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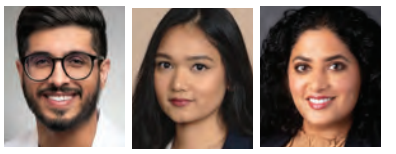

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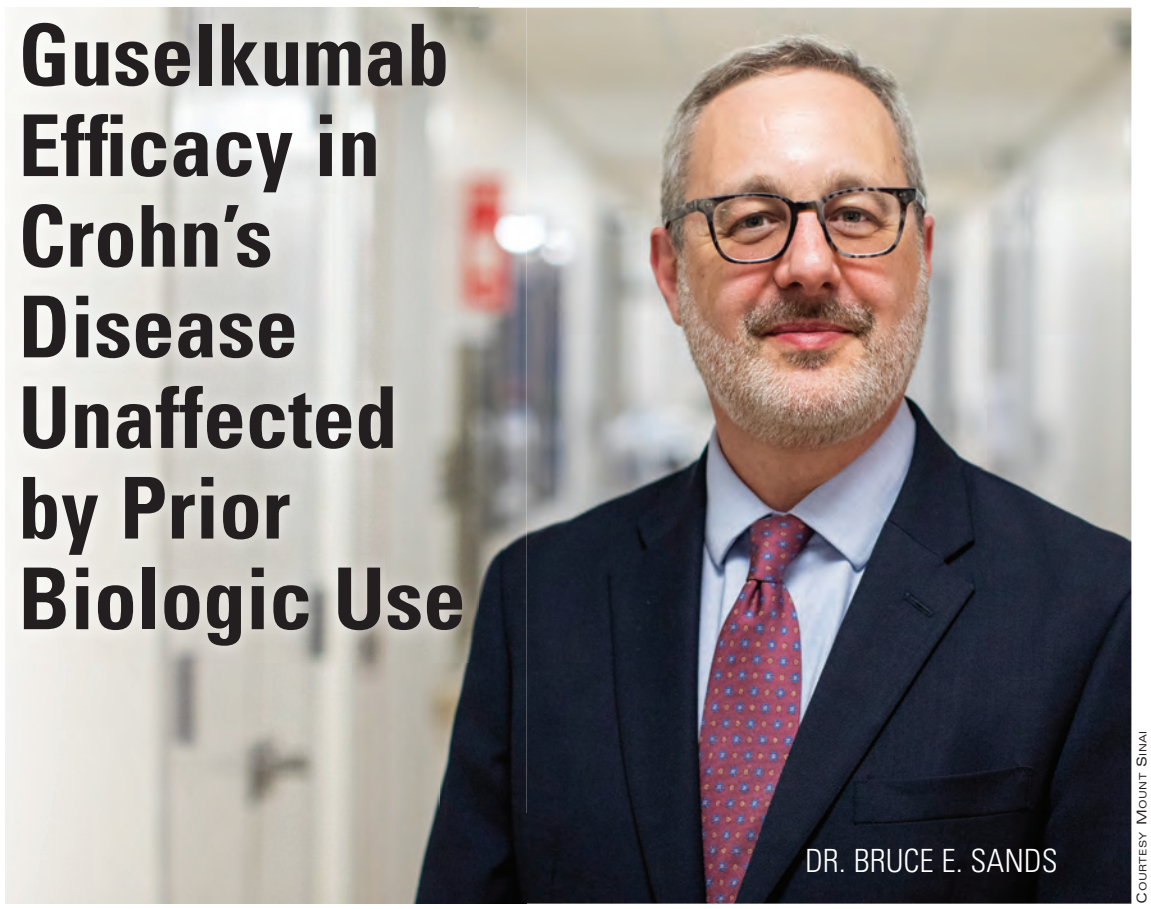
GI&Hepatology News

February 2025 Volume 19 / Number 2

Guselkumab Efficacy in Crohn's Disease Unaffected by Prior Biologic Use



DR. BRUCE E. SANDS

COURTESY MOUNT SINAI

BY BECKY MCCALL

FROM UEG 2024

VIENNA — Guselkumab has been shown to be efficacious vs placebo in patients with moderately to severely active Crohn's disease (CD), regardless of prior biologic therapy exposure, according to a pooled analysis of the two phase 3 double-blind GALAXI 2 and 3 studies.

"We found that guselkumab was effective in both biologic-naive and biologic-inadequate subpopulations," said coinvestigator Bruce E. Sands, MD, AGAF, gastroenterologist from Icahn School of Medicine at Mount Sinai, New York City.

These latest results add to the primary results of the studies reported earlier in 2024 that guselkumab was shown to be superior to both placebo and ustekinumab in the same patient population with moderately to severely active CD.

Sands reported the new data in a presentation at the United European Gastroenterology (UEG) Week 2024.

Guselkumab potently blocks interleukin (IL)–23 and binds to CD64, a receptor on cells that produce IL-23. The dual-acting IL-23p19 subunit inhibitor agent is currently under review

See **Guselkumab** · *page 20*

FIT Completion and Yield Similar in Younger and Older Adults

BY MEGAN BROOKS

Adults aged 45-49 years are as likely as are those aged 50 years to complete a fecal immunochemical test (FIT) as an initial screen for colorectal cancer (CRC) and follow-up with a colonoscopy if needed, a new study has found.

The study also found a similar low 3% rate of CRC detected at colonoscopy in both the younger and older adults.

"Our study suggests that adults ages 45-49 have a colorectal cancer risk that is similar to what we see in adults age 50," senior author Jeffrey K. Lee, MD, MPH, gastroenterologist and research scientist at Kaiser Permanente Northern California Division of Research (DOR) in Oakland, California, said in a news release.

"The low number of cancers we found also provides support for initially offering younger adults a non-invasive test, like FIT, to determine which patients would benefit from a colonoscopy," Lee noted.

Timely and Important Question

"This study addresses a timely and important clinical question, namely, is FIT an acceptable screening modality in patients aged 45-49," Ziad F. Gellad, MD, MPH, AGAF, professor of medicine, Duke University Medical Center, Durham, North Carolina, who was not involved in the study, said in an interview.

"The finding that FIT completion and yield in younger patients is similar to those aged 50 and above is good news because it supports the use

See **Completion** · *page 16*

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LETTER FROM THE EDITOR

Healthcare AI: Balancing Safety and Innovation

Artificial intelligence (AI) applications are expanding rapidly in healthcare. AI-powered tools are increasingly used in everyday medical practice, assisting clinicians with tasks such as diagnosis, treatment planning, data analysis, and patient monitoring, effectively integrating AI into routine clinical decision-making. Despite its potential to fundamentally transform the practice of medicine and healthcare delivery, AI in healthcare remains largely unregulated, with a lack of common standards to guide responsible design, development, and adoption of AI-based tools to guide clinical care.

But this is changing. In mid-January, the US Department of Health & Human Services released its Strategic Plan for the Use of AI in Health, Human Services, and Public Health (available at www.healthit.gov), presenting an approach to catalyze innovation, promote trustworthy AI development, democratize technologies and resources, and cultivate AI-empowered workforces and organizational cultures. While there is no immediate regulatory impact, the plan does provide important insights into how the federal government thinks about AI, which will be a part of driving regulations in the future. As crucial stakeholders in the health AI universe and advocates for its responsible use in clinical practice, it is critical that we as clinicians keep abreast of developments in this rapidly evolving space.

Dr. Adams

'Despite its potential to fundamentally transform the practice of medicine and healthcare delivery, AI in healthcare remains largely unregulated.'

In this month's issue of *GI & Hepatology News*, we summarize a recent systematic review and meta-analysis highlighting worsening health disparities for Hispanic adults with MASLD. We also report the results of an industry-sponsored study comparing the real-world clinical effectiveness of GI Genius (an AI-driven tool) with that of standard colonoscopy.

In February's Member Spotlight, we introduce you to international AGA member Dr. Tossapol Kerdsirichairat (clinical associate professor of gastroenterology at Bumrungrad International Hospital in Bangkok, Thailand), who shares his insights regarding the challenges and rewards of practicing gastroenterology at one of the largest private hospitals in Southeast Asia. 'Tos' is one of roughly 25% of AGA members who live and work outside the United States.

Finally, this month's In Focus column from The New Gastroenterologist focuses on management of chronic constipation, a highly prevalent condition that significantly impacts the quality of life of many of our patients. We hope you enjoy this and all the exciting content in our February issue. ▮

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

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GI&Hepatology News

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.

