



9 • CLINICAL PRACTICE UPDATE
Managing GI and Liver Conditions in
Pregnant Patients



18 • PERSPECTIVES
Debating Surgical vs Endoscopic
Excision of Large Colon Polyps



22 • MEMBER SPOTLIGHT
Advocating for Better Care of Women
With GI Disorders



Official newspaper of the AGA Institute

mdedge.com/gihepnews

GI & Hepatology News

March 2025

Volume 19 / Number 3

Fecal Hemoglobin Levels From Negative FITs Signal CRC Risk



Specimen tubes are prepared for fecal immunochemical testing, which can determine the presence of occult blood in samples.

BY DIANA SWIFT

FROM GASTROENTEROLOGY

The chance of detecting colorectal cancer (CRC) in subsequent screenings increases by up to 13-fold in the presence of a detectable fecal hemoglobin (f-Hb) concentration in a prior negative fecal immunochemical test (FIT), according to a large international meta-analysis assessing dose-response relationships across 13 studies.

These findings support the development of risk-stratified screening strategies based on these concentrations, according to

researchers led by Danica M.N. van den Berg, MSc, a PhD candidate and econometrics researcher in the department of public health at Erasmus MC, University Medical Center in Rotterdam, the Netherlands.

Higher f-Hb concentrations in prior negative screening tests are strongly associated with an increased risk of detecting colorectal neoplasia in subsequent screenings, van den Berg said in an interview. "Gastroenterologists and other clinicians should consider the value of f-Hb concentrations in refining screening protocols and personalizing patient care to detect colorectal neoplasia earlier and more accurately."

See **Hemoglobin** • page 17

Obesity Linked With Malignant Progression of Barrett's Esophagus

BY CAROLYN CRIST

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Obesity appears to be associated with malignant progression of Barrett's esophagus (BE), according to a recent systematic review and meta-analysis.

A dose-response relationship exists between body mass index (BMI) and esophageal adenocarcinoma (EAC) or high-grade dysplasia (HGD), the authors found.

"Obesity has been implicated in the pathogenesis of many reflux-related esophageal disorders such as gastroesophageal reflux disease (GERD), BE, and EAC," said senior author Leo Alexandre, MRCP, PhD, a clinical associate professor and member of the Norwich Epidemiology Centre at the University of East Anglia and gastroenterologist with the Norfolk & Norwich University Hospital NHS Foundation Trust, both in Norwich, England.

"Guidelines advocate obesity as a criterion for targeted screening for BE in patients with chronic reflux symptoms," he said. "While obesity is a recognized risk factor for both BE and EAC, it's been unclear whether obesity is a risk factor for malignant progression."

The study was published in *Clinical Gastroenterology and Hepatology* (2024 Sep. doi: 10.1016/j.cgh.2024.07.041).

Analyzing Risk

BE, which is the only recognized precursor lesion to

See **Obesity** • page 21

BE ON THE FOREFRONT

Advance your work — and patient outcomes — with the global digestive disease community at DDW® 2025 in San Diego, CA, or online.

DDW2025
Digestive Disease Week®
MAY 3-6, 2025 | SAN DIEGO, CA
EXHIBIT DATES: MAY 4-6, 2025

Get early bird discounts through Feb. 26.
Register now at ddw.org/register.

PRST STD
U.S. POSTAGE
PAID
HARRISBURG, PA
PERMIT 500

CHANGE SERVICE REQUESTED

GI & HEPATOLOGY NEWS
17550 N Perimeter Drive,
Suite 110
Scottsdale, AZ 85255-7829

LETTER FROM THE EDITOR

The Value of Public Service

Former Secretary of State Condoleezza Rice once said: “There is no greater challenge and there is no greater honor than to be in public service.” It has been a challenging few months for public servants, including the thousands of federal healthcare and public health workers who care for our veterans, provide critical services to underserved communities, work to fund high-impact biomedical research that improves health outcomes, and otherwise further important public health goals.

From the VA to the Department of Health & Human Services and its operating divisions, including the Centers for Disease Control and Prevention, National Institutes of Health, Centers for Medicare & Medicaid Services, and others, dedicated federal civil servants have had their work ethic, commitment, and productivity questioned in late-night emails from anonymous authors. They have been encouraged indiscriminately to resign and “move from [their] lower-productivity jobs in the public sector to higher-productivity jobs in the private sector,” and been subjected to vague threats of future job loss regardless of role, duration of service,



Dr. Adams

‘I hope for the greater good that we can work together to uphold the value of public service, of community, of civility — both for the sake of our democracy and to preserve our nation’s health.’

performance, or political persuasion. This includes the roughly 30% of federal employees who are themselves US military veterans.

In essence, the message is that their work does not matter, and their service and sacrifice is not valued (which, of course, could not

be further from the truth). These actions, along with a plethora of other divisive policies, not only threaten our democratic principles, but also serve to degrade our collective values and norms.

We are at a “fork in the road” as a nation. I hope for the greater good that we can work together to uphold the value of public service, of community, of civility — both for the sake of our democracy and to preserve our nation’s health.

In our March issue, we celebrate

National Colorectal Cancer Awareness Month with relevant summaries of emerging science, highlights of AGA resources, and a Perspectives column addressing the pros and cons of endoscopic vs surgical management of large colon polyps. This month’s Member Spotlight features Dr. Pooja Singhal (Oklahoma Gastro Health and Wellness), who describes how she integrates wellness principles into her clinical practice, discusses the evolution of her interest in women’s digestive health, and shares how she serves her community outside of medicine. ■

*Megan A. Adams, MD, JD, MSc
Editor in Chief*

Member SPOTLIGHT

See page 22



Official newspaper of the AGA Institute
mdedge.com/gihepnews

GI & Hepatology News

EDITOR IN CHIEF, GI & HEPATOLOGY NEWS

Megan A. Adams, MD, JD, MSc

EDITOR IN CHIEF, THE NEW GASTROENTEROLOGIST

Judy Trieu, MD, MPH

ASSOCIATE EDITORS

Ziad F. Gellad, MD, MPH, AGAF

David Katzka, MD

Bharati Kochar, MD, MS

Marc S. Piper, MD, MSc

Janice H. Jou, MD, MHS

Gyanprakash A. Ketwaroo, MD, MSc

Kimberly M. Persley, MD, AGAF

EDITORS EMERITUS, GI & HEPATOLOGY NEWS

John I. Allen, MD, MBA, AGAF

Colin W. Howden, MD, AGAF

Charles J. Lightdale, MD, AGAF

EDITORS EMERITUS, THE NEW GASTROENTEROLOGIST

Vijaya L. Rao, MD

Bryson Katona, MD, PhD

AGA INSTITUTE STAFF

Managing Editor, GI & HEPATOLOGY NEWS and THE NEW GASTROENTEROLOGIST,
Danielle Kiefer

Vice President of Communications Jessica Duncan

OFFICERS OF THE AGA INSTITUTE

President Maria Abreu, MD, AGAF

President-Elect Lawrence Kim, MD, AGAF

Vice President Byron L. Cryer, MD, AGAF

Secretary/Treasurer John I. Allen, MD, MBA, AGAF

©2025 by the AGA Institute. All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without permission in writing from the publisher.

GI & HEPATOLOGY NEWS is the official newspaper of the American Gastroenterological Association (AGA) Institute and provides the gastroenterologist with timely and relevant news and commentary about clinical developments and about the impact of healthcare policy. Content for **GI & HEPATOLOGY NEWS** is developed through a partnership of the newspaper’s medical board of editors (Editor in Chief and Associate Editors), Frontline Medical Communications Inc. and the AGA Institute Staff. “News from the AGA” is provided exclusively by the AGA, AGA Institute, and AGA Research Foundation. All content is reviewed by the medical board of editors for accuracy, timeliness, and pertinence. To add clarity and context to important developments in the field, select content is reviewed by and commented on by external experts selected by the board of editors.

The ideas and opinions expressed in **GI & HEPATOLOGY NEWS** do not necessarily reflect those of the AGA Institute or the Publisher. The AGA Institute and Frontline Medical Communications Inc. will not assume responsibility for damages, loss, or claims of any kind arising from or related to the information contained in this publication, including any claims related to the products, drugs, or services mentioned herein. Advertisements do not constitute endorsement of products on the part of the AGA Institute or Frontline Medical Communications Inc.

POSTMASTER Send changes of address (with old mailing label) to GI & Hepatology News, Subscription Service, 17550 N Perimeter Drive, Suite 110, Scottsdale, AZ 85255-7829.

RECIPIENT To change your address, contact Subscription Services at 1-800-430-5450. For paid subscriptions, single issue purchases, and missing issue claims, call Customer Service at 1-833-836-2705 or e-mail custsvc.gihep@fulcoinc.com

The AGA Institute headquarters is located at 4930 Del Ray Avenue, Bethesda, MD 20814, ginews@gastro.org.

GI & HEPATOLOGY NEWS (ISSN 1934-3450) is published monthly for \$230.00 per year by Frontline Medical Communications Inc., 283-299 Market Street (2 Gateway Building), 4th Floor, Newark, NJ 07102. Phone 973-206-3434

MDedge®



FRONTLINE MEDICAL COMMUNICATIONS SOCIETY PARTNERS

Editor Richard Pizzi

Creative Director

Louise A. Koenig

Director, Production/

Manufacturing

Rebecca Slebodnik

Director, Business

Development

Cheryl Wall

978-356-0032 cwall@mdedge.com

E-mail ginews@gastro.org

FRONTLINE MEDICAL COMMUNICATIONS

Corporate

VP, Sales Mike Guire

VP, Partnerships Amy Nadel

Director, Circulation Jared Sonners

Senior Director, Content Content

Patrick Finnegan

Managing GI and Liver Conditions During Pregnancy: New Guidance From AGA

BY CAROLYN CRIST

FROM GASTROENTEROLOGY

Clinicians should be aware of how to manage certain gastrointestinal (GI) and liver conditions associated with pregnancy, such as hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, and acute fatty liver of pregnancy, according to a clinical practice update (CPU) from the American Gastroenterological Association.

Notably, procedures, medications, or other interventions intended to improve maternal health shouldn't be withheld solely because the patient is pregnant, the authors wrote. Instead, treatments should be personalized based on a risk-benefit assessment.

"Pregnancy causes significant physiological changes that can affect the GI tract and liver function. Some common conditions — such as nausea, vomiting, gastroesophageal reflux disease (GERD), and constipation — may be exac-

medications, or interventions just because they're pregnant, the authors wrote. Instead, taking an individual approach will help clinicians decide what to do based on the risks and benefits.

At the beginning of pregnancy, early treatment of nausea and vomiting can reduce progression to hyperemesis gravidarum, the authors wrote. Stepwise treatment can include vitamin B6, doxylamine, hydration, and adequate nutrition, followed by ondansetron, metoclopramide, promethazine, and intravenous glucocorticoids in moderate to severe cases.

Constipation may also pose a problem because of hormonal, physiological, and medication-related changes. Treatment options can include dietary fiber, lactulose, and polyethylene glycol-based laxatives.

Patients with certain conditions — such as complex inflammatory bowel disease (IBD), advanced cirrhosis, or liver transplant — should work with a multidisciplinary team to coordinate birth, preferably in a tertiary care center, the authors wrote.

For patients with IBD, clinical remission helps to improve pregnancy outcomes, including before conception, during pregnancy, and throughout the postpartum period. Biologic agents should be used during pregnancy and post partum, though methotrexate, thalidomide, and S1P-receptor modulators should be stopped at least 6 months before conception.

