)
- IHC
- Subjective interpretation
- Methylated DNA markers
- Quantitatively assessed
- No subjective bias
- Easily scalable
- MicroRNAs

CYTOSPONGE
ESOPHACAP
JASSS BALLOON/ESOCHEK
**BE MDM Discovery and Validation**

- **Marker Discovery (RRBS)**
- **Biological Marker validation (qMSP)**
- **Whole Esophageal Brushings**
- **SOS 1 trial**
  - 40 patients
  - 20 BE cases
  - 20 controls

Selected best tolerated, safe sponge configuration with optimal DNA yield

Iyer et al, Am J Gastro 2018

**BE MDM Selection**

**Cases**
- > 1 cm BE
- *Clinical endoscopy*

**Controls**
- No known BE
- *Clinical endoscopy*

**SOS Test**

**Clinical EGD**

**BE Endoscopy + Histology**

Successful swallow and retrieval

Endoscopic evaluation

BE or no BE Esophagitis

Iyer et al, Am J Gastro 2020
High MDM levels in cases vs controls

- ZNF682, VAV3, NDRG4, BMP3, ZNF568

5 MDM Panel Performance

- ZNF682, VAV3, NDRG4, BMP3, ZNF568

AUC: 0.97 (0.94-0.99)

Sensitivity

Iyer et al, Am J Gastro 2020
Marker Selection: Independent Validation

<table>
<thead>
<tr>
<th></th>
<th>Training Set</th>
<th>Test Set</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=201</td>
<td>N=90</td>
</tr>
<tr>
<td>BE=112, C=89</td>
<td>BE=61, C=29</td>
<td></td>
</tr>
</tbody>
</table>

Sensitivity 91% 92%
Specificity 90% 90%

Accuracy (other studies)

<table>
<thead>
<tr>
<th>Device/Marker</th>
<th>Design</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 mm Sponge</td>
<td>Case Control N=1110</td>
<td>80%</td>
<td>92%</td>
</tr>
<tr>
<td>TFF3 (UK)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 mm Sponge</td>
<td>Case Control N=191</td>
<td>76%</td>
<td>77%</td>
</tr>
<tr>
<td>TFF3 (USA)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18 mm Balloon</td>
<td>Case Control N=86</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>MDMs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20 mm Sponge</td>
<td>Case Control N=95</td>
<td>94%</td>
<td>62%</td>
</tr>
<tr>
<td>MDMs</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Moinova Sci Trans Med 2018
- DDW 2019
- Wang CCR 2019
Several ongoing prospective studies in the US

**EsophaCap**
- NCT04214119
- NCT03961945
- NCT03060642

**EsoChek**
- NCT04295811
- NCT04293458
- NCT04880044

Cytosponge-trefoil factor 3 versus usual care to identify Barrett’s oesophagus in a primary care setting: a multicentre, pragmatic, randomised controlled trial

- 113 GP primary care clinics
- PPI 6 m
- 2769 (39%) interested
- 1750 swallowed tethered cell collection system
- 231 Positive
- 6983 tethered cell collection system
- Randomization
- 6531 Usual Care
- 1 sponge detachment
- 4% sore throat
- Acceptability score 9
- 59% PPV
- 140 BE on EGD
- 13 BE on EGD

Lancet 2020
Tethered Cell Collection System arm: BE dysplasia + Stage 1 EAC

Optical Capsule Endomicroscopy

- Tethered capsule (reusable)
  - 25 by 13mm
- OFDI and Near-infrared wavelength imaging (≈VLE)
- Cross sectional images of esophagus
- Squamous Versus BE
- Multicenter Study
  - 116/149 (79%) BE patients swallowed
  - BE detected on TCE
  - High correlation with endoscopy

Dong et al, CGH 2021
Exhaled Volatile Organic Compounds

- Three metal oxide sensors interact with exhaled VOCs
- Digital breath print specific to BE
- High patient uptake

<table>
<thead>
<tr>
<th>USA</th>
<th>Netherlands</th>
</tr>
</thead>
<tbody>
<tr>
<td>BE : N=101, Control : N=89</td>
<td>BE : N=129, GERD : N=141, Control : N=132</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>90%</td>
<td>69%</td>
</tr>
<tr>
<td>90%</td>
<td>53%</td>
</tr>
</tbody>
</table>