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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

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GLP-1 RAs Safe in the Perioperative Period: New Guidance

BY DIANA SWIFT

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

The majority of patients may safely take glucagon-like peptide 1 receptor agonists (GLP-1 RAs) before elective surgery and gastrointestinal endoscopies, according to updated guidance published jointly by AGA and four other medical societies.

The new guidance, contrasting with earlier recommendations, says these incrementally used agents can be taken up until the day of surgery, but patients are advised to follow a liquid diet for 24 hours before the procedure (Clin Gastroenterol Hepatol. 2024 Oct. doi: 10.1016/j.cgh.2024.10.003). The decision to proceed with endoscopy and other procedures should be based on shared decision-making with the patient and interdisciplinary care teams in conjunction with minimization of the aspiration risk from delayed gastric emptying, the guidance stresses.

Dr. Schulman

'Nearly all institutions have been forced to revise preprocedural protocols, despite a lack of high-level evidence to suggest that these adjustments are necessary.'

The five endorsing organizations include AGA, along with the American Society for Metabolic and Bariatric Surgery, American Society of Anesthesiologists (ASA), International Society of Perioperative Care of Patients With Obesity, and Society of American Gastrointestinal and Endoscopic Surgeons. The societies emphasize that the statement is intended as guidance only and is not an evidence-based formal guideline.

GLP-1 RAs are known to delay gastric emptying, raising concerns about regurgitation, aspiration, and airway compromise during anesthesia. Rare serious adverse events have also been observed (JAMA. 2023;330[18]:1795-1797), prompting the ASA in 2023 to recommend holding these agents for 1 week for the injectable form and 1 day for the oral form before all procedures requiring anesthesia.

That abundance of caution, however, had negative impacts of its own. "This guidance has led to cancellations and postponements of many endoscopic and surgical procedures or required patients to undergo general anesthesia who may otherwise have had their procedures performed under moderate sedation," said guidance coauthor Allison R. Schulman, MD, MPH, an associate professor of medicine and surgery and chief of endoscopy at the University of Michigan in Ann Arbor. "Nearly all institutions have been forced to revise preprocedural protocols, despite a lack of high-level evidence to suggest that these adjustments are necessary."

"Studies have yielded mixed results as to whether patients on GLP-1s are at increased risk of these events, and the limited data available are inconsistent," Schulman said. "As a result, there are inconsistencies in the recommendations from various societies leading to growing uncertainty with proceduralists on how to provide safe, effective, and timely procedural care to patients taking GLP-1 RAs."

The new joint-society guidance may alleviate some of the uncertainty. Among the recommendations:

- Continuing GLP-1 RAs in the perioperative period should be based on shared decision-making with the patient and all care teams balancing the metabolic need for the GLP-1 RA with individual patient risk.
- Certain variables may increase the risk for delayed gastric emptying and aspiration with the periprocedural use of GLP-1 RAs: **escalation phase** — This phase vs the maintenance phase is associated with a higher risk for delayed gastric emptying; **higher dose** — the higher the dose, the greater the risk for gastrointestinal (GI) side effects; **weekly dosing** — GI side effects are more common with weekly vs daily formulations; **presence of GI symptoms** — nausea, vomiting, abdominal pain, dyspepsia, and constipation may suggest delayed gastric emptying; and **medical problems beyond GLP-1 RA indications with GI effects** — assess for such conditions as bowel dysmotility, gastroparesis, and Parkinson's disease.
- Risk factors should be assessed in advance to allow sufficient time to adjust preoperative care, including diet modification and medication bridging if GLP-1 RA cessation is deemed advisable.
- If retained gastric contents are a concern on the day of a procedure, point-of-care gastric ultrasound could be used to assess aspiration risk, resources permitting.
- The aspiration risk from delayed gastric emptying should be minimized by preoperative diet modification and/or altering the anesthesia plan to consider rapid sequence induction of general anesthesia for tracheal intubation. A 24-hour preoperative liquid diet, as before colonoscopy and bariatric surgery, can be utilized when delayed gastric emptying is a concern.
- When concern about retained gastric contents exists on procedure day, providers should engage patients in a shared decision-making model and consider the benefits and risks of rapid-sequence induction of general anesthesia for tracheal intubation to minimize aspiration risk vs procedure cancellation.

Dr. Purow

"Safe continuation of surgery and gastrointestinal endoscopy, and prevention of procedure cancellation, for patients on GLP-1 RAs can be prioritized following the recommendations above, as would occur for other patient populations with gastroparesis," the guidance panel wrote.

Commenting on the statement but not involved in it, David B. Purow, MD, managing director of the Digestive Health Center at Northwell Health/Huntington Hospital in Huntington, New York, said the recommendations will encourage clinicians to be more discerning about actual risk in individual cases rather than follow the previous blanket recommendation to stop these agents before procedures requiring sedation.

While GLP-1 RAs were prescribed for the relatively small number of patients with diabetes, he said, the risk was not apparent but became clearer with the widespread use of these agents for weight loss — often unregulated and undisclosed to care providers.

"The pendulum shifted too far the other way, and now it's shifted back," he said in an interview. "The new guidance is great because now we can be more thoughtful about managing individual patients." He cited, for instance, the recommendations on the greater risk in patients in the dose-escalation phase or on higher doses, and the risk-reducing measure of a liquid diet for 24 hours before surgery.

His center is already using point-of-care ultrasound and recently had a case in which a patient who forgot and took his GLP-1 RA before a scheduled procedure was found on ultrasound to have a full stomach. "In some cases, these drugs can cause an almost gastroparesis level of delayed emptying," Purow said.

'The pendulum shifted too far the other way, and now it's shifted back. The new guidance is great because now we can be more thoughtful about managing individual patients.'

Purow thinks this early guidance will probably progress to firm guidelines within a year. Schulman is more cautious. "Our understanding of this complex topic is increasing rapidly, and ongoing clinical research will ultimately lead to evidence-based guidelines in this changing landscape," she said.

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Schulman is a consultant for Apollo Endosurgery, Boston Scientific, Olympus, Microtech, and Fractyl. Purow had no competing interests to declare. ■

Liver Stiffness Measurement Predicts Long-Term Outcomes in Pediatric Biliary Atresia

BY WILL PASS
MDedge News

FROM GASTROENTEROLOGY

Liver stiffness measurement (LSM) using vibration-controlled transient elastography (VCTE) predicts long-term outcomes among pediatric patients with biliary atresia, according to investigators.

These findings suggest that LSM may serve as a noninvasive tool for risk stratification and treatment planning in this population, reported lead author Jean P. Molleston, MD, of Indiana University School of Medicine, Indianapolis, and colleagues.


Dr. Molleston

"Biliary atresia is frequently complicated by hepatic fibrosis with progression to cirrhosis and portal hypertension manifested by ascites, hepatopulmonary syndrome, and variceal bleeding," the investigators wrote in *Gastroenterology* (2024 Oct. doi: 10.1053/j.gastro.2024.09.035). "The ability to predict these outcomes can inform clinical decision-making."

To this end, VCTE has been gaining increasing support in the pediatric setting.

"Advantages of VCTE over liver biopsy include convenience, cost, sampling bias, and risk," the investigators wrote. "VCTE potentially allows (1) fibrosis estimation, (2) prediction of portal hypertension complications/survival, and (3) ability to noninvasively monitor liver stiffness as a fibrosis surrogate."

The present multicenter study aimed to gauge the prognostic utility of VCTE among 254 patients, aged 21 years or younger, with biliary atresia. All patients had a valid baseline LSM, plus longitudinal clinical and laboratory data drawn from studies by the Childhood Liver Disease Research Network (ChiLDReN). Liver stiffness was assessed noninvasively with FibroScan devices, adhering to protocols that required at least 10 valid measurements and a variability of less than 30%.


ARINDAM GHOSH/DREAMSTIME

The primary outcomes were survival with native liver (SNL), defined as the time to liver transplantation or death, and a composite measure of liver-related events, including the first occurrence of transplantation, death, ascites, variceal bleeding, or hepatopulmonary syndrome. Secondary outcomes focused on the trajectory of platelet decline, a marker of disease progression. The study also explored the relationship between baseline LSM and conventional biomarkers, including platelet count, albumin, and bilirubin.