For patients with chronic hepatitis B, serum hepatitis B virus DNA and liver biochemical levels should be tested. Patients with a serum level > 200,000 IU/mL during the third trimester should be considered for treatment with tenofovir disoproxil fumarate.

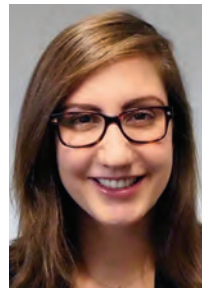
For patients on immunosuppressive therapy for chronic liver diseases or after liver transplantation, therapy should continue at the lowest effective dose. However, mycophenolate mofetil shouldn't be administered during pregnancy.

Intrahepatic cholestasis of pregnancy may be diagnosed during the second or third trimester based on pruritus and a serum bile acid level > 10 $\mu\text{mol/L}$. Treatment should include oral ursodeoxycholic acid, with a total daily dose of 10-15 mg/kg.

Other pregnancy-related liver diseases — such as pre-eclampsia; hemolysis, elevated liver enzymes, and low platelets syndrome; and acute fatty liver of pregnancy — require careful birth planning and evaluation for possible liver transplantation. For certain high-risk patients, daily

aspirin should start at week 12 of gestation.

In addition, elective endoscopic procedures should wait until after birth, and nonemergent but necessary procedures should be performed during the second trimester. Patients with cirrhosis should undergo evaluation for esophageal



Dr. Shmidt

'GI practitioners should be counseling women well in advance of pregnancy and recruiting all relevant stakeholders as early as possible, even prior to conception. This way, pregnancy care is not reactive, but instead proactive.'

varices, and upper endoscopy should happen during the second trimester to guide beta-blocker therapy or endoscopic variceal ligation.

Endoscopic retrograde cholangiopancreatography can be performed for urgent indications, such as choledocholithiasis, cholangitis, and some gallstone pancreatitis cases, ideally during the second trimester.

Cholecystectomy is considered safe during pregnancy, with a laparoscopic approach as the standard of care regardless of trimester, though the second trimester is ideal.

Pregnancy-Related Updates in Practice

Ultimately, clinicians should familiarize themselves with the best practice advice to feel comfortable when counseling and managing pregnancy-related concerns, especially high-risk patients, said Eugenia Shmidt, MD, associate professor of gastroenterology, hepatology, and nutrition, and founder of the IBD Preconception and Pregnancy Planning Clinic at the University of Minnesota, Minneapolis.

"Half of all patients with GI and liver disease are women, and oftentimes, they don't have appropriate guidance regarding reproductive health in the context of their disease," she said. "There exists a very large knowledge gap in this area, particularly because most clinical trials exclude pregnant people."

Most importantly, the advice statements can guide practitioners on how to help pregnant patients make informed reproductive decisions, she added.

"This CPU makes it clear that preconception counseling and multidisciplinary care are key in optimizing reproductive health, regardless of the underlying GI or liver disease," Shmidt said. "GI practitioners should be counseling women well in advance of pregnancy and recruiting all relevant stakeholders as early as possible, even prior to conception. This way, pregnancy care is not reactive, but instead proactive."

The authors received no specific funding for this update. Kothari and Shmidt reported no relevant disclosures. ■



Dr. Kothari

'This clinical practice update stresses the need for coordinated, multidisciplinary care among obstetricians, gastroenterologists, hepatologists, and maternal-and-fetal medicine experts to ensure optimal outcomes, particularly in complex or high-risk cases.'

erbated, and underlying GI or liver diseases can behave differently during pregnancy," said lead author Shivangi Kothari, MD, associate professor of medicine and associate director of endoscopy at the University of Rochester Medical Center and Strong Memorial Hospital, both in Rochester, New York.

"These conditions can pose significant risks to both the mother and fetus, and their management requires a specialized, updated approach," she said. "This clinical practice update stresses the need for coordinated, multidisciplinary care among obstetricians, gastroenterologists, hepatologists, and maternal-and-fetal medicine experts to ensure optimal outcomes, particularly in complex or high-risk cases."

The update was published online in *Gastroenterology* (2024 Aug. doi: 10.1053/j.gastro.2024.06.014).

Pregnancy-Related Concerns

The best path to optimal outcomes is to start early, the authors wrote. Before pregnancy, patients should consider preconception and contraceptive care counseling with a multidisciplinary team that can address GI and liver issues, especially among reproductive-age people who want to become pregnant.

Once pregnant, though, patients shouldn't be deterred from receiving procedures,

New Risk Score Might Improve HCC Surveillance Among Cirrhosis Patients

BY WILL PASS

MDedge News

FROM GASTROENTEROLOGY

A newly validated risk stratification tool could potentially improve hepatocellular carcinoma (HCC) surveillance among patients with cirrhosis, based on a recent phase 3 biomarker validation study.

The Prognostic Liver Secretome Signature With Alpha-Fetoprotein Plus Age, Male Sex, Albumin-Bilirubin, and Platelets (PAaM) score integrates both molecular and clinical variables to effectively classify cirrhosis patients by their risk of developing HCC, potentially sparing low-risk patients from unnecessary surveillance, lead author Naoto Fujiwara, MD, PhD, of the University of Texas Southwestern Medical Center, Dallas, and colleagues reported.

“Hepatocellular carcinoma risk stratification is an urgent unmet need for cost-effective screening and early detection in patients with cirrhosis,” the investigators wrote in *Gastroenterology* (2024 Nov. doi: 10.1053/j.gastro.2024.10.035). “This study represents the largest and first phase 3 biomarker validation study that establishes an integrative molecular/clinical score, PAaM, for HCC risk stratification.”

The PAaM score combines an 8-protein prognostic liver secretome signature with traditional clinical variables, including alpha-fetoprotein (AFP) levels, age, sex, albumin-bilirubin levels, and platelet counts. The score stratifies patients into high-, intermediate-, and low-risk categories.

The PAaM score was validated using 2 independent prospective cohorts in the United States: the statewide Texas Hepatocellular Carcinoma Consortium (THCCC) and the

nationwide Hepatocellular Carcinoma Early Detection Strategy (HEDS). Across both cohorts, 3484 patients with cirrhosis were followed over time to assess the development of HCC.

In the Texas cohort, comprising 2156 patients with cirrhosis, PAaM classified 19% of patients as high risk, 42% as intermediate risk, and 39% as low risk. The annual incidence of HCC was significantly different across these groups, with high-risk patients experiencing a 5.3% incidence rate, versus 2.7% for intermediate-risk patients and 0.6% for low-risk patients (P less than .001). Compared with those in the low-risk group, high-risk patients had sub-distribution hazard ratio (sHR) of 7.51 for developing HCC, while intermediate-risk patients had an sHR of 4.20.

In the nationwide HEDS cohort, which included 1328 patients, PAaM similarly stratified 15% of participants as high risk, 41% as intermediate risk, and 44% as low risk. Annual HCC incidence rates were 6.2%, 1.8%, and 0.8% for high-, intermediate-, and low-risk patients, respectively ($P < .001$). Among these patients, sub-distribution hazard ratios for HCC were 6.54 for high-risk patients and 1.77 for intermediate-risk patients, again underscoring the tool’s potential to identify individuals at elevated risk of developing HCC.

The PAaM score outperformed existing models like the aMAP score and the PLSec-AFP molecular marker alone, with consistent superiority across a diverse range of cirrhosis etiologies, including metabolic dysfunction-associated steatotic liver disease (MASLD), alcohol-associated liver disease, and cured hepatitis C virus (HCV) infection.

Based on these findings, high-risk

Nancy S. Reau, MD, AGAF, of RUSH University in Chicago, Illinois, highlighted both the promise and challenges of the PAaM score for HCC risk stratification, emphasizing that current liver cancer screening strategies remain inadequate, with only about 25% of patients receiving guideline-recommended surveillance.

“An easy-to-apply cost-effective tool could significantly improve screening strategies, which should lead to earlier identification of liver cancer — at a time when curative treatment options are available,” Reau said.

PAaM, however, may be impractical for routine use. “A tool that classifies people into three different screening strategies and requires longitudinal applications and re-classification could add complexity,” she explained, predicting that “clinicians aren’t going to use it correctly.”

Reau was particularly concerned about the need for repeated assessments over time. “People change,” she said. “A low-risk categorization

by PAaM at the age of 40 may no longer be relevant at 50 or 60 as liver disease progresses.”

Although the tool is “exciting,”

Reau suggested that it is also “premature” until appropriate reclassification intervals are understood.

She also noted that some patients still develop HCC despite being considered low risk, including cases of HCC that develop in non-cirrhotic HCV infection or MASLD.

Beyond the above clinical considerations, Reau pointed out several barriers to implementing PAaM in routine practice, starting with the under-recognition of cirrhosis. Even if patients are identified, ensuring both clinicians and patients adhere to screening recommendations remains a challenge.

Finally, financial considerations may pose obstacles.

“If some payers cover the tool and others do not, it will be very difficult to implement,” Reau concluded.

Reau reported no conflicts of interest.



Dr. Reau

patients might benefit from more intensive screening strategies, Fujiwara and colleagues suggested, while intermediate-risk patients could continue with semi-annual ultrasound-based screening. Of note, low-risk patients — comprising about 40% of the study population — could potentially avoid frequent screenings, thus reducing healthcare costs and minimizing unnecessary interventions.

“This represents a significant step

toward the clinical translation of an individual risk-based HCC screening strategy to improve early HCC detection and reduce HCC mortality,” the investigators concluded.

This study was supported by the National Cancer Institute, Department of Veterans Affairs, the Japan Society for the Promotion of Science, and others. The investigators disclosed additional relationships with Boston Scientific, Sirtex, Bayer, and others. ■

Suboptimal Diets Tied to Global Doubling of GI Cancer Cases

BY DIANA SWIFT

FROM GASTROENTEROLOGY

More than one in five new gastrointestinal (GI) cancer cases globally were attributable to suboptimal dietary intake, according to a recent study.

Writing in *Gastroenterology*

(2024 July. doi: 10.1053/j.gastro.2024.07.009), researchers led by Li Liu, PhD, of the department of epidemiology and biostatistics, Ministry of Education Key Lab of Environment and Health, School of Public Health, Tongji Medical College, Huazhong University of Science and Technology in Wuhan,

China, reported that excessive consumption of processed meats (the biggest culprit), insufficient fruit intake, and insufficient whole-grain intake were the leading dietary risk factors. In addition, the number of diet-related cases doubled from 1990 to 2018.

“In regions with limited access

to healthy foods, policy interventions like taxing unhealthy foods and subsidizing nutritious options may help shift dietary patterns and reduce cancer risk,” Liu said in an interview.

The study examined meta-analyses from 184 countries

Continued on following page

Continued from previous page

in seven regions for the period 1990-2018 looking at rates of six major GI cancers: colorectal, liver, esophageal, pancreatic, and gallbladder/biliary tract. Among these, the age-standardized incidence of liver, pancreatic, and colorectal increased significantly over the past 3 decades (Cancer Commun [Lond]. 2021 Nov;41[11]:1137-1151).

The research team used a comparative risk assessment model to estimate the impact of diet on

countries. The findings support the development of targeted diet-related public health interventions in various regions and nations to reduce GI cancer incidence, the authors wrote.

Among the study's specific findings:

- In 2018, 21.5% (95% uncertainty interval [UI], 19.1-24.5) of incident GI cancer cases globally were attributable to suboptimal diets, a relatively stable proportion since 1990 (22.4%; 95% UI, 19.7-25.6).



Dr. Liu

'In regions with limited access to healthy foods, policy interventions like taxing unhealthy foods and subsidizing nutritious options may help shift dietary patterns and reduce cancer risk.'