DDW 2019, Peters, Gut 2020

ACG Clinical Guideline: Diagnosis and Management of Barrett’s Esophagus

- Screening: males with chronic and/or frequent reflux and 2 or more risk factors
  - Caucasian race
  - Central obesity
  - Ever smoking
  - Confirmed family history in a first degree relative
- Screening is NOT recommended in females
  - Low risk of EA
- Unsedated TNE is an alternative
- Consider life expectancy of patient

Am J Gastroenterology 2016
### BE Screening Guidelines

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>In patients with multiple risk factors for esophageal adenocarcinoma, screening is <strong>recommended</strong>(^1) (weak recommendation, moderate quality evidence)</td>
<td>Consider in at-risk population</td>
<td>EGD may be considered</td>
<td>Screening can be considered in patients with chronic reflux symptoms and multiple risk factors (at least three of age 50 years or older, white race, male sex, obesity). Decrease by one point in presence of at least one first-degree relative with Barrett's or EAC. Screening with endoscopy is not feasible or justified for an unselected population with gastro-oesophageal reflux symptoms(^5)</td>
</tr>
<tr>
<td>Screening the general population <strong>not recommended</strong>(^1) (strong recommendation, moderate quality evidence)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Common themes
1. Chronic GERD (symptoms)
2. Multiple risk factors
3. No population screening

- family history of EAC or BE (high risk)\(^3\)
- Use, and intra-abdominal distribution of fat
- Population with gastro-oesophageal reflux symptoms

#### Unresolved Questions
- 43
- 44
Who to Screen?
GERD alone inadequate, GERD+ (other risk factors) risk scores

AUC (BE)
GERD = 0.58
GERD+ = 0.67 - 0.69

EAC and GEJAC Prediction Tool

Validation of Tools for Predicting Incident Adenocarcinoma of the Esophagus (EAC) or Esophagogastric Junction (EGJAC)

206,974 people examined 1964-1973
319 cancer cases mean 32 years later

Tools predicted cancer better than GERD alone


Rubenstein, AJG 2021
GERD + Tools predicted EAC/GEJAC better than GERD alone

EAC and GEJAC: Absolute Risk

Lifetime EAC + GEJAC risk: 4th Quartile of Kunzman Score ≈ 5% (Lifetime risk of CRC)
**BE Screening Paradigm?**

- **Standard endoscopy**
  - Confirmatory diagnosis using standard endoscopy

- **Non-endoscopic devices**
  - Triage testing using minimally invasive non-endoscopic cell sampling devices

- **Risk prediction algorithm**
  - App-based algorithm to enrich at-risk groups in the general population

---

**Comparative Cost-Effectiveness of Reflux Based and Reflux Independent Strategies of Barrett’s Esophagus Screening**

### Population
- 3 scenarios with 50 year old individuals:
  1. GERD-based (white men) with BE prevalence 8.0%
  2. GERD-independent (all races, men & women) with BE prevalence 5.0%
  3. GERD-independent (all races, men & women) with BE prevalence 1.6%

### Interventions
- sEGD
- Swallowable Devices w/ Biomarkers
- E-Nose
- hTNE/mTNE

### Results
- Screening individuals aged 50 years old in a GERD-independent manner with minimally invasive non-endoscopic tests is cost effective compared to no screening.
- Non-endoscopic swallowed capsule sponge based strategies were the favorable strategies in all three screening scenarios compared to other endoscopic BE screening modalities.

**Author**
Sami, Iyer et al. AJG. 2021
Is detection of more BE alone sufficient to improve EAC outcomes?

Screening tool (simple, acceptable, accurate, and cost-effective):
- TNE
- Cytology sponge
- Capsule endomicroscopy
- Future blood biomarkers

Target population (Caucasian male, age ≥50 years, chronic GERD, positive family history, centrally obese):
- Validation of M-BERET and other BE risk prediction models.
- Future blood biomarkers.

Screen for BE

Detect and treat prevalent HGD/EAC

surveillance

Risk stratify remaining patients with BE:
- Clinical: LSBE.
- Histological: LGD, p53.
- Future blood biomarkers.
- Combination of the above.

Low risk = observe or discharge
High risk = endotherapy or chemoprevention

CGH 2014
Summary

- BE screening has the potential to improve EAC outcomes
  - Increasing detection of those at EAC risk
- Minimally invasive non-endoscopic BE detection tools substantial progress
  - Safe and accurate
  - Increase access and participation
  - May enter clinical realm in near future
- Identifying target population, improved dysplasia detection and risk stratification critical next steps

Questions?

Speaker: Prasad G. Iyer, MD, MS, FACG

Moderator: Christina Tofani J. Tofani, MD
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