LSM was a strong predictor of long-term outcomes. Specifically, Kaplan-Meier analysis showed significant differences in 5-year SNL across LSM strata ($P < .001$). Children with LSM values less than 10 kPa had excellent 5-year SNL rates (LSM 10 to < 15 kPa, 88.9%; 95% CI, 75.1%-95.3%), while those with LSM of at least 15 kPa exhibited substantially lower 5-year SNL (58.9%; 95% CI, 46.0%-69.7%).

Similarly, event-free survival (EFS) rates declined as LSM values increased ($P < .001$). Participants with LSM less than 10 kPa had a 5-year EFS rate of 92.2% versus with 61.2% for those with LSM of at least 15 kPa.

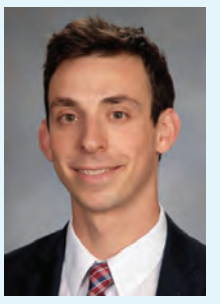
LSM also predicted platelet decline. For every twofold increase in baseline LSM, platelet counts declined by an additional 4,000/mm^3 per year ($P < .001$). This association was illustrated through predicted trajectories for participants with LSM values of 4, 7, 12, 18, and 42 kPa, corresponding to different percentiles of disease severity.

Cox proportional hazards analysis indicated that a twofold increase in LSM was associated with a hazard ratio of 3.3 ($P < .001$) for liver transplant or death. While LSM had good discrimination on its own (C statistic = 0.83), it did not significantly improve predictive accuracy when added to models based on platelet count, albumin, and bilirubin.

"This noninvasive measurement could potentially be used to predict natural history, stratify patients for clinical trials, plan interventions, and provide anticipatory guidance," Molleston and colleagues concluded.

This study was supported by grants from the National Institute of Diabetes, Digestive and Kidney Diseases; National Institutes of Health; Childhood Liver Disease Research Network; and others. The investigators disclosed no conflicts of interest. ■

Grading liver stiffness using elastography is a widely utilized tool in adult populations, and its application is expanding in pediatric hepatology clinics. Clinicians incorporate liver stiffness measurements (LSM) alongside clinical findings and biochemical markers to noninvasively assess the degree of hepatic fibrosis and cirrhosis. Molleston and colleagues leveraged the robust data from the National Institute of Diabetes and Digestive and Kidney Diseases–supported network ChiLDReN and found that LSM in children with biliary atresia (BA) correlate with the progression to complications associated with portal hypertension and liver transplantation. While these findings are not unexpected, this compelling investigation accomplishes the important function of validating the utility of elastography in this cohort.


Dr. Bennett


Dr. Rand

Prognosticating the timeline of complications stemming from biliary atresia is a central tenet of pediatric hepatology. Helping families understand what the future may hold for their child is critical in fostering long-term relationships between clinicians and caregivers. Furthermore, establishing clear expectations regarding follow-up care and monitoring is beneficial for both providers and patients. Of particular importance is minimizing the need for invasive procedures, such as liver biopsy, which, while relatively safe, remains burdensome and is rarely used to assess fibrosis in BA.

Pediatric hepatologists already consider multiple factors — including age at hepatoportoenterostomy, subsequent clearance of cholestasis, exam findings such as splenomegaly, and platelet count — to predict the clinical course of infants with BA. The addition of a data-driven approach to interpreting liver stiffness measurements represents a valuable new tool in this expanding repertoire, offering an encouraging prospect for both providers and families navigating the complexities of pediatric liver disease.

Aaron Bennett, MD, is a fellow in the Division of Gastroenterology, Hepatology and Nutrition at Children's Hospital of Philadelphia in Pennsylvania. Elizabeth B. Rand, MD, is the medical director of the Liver Transplant Program, director of the Gastroenterology Fellowship Program, and director of the Advanced Transplant Hepatology Program at Children's Hospital of Philadelphia.

Lipophilic Statins May Protect Against HCC in Select Liver Disease Patients

BY WILL PASS
MDedge News

FROM GASTRO HEP ADVANCES

Lipophilic statins are associated with reduced risk of developing hepatocellular carcinoma (HCC) among patients with hepatic fibrosis and cirrhosis, according to investigators.

These findings also pave the way for new research into targeted therapies, personalized prevention strategies, and broader applications in high-risk populations, Erik Almazan, MD, and Raymond T. Chung, MD, of Harvard Medical School, Boston, Massachusetts, reported.

"Statins, metformin, and aspirin are low-cost medications often prescribed for the management of diseases associated with metabolic syndrome that have been associated with reduced HCC risk, the investigators wrote in *Gastro Hep Advances* (2024 Aug. doi: 10.1016/j.gastha.2024.08.014). "Despite these findings, few studies have focused on populations in the US or without hepatitis B virus (HBV) or hepatitis C virus (HCV)."

To address this knowledge gap, Almazan and Chung retrospectively analyzed data from 3677 patients with hepatic fibrosis and cirrhosis, drawn from the *All of Us* Controlled Tier Dataset v7, which spans May 2018 to July 2022.

Within this population, 94 patients had HCC, while 3583 served as controls. Lipophilic statin use was compared with hydrophilic statins, metformin, and aspirin. Multivariable logistic regression controlled for confounders including age, sex, race, and the presence of HBV or HCV.

Participants in the HCC cohort were older (mean age, 64 vs 58 years), were more likely to be male (64.1% vs 50.0%), and had higher rates of chronic HBV (9.6% vs 2.5%) and chronic HCV (36.2% vs. 20.5%) compared to controls ($P \leq .01$).

As a class, lipophilic statins were associated with a 36% reduced risk of HCC (odds ratio [OR], 0.64; 95% CI, 0.41-1.00; $P < .05$). Specifically, atorvastatin was associated with a 41% reduced risk (OR, 0.59; 95% CI, 0.37-0.93; $P = .02$), while simvastatin was associated with a 54% reduced risk (OR, 0.46; 95% CI, 0.22-0.97; $P = .04$).

In contrast, hydrophilic statins, such as pravastatin and rosuvastatin, showed no significant association with HCC risk. Similarly, no protective association was observed for metformin or aspirin.

These findings suggest that lipophilic statins could provide a practical and cost-effective strategy for HCC prevention, particularly in patients with metabolic syndrome or alcohol-related liver disease, according to Almazan and Chung. These high-risk groups often lack accessible and noninvasive prevention options, further highlighting the clinical relevance of these results.

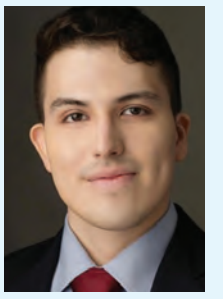
The investigators proposed that the chemopreventive effects of lipophilic statins may be linked to their ability to passively diffuse into cells and modulate pathways involved in cancer development, such as the mevalonate pathway. These potential mechanisms remain poorly understood.

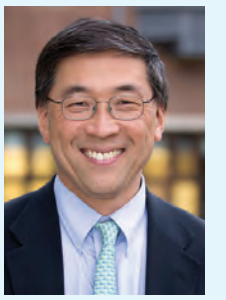
Almazan and Chung also pointed out several study limitations, including lack of granular data on statin doses and treatment duration, absence of serologic and imaging confirmation of hepatic fibrosis and cirrhosis, and a study cohort drawn from populations historically underrepresented in medical research, potentially limiting generalizability to the broader US population.

"Nevertheless, we believe that our study adds valuable information to the literature on statin use and its association with HCC with data from a US-based sample inclusive of individuals with risk factors other than HBV and HCV," the investigators wrote. "These results provide further support for trials (such as NCT05028829) evaluating the utility of lipophilic statins for chemoprevention in HCC for persons at risk."

This study was supported by various National Institutes of Health grants. The investigators disclosed no conflicts of interest. ■

Hepatocellular carcinoma (HCC) incidence continues to increase in the United States. Because of its poor prognosis and limited treatment options, prevention strategies are critically needed, yet there are no Food and Drug Administration–approved treatments for HCC prevention. In the United States, metabolic syndrome has a high prevalence and is a significant contributor to HCC burden. Many individuals with metabolic syndrome are eligible for statin therapy, which has been associated with HCC chemoprevention. Evidence suggests that lipophilic statins may be more effective chemopreventive agents than hydrophilic statins. However, previous studies have largely focused on populations with hepatitis C virus, making it unclear whether these findings are generalizable to individuals with other liver disease etiologies.