GI cancer independent of energy intake and adiposity. Although the principal dietary risk factors varied across individual cancers, suboptimal intake of the three aforementioned components was responsible for 66.51% of all diet-attributable GI cancers in 2018. The global mean processed meat consumption was 17 g/d in 2018, falling to a low in South Asia of 3 g/d.

The investigators also found diet-linked cancer incidence positively correlated with the Socio-demographic Index (SDI), an integrated measure of national development, income, and fertility. Incidence varied across world regions, with the highest proportion of cases in Central and Eastern Europe, Central Asia, Latin America, the Caribbean, and in high-income

- Absolute diet-attributable cases doubled from 580,862 (95% UI, 510,658-664,076) in 1990 to 1,039,877 (95% UI, 923,482-1,187,244) in 2018.
- Excessive processed meat consumption (5.9%; 95% UI, 4.2%-7.9%), insufficient fruit intake (4.8%; 95% UI, 3.8%-5.9%), and insufficient whole-grain intake (3.6%; 95% UI, 2.8%-5.1%) were the most significant dietary risk factors in 2018 — a shift from 1990 when the third major concern was insufficient non-starchy vegetable intake.

Given the well-established link between diet and GI cancers, the incidence findings came as no surprise. "However, the dramatic doubling of diet-attributable cases over the past few decades was

truly unexpected," Liu said. "This increase can likely be attributed to global population growth and aging. While aging is an irreversible process, we can still reduce the growing burden of diet-related GI cancers by focusing on modifiable behaviors, particularly through targeted dietary interventions."

A Modifiable Risk Factor

Commenting on the analysis but not involved in it, Andrew T. Chan, MD, MPH, a professor of medicine at Harvard Medical School and a



Dr. Chan

'Although much work needs to be done to clarify the precise mechanisms underlying this association, there are substantial data that diet may cause changes in the gut microbiome, which in turn promotes cancer.'

gastroenterologist at Massachusetts General Hospital, both in Boston, noted that his own group's studies also support the association of diet with an increased risk for GI cancers, particularly colorectal cancers.

"Although much work needs to be done to clarify the precise mechanisms underlying this association, there are substantial data that diet may cause changes in the gut microbiome, which in turn promotes cancer," Chan said in an interview. "Going forward, we are working to develop strategies in which diet is modified to mitigate the risk of cancer associated with suboptimal diets."

In other study findings, Liu's group observed that two regional groups, Central and Eastern Europe, Central Asia, Latin America, and the Caribbean, as well as high-income

countries, bore the top three diet-attributable burdens worldwide in 2018, all driven mostly by an upward-trending excess of processed meat.

By regions, Central and Eastern Europe and Central Asia experienced the highest attributable burden across regions in 1990 (31.6%; UI, 27.0%-37.4%) and 2018 (31.6%; UI, 27.3%-36.5%).

As for the impact of the SDI, the authors explained that diet-attributable GI cancer burden was higher among adults with higher education and living in urban areas than among those with lower education and rural residency. "Some dietary habits tended to be worse in higher-SDI countries, specifically, higher consumption of processed meats," they wrote.

Although the proportional attributable GI incidence remains relatively stable, they added, the doubling of absolute cases from 1990 to 2018, along with the discrepancies between urbanicity and countries/regions, supports more targeted preventive measures.

And while the diet-GI cancer connection is clear, they agreed with Chan in that "the precise pathogenesis from suboptimal diets to these cancers remains unclear and requires further basic studies to clarify the mechanism."

In the meantime, the findings "underscore the urgent need for proactive public health interventions. Diet, as a modifiable risk factor, still offers substantial potential for improvement," Liu said.

This study was funded by the National Natural Science Foundation of China and the American Cancer Society. The authors and Chan disclosed no relevant conflicts of interest. ■

NEWS FROM THE AGA

Colorectal Cancer Awareness Month Is Here!

Happy Colorectal Cancer (CRC) Awareness Month! Today, CRC is the third-most common cancer in men and women in the United States. But there is good news: We know that screening saves lives. That's why we need to raise awareness about the importance of getting screened starting at age 45 all throughout the year, but especially during CRC Awareness Month.

We have a variety of resources for both physicians and patients to navigate the CRC screening process.

Clinical Guidance

AGA's clinical guidelines and clinical practice updates provide evidence-based recommendations to guide your clinical practice decisions. Visit AGA's new toolkit on CRC (gastro.org/guideline-toolkits) for the latest guidance on topics including colonoscopy follow-up, liquid biopsy, appropriate and tailored polypectomy, and more.

Patient Resources

AGA's GI Patient Center can help your patients

understand the need for CRC screening, colorectal cancer symptoms and risks, available screening tests, and the importance of preparing for a colonoscopy.

Visit www.patient.gastro.org to access patient education materials.

Join the Conversation

We will be sharing resources and encouraging CRC screenings on social media all month long. Join us as we remind everyone that 45 is the new 50. ■

The New Gastroenterologist

How to Discuss Lifestyle Modifications in MASLD

BY NEWSHA NIKZAD, MD;
DANIEL J. HUYNH, BS;
NIKKI DUONG, MD

Metabolic dysfunction–associated steatotic liver disease (MASLD) is a spectrum of hepatic disorders closely linked to insulin resistance, dyslipidemia, hypertension, and obesity.¹ An increasingly prevalent cause of liver disease and liver-related deaths worldwide, MASLD affects at least 38% of the global population.² The immense burden of MASLD and its complications demand attention and action from the medical community.

Lifestyle modifications involving weight management and dietary composition adjustments are the foundation of addressing MASLD, with a critical emphasis on early intervention.³ Healthy dietary indices and weight loss can lower enzyme levels, reduce hepatic fat content, improve insulin resistance, and overall, reduce the risk of MASLD.³ Given the abundance of literature that exists on the benefits of lifestyle modifications on liver and general health outcomes, clinicians should be prepared to have informed, individualized, and culturally concordant conversations with their patients about these modifications. This Short Clinical Review aims to guide effective discussion of early lifestyle interventions addressing MASLD, while considering patient-specific motivators, cultural backgrounds, and potential obstacles to lifestyle changes.

Initiate the Conversation

Conversations about lifestyle modifications can be challenging and



Dr. Nikzad

complex. If patients themselves are not initiating conversations about dietary composition and physical activity, then it is important for clinicians to start a productive discussion.

The use of non-stigmatizing, open-ended questions can begin this process. For example, clinicians can consider asking patients: “How would you describe your lifestyle habits, such as foods you usually eat and your physical activity levels? What do you usually look for when you are grocery shopping or thinking of a meal to cook? Are there ways in which you stay physically active throughout the day or week?”⁴ (see Table 1). Such questions can provide significant insight into patients’ activity and eating patterns. They also eliminate the utilization of words such as “diet” or “exercise” that may have associated stigma, pressure, or negative connotations.⁴

Regardless, some patients may not feel prepared or willing to

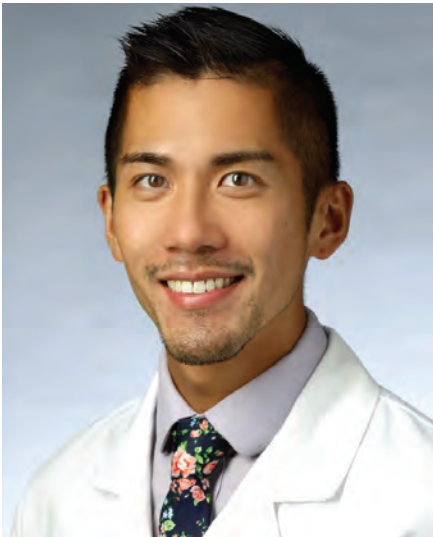


Dr. Huynh

discuss lifestyle modifications during a visit, especially if it is the first clinical encounter when rapport has yet to even be established.⁴ Lifestyle modifications are implemented at various paces, and patients have their individual timelines for achieving these adjustments. Building rapport with patients and creating spaces in which they feel safe discussing and incorporating changes to various components of their lives can take time. Patients want to trust their providers while being vulnerable. They want to trust that their providers will guide them in what can sometimes be a life-altering journey. It is important for clinicians to acknowledge and respect this reality when caring for patients with MASLD. Duong often utilizes this phrase, “It may seem like you are about to walk through fire, but we are here to walk with you. Remember, what doesn’t challenge you, doesn’t change you.”

Identify Motivators of Engagement

Identifying patients’ motivators of engagement will allow clinicians to guide patients through not only the introduction, but also the maintenance of such changes (see Table 2). Improvements in dietary composition and physical activity are often recommended by clinicians who are inevitably and understandably concerned about the consequences of MASLD. Liver diseases, specifically cirrhosis and hepatocellular carcinoma, as well as associated metabolic disorders, are consequences that could result from poorly controlled MASLD. Though these consequences should



Dr. Duong

be conveyed to patients, this tactic may not always serve as an impetus for patients to engage in behavioral changes.⁵

Clinicians can shed light on motivators by utilizing these suggested prompts: “What motivates you to come to our appointments and care for your health? What entails a meaningful life for you — what do or would you enjoy doing? What would make implementing lifestyle changes important to you?” Patient goals may include “being able to

Given the abundance of literature that exists on the benefits of lifestyle modifications, clinicians should be prepared to have informed, individualized, and culturally concordant conversations with their patients.

keep up with their grandchildren,” “becoming a runner,” or “providing healthy meals for their families.”^{5,6} Engagement is more likely to be feasible and sustainable when lifestyle modifications are tied to goals that are personally meaningful and relevant to patients.

Within the realm of physical activity specifically, exercise can be individualized to optimize motivation as well. Both aerobic exercise and resistance training are associated independently with benefits such as weight loss and decreased hepatic adipose content.³ Currently, there is no consensus regarding the optimal type of physical activity for patients with MASLD; therefore, clinicians should encourage patients

Table 1. Example Prompts Using Sensitive Language to Understand Lifestyle Habits

Dietary Index
How would you describe your lifestyle habits, such as food you usually eat and your physical activity levels?
What is your favorite meal?
How do you feel about your lifestyle habits, including food and physical activity?
What do you usually look for when you are grocery shopping or thinking of a meal to cook?
Physical Activity
How physically active are you throughout the day or week?
Are there ways in which you stay physically active throughout the day or week?
What motivates you to come to our appointments and care for your health?
What entails a meaningful life for you — what do you or would you enjoy doing?
What would make implementing lifestyle changes important to you?

Source: Dr. Nikzad, Mr. Huynh, and Dr. Duong

to personalize physical activity.³ While some patients may prefer aerobic activities such as running and swimming, others may find more fulfillment in weightlifting or high-intensity interval training. Furthermore, patients with cardiopulmonary or musculoskeletal health contraindications may be limited to specific types of exercise. It is appropriate and helpful for clinicians to ask patients, “What types of physical activity feel achievable and realistic for you at this time?” If physicians can guide patients with MASLD in identifying types of exercise that are safe and enjoyable, their patients may be more motivated to implement such lifestyle changes.

It is also crucial to recognize that lifestyle changes demand active effort from patients. While sustained improvements in body weight and dietary composition are the foundation of MASLD management, they can initially feel cumbersome and abstract to patients. Physicians can help their patients remain motivated by developing small, tangible goals such as “reducing daily caloric intake by 500 kcal” or “participating in three 30-minute fitness classes per week.” These goals should be developed jointly with patients, primarily to ensure that they are tangible, feasible, and productive.

A Culturally Safe Approach

Additionally, acknowledging a patient’s cultural background can be conducive to incorporating patient-specific care into MASLD management. For example, qualitative studies have shown that people from Mexican heritage traditionally complement dinners with soft drinks. While meal portion sizes vary amongst households, families of Mexican origin believe larger portion sizes may be perceived as healthier than Western diets since their cuisine incorporates more vegetables into each dish.⁷

Eating rituals should also be considered since some families expect the absence of leftovers on the plate.⁷ Therefore, it is appropriate to consider questions such as, “What are common ingredients in your culture? What are some of your family traditions when it comes to meals?” By integrating cultural considerations, clinicians can adopt a culturally safe approach, empowering patients to make lifestyle modifications tailored toward their unique social identities. Clinicians should avoid

Table 2. Prompts to Guide Patients Through Effective and Sustainable Lifestyle Changes

Improve motivation
Ask about personal goals (example questions as in Table 1)
Ask about preferred food ingredients/cuisines (ie, ‘What are some of your favorite meals?’)
Ask about preferred forms of physical activity (ie., ‘What types of physical activity do you enjoy? Would you prefer to [insert activity] or [insert activity]? What type of activity would be feasible for your current schedule? Is there anything that concerns you or makes you unsure about that specific activity?’)
Set small, tangible goals with patients (ie, Start with a mutually designed plan that is simple and includes frequency, intensity, type, time, volume, and progression)
Identify barriers and incorporate social determinants of health
Ask explicitly about barriers (ie, ‘Is there any part of your life that makes it feel like making lifestyle changes is not possible or would be too challenging? Is there a way that I can help you with any barriers to making lifestyle changes?’)
Provide accessible education/educational resources
Creatively identify solutions with patients
Dietician referrals
Food pantries/coupon programs
Community exercise programs
Community nutritional information classes

Source: Dr. Nikzad, Mr. Huynh, and Dr. Duong

generalizations or stereotypes about cultural values regarding lifestyle practices, as these can vary among individuals.

Identify Barriers to Lifestyle Changes and Social Determinants of Health

Even with delicate language from providers and immense motivation from patients, barriers to lifestyle changes persist. Studies have shown that patients with MASLD

Physicians can effectively guide patients through lifestyle changes by identifying each patient’s unique knowledge gap and determining the most effective, accessible form of education.

perceive a lack of self-efficacy and knowledge as major barriers to adopting lifestyle modifications.^{8,9} Patients have reported challenges in interpreting nutritional data, identifying caloric intake and portion sizes. Physicians can effectively guide patients through lifestyle changes by identifying each patient’s unique knowledge gap and determining the most effective, accessible form of education. For example, some patients may benefit from jointly interpreting a nutritional label with their healthcare providers, while others may require educational materials and interventions provided by a registered dietician.

Understanding patients’ professional or other commitments can help physicians further individualize recommendations. Questions such as, “Do you have work or other responsibilities that take up some of your time during the day?” minimize presumptive language about employment status. It can reveal whether patients have schedules that make certain lifestyle changes more challenging than others. For example, a patient who is an overnight delivery associate at a warehouse may have a different routine from another patient who is a family member’s caretaker. This framework allows physicians to build rapport with their patients and ultimately, make lifestyle recommendations that are more accessible.

Though MASLD is driven by inflammation and metabolic dysregulation, social determinants of health play an equally important role in disease development and progression.¹⁰ As previously discussed, health literacy can deeply influence patients’ abilities to implement lifestyle changes. Furthermore, economic stability, neighborhood and built environment (ie, access to fresh produce and sidewalks), community, and social support also impact lifestyle modifications. It is paramount to understand the tangible social factors in which patients live. Such factors can be ascertained by beginning the dialogue with “Which grocery stores do you find most convenient? How do you travel to obtain food/attend community exercise programs?” These questions may offer insight into physical

barriers to lifestyle changes. Physicians must utilize an intersectional lens that incorporates patients’ unique circumstances of existence into their individualized health care plans to address MASLD.

Summary

- Communication preferences, cultural backgrounds, and sociocultural contexts of patient existence must be considered when treating a patient with MASLD.
- The utilization of an intersectional and culturally safe approach to communication with patients can lead to more sustainable lifestyle changes and improved health outcomes.
- Equipping and empowering physicians to have meaningful discussions about MASLD is crucial to combating a spectrum of diseases that is rapidly affecting a substantial proportion of patients worldwide. ■

Nikzad is in the department of internal medicine at University of Chicago Medicine, Illinois (@NewshaN27). Huynh is a medical student at Stony Brook University Renaissance School of Medicine, Stony Brook, New York (@daniel-huynhhh). Duong is in the division of gastroenterology and hepatology at Stanford University, Palo Alto, California (@doctornikkid). They have no conflicts of interest.

References

1. Mohanty A. MASLD/MASH and weight loss. *GI & Hepatology News*. 2023 Oct. *Data Trends* 2023:9-13.
2. Wong VW et al. Changing epidemiology, global trends and implications for outcomes of NAFLD. *J Hepatol*. 2023 Sep. doi: 10.1016/j.jhep.2023.04.036.
3. Zeng J et al. Therapeutic management of metabolic dysfunction associated steatotic liver disease. *United European Gastroenterol J*. 2024 Mar. doi: 10.1002/ueg2.12525.
4. Berg S. How patients can start—and stick with—key lifestyle changes. *AMA Public Health*. 2020 Jan. <https://www.ama-assn.org/delivering-care/public-health/how-patients-can-start-and-stick-key-lifestyle-changes>.
5. Berg S. 3 ways to get patients engaged in lasting lifestyle change. *AMA Diabetes*. 2019 Jan.
6. Teixeira PJ et al. Motivation, self-determination, and long-term weight control. *Int J Behav Nutr Phys Act*. 2012 Mar. doi: 10.1186/1479-5868-9-22.
7. Aceves-Martins M, et al. Cultural factors related to childhood and adolescent obesity in Mexico: A systematic review of qualitative studies. *Obes Rev*. 2022 Sep. doi: 10.1111/obr.13461.
8. Figueroa G, et al. Low health literacy, lack of knowledge, and self-control hinder healthy lifestyles in diverse patients with steatotic liver disease. *Dig Dis Sci*. 2024 Feb. doi: 10.1007/s10620-023-08212-9.
9. Wang L, et al. Factors influencing adherence to lifestyle prescriptions among patients with nonalcoholic fatty liver disease: A qualitative study using the health action process approach framework. *Front Public Health*. 2023 Mar. doi: 10.3389/fpubh.2023.1131827.
10. Andermann A and CLEAR Collaboration. Taking action on the social determinants of health in clinical practice: A framework for health professionals. *CMAJ*. 2016 Dec. doi: 10.1503/cmaj.160177.

New Guideline on EoE Reflects Decade of Advances in Diagnosis and Management

BY CAROLYN CRIST

Clinicians should be aware of the latest developments in the diagnosis and management of eosinophilic esophagitis (EoE), including new biologics approved for treatment and the elimination of proton-pump inhibitor (PPI) trials for diagnosis, according to a new clinical guideline from the American College of Gastroenterology (ACG).

As an update to the 2013 version, the guideline covers paradigm-shifting changes in EoE knowledge about risk factors, pathogenesis, validated outcome metrics, new nomenclature, and pediatric-specific considerations.

"There have been multiple advances across diagnosis, treatment, monitoring, and other aspects of EoE management in the

10.14309/ajg.0000000000003194).

EoE Diagnosis

EoE is a chronic allergen-induced, type 2 immune-mediated disease of the esophagus, which is characterized by symptoms of esophageal dysfunction (such as dysphagia and food impaction) and an eosinophilic predominant infiltrate in the esophagus, the authors wrote.

A diagnosis should be based on the presence of esophageal dysfunction symptoms and at least 15 eosinophils per high-power field on esophageal biopsy, particularly after ruling out non-EoE disorders. A critical change from the 2013 guideline eliminates the requirement of a PPI trial for diagnosis.

Endoscopic evaluation is critical for diagnosis, assessing treatment response, and long-term mon-

basophils, natural killer cells, and fibroblasts in EoE, the authors postulate that using the EoE histologic scoring system may become more relevant in the future, particularly around findings such as persistent

been uncovered, and this has led to successful strategies for disease intervention, including precision therapy."

For treatment of EoE, the goals include improving patient symp-



Dr. Rothenberg

'We now understand that the esophagus is an immune-responsive organ and that food allergies can be manifested as EoE. Investment in science is paying off as the basic disease pathoetiology has been uncovered, and this has led to successful strategies for disease intervention, including precision therapy.'

basal zone hyperplasia or lamina propria fibrosis as drivers of ongoing symptoms when eosinophil counts decline.

A Better Understanding of Pathogenesis

"While EoE is considered a relatively new disease, there has been a concerted effort by researchers and clinicians to work together, in partnership with patients, to better understand the basic disease pathogenesis and develop the best treatment approaches," said Marc Rothenberg, MD, PhD, director of allergy and immunology at Cincinnati Children's Hospital Medical Center, Ohio. Rothenberg wasn't involved with the update.

"A lot of progress has been made since the initial thought that esoph-

toms and quality of life, improving endoscopic and histologic findings, normalizing growth and development in children, maintaining nutrition, and preventing complications such as food impaction or perforation.

This means addressing both the inflammatory and fibrostenotic aspects of the disease, the authors wrote. Pharmacologic or dietary therapies can treat the inflammatory component and may lead to esophageal improvements, whereas esophageal dilation can treat strictures and luminal narrowing. Notably, treatment choices should be individualized based on disease characteristics and patient preferences.

In general, PPIs are suggested as treatment, even beyond reflux



Dr. Dellon

'The guidelines aimed to provide practical and evidence-based recommendations that could be implemented in daily practice, as well as to provide advice on a number of aspects of diagnosis and management of EoE where there might not be a definitive evidence base, but where clinical questions commonly arise.'

decade since the last ACG guidelines and in the 5 years since the last AGA [American Gastroenterological Association] guidelines [Gastroenterology. 2020 May. doi: 10.1053/j.gastro.2020.02.038], including new drug approvals globally for EoE," said lead author Evan Dellon, MD, AGAF, professor of gastroenterology and hepatology and director of the Center for Esophageal Diseases and Swallowing at the University of North Carolina School of Medicine, Chapel Hill.

"The guidelines aimed to provide practical and evidence-based recommendations that could be implemented in daily practice, as well as to provide advice on a number of aspects of diagnosis and management of EoE where there might not be a definitive evidence base, but where clinical questions commonly arise," he said.

The update was published online in *The American Journal of Gastroenterology* (2025 Jan. doi:

itoring, the authors wrote. The guideline advises using the EoE endoscopic reference score (EREFS) to characterize endoscopic findings, a recommendation that was also endorsed in 2022 guidelines by the American Society for Gastrointestinal Endoscopy (Gastrointest Endosc. 2022 Oct;96[4]:576.e1-592.e1). EREFS classifies five key EoE features, including edema, rings, exudates, furrows, and strictures, by severity.

For histologic features of EoE to be assessed, at least six esophageal biopsies should be taken from at least two esophageal levels (such as proximal/mid and distal halves), specifically targeted in areas of furrows or exudates.

In addition, peak eosinophil counts should be quantified on esophageal biopsies from every endoscopy performed for EoE, which will help with subsequent management and monitoring.

As new research expands on the role of mast cells, T cells,



Dr. Chang

'This new 2025 guideline summarizes and synthesizes key studies in support of proton-pump inhibitors, topical steroids, dietary therapy, and biologics for EoE. ... The guidelines are clinically relevant in providing practical suggestions (such as medication dosing) and expert opinions on key concepts in managing EoE.'

ageal eosinophilia was a ramification of acid reflux disease," said Rothenberg, the founding director and a principal investigator of the Consortium of Eosinophilic Gastrointestinal Disease Researchers.