Dr. Almazan


Dr. Chung

Our findings support the chemopreventive potential of lipophilic statins in patients with hepatic fibrosis and cirrhosis, regardless of the underlying cause. If lipophilic statins are confirmed as effective chemopreventive agents, HCC prevention could begin in the primary care setting. For example, primary care providers treating patients with metabolic syndrome and an indication for statin therapy could select treatment with lipophilic statins over hydrophilic statins. This approach would be cost-effective, relatively simple to implement, and beneficial to many patients, including those from lower socioeconomic backgrounds who are at higher risk.

Large-scale clinical trials and basic science studies are necessary to confirm the role of lipophilic statins in HCC prevention. Supporting precision medicine initiatives like the *All of Us* Research Program could help identify individuals most likely to benefit and address gaps in current HCC prevention strategies.

Erik Almazan, MD, is a resident physician at Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts. Raymond T. Chung, MD, is director of the Hepatology and Liver Center at Massachusetts General Hospital and Harvard Medical School, Boston. They have no conflicts to disclose.


Mohammed Haneefa Nizamudeen/Stock/Getty Images

Hispanic Patients Face Disparities in MASLD

BY WILL PASS
MDedge News

FROM CLINICAL GASTROENTEROLOGY AND HEPATOLOGY

Hispanic adults in the United States experience significantly higher risk of metabolic dysfunction–associated steatotic liver disease (MASLD) and metabolic dysfunction–associated steatohepatitis (MASH), compared with non-Hispanic adults, according to a new systematic review and meta-analysis.

These findings underscore worsening health disparities in MASLD management and outcomes in this patient population, Kaleb Tesfai, BS, of the University of California, San Diego (UCSD), and colleagues reported.

Previously, a 2018 meta-analysis (Clin Gastroenterol Hepatol. 2018 Feb. doi: 10.1016/j.cgh.2017.09.041) found that Hispanic individuals had a higher MASLD prevalence than non-Hispanic White and Black individuals, along with an elevated relative risk of MASH.

"In the setting of the evolving obesity epidemic, prevalence of MASLD has increased and characteristics of patient populations of interest have changed since the time of this prior meta-analysis," Tesfai and colleagues wrote in *Clinical Gastroenterology and Hepatology* (2024 Jul. doi: 10.1016/j.cgh.2024.06.038). "Importantly, MASH has become a leading indication for liver transplant, thereby impacting long-term clinical outcomes. As such, accurate, updated prevalence rates and relative risk estimates of MASLD, MASH, advanced fibrosis/cirrhosis, and clinical outcomes for Hispanic adults in the US remain poorly characterized."

'Our systematic review and meta-analysis highlights the worsening health disparities experienced by Hispanic adults in the US, with significant increase in the relative risk of MASLD and MASH ... compared with prior estimates.'

The present meta-analysis focused specifically on Hispanic adults in the United States; it compared their disease prevalence, severity, and risk to non-Hispanic adults. Twenty-two studies, conducted between January 1, 2010, and December 31, 2023, were included, comprising 756,088 participants, of whom 62,072 were Hispanic.

Study eligibility required reported data on the prevalence of MASLD, MASH, or advanced fibrosis, as well as racial or ethnic subgroup analyses. Studies were excluded if they did not use validated diagnostic methods, such as liver biopsy or imaging, or if they lacked stratification by Hispanic ethnicity. Prevalence estimates and relative risks were calculated using random-effects models. The analysis also accounted for potential confounding factors, including demographic characteristics, metabolic comorbidities, and social determinants of health (SDOH).

The pooled prevalence of MASLD among Hispanic adults was 41% (95% CI, 30%-52%), compared with 27% in non-Hispanic populations, reflecting a relative risk (RR) of 1.50 (95% CI, 1.32-1.69). For MASH, the pooled prevalence among Hispanic adults with MASLD was 61% (95% CI, 39%-82%), with an RR of 1.42 (95% CI, 1.04-1.93), compared with non-Hispanic adults.

"Our systematic review and meta-analysis highlights the worsening health disparities experienced by Hispanic adults in the US, with significant increase in the relative risk of MASLD and MASH in contemporary cohorts compared with prior estimates," the investigators wrote.

Despite these elevated risks for MASLD and MASH, advanced fibrosis and cirrhosis did not show statistically significant differences between Hispanic and non-Hispanic populations.

The study also characterized the relationship between SDOH and detected health disparities. Adjustments for factors such as income, education, and healthcare access eliminated the independent association between Hispanic and MASLD risk, suggesting that these structural inequities play a meaningful role in disease disparities.

Still, genetic factors, including PNPLA3 and TM6SF2 risk alleles, were identified as contributors to the higher disease burden in Hispanic populations.

"Public health initiatives focused on increasing screening for MASLD and MASH and enhancing health care delivery for this high-risk group are critically needed to optimize health outcomes for Hispanic adults in the US," the authors wrote.

This study was supported by various institutes at the National Institutes of Health, Gilead Sciences, and the SDSU-UCSD CREATE Partnership. The investigators disclosed additional relationships with Eli Lilly, Galmed, Pfizer, and others. ■

Tapering Corticosteroids in Severe Alcohol-Associated Hepatitis

BY CAROLYN CRIST

FROM AASLD 2024

SAN DIEGO — In patients with severe alcohol-associated hepatitis (SAH), tapering corticosteroids appears to be safer and as effective as a conventional fixed dose, according to new research.

"Although several drugs have been evaluated for severe alcohol-associated hepatitis, none have succeeded in practice. Corticosteroids remain the mainstay of treatment; however, infections remain a major concern in 25%-40% of cases," said Anand Kulkarni, MD, director of critical care hepatology at the Asian Institute of Gastroenterology in Hyderabad, India.

"There are no standard society guidelines for steroid dosing, and our current practices stem from studies in the 1970s, so there's a major knowledge gap around optimal dosing and if stepwise tapering helps," said Kulkarni, who presented the findings at The Liver Meeting 2024: American Association for the Study of Liver Diseases (AASLD).

Assessing Tapered Doses

In a multicenter, open-label randomized controlled trial, 254 patients with SAH from four Indian centers and one Canadian center were randomized to receive either a fixed or tapering dose of 40 mg prednisolone daily for 4 weeks. The patients in the tapering group received a starting dose of 40 mg, which was reduced by 10 mg weekly over 4 weeks.

While taking corticosteroids, 66% of those in the fixed dose group and 55% of those in the tapering group also received prophylactic antibiotics.

The mean age of participants was 41.1 years, the median Model for End-Stage Liver Disease score was 25.6, and 98.4% were men.

The primary objective was to compare the incidence of drug-related adverse events, infections, hospitalization, and mortality through day 90.

The duration of corticosteroid therapy was 22 days in the fixed dose group and 23 days in the tapering dose group.

Overall, the proportion of steroid responders was similar in both groups, at 80.3% in the fixed dose group and 82.5% in the tapering dose group.

However, the incidence of drug-related adverse events was significantly higher in the fixed dose group (52%) than in the tapering dose group (36.2%). The most common adverse events in both groups were infection, hyperglycemia, and hematochezia.

At 90 days, the incidence of infection was significantly lower in the tapering group (19.7%) than in the fixed dose group (33.1%). In both groups, the most common infection sites were the lungs (28.3%) and urinary tract (22.4%).

In terms of liver-related outcomes, some patients developed hepatic encephalopathy (11.8% in fixed dose vs 6.3% in tapering dose) and acute variceal bleed (3.1% in each group), as well as acute kidney injury (26.8% in fixed dose vs 18.9% in tapering dose).

Hospitalization within 90 days was required in 44.1% of the fixed dose group and 33.1% of the tapering dose group. Survival at day 90 was 83.5% in the fixed dose group and 86.6% in the tapering group. Relapse of alcohol use by day 90 occurred in 13.4% of the fixed dose group and 12.6% of the tapering group.

"Rapid tapering in severe alcohol-associated hepatitis reduces infections and hospitalizations but doesn't have a significant impact on survival," Kulkarni concluded. Given the high risk for infection in patients with SAH and limited certainty around benefits, the data may also call into question whether to give steroids to these patients

Continued on following page

AGA Legacy Society Members Sustain GI Research

Research creates successful practices. Patients benefit from gastroenterology research daily in practices. Scientists are working hard to develop new treatments and therapies, and to discover cures to advance the field and better patient care. But they can't do this without research funding.

AGA Legacy Society members have answered this call for support. They recognize the value that research has had in their profession, both in academic medicine and in private practice, and are showing their appreciation by giving back.