"We now understand that the esophagus is an immune-responsive organ and that food allergies can be manifested as EoE. Investment in science is paying off as the basic disease pathoetiology has

symptoms. In EoE, PPIs can decrease eotaxin-3 cytokines that recruit eosinophils to the esophagus, improve esophageal barrier function, and maintain esophageal epithelial transcriptional homeostasis. Although potassium-competitive acid-blocker medications have been studied in EoE, data remain limited. H2-receptor blockers don't appear to be effective for EoE.

Swallowed topical corticosteroids have shown histologic efficacy, the authors reported, particularly in recent phase 3 trials of budesonide oral suspension (BOS) and budesonide orodispersible tablet (BOT). BOS was approved for EoE by the US Food and Drug Administration (FDA) in 2024, and BOT was approved for EoE by the European Medicines Agency in 2018.

In terms of dietary elimination, a range of options appear to be effective for patients, including the six-food elimination diet, which has been studied most. However, less restrictive or step-up approaches (such as four-food elimination or one-food elimination of milk) may be better for patients, the authors wrote. Ultimately,

Allergy test-directed elimination diets aren't currently recommended because EoE has delayed hypersensitivity, so skin prick, patch, or serum Ig allergy tests tend to have limited success in predicting EoE food triggers.

the “optimal” choice is one that patients and families can adhere to and have the resources to complete.

In addition, they noted that allergy test-directed elimination diets aren't currently recommended because EoE has delayed hypersensitivity, so skin prick, patch, or serum Ig allergy tests tend to have limited success in predicting EoE food triggers.

In terms of biologic treatments, dupilumab is recommended for ages 12 years or older who do not respond to PPI therapy, as well as suggested for ages 1-11 years based on previous clinical trial data. The FDA approved the use of dupilumab for ages 1-11 years in February 2024.

In this update, the authors declined to make recommendations about other biologics such as cendakimab, benralizumab, liren-telimab, mepolizumab, or reslizumab. They also advised against using omalizumab as a treatment for EoE.

“This new 2025 guideline summarizes and synthesizes key studies in support of proton-pump inhibitors, topical steroids, dietary

therapy, and biologics for EoE. Additionally, the guidelines are clinically relevant in providing practical suggestions (such as medication dosing) and expert opinions on key concepts in managing EoE,” said Joy Weiling Chang, MD, assistant professor of gastroenterology at the University of Michigan, Ann Arbor, who specializes in patient-physician preferences and decision-making in EoE care.

“It's an exciting time to take

care of patients with EoE with many new therapies, but the rapidly evolving options can be overwhelming,” said Chang, who wasn't involved with the update. “Since there are no clinical effectiveness studies between the various treatments, and therapies can differ so much (with delivery and daily use, monitoring, cost), electing EoE treatment is an ideal opportunity for shared decision-making. Equipped with these

clinical guidelines, clinicians can be empowered to elicit and consider patient preferences and values in the management of this chronic disease.”

The authors received no specific funding for this update. Dellon and Rothenberg reported receiving research funding and consultant roles with numerous pharmaceutical companies and organizations. Chang reported no relevant disclosures. ■



Complete Clinical Updates for Today's Practice

May 3-4 | San Diego & Virtual

Enhance your delivery of care and improve patient outcomes.

You will engage with experts, fostering collaborative learning and knowledge acquisition.

This course incorporates evidence-based practices and technology to inform diagnosis and treatment.

Hear about the latest cutting-edge research and get the latest clinical practice updates.

Register at pgcourse.org

Register by Feb. 26 and save!

 | 

BE ON THE FOREFRONT

Advance your work — and patient outcomes — with the global digestive disease community at DDW® 2025 in San Diego, CA, or online.



4,000+ posters across GI and hepatology.



400+ education sessions in 17 tracks.



300 industry supporters in the Exhibit Hall.



Connect with colleagues from around the world.

Get early bird discounts through Feb. 26. Register now at ddw.org/register.



DDW2025
Digestive Disease Week®
MAY 3-6, 2025 | SAN DIEGO, CA
EXHIBIT DATES: MAY 4-6, 2025

AGA Clinical Practice Update: P-CABs Can Help When PPI Therapy Fails

BY CAROLYN CRIST

FROM GASTROENTEROLOGY

Clinicians generally shouldn't use potassium-competitive acid blockers (P-CAB) as first-line therapy for acid-related conditions, nonerosive gastroesophageal reflux disease (GERD), or peptic ulcer disease, according to a recent clinical practice update from the American Gastroenterological Association (AGA).

However, P-CABs are recommended in place of proton-pump inhibitors (PPIs) for most patients with *Helicobacter pylori* and other conditions where patients haven't responded to PPIs.

"P-CABs are a newer medication class now available in the US, associated with more rapid, potent, and prolonged gastric acid inhibition than PPI formulations," said lead author Amit Patel, MD, a gastroenterologist at the Duke University School of Medicine and Durham Veterans Affairs Medical Center, Durham, North Carolina.

"P-CABs have potentially significant clinical benefits in the management of *Helicobacter pylori* infection and GERD, particularly more severe erosive esophagitis," he said. "Emerging data are affording additional insights into the clinical benefits of P-CABs in settings such as on-demand therapy for

reflux-associated symptoms, bleeding gastroduodenal ulcers, and endoscopic eradication therapy for Barrett's esophagus."

The update was published in *Gastroenterology* (2024 Sep. doi: 10.1053/j.gastro.2024.06.038).

P-CAB Developments

For most patients, PPIs and histamine-2 receptor antagonists remain



Dr. Patel

the primary way to inhibit gastric acid secretion for common upper gastrointestinal conditions, the authors wrote. However, P-CABs such as vonoprazan and tegoprazan may provide relief

when PPIs have limitations.

Unlike PPIs, P-CABs are considered acid-stable, don't require pre-meal dosing, aren't prodrugs, and don't require conversion to an active form to provide pharmacologic effects. They tend to have longer half-lives and more rapid onset. Serum gastrin levels typically remain higher with P-CABs.

In terms of safety, randomized trial data indicate that P-CABs are generally well tolerated and have short-term and medium-term safety similar to PPIs. Because of potent

acid suppression, enteric infection risks remain higher, though long-term safety data are needed, the authors wrote.

Overall, P-CABs appear to be equally as potent or more potent than PPIs, though more potent acid inhibition isn't necessarily associated with better outcomes, the authors wrote. For most foregut acid-related disorders — such as heartburn and prevention of nonsteroidal anti-inflammatory drug-associated ulcers — P-CABs can help when patients fail PPI therapy.

In general, though, nonclinical factors related to cost, barriers to obtaining medication, and limited long-term safety data may outweigh the advantages of P-CABs, especially if clinical superiority isn't yet known, the authors wrote.

For GERD, clinicians generally shouldn't use P-CABs as first-line therapy for patients with uninvestigated heartburn symptoms or nonerosive reflux disease. However, P-CABs should be used for those with documented acid-related reflux who fail therapy with twice-daily PPIs. They may also be appropriate for on-demand heartburn therapy, although more evidence is needed.

For erosive esophagitis, P-CABs generally shouldn't be used for milder cases but can be considered

for patients with more severe cases that haven't responded to PPIs, including refractory esophagitis.

For *H pylori*, P-CABs should be used in place of PPIs for eradication regimens, including among patients with clarithromycin-resistant strains. In contrast with most of the other indications in the update, the short-term duration of *H pylori* treatment reduced the authors' concerns about P-CAB costs and safety.

For peptic ulcer disease, P-CABs generally shouldn't be used as first-line treatment or prophylaxis. However, the rapid onset and potent acid inhibition could be useful for patients with bleeding gastroduodenal ulcers and high-risk stigmata.

"Emerging data will allow refinements in the populations and clinical settings for which P-CABs at various doses may be considered and advised — and may reveal more clinical scenarios in which they can provide meaningful benefit," Patel said. "Further investigations, including additional populations and novel indicators, as well as evaluating long-term safety data and cost-effectiveness, are warranted, as P-CABs are incorporated more broadly into clinical practice worldwide."

The authors received no specific funding for this update. Patel reported no relevant disclosures. ■

Low-Dose Aspirin Cuts CRC Recurrence

BY MEGAN BROOKS

Low-dose aspirin reduced colorectal cancer (CRC) recurrence rates by more than half in patients with tumors harboring mutations in the PI3K signaling pathway, according to findings from the phase 3 ALASCCA trial.

These results stress "the importance of upfront genomic testing" in patients with CRC, said Anna Martling, MD, PhD, from Karolinska Institutet, Stockholm, Sweden, who reported the findings at the American Society of Clinical Oncology (ASCO) Gastrointestinal Cancers Symposium 2025 in San Francisco.

This is the first trial to show that

mutations in the PI3K signaling pathway, beyond *PIK3CA* alterations, predict aspirin response, "expanding the targetable patient population substantially," Martling added. Genetic mutations along the PI3K signaling pathway are found in about 30% of CRCs.

While aspirin as chemoprevention in CRC has been studied, data confirming its effectiveness as well as uptake of this approach in practice have been lacking, explained ASCO expert commenter Pamela Kunz, MD, with Smilow Cancer Hospital and Yale Cancer Center, New Haven, Connecticut.

"It's really clear that this is a practice-changing study," said Kunz.

The findings indicate that this approach "checks all of the boxes: It's effective, it's low risk, it's inexpensive, and it's easy to administer."

The trial included 626 patients with stages II-III colon cancer (67%) or stages I-III rectal cancer (33%) across 33 hospitals in Sweden, Denmark, Finland, and Norway.

Patients were stratified into two groups based on specific PI3K pathway alterations. Group A (n = 314) included patients with *PIK3CA* mutations in exon 9 and/or 20, and group B (n = 312) included those with other PI3K pathway mutations, including *PIK3CA* mutations outside exon 9/20, or mutations

in *PIK3R1* or *PTEN* genes.

Participants in both groups were randomly allocated 1:1 to 160 mg/d of aspirin or placebo for 3 years. The primary outcome was CRC recurrence; disease-free survival was a secondary outcome.

Compared with placebo, aspirin reduced the risk for recurrence by 51% (hazard ratio [HR], 0.49) in patients with *PIK3CA* mutations, with a 3-year recurrence rate of 7.7% in those taking aspirin vs 14.1% in the placebo group.

Both Martling and Kunz predicted that these findings will change clinical practice. "I anticipate that we'll be seeing adoption of this [strategy]," Kunz said. ■

CRC Screening May be Optimized

Hemoglobin from page 1

Published in *Gastroenterology* (2024 Nov. doi: 10.1053/j.gastro.2024.10.047), the study was prompted by prior research showing individuals with f-Hb concentrations just below the positivity cutoff had an elevated CRC risk vs those with low or no f-Hb. “However, global variations in FIT positivity cutoffs and f-Hb category definitions complicated cross-study comparisons,” van den Berg said. Given the lack of an established

was, however, wide variability in the stool positivity cut-offs in the included studies, ranging from 10 µg f-Hb/g to 80 µg f-Hb/g.

With an overall effect size of 0.69 (95% CI, 0.59-0.79), pooled analysis revealed that in the next screening round, individuals with f-Hb concentrations in stool of 5, 10, 20, and 40 µg/g had a 3-fold, 5-fold, 8-fold, and 13-fold higher risk for colorectal neoplasia, respectively, vs individuals showing 0 µg/g. Although

there was significant study heterogeneity ($I^2 = 97.5\%$, $P < .001$), sensitivity analyses confirmed the consistency of findings. Interestingly, subgroup analyses indicated that

f-Hb concentrations from a previous negative test were especially predictive of advanced neoplasia in subsequent screenings.