"I donated to the AGA Research Foundation to ensure the vitality of our specialty, and to fund the research of future generations of gastroenterologists," said Michael Camilleri, MD, AGAF, of Mayo Clinic, Rochester, Minnesota, and an AGA Legacy Society member. "Funding from organizations like the AGA Research Foundation is crucial for young scientists and gastroenterologists to launch their careers. At the start of my career, I received two AGA research awards. I felt it was my turn to support the mission of the organization that I regard as my academic home away from home institution."

AGA Legacy Society members see the promise the future holds and are committed to furthering research in gastroenterology and hepatology through their generous donations.

AGA members who make gifts at the AGA Legacy Society level any time before Digestive Disease Week® (DDW) 2025 will receive an invitation to the AGA Research Foundation Benefactor's Event in San Diego, California. Interested in learning more about AGA Legacy Society membership? Contact foundation@gastro.org or visit https://foundation.gastro.org/our-donors/aga-legacy-society/.

Continued from previous page

at all, said session co-moderator Aleksander Krag, MD, professor of clinical medicine at the University of Southern Denmark, Odense, and secretary general of the European Association for the Study of Liver 2023-2025.

"Since there are no other treatments available as of now, we'll still continue to give steroids," Kulkarni noted. But "tapering the dose should be beneficial."

Although steroid therapy has been considered the "mainstay treatment" for SAH for 50 years, it doesn't always lead to long-term improvement in liver values or survival, said Prasun Jalal, MD, the Stan and Sue Partee Endowed Chair in Hepatology at Baylor College of Medicine, Houston, Texas, who wasn't involved with the study.

Researchers are looking to other connections, such as the gut microbiome, to find treatments for advanced alcoholic liver disease, Jalal said in an interview. In a small pilot study, he and colleagues found that intestinal microbiota transplantation (IMT) appears to be safe and effective for these patients.

"Early analyses suggest that IMT has a favorable outcome on the prognosis of patients with severe alcohol-associated hepatitis and is safe," Jalal said. "A longer follow-up study with a larger sample size is in progress."

Kulkarni and Krag reported no relevant disclosures. Jalal has speaking and teaching relationships with AbbVie and Madrigal.

Avoid Getting Stuck: A Practical Guide to Managing Chronic Constipation

BY HAMZA SALIM DO; ANNI CHOWDHURY DO; AND LAVANYA VISWANATHAN MD, MS

Introduction

Constipation affects one in six people worldwide and accounts for one third of outpatient visits. Chronic constipation is defined by difficult, infrequent, and/or incomplete defecation, quantified by less than three spontaneous bowel movements per week, persisting for at least 3 months. Patients may complain of straining during defecation, incomplete evacuation, hard stools (Bristol stool scale [BSS] type 1-2), and fullness or bloating. Chronic constipation can be subclassified as either a primary or secondary disorder. Our discussion aims to provide further insight into classification, evaluation, and management of the different forms of chronic constipation for the gastroenterologist.

Primary Constipation Disorders

Primary constipation includes disorders of the colon or anorectum. This includes irritable bowel syndrome with constipation (IBS-C), chronic idiopathic constipation (CIC), slow transit constipation (STC), dyssynergic defecation, and pelvic floor disorders.

IBS-C

IBS-C is a chronic disorder of the gut-brain axis with a worldwide prevalence of 1.3% and a prevalence of 6%-16% in the United States, United Kingdom, and Canada, with females more likely to seek care than males. The economic impact of IBS-C is estimated to be $1.5 billion–$10 billion per year in the United States alone. The distinguishing characteristic is abdominal pain; however, IBS-C can present with a constellation of symptoms. The diagnostic paradigm has shifted from IBS being a diagnosis of exclusion to now using a positive diagnostic strategy. Using this Rome IV criteria, one can make the diagnosis with > 95% accuracy.

CIC

CIC, previously defined as functional constipation, is a disorder defined by incomplete defecation and difficult or infrequent stool. CIC is diagnosed in patients without an underlying anatomic or structural abnormality. Rome IV Criteria helps further classify the defining characteristics of chronic idiopathic constipation.

STC

STC is characterized by impaired colonic transit time in the absence of pelvic floor dysfunction. It presents with infrequent bowel movements, diminished urgency, and/or straining with defecation.

Defecatory Disorders: Dyssynergic Defecation and Pelvic Floor Dysfunction

Defecatory disorders (DDs) result from alterations in the colonic-neural pathway with an unclear pathogenesis. A firm understanding of colonic physiology is necessary to identify DDs. The right colon helps to store and mix stool contents, the left colon helps add water to the stool, and the anal canal and rectum enable defecation and maintain continence. Any alteration along this physiologic pathway results in DDs.

DDs primarily develop via maladaptive pelvic floor contraction during defecation or from muscle or nerve injury and include functional outlet obstruction, anorectal dyssynergia, and pelvic floor dysfunction. Increased resistance to defecation results from anismus, paradoxical anal sphincter contraction, or incomplete relaxation of the pelvic floor and external anal sphincter. This muscle incoordination is described as dyssynergia. DDs can involve either muscle or nerve dysfunction or a combination of the two. Reduced rectal sensation caused by reduced sensory triggers can cause stasis of stool, thus propagating the cycle of constipation. Over time, excessive straining can weaken the pelvic floor, increasing the risk of excessive perineal descent, rectal intussusception, solitary rectal ulcer syndrome, and pudendal neuropathy. Thus, identification of DDs is crucial in patients with chronic constipation.

Secondary Constipation Disorders

Secondary constipation disorders are a result of an alternative process and warrant a thorough review of outpatient medications and medical history. The most common causes of secondary constipation span a wide differential.

Dr. Salim (@hamsalim07 on X) is based in the Department of Internal Medicine, University of Texas Medical Branch, Galveston. **Dr. Chowdhury** (annicho.med on Instagram) is a fellow in the Department of Gastroenterology, Hepatology, and Nutrition, University of Texas MD Anderson Cancer Center, Houston. **Dr. Viswanathan** (@LavanyaMD on X) is associate professor, University of Texas MD Anderson Cancer Center. The authors declare no conflict of interest.

Clinical Evaluation

The evaluation of constipation begins with a thorough history. Description of bowel habits should include frequency, duration, straining, stool consistency using a Bristol stool chart, complete vs incomplete evacuation, pain, bloating, and use of digital maneuvers (vaginal splinting or digital stool removal). One should inquire about back trauma/surgeries and obstetric history to include vaginal forceps injury or episiotomy.

With increased smartphone use, toilet time on average has increased and can contribute to maladaptive bowel habits. Patients may not realize they are constipated, so patient education is critical. A patient with daily bowel movements ranging between BSS type 1-6 with incomplete evacuation might complain of diarrhea but may in fact have constipation with overflow diarrhea, for example. Medical history is also clinically relevant, as systemic conditions can cause secondary constipation. A constipated patient should also be asked what therapies he/she has tried prior to gastroenterology referral as primary care referrals for constipation account for 8 million visits to gastroenterology per year.

While a sensitive topic, inquire about abuse history, especially in those with childhood constipation symptoms. There is a positive correlation between childhood constipation and physical, emotional, and sexual abuse, and for any number of reasons, your patient may be reluctant to share this or undergo a digital rectal exam (DRE). In such cases, be sensitive in asking for this history in private rather than with other family members around and always perform this exam with a chaperone present.

A detailed physical exam is an indispensable tool all gastroenterologists must master when evaluating a constipated patient. Some key exam findings include abdominal distention, high-pitched bowel sounds, and presence of a succussion splash indicating obstructive pathology. Dry skin and brittle hair indicate hypothyroidism while hypermobile joints and skin laxity suggest connective tissue disease. Finally, a physical examination is incomplete without a DRE.

DRE

DRE is an often-overlooked physical exam component which provides helpful insight that can guide management. An informed DRE can help identify structural disorders such as fissure, hemorrhoids, anorectal mass, fecal impaction, rectal

prolapse, and excessive perineal descent syndrome. Unless contraindicated, DRE should be a standard part of the workup of a patient with chronic constipation.

Workup

Colonoscopy

The role of colonoscopy in chronic constipation is low yield and indicated only if alarm signs are present. When no organic causes can be identified, the patient is deemed to have a functional bowel or motility disorder leading to constipation.

Colonic Transit Time

Colonic transit time (CTT) can be evaluated by assessing the presence of radio-opaque sitz markers in the colon with an abdominal x-ray 5 days after ingestion. The presence of five or more sitz markers may indicate STC. However, this can also signal an obstructive defecatory disorder. Colon scintigraphy can determine whether there is diffuse colonic dysmotility or dysfunction in a specific segment of the colon.

Anorectal Function Testing (AFT)

AFT can evaluate DDs, such as fecal incontinence, dyssynergic defecation, rectal sensory disorders, anorectal pain, and rectal prolapse. AFT comprises three tests: anorectal manometry (ARM), balloon expulsion test (BET), and rectal sensory testing. These assess the defecation, continence, and sensory mechanisms of the rectum, respectively.

ARM testing employs a thin, flexible probe with an attached sensor that is inserted into the rectum to measure internal and external sphincter pressures while at rest, squeezing, and bearing down to give a functional assessment of sphincter tone. Cough or party balloon test assesses continence and sphincter strength. Rectal sensation is assessed by inflating a balloon incrementally and asking the patient to indicate first sensation, urgency to defecate, and discomfort. If both ARM and BET are abnormal, the patient meets diagnostic criteria for dyssynergic defecation.

Pelvic floor disorders can be further assessed by MR defecography or barium defecography. Barium defecography is the more widely available of the two. MR defecography is a dynamic study that directly assesses pelvic floor muscles and endopelvic fascia during various stages of defecation and considered superior. This testing modality can distinguish between functional causes such as dyssynergia or pelvic floor dysfunction and structural causes of obstruction such as rectocele, rectal prolapse, or rectal intussusception. MR defecography is helpful when dyssynergia is suggested by ARM with a normal BET or if there is an absent recto-anal inhibitory reflex on ARM, which may suggest rectal intussusception.

Management

CIC

Incorporating 20-30 g of total soluble fiber, such as psyllium in individuals with low dietary fiber intake is the first-line recommendation for CIC. If response to a trial of fiber supplementation is inadequate, over-the-counter (OTC) osmotic laxatives such as polyethylene glycol and magnesium oxide can be incorporated. In the event of failure of OTC osmotic laxatives, lactulose can be considered. Stimulant laxatives such as senna, bisacodyl, or sodium picosulfate can be added as an adjunctive measure for short periods of time, defined as daily for 4 weeks or less.

There is a positive correlation between childhood constipation and physical, emotional, and sexual abuse, and for any number of reasons, your patient may be reluctant to share this or undergo a digital rectal exam.

If these measures are inadequate, pharmacological therapy with secretagogues and 5HT agonists can be considered. Prucalopride, a selective agonist of serotonin 5-HT4 receptors, is approved for CIC, prescribed 2 mg daily. It can also be used in patients with global motility delays, such as gastroparetics with constipation. Vibrant is a non-pharmacologic, orally ingested, vibrating, and programmable capsule device that has recently received Food and Drug Administration approval for treatment of chronic constipation by stimulating the intestinal wall, thereby promoting colonic contractile activity to achieve more spontaneous bowel movements. Further studies are required to assess its efficacy. Additionally, if there is inadequate response to all the above, it would be prudent to evaluate for the presence of pelvic floor dysfunction as well.

IBS-C

Similar to CIC, treatment for mild IBS-C starts with osmotic laxatives with the additional component of pain control. Antispasmodics can be used to manage the abdominal pain, cramping, and spasms associated with IBS-C. Antispasmodics available in the United States include anticholinergic agents that cause smooth muscle relaxation, such as dicyclomine or hyoscyamine or direct smooth muscle relaxants such as peppermint oil. IBS-C patients with moderate symptoms may need escalation of therapy to secretagogues or 5HT agonists. Secretagogues increase fluid retention in the colonic lumen to promote bowel movements and improve visceral hypersensitivity. Lubiprostone is an intestinal chloride channel activator, indicated only for adult women with IBS-C. Linaclotide and plecanatide are guanylate cyclase-C activators which increase intestinal chloride and bicarbonate secretion, and both are indicated in IBS-C and CIC. Tenapanor inhibits the sodium/hydrogen exchanger in the gastrointestinal tract, leading to increased water secretion, and is recommended for IBS-C in adults who have failed secretagogues.

All four of these drugs can be considered for moderate to severe IBS-C symptoms. In the case of severe IBS-C symptoms, Tegaserod, a 5-HT4 receptor partial agonist has been approved in women under 65 without significant cardiovascular or cerebrovascular disease. Regardless of IBS-C symptom severity, persistent visceral hypersensitivity can be treated with low-dose neuromodulators.

Opioid-Induced Constipation (OIC)

In patients with OIC, peripherally acting mu-opioid receptor antagonists such as methylnaltrexone and naloxegol can be beneficial where stimulant laxatives are insufficient. Additionally, lubiprostone is indicated in OIC in non-cancer patients. At present, there are no head-to-head trials comparing efficacy of these medications.

Defecatory Disorders

Biofeedback therapy is the cornerstone of treatment for dyssynergic defecation, focusing on neuromuscular training to restore a normal pattern of defecation by teaching patients to tense the abdomen and relax the pelvic floor muscles and anal sphincter. It retrains the body to coordinate abdominal, rectal, and anal muscles to achieve synchronous contraction to achieve complete evacuation. It also increases awareness and response to rectal fullness or the need to defecate.

Biofeedback makes patients aware of counterproductive subconscious actions such as contracting of their anal sphincter during defecation followed by simulated defecation training with focus on how to tighten abdominal muscles and relax pelvic floor muscles to initiate and complete defecation. This is performed in the office with a physiotherapist or trained nurse for at least six sessions or at home where patients are encouraged to perform the exercises for 20 minutes, twice a day. These sessions utilize tools such as manometry probes, electromyography probes, simulated balloon, or home biofeedback training devices to provide visual feedback while practicing abdominophrenic breathing. Biofeedback is particularly helpful in patients suffering from constipation. Patients with defecatory disorders can also benefit from pelvic floor physical therapy which focuses on strengthening the pelvic and puborectal muscles, external anal sphincter, and pelvic muscles. This is more useful in patients with fecal incontinence. Despite all these treatments, a subset of patients may still not respond and may qualify for surgical evaluation.

Defecatory disorders (DDs) result from alterations in the colonic-neural pathway with an unclear pathogenesis. A firm understanding of colonic physiology is necessary to identify DDs.

Conclusion

While constipation is seldom life-threatening, it has a negative impact on patient quality of life and poses a significant financial burden on our overall healthcare system. The complexity of this condition should be appreciated and understood in order for a complete and thorough evaluation. We trust that our practical guide should serve as a useful tool in the evaluation of a chronically constipated patient. ■

For a longer version of this article, including the full list of references and two graphics, please visit MDedge.com/gihepnews.

A Good FIT for Younger Adults

Completion from page 1

of this screening modality in the younger cohort," said Gellad, section chief, gastroenterology, Durham VA Health Care System.

The study was published online in *Annals of Internal Medicine* (2024 Oct. doi: 10.7326/M24-0743).

In 2021, the US Preventive Services Task Force lowered the age to start CRC screening from 50 to 45 years, in response to studies showing an increased rate of CRC in adults aged 45-49 years.

The decision to start CRC screening at age 45 was made based on modeling studies, which are dependent on assumptions, co-first author Theodore R. Levin, MD, who is also a gastroenterologist and research scientist at Kaiser Permanente DOR, said in an interview.

"We thought it was important to collect real-world data on the experience of screening in this age group. We had no basis to know whether younger people would take up screening or if the yield of screening would be sufficiently high to warrant starting screening in this age group," said Levin.

The researchers compared FIT screening completion and outcomes in 213,928 patients aged 45-49 years and 53,804 patients aged 50 years who received a FIT kit for the first time. The patients were from Kaiser Permanente Northern California, Washington, and Colorado.

Overall, FIT completion rates were slightly higher in the younger adults than in the 50-year-olds (38.9% vs 37.5%; adjusted risk ratio [aRR], 1.05), although the younger patients from Colorado were substantially less likely to complete a FIT (30.7% vs 40.2%; aRR, 0.77).

In the overall 45- to 49-year age group, 3.6% of adults had a positive FIT result, only slightly lower than the 4% positivity rate in the 50-year age group (aRR, 0.91).

Dr. Lee

Dr. Gellad

About two thirds of adults in both groups who had a positive FIT result went on to have a colonoscopy within 3 months of receiving the test result.