“This is a strategy worth pursuing and evaluating in the United States,” said gastroenterologist Theodore R. Levin, MD, a research scientist at Kaiser Permanente Division of Research in Northern California, commenting on the study but not involved in it. “However, there is no currently available FIT brand in the US that reports f-Hb concentration. All FITs in the US report as a qualitative positive-negative result.”

The Dutch investigation aligns with prior studies demonstrating a positive association between f-Hb concentrations in previous screenings and the detection of colorectal neoplasia. “Our working hypothesis was that risk increases in a decreasing manner as f-Hb concentrations rise, and the findings supported this hypothesis,” van den Berg said.

Other research (*Clin Gastroenterol Hepatol.* 2024 Nov. doi: 10.1016/j.cgh.2024.09.036) has projected f-Hb level risk stratification to be effective and perhaps cost-effective in reducing delayed diagnosis of colorectal cancer.

Feasibility of Implementation

In large national screening programs in Europe, Asia, and Australia, as well as those of Kaiser Permanente and the Veterans Health Administration in the United States, information on f-Hb concentrations is already available.

“Therefore, incorporating an Hb-based approach should be relatively easy and affordable,” van den Berg said, and may help to optimize resource use while maintaining high detection rates. “However, the more critical question is whether such an approach would be acceptable to the target population.” To that end, randomized controlled trials in Italy and the Netherlands are offering tailored invitation intervals

key focus will be understanding the acceptability of risk-stratified colorectal cancer screening based on f-Hb among the target population and addressing any information needs they may have, as these are critical factors for successful implementation,” said van den Berg. Her group is currently studying the most effective and cost-effective risk-based strategy for CRC screening based on f-Hb levels.

The authors cautioned that since individuals with undetectable f-Hb levels make up the majority of those with negative FIT results, care must be taken that reducing screening frequency for this low-risk group

does not lead to unfavorable outcomes at the population level.

This study was funded by the Dutch Organization for Scientific Research, which had no role in study design, data collection, analysis, interpretation, or writing.

The authors declared no competing interests. Levin disclosed no competing interests relevant to his comments. ■



Ms. van den Berg

‘Incorporating an Hb-based approach should be relatively easy and affordable. However, the more critical question is whether such an approach would be acceptable to the target population.’



Dr. Levin

‘This is a strategy worth pursuing and evaluating in the United States. However, there is no currently available FIT brand in the US that reports f-Hb concentration.’

based on prior f-Hb concentrations and may provide insight into the real-world application of risk-stratified screening.

Among the many variables to be considered in the context of population-wide screening are cost-effectiveness, acceptability, and practicality, as well as invitation intervals, positivity cut-off levels, and start and stop ages for screening. “A

 **aga gi patient center**
For all your digestive health needs



We've got your patients covered

Send your patients to the **AGA GI Patient Center** for expert information on their digestive conditions, including symptoms, treatment options and more.

For more information, visit patient.gastro.org.

Surgical vs Endoscopic Excision of Large Colon Polyps

Dear colleagues,

We now have the ability to remove almost any large colon polyp endoscopically using a variety of techniques — from the widely used endoscopic mucosal resection to the increasingly prevalent endoscopic submucosal dissection. Yet, in this new era, are there specific polyps for which we should exercise caution and consult a surgeon first?

In this issue of Perspectives, Dr. Jeffrey Mosko and Dr. Moamen Gabr discuss the importance of careful polyp selection and argue

that almost all polyps can be safely removed endoscopically, with low recurrence rates. In contrast, Dr. Ira Leeds from colorectal surgery offers a counterpoint, urging caution when managing polyps in the cecum and rectum while highlighting the role of minimally invasive surgical approaches. We hope these discussions provide valuable insights to support your approach to managing large colorectal polyps, especially in an era of



Dr. Ketwaroo

increasing colon cancer screening.

We also welcome your thoughts on this topic — join the conversation on X at @AGA_GIHN.

Gyanprakash A. Ketwaroo, MD, MSc, is associate professor of medicine, Yale University, New Haven, and chief of endoscopy at West Haven VA Medical Center, both in Connecticut. He is an associate editor for GI & Hepatology News.

Advantages of Endoscopic Resection for Large Colon Polyps

BY MOAMEN GABR, MD, MSC, AND JEFFREY D. MOSKO, MD, MSC

Endoscopy has revolutionized the management of large colorectal polyps, offering a minimally invasive alternative to surgical resection. The dawn of endoscopic resection in the late 20th century, particularly the evolution of endoscopic mucosal resection (EMR) in Japan, marked a paradigm shift in the treatment of colonic lesions by enabling the removal of lesions that would otherwise necessitate surgery.

Endoscopic resection of colorectal polyps is generally performed in an outpatient setting, allowing patients to recover at home the same day. This minimizes disruption to daily life and significantly enhances patient satisfaction.

Most procedures are performed under moderate or deep sedation eliminating the need for general anesthesia. This represents a critical benefit, particularly for patients who are at higher risk of anesthesia-related complications.

Endoscopic resection reduces healthcare costs by eliminating prolonged hospital stays and complex perioperative care. Additionally, preserving the colon's structure and function avoids long-term consequences such as altered bowel habits or ostomy dependence, common with surgical interventions.



Dr. Gabr

The advantages of endoscopic intervention are clear: safety, cost-effectiveness, organ preservation, and convenience for patients.

Lesion Selection

The superiority of endoscopic resection relies on selecting lesions appropriately, specifically those with a low risk of lymph node metastases. This meticulous process should include assessing a lesion's size, location, morphology, granularity, microvascular and surface pit pattern using a combination of high-definition white-light endoscopy, virtual chromoendoscopy, and image magnification.



Dr. Mosko

Gross morphologic assessment utilizes the Paris and LST classifications. Combining the Paris classification, lesion granularity, and location is both straightforward and revealing. Ulcerated/excavated lesions (0-III) are concerning for deep invasion. Depressed (0-IIc) morphologies are strongly associated with T1 CRC. Nodular lesions (0-Is or IIa + Is) have a higher risk of T1 colorectal cancer (CRC), compared with flat

Advantages continued on following page

Blurred Lines: Polyp Needing Surgical Versus Endoscopic Excision

BY IRA LEEDS, MD

I am grateful for the invitation to join in discussion with Gabr and Mosko on the ever-increasing role of endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD). However, as a surgeon, I do carry at least mild trepidation entering one of the literary “safe spaces” of my gastroenterology colleagues.

With the increasing evidentiary support of EMR approaches and the increasing experience of those performing ESD, these two techniques are quickly becoming the options of choice. As these practices become ubiquitous, it is important to recognize both their advantages and limitations, compared with available surgical options. The decision to proceed with EMR and ESD is essentially a turning point away from early surgical referral for a complex lesion. In this discussion, I intend to highlight when EMR and ESD have a clear advantage to early surgical referral, why I believe that early



Dr. Leeds

surgical referral is still superior to advanced endoscopic techniques in the rectum, and why the approach for right-sided lesions should hinge on careful shared decision-making.

Endoscopic approaches nearly always beat surgical approaches when considering short-term risks. Even in the best surgical series, colorectal surgery typically leads to complications in 10%-15% of patients, 1%-5% being serious. Moreover, transabdominal surgical interventions (ie, colectomy) require considerable recovery involving at least a few days in the inpatient setting and over

a month of activity restrictions. Finally, there is a minority of chronically unwell patients who cannot tolerate surgical intervention but may be fortunate enough to have a lesion that with enhanced attention can be endoscopically resected. While EMR and ESD also contribute a disproportionate burden of complications to endoscopy practice, overall complication rates are still favorable when compared with surgical resection.

Moreover, the most feared short-term complication of EMR and ESD, perforation, has the added benefit of a “controlled failure” to colectomy. Advanced endoscopic approaches already require a prepared colon, and patients are

Blurred continued on following page

Read more!

Please find full-length versions of these debates online at MDedge.com/gihepnews/perspectives.

Advantages *continued from previous page* lesions (0-IIa or 0-IIb). Nongranular lesions (0-Is and 0-IIa + Is) have a higher risk of covert cancer. Finally, the recto-sigmoid location is associated with an increased risk of T1 CRC (vs proximal locations).

Endoscopic surface pattern assessment increases one's diagnostic accuracy. There are three primary endoscopic surface pattern classifications: NBI International Colorectal Endoscopic (NICE), Japanese NBI expert team (JNET), and Kudo pit pattern classifications. Colonic lesions that have a NICE Type 3, JNET 3, or Kudo type Vn pattern should be referred promptly for surgical resection. Lesions with a JNET 2B or Kudo type VI carry a higher risk of superficial T1 CRC but can still be removed endoscopically (see below) in expert centers. All other lesions should undergo endoscopic resection.

Endoscopic Resection Techniques

Endoscopic resection of large colorectal polyps encompasses two primary techniques: EMR and endoscopic submucosal dissection (ESD), each tailored to specific lesion characteristics and operator expertise.

EMR, the technique of choice for the vast majority of lesions, relies on injecting a submucosal cushion to lift the lesion before excision. Recent advances, including enhanced snare designs and underwater EMR, have improved en-bloc resection rates, significantly reducing recurrence and enhancing the efficacy of this technique.

ESD offers unparalleled precision for en-bloc resection of complex lesions, particularly those with fibrosis or high-risk features. Cutting-edge innovations, such as traction devices, have streamlined the procedure, addressing the traditional challenges of ESD. Despite being more time intensive, ESD minimizes recurrence and provides complete histopathological evaluation, critical for the management of malignant or pre-malignant lesions.

For non-lifting polyps, newer techniques such as endoscopic full-thickness resection (eFTR), using tools like the Full-Thickness Resection Device (FTRD), enable resection of up to 2-3 cm of the colonic or rectal wall. This ensures complete removal of any lesion and its underlying tissue, effectively preventing recurrence.

These advancements demonstrate how endoscopy can tackle even the most challenging colorectal polyps, reinforcing its position as the preferred treatment modality.

Perceived Limitations

With ongoing refinement over the last 2 decades, many of the perceived limitations (below) of endoscopic

resection have now been overcome.

- **Difficult locations/access:** Historically lesions at the anorectal junction, ileocecal valve, appendiceal orifice, and anastomoses were preferentially sent for surgery. In spite of unique technical challenges at each of these locations, there is now compelling data supporting EMR for these scenarios. We now also have techniques aimed at enabling the resection of lesions with poor access including patient repositioning, distal attachments, variable endoscope diameter/flexibility, traction, and overtube devices.

- **Recurrence:** In the past, recurrence after endoscopic resection of lesions > 20 mm has been reported to be as high as 20%. With our current systematic approach to complete resection, meticulous examination of the post-resection defect for residual polyp tissue, adjunctive techniques to address submucosal fibrosis (hot avulsion, CAST, submucosal release), and thermal ablation to the resection margin (EMR-T), the risk of recurrence for piecemeal resections can be decreased to < 5%. In fact, some groups argue for the en-bloc resection of all large colorectal lesions based on the extremely low (< 1%) recurrence rates and potential for decreased follow-up.

- **Post-resection bleeding:** Post-resection bleeding is no longer a major limitation of any endoscopic approach because of the combination of improved intra-procedural hemostatic and resection techniques, optimized electrosurgical technology, and enhanced defect closure capabilities and devices (with prophylactic defect closure now supported by randomized control trial level data).

- **Perforation:** Deep mural injury (DMI), once an endoscopists' worst fear during resection, is no longer a surgical emergency. It can now be predicted, identified (Sydney classification), and successfully managed. In spite of more widespread aggressive resection strategies, the risk of emergency surgery in patients undergoing EMR and even ESD (where the risk of DMI is significantly higher) is extremely low.

Endoscopic resection for large colorectal polyps is effective, available, minimally invasive, and organ sparing making it the standard of care for the management of colonic polyps. With ongoing iteration in techniques, more invasive surgical approaches can be avoided in almost all patients with benign and low-risk T1 colorectal cancers. ■

Gabr is associate GI division director at the University of Cincinnati, Ohio. Mosko is an assistant professor at the University of Toronto and a staff gastroenterologist at St. Michael's Hospital. The authors declare no conflicts of interest.

Blurred *continued from previous page* given strict return instructions. Hence, the yearly handful of postprocedural perforations that I get called upon to assist with typically tolerate a routine surgical exploration, repair or resection, and recover at rates equal to or better than elective colon resections. For these reasons, lesions that can be endoscopically removed within appropriate risk tolerances can and should be considered for EMR or ESD at time of diagnosis.

There are two clinical scenarios where this consideration for up-front EMR or ESD requires further caution. First, any rectal lesion considered for advanced endoscopic techniques really needs to be done in multidisciplinary conference with a colorectal surgeon. In the modern era of colorectal surgery, surgeons now have numerous approaches to reach the rectum that bridge the gap between traditional endoscopy and transabdominal resection. For many rectal lesions, transanal laparoscopic and robotic approaches offer the opportunity for local excision. The most commonly practiced approach, transanal minimally invasive microsurgery (TAMIS), provides many of the benefits of endoscopy (eg, same-day discharge, no activity restrictions, limited perioperative physiologic stress, low complication rates) while providing the surgical precision, repair strategies, and specimen orientation of conventional surgery. Anecdotally, the time it takes to do a high-quality TAMIS excision in the rectum can be substantially less than that required for a comparable ESD.

For rectal lesions in particular, specimen quality is paramount for oncologic prognosis. Regardless of any intrinsic favorable histopathology or deft hand of the endoscopist, a TAMIS approach will typically provide for a deeper partial-thickness or even full-thickness excision. More times each year than I would like, I find myself at a multidisciplinary tumor board discussing an endoscopically removed rectal lesion done in a piecemeal fashion or insufficient deep ESD where appropriate risk stratification is impossible and we end up offering patients

a likely overly aggressive proctectomy or a potentially oncologically unsound re-excision. Consideration of EMR/ESD vs TAMIS up front would allow better sorting of which technique is most suited to which lesion and avoid these diagnostic dilemmas that seem to be only more common as EMR and ESD practices proliferate.

For a different set of reasons, an advanced cecal adenoma may also be more suited to upfront surgical considerations. Right-colon lesions can be more challenging for surveillance for a host of reasons. Procedurally, right-colon lesions are undeniably more difficult. The thin-walled cecum can be unforgiving for repeated polypectomies. Despite its being an uncomfortable subject for colonoscopists, the evidence suggests that getting to the cecum is not consistent or 100% expected. Finally, patients can be unwilling to undergo serial bowel preparation and endoscopic examination. In contrast, a laparoscopic right colectomy avoids these issues while also attributing little additional risk. Laparoscopic right-colon operations have overall complication rates of less than 10% and major complications of less than 1%. Hospital stays for laparoscopic right colectomy are typically 3 days or less. Finally, surgery reduces both the frequency of surveillance, and a shortened colon makes surveillance easier.

Advanced polypectomy techniques broaden our ability to address even difficult lesions under the ideally aligned degree of invasive procedure. However, like any procedure, these techniques have their own advantages and limitations. There will always be a minority of premalignant colon lesions that are best suited to surgery-first approaches to treatment. In my practice, maintaining open lines of communication and regular interaction with my endoscopy colleagues naturally leads to polyps being addressed in their most suitable fashion. ■

Leeds is assistant professor of surgery at the Yale School of Medicine, New Haven, Connecticut and a staff surgeon at the VA Connecticut Healthcare System. He declares no conflicts of interest.

Random Biopsy Improves IBD Dysplasia Detection, With Caveats

BY WILL PASS

MDedge News

FROM CLINICAL GASTROENTEROLOGY
AND HEPATOLOGY

Random biopsy during colonoscopy improves dysplasia detection among patients with inflammatory bowel disease (IBD), but level of benefit depends on equipment and disease characteristics, according to a recent review and meta-analysis.

Random biopsies collected in studies after 2011 provided limited additional yield, suggesting that high-definition equipment alone may be sufficient to achieve a high detection rate, lead author Li Gao, MD, of Air Force Medical University, Xi'an, China, and colleagues reported. In contrast, patients with primary sclerosing cholangitis (PSC) consistently benefited from random biopsy, offering clearer support for use in this subgroup.

"Random biopsy has been proposed as a strategy that may detect dysplastic lesions that cannot be identified endoscopically, thus minimizing the occurrence of missed colitis-associated dysplasia during colonoscopy," the investigators wrote in *Clinical Gastroenterology and Hepatology* (2024 Jul. doi: 10.1016/j.cgh.2024.05.045). However, the role of random biopsies in colonoscopic surveillance for patients with IBD remains a topic of ongoing debate."

The SCENIC guidelines remain inconclusive on the role of random biopsy in IBD surveillance, the investigators noted, while other guidelines recommend random biopsy with high-definition white-light endoscopy, but not chromoendoscopy.

The present meta-analysis aimed to characterize the impact of random biopsy on dysplasia detection. The investigators aggregated prospective and retrospective studies published in English through September 2023, all of which compared random biopsy with other surveillance techniques and reported the proportion of dysplasia detected exclusively through random biopsy.

"To the best of our knowledge, this systematic review and meta-analysis was the first comprehensive summary of the additional yield of random biopsy during colorectal cancer surveillance in

Patients with inflammatory bowel diseases (IBD) with colonic involvement are at two- to threefold increased risk of colorectal cancer (CRC), compared with the general population. The development and progression of dysplasia in these patients with IBD does not follow the typical adenoma-carcinoma sequence; rather, patients with IBD at increased risk of colorectal cancer may have field cancerization changes. Historically, these mucosal changes have been difficult to visualize endoscopically, at least with standard definition endoscopes. As a result, systematic, four-quadrant, random biopsies — 8 in each segment of the colon, totaling 32 biopsies — are recommended for dysplasia detection. The practice has been adopted and accepted widely. Over time, there have been significant advancements in the management of IBD, with improved colonoscopic resolution, adjunct surveillance techniques, focus on quality of colonoscopic exams and evolution of treatments and treatment targets, and these have resulted in a reduction in the risk of CRC in patients with IBD. The value of random biopsies for dysplasia surveillance in patients with colonic IBD has been questioned.



Dr. Singh

patients with IBD," Gao and colleagues noted.

The final dataset comprised 37 studies with 9051 patients undergoing colorectal cancer surveillance for IBD. Patients had diverse baseline characteristics, including different proportions of ulcerative colitis and Crohn's disease, as well as varying prevalence of PSC, a known risk factor for colorectal neoplasia.

The pooled additional yield of random biopsy was 10.34% in per-patient analysis and 16.20% in per-lesion analysis, meaning that approximately 1 in 10 patients and 1 in 6 lesions were detected exclusively through random biopsy. Despite these benefits, detection rates were relatively low: 1.31% per patient and 2.82% per lesion.

In this context, the systematic review and meta-analysis from Gao and colleagues provides critical insights into the yield of random biopsies for dysplasia surveillance in patients with IBD. Through a detailed analysis of 37 studies published between 2003 to 2023,

with 9051 patients who underwent dysplasia surveillance with random biopsies, they ascertained the incremental yield of random biopsies. Overall, 1.3% of patients who underwent random biopsies were detected to have dysplasia. Of these, 1 in 10 patients were detected to have dysplasia only on random biopsies. On per-lesion analysis, one in six dysplastic lesions were detected only on random biopsies. Interestingly, this yield of random biopsies varied markedly depending on the era, as a surrogate for quality of colonoscopies. In studies that fully enrolled and published before 2011 (majority of patients recruited in the 1990s to early 2000s), the per-patient incremental yield of random biopsies was 14%; this dropped precipitously to 0.4% in studies published after 2011 (majority of patients recruited in late 2000s to 2010s). The incremental yield of random biopsies remained markedly high in studies with a high proportion of patients with primary sclerosing cholangitis (PSC), a

condition consistently associated with a four- to sixfold higher risk of CRC in patients with IBD.

These findings lend support to the notion that improvements in endoscopy equipment with wide adoption of high-definition white-light colonoscopes and an emphasis on quality of endoscopic examination may be leading to better endoscopic detection of previously "invisible" dysplastic lesions, leading to a markedly lower incremental yield of random biopsies in the current era. This questions the utility of routinely collecting 32 random biopsies during a surveillance exam for a patient with IBD at increased risk of CRC (as long as a thorough high-quality exam is being performed), though there may be subpopulations such as patients with PSC where there may be benefit. Large ongoing trials comparing the yield of targeted biopsies vs random and targeted biopsies in patients with IBD undergoing dysplasia surveillance with high-definition colonoscopes will help to definitively address this question.

Siddharth Singh, MD, MS, is associate professor of medicine and director of the UCSD IBD Center in the division of gastroenterology, University of California, San Diego. He declares no conflicts of interest relative to this article.

Subgroup analyses showed a decline in random biopsy additional yield over time. Studies conducted before 2011 reported an additional yield of 14.43% in per-patient analysis, compared to just 0.42% in studies conducted after 2011. This decline coincided with the widespread adoption of high-definition endoscopy.

PSC status strongly influenced detection rates throughout the study period. In patients without PSC (0%-10% PSC prevalence), the additional yield of random biopsy was 4.83% in per-patient analysis and 11.23% in per-lesion analysis. In studies where all patients had PSC, the additional yield increased dramatically to 56.05% and 45.22%, respectively.

"These findings highlight the incremental benefits of random biopsy

and provide valuable insights into the management of endoscopic surveillance in patients with IBD," the investigators wrote. "Considering the decreased additional yields in studies initiated after 2011, and the influence of PSC, endoscopy centers lacking full high-definition equipment should consider incorporating random biopsy in the standard colonoscopy surveillance for IBD patients, especially in those with PSC."

This study was supported by the National Key R&D Program of China, the Key Research and Development Program of Shaanxi Province, and the Nanchang High-Level Scientific and Technological Innovation Talents "Double Hundred Plan" project. The investigators disclosed no conflicts of interest. ■

Study Shows 4% Increase in Risk

Obesity from page 1

EAC, is associated with a 30-fold increase in the incidence of the aggressive cancer. Typically, malignant progression occurs when nondysplastic BE epithelium progresses to low-grade dysplasia (LGD) and then HGD, followed by invasive adenocarcinoma.



Dr. Alexandre

'The most obvious pathologic link is via GERD, with the mechanical effect of visceral obesity promoting the GERD directly, and the sequence of Barrett's dysplasia to cancer indirectly.'

Current guidelines suggest that patients with BE undergo endoscopic surveillance for early detection of adenocarcinoma. However, clinical risk factors could help with risk stratification and a personalized approach to long-term BE management, the authors wrote.

Alexandre and colleagues reviewed case-control or cohort studies that reported on the effect of BMI on the progression of nondysplastic BE or LGD to EAC, HGD, or esophageal cancer (EC). Then they estimated the dose-response relationship with a two-stage dose-response meta-analysis.