Adenoma detection during colonoscopy was slightly lower in the younger than in the older group (58.8% vs 67.7%; aRR, 0.88).

'The low number of cancers we found also provides support for initially offering younger adults a non-invasive test, like FIT, to determine which patients would benefit from a colonoscopy.'

However, yields were similar for adenoma with advanced histology (13.2% vs 15.9%; aRR, 0.86), polyp with high-grade dysplasia (3.4% vs 5.1%; aRR, 0.68), sessile serrated lesion (10.3% vs 11.7%; aRR, 0.92), and CRC (2.8% vs 2.7%; aRR, 1.10).

FIT First Fits With Younger Adults' Busy Lives

"Overall, people under 50 have lower incidence of cancer than people in their 50s, 60s, and 70s. However, if you do a test like FIT first, you can improve the yield of colonoscopy, which is a much more efficient strategy," Levin said.

He noted that younger people are the least likely to be screened.

"They are busy with work and family responsibilities and may not

Continued on following page

Breath Gas Patterns Predict Response to Low FODMAP Diet

BY JOHN WATSON

FROM ACG 2024

PHILADELPHIA — Non-fasting breath gas patterns may help identify patients with irritable bowel syndrome (IBS) who are most likely to respond to a low fermentable oligo-, di-, monosaccharides and polyols (FODMAP) diet, according to a new study.

The low FODMAP diet is the most evidence-based dietary therapy for patients with IBS, but we know that "only about 50% of our patients respond to it," said principal investigator Prashant Singh, MD, assistant professor at the University of Michigan in Ann Arbor. "Exhaled breath gases represent bacterial fermentation of dietary carbohydrates. These measurements could provide a simple biomarker for response to low FODMAP diets."

Even before starting the low FODMAP diet, "you could see notable differences in breath test patterns between responders and nonresponders," he said. "We saw that low FODMAP responders had higher hydrogen (H2) and lower methane (CH4) at baseline than nonresponders and had a greater drop in hydrogen following FODMAP restriction vs nonresponders."

He added that these results imply that responders to this diet may exhibit differences in baseline microbiota composition regarding saccharolytic capacity and/or methanogens.

Singh presented the findings at the American College of Gastroenterology (ACG) 2024 Annual Scientific Meeting.

MOMENT RF/GETTY IMAGES

Breaths That Can Predict Response

To determine if pre-intervention non-fasting breath patterns are associated with a clinical response to low FODMAP diets, Singh and colleagues enrolled 284 self-selected participants (mean age, 45.2 years) with mild to moderate gastrointestinal (GI) symptoms. Participants used an app-connected breath analyzer to record hourly, non-fasting H2 and CH4 levels during waking hours, in addition to logging meal content and symptom severity (bloating, abdominal pain, and flatulence) on a 0-10 scale.

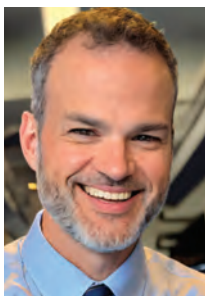
Patients were directed to consume their habitual diet for 1 week, before following an app-directed low FODMAP diet for 1 week. Responders were defined as those with a ≥ 30% reduction in at least one mean symptom score. The researchers then compared average hourly H2 and CH4 levels and symptom scores at baseline between low FODMAP diet responders and nonresponders.

Of the participants, 111 were classified as responders and 173 as nonresponders. There were no significant differences between the groups in gender, age, body mass index, or FODMAP per calorie.

Following FODMAP restriction, responders had consistently lower abdominal pain throughout the day and lower bloating and flatulence predominantly in the latter part of the day. Nonresponders experienced no significant changes in key abdominal symptoms after adopting the low FODMAP diet.

The researchers found that breath tests taken at baseline revealed predictive trends between the groups, even though average FODMAP consumption did not significantly differ between them. Baseline H2 levels were higher among responders than among nonresponders, especially in the morning and evening. However, responders had lower baseline CH4 levels throughout the day.

Following FODMAP restrictions, responders had a significant drop in non-fasting H2 but not CH4, whereas nonresponders did not have a significant drop in either.



Dr. Staller

The study was limited by the fact that participants were not clinically diagnosed with IBS, their GI symptoms were mild overall, and no data were available on stool consistency/frequency or fecal microbiome composition for correlation with exhaled breath gas levels.

A Potential New Biomarker

Session co-moderator Kyle Staller, MD, MPH, director of the Gastrointestinal Motility Laboratory at Mass General and associate professor of medicine at Harvard Medical School in Boston, Massachusetts, said in an interview that if validated, these findings provide hope for better directing low FODMAP diets to those patients who may benefit.

There are some patients who may or may not respond to a FODMAP diet, for reasons we don't yet know, possibly related to fermentation of gas, and it's helpful to know before starting treatment, he said. It may help us with more of "a precision medicine approach before we really torture people with diets that can be very difficult to adhere to."

Staller, who was not involved in the study, added that, "People tend to really focus on small intestinal bacteria overgrowth when it comes to hydrogen and methane production, but in reality, this is really a very agile day-to-day, meal-to-meal responsiveness.

"It's a different paradigm," he continued. "I'd also like to see more data as to why we see the diurnal rhythm" and whether potential factors such as intestinal transit times are playing a role.

'People tend to really focus on small intestinal bacteria overgrowth when it comes to hydrogen and methane production, but in reality, this is really a very agile day-to-day, meal-to-meal responsiveness.'

Singh reported receiving royalties from UpToDate. Staller reported receiving research support from Ardelyx and Restasis and serving as a consultant to Anji, Ardelyx, GI Supply, Mahana, Restasis, and Sanofi. Funding associated with the study was not available at the time of publication. ■

Continued from previous page

realize that they are at risk for CRC. It is important to offer them a test that is easy to perform and does not require them to miss a day of work or arrange for a driver. They should be offered an option to screen with a stool-based test as an easy way to fit CRC screening into their busy lives," Levin said.

Gellad said the study also highlights the limitations of FIT, "namely, that the low uptake and suboptimal colonoscopy follow-up of positive tests, also extend into the lower age group."

Additionally, Gellad said he hopes other large systems will replicate this study to address the generalizability of these findings outside the Kaiser system.

The study was funded by the Kaiser Permanente Sydney R. Garfield Memorial Fund. Disclosures for study authors are available with the original article. Gellad consulted for Merck and Novo Nordisk and is a co-founder of Higgs Boson. ■

Member SPOTLIGHT

Endoscopist Brings Cutting-Edge Tech to Asia-Pacific Region

BY JENNIFER LUBELL

MDedge News

As the COVID-19 crisis unfolded in early 2020, Tossapol Kerdsirichairat, MD, faced another challenge: his mother's ovarian cancer diagnosis.

"She chose to remain in Thailand, so I decided to relocate to care for her," said Dr. Kerdsirichairat, an interventional endoscopist who completed fellowships at the University of Michigan, Ann Arbor, and Johns Hopkins University in Baltimore, Maryland. The move to Bangkok turned out to be one of the best decisions of his life, he said, as he could support his mother while introducing advanced endoscopic techniques and devices to the region.

"Bangkok is a hub for medical innovation in Asia, offering opportunities to work with a diverse patient population and access to cutting-edge technology," said Kerdsirichairat, who works at Bumrungrad International Hospital as a clinical associate professor.

Establishing a high-risk gastrointestinal (GI) cancer program that included pancreatic cancer screening for high-risk individuals was one of his core achievements at Bumrungrad. The program is the first of its kind in Thailand and one of the few in the Asia-Pacific region.

"I guide patients and families through understanding their risks and implementing preventive strategies, collaborating with multidisciplinary teams to ensure comprehensive care. It's incredibly rewarding to see the impact of early tumor detection," said Kerdsirichairat, an international member of AGA who was a participant in the AGA Young Delegates Program.

He has set several records in Thailand for the smallest tumor detected, including a 0.3-millimeter (mm) esophageal tumor, a 0.8-mm tumor for stomach cancer, a 5-mm pancreatic tumor, and a 1-mm tumor for colon cancer.

"These were detected through high-standard screening programs, as patients often do not develop symptoms from these subtle lesions," said Kerdsirichairat, who discussed in an interview the unique challenges of practicing overseas.

Courtesy Bumrungrad International Hospital

Dr. Tossapol Kerdsirichairat

Why did you choose GI?