Overall, 20 observational studies reported data on 38,565 adult patients, including 1684 patients who were diagnosed with EAC, HGD, or EC. The studies enrolled patients between 1976 and 2019 and were published between 2005 and 2022. Most were based in Europe or the United States, and 74.4% of participants were men.

Among 12 cohort studies with 19,223 patients who had baseline nondysplastic BE or LGD, 816 progressed to EAC, HGD, or EC. The pooled annual rate of progression was 0.03%. Among eight cohort studies with 6647 male patients who had baseline nondysplastic BE or LGD, 555 progressed to EAC, HGD, or EC. The pooled annual rate of progression was 0.02%.

In addition, among 1992 female patients with baseline nondysplastic BE or LGD, 110 progressed to EAC, HGD, or EC. The pooled annual rate of progression was 0.01%, which wasn't a significant difference compared with the progression rate among male patients.

Based on meta-analyses, obesity

was associated with a 4% increase in the risk for malignant progression among patients with BE (unadjusted odds ratio, 1.04; 95% CI, 1.00-1.07; $P < .001$).

Notably, each 5-unit increase in BMI was associated with a 6% increase in the risk of developing HGD or EAC (adjusted odds ratio, 1.06; 95% CI, 1.02-1.10; $P < .001$).

"Although the exact mechanisms by which obesity promotes esophageal carcinogenesis is not fully understood, several possible mechanisms may explain it," Alexandre said. "The most obvious pathologic link is via GERD, with the mechanical effect of visceral obesity promoting the GERD directly, and the sequence of Barrett's dysplasia to cancer indirectly. In addition, it has been demonstrated in experimental studies that gastric acid and bile acid drive malignant changes in esophageal epithelium through stimulation of proliferation, inhibition of apoptosis, and generation of free radicals."

Considering Risk

This study highlights the importance of recognizing the association

between obesity and cancer risks, said Prateek Sharma, MD, professor of medicine and director of gastrointestinal training at the University of Kansas School of Medicine, Kansas City, Kansas.

Sharma, who was not involved with this study, coauthored an American Gastroenterological Association technical review on the



Dr. Sharma

'Obesity is a known risk factor for esophageal adenocarcinoma and may be a modifiable risk factor. Showing that BMI is related to neoplastic progression in Barrett's esophagus may impact surveillance intervals.'

management of BE (Gastroenterology. 2011 Mar. doi: 10.1053/j.gastro.2011.01.031).

"Obesity is a known risk factor for esophageal adenocarcinoma and may be a modifiable risk factor," he said. "Showing that BMI is

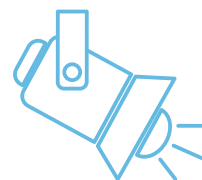
related to neoplastic progression in Barrett's esophagus may impact surveillance intervals."

Future research should look at additional obesity-related factors, such as visceral obesity and malignant progression of BE, as well as whether diet, lifestyle, and bariatric interventions can reduce the risk for progression.

"The next steps also include plugging BMI into risk scores and risk stratification models to enable targeted surveillance among high-risk groups," Sharma said.

One of the study coauthors received funding as a National Institute for Health Research Academic clinical fellow. No other funding sources were declared. Alexandre and Sharma reported no relevant disclosures. ■

Call for Nominations



Member SPOTLIGHT

Nominate your colleagues to be featured in Member Spotlight.
Email GINews@gastro.org.



► **aga** gi career search

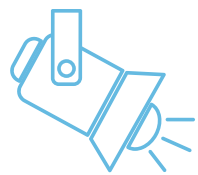
Finding the right job or candidate is at your fingertips

Your career hub across all disciplines and specialties in GI.

Start your search today at

GICareerSearch.com

COM19-024



Member SPOTLIGHT

GI Doc Empowers Female Patients To Be Themselves

BY JENNIFER LUBELL

MDedge News

Pooja Singhal, MD, AGAF, will never forget the time a female patient came in for gastroesophageal reflux disease and dysphagia treatment, revealing that she had already gone through multiple gastroenterologists (GIs) to help diagnose and treat her ailments.

"We spent a whole visit talking about it," said Singhal, a gastroenterologist, hepatologist, and obesity medicine specialist at Oklahoma Gastro Health and Wellness in Oklahoma City. During the exam, she discovered that her middle-aged patient was wearing an adult diaper for diarrhea and leakage.

Previous GIs told the patient they couldn't help her and that she had to live with these symptoms. "I was just so shocked. I told her: This is not normal. Let's talk more about it. Let's figure out how we can manage it," said Singhal, who has spent her career advocating for more education about GI conditions.

There are real barriers to patients opening up and sharing their symptoms, especially if they're female. All GI doctors, but women GIs in particular, face a huge burden of fighting the stigma of disorders of brain-gut interaction and gaining trust of their patients to improve quality of life, while ensuring that the correct knowledge gets across to the public, said Singhal.

An alumna of the American Gastroenterological Association's (AGA) Future Leaders Program, Singhal has served as the private practice course director for AGA's Midwest Women in GI Workshop. She is also a four-time recipient of the SCOPY award for her work in raising community awareness of colorectal cancer prevention in Oklahoma. In an interview, she discussed the critical role women GI doctors play in assisting the unique needs of female patients, and why it takes a village of doctors to treat the complexities of GI disorders.

Why did you choose GI, and more specifically, what brought about your interest in women's GI issues?

GI is simply the best field. While I was doing my rotation in GI as a resident, I was enthralled and humbled that the field of gastroenterology offered an opportunity to prevent



Dr. Pooja Singhal practices at Oklahoma Gastro Health and Wellness in Oklahoma City.

cancer. Colon cancer is the second leading cause of cancer-related deaths, and when I realized that we could do these micro-interventions during a procedure to remove polyps that could potentially turn into cancer — or give us an opportunity to remove carcinoma in situ — that's what really inspired me and piqued my interest in GI. As I continued to learn and explore GI more, I appreciated the opportunity the field gave us in terms of using both sides of our brains equally, the right side and the left side.

I love the diagnostic part of medicine. You have this privilege to be able to diagnose so many different diseases and perform procedures using technical skills, exploring everything from the esophagus, liver, pancreas, small bowel, and colon.

But what I really appreciate about gastroenterology is how it's piqued my interest in women's digestive health. How it became very close to my heart is really from my patients. I've learned a lot from my patients throughout the years. When I was much younger, I don't know if I really appreciated the vulnerability it takes as a woman to go to a physician and talk about hemorrhoids and diarrhea.

One of the comments I often receive is: "Oh, thank God you're a female GI. I can be myself. I can share something personal and you would understand."

Your practice places a specific emphasis on health and wellness. Can you provide some examples

of how you incorporate wellness into treatment?

I feel like wellness is very commonplace now. To me, the definition of wellness is about practicing healthy habits to attain your maximum potential, both physically and mentally — to feel the best you can. My practice specifically tries to achieve that goal by placing a strong emphasis on education and communication. We provide journals where patients can keep track of their symptoms. We encourage a lot of discussion during visits, where we talk about GI diseases and how to prevent them, or to prevent them from happening again. If you're going to do a hemorrhoid treatment that offers hemorrhoid banding, we talk about it in detail

with the patient; we don't just do the procedure.

We have a dietitian on staff for conditions like inflammatory bowel disease, Crohn's and ulcerative colitis, celiac disease, irritable bowel syndrome. Some of our older patients have pelvic organ prolapse and fecal incontinence. We have a pelvic floor therapist and a urogynecologist, and we work very closely with ob-gyn teams. My practice also takes pride in communicating with primary care physicians. We've had patients who have had memory loss or dementia or are grieving the loss of a loved one. And we prioritize communicating and treating patients as a whole and not focusing on just their GI symptoms.

As an advocate for community education on GI disorders, where is education lacking in this field?

I think education is lacking because there is an information delivery gap. I feel the public consumes information in the form of short social media reels. The attention span is so short and any scientific information, especially around diseases, can be scary and overwhelming. Whereas I think a lot of the medical community still interacts and exchanges information in terms of journals and publications. So, we are not really trained necessarily to talk about diseases in very simple terms.

We need more advocacy efforts on Capitol Hill. AGA has been good about doing advocacy work. I had an opportunity to go to Capitol Hill a couple of times and really advocate



Dr. Singhal and her GI clinic team attend a colon cancer public educational event in Oklahoma City.

for policy around obesity medicine coverage and procedure coverage. I was fortunate to learn so much about healthcare policy, but it also made me appreciate that there are a lot of gaps in terms of understanding common medical diseases.

You're trained in the Orbera IntraGastric Balloon System for weight reduction. How is this procedure different from other bariatric procedures?

IntraGastric balloon is Food and Drug Administration approved for weight loss. It's a temporary medical device, so it's reversible. No. 2, it's a nonsurgical intervention, so it's usually done in an outpatient setting. We basically place a deflated gastric balloon endoscopically, similar to an upper endoscopy method. We take a pin endoscope, a deflated balloon, which is made of medical-grade material, and we inflate it with adequate fluid. The concept is when the balloon is inflated, it provides satiety. It reduces the amount of space in the stomach for food. It slows down how quickly the food is going to leave. So you feel full much of the time. And it also helps decrease a hormone called ghrelin, which is responsible for hunger. It can make a big difference when people are gaining weight and in that category of overweight before they progress to obese.

As I tell everybody, obesity is a chronic lifelong disease that is very complex and requires lifelong efforts. So, it's truly a journey. What's made this procedure a success is

follow-up and the continued efforts of dietitians and counseling and incorporating physical exercise, because maintenance of that weight loss is also very important. Our goal is always sustained weight loss and not just short-term weight loss.

As the practice course director for the AGA's Midwest Women in GI Workshop, can you tell me how this course came about? What does the workshop cover?

This workshop is a brainchild of AGA. This will be the third year of having these workshops. It's been divided into regional workshops, so more people can attend. But it arose from the recognition that there is a need to have a support system, a forum where discussions on navigating career and life transitions with grace can happen, and more resources for success can be provided.

There is so much power in learning from shared experiences. And I think that was huge, to realize that we are not alone. We can celebrate our achievements together and acknowledge our challenges together, and then come together to brainstorm

and innovate to solve problems and advocate for health equity.

You've been involved with community, non-profit organizations like the Homeless Alliance in Oklahoma City. How has this work enriched your life outside of medicine?

I feel like we sometimes get tunnel vision, talking to people in the same line of work. It was extremely important for me to broaden my horizons by learning from people outside of the medical community and from organizations like Homeless Alliance, which allowed me a platform to understand what my community needs. It's an incredible organization that helps provide shelter for not only human beings, but also pets. The freezing

temperatures over the last few months provided unique challenges like overflow in homeless shelters. I've learned so many things, such as how to ask for grants and how to allocate those funds. It has been absolutely enriching to me to learn about my community needs and see what an amazing difference people in the community are making. ■



Dr. Singhal celebrates the 1-year anniversary of her solo practice with her family and GI team at Oklahoma Gastro Health and Wellness.

COURTESY DR. POOJA SINGHAL

Lightning Round

Dream job if you weren't a gastroenterologist?

Archaeologist. I love discovering treasure.

Inspirational people?

My parents

Best Halloween costume you ever wore?

Cat Woman

Favorite type of music?

Hip Hop

Cat person or dog person?

Dog — I have a pitbull named Baloo

Favorite sport?

Basketball

Song you have to sing along with when you hear it?

Happy by Pharrell Williams

Introvert or extrovert?

Extrovert

Favorite holiday?

Thanksgiving and Diwali

Optimist or pessimist?

Optimist