Gastroenterology is a specialty that uniquely integrates procedural skill, clinical decision-making, and a deep understanding of complex biological systems. I was drawn especially to the ability to make a direct and meaningful impact in patients' lives through advanced endoscopic procedures, while also addressing both acute and chronic diseases, and focusing on cancer prevention. It is incredibly rewarding to perform an endoscopic retrograde cholangiopancreatography [ERCP] for cholangitis and see a patient return to normal the very next day, or to perform an endoscopic ultrasound [EUS] for pancreatic cancer screening in high-risk individuals and detect a sub-centimeter pancreatic tumor.

Realizing that early detection can improve survival by threefold after surgery is a powerful reminder of the difference we can make in patients' lives. This specialty requires a delicate balance of precision and empathy, which perfectly aligns with my strengths and values as a physician.

You have a wide variety of clinical interests, from endoscopic procedures to cancer research to GERD. What's your key subspecialty and why?

My primary specialty is advanced endoscopy, which includes techniques such as EUS, ERCP, and endoscopic resection of precancerous and early cancerous lesions. I also focus on cutting-edge, evidence-based techniques recently included in clinical guidelines, such as Transoral Incisionless Fundoplication [TIF]. These minimally invasive options allow me to diagnose and treat conditions that once required surgery. The precision and innovation involved in advanced endoscopy enable me to effectively manage complex cases — from diagnosing early cancers to managing bile duct obstructions and resecting precancerous lesions.

Can you describe your work in cancer genetics and screening?

I am deeply committed to the early detection of gastrointestinal cancers, particularly through screening for precancerous conditions and hereditary syndromes. During my general GI training at the University of Michigan, I had the privilege of working with Grace Elta, MD, AGAF, and Michelle Anderson, MD, MSc, renowned experts in pancreatic cancer management. I was later trained by Anne Marie Lennon, PhD, AGAF, who pioneered the liquid biopsy technique for cancer screening through the CancerSEEK project, and Marcia (Mimi) Canto, MD, MHS, who initiated the Cancer of the Pancreas Screening project for high-risk individuals of pancreatic cancer.

I also had the distinction of being the first at Bumrungrad International Hospital to perform endoscopic drainage for pancreatic fluid collections in the setting of multi-organ failure. This endoscopic approach has been extensively validated in the medical literature as significantly improving survival rates compared to surgical drainage. My training in this specialized procedure was conducted under the guidance of the premier group for necrotizing pancreatitis, led by Martin Freeman, MD, at the University of Minnesota.

Later, I contributed to overseeing the Inherited Gastrointestinal Malignancy Clinic of MyCode, a large-scale population-based cohort program focused on cancer screening in Pennsylvania. By December 2024, MyCode had collected blood samples from over 258,000 individuals, analyzed DNA sequences from over 184,000, and provided clinical data that benefits over 142,000 patients. It's not uncommon for healthy 25-year-old patients to come to our clinic for colon cancer screening after learning from the program that they carry a cancer syndrome, and early screening can potentially save their lives.

What are the key differences between training and practicing medicine in the United States and in an Asian country?

The US healthcare system is deeply rooted in

Lightning round

Texting or talking?
Talking. It's more personal and meaningful.

Favorite city in the US?
Ann Arbor, Michigan

Cat or dog person?
Dog person

Favorite junk food?
Pizza

Number of cups of coffee you drink per day?
Two – just enough to stay sharp, but not jittery.

Dream job, if you weren't a GI?
Architect

Best place you went on vacation?
Kyoto, Japan

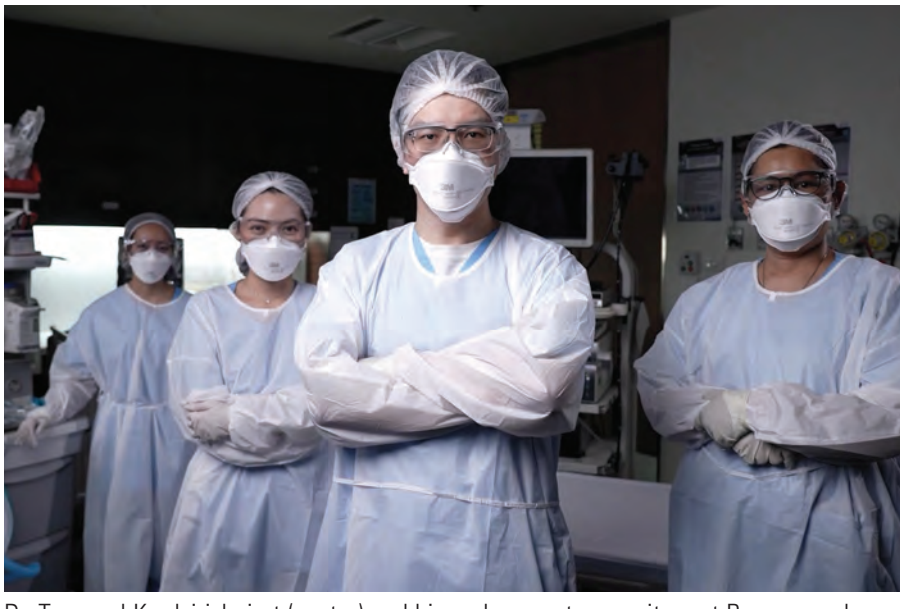
Favorite sport?
Skiing

Favorite ice cream?
Matcha green tea

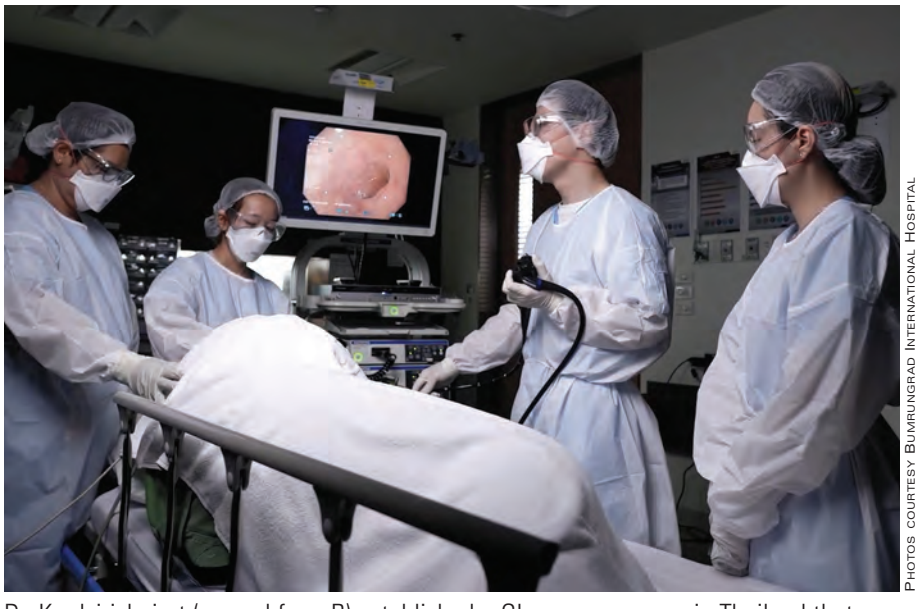
Song you have to sing along with when you hear it?
"Everybody" by Backstreet Boys

Favorite movie or TV show?
Forrest Gump and *Friends*

Optimist or pessimist?
Optimist. I believe in focusing on solutions and possibilities.



Dr. Tossapol Kerdsirichairat (center) and his endoscopy team suit up at Bumrungrad International Hospital, Bangkok, Thailand.



Dr. Kerdsirichairat (second from R) established a GI cancer program in Thailand that included pancreatic cancer screening for high-risk individuals.

PHOTOS COURTESY BUMRUNGRAD INTERNATIONAL HOSPITAL

evidence-based protocols and multidisciplinary care, driven by an insurance-based model. In contrast, many Asian countries face challenges such as the dependency on government approval for certain treatments and insurance limitations. Practicing in Asia requires navigating unique cultural, economic, and systemic differences, including varying resource availability and disease prevalence.

What specific challenges have you faced as a GI in Thailand?

As an advanced endoscopist, one of the biggest challenges I faced initially was the difficulty in obtaining the same devices I used in the US for use in Thailand. With support from device companies and mentors in the US, I was able to perform groundbreaking procedures, such as the TIF in Southeast Asia and the first use of a full-thickness resection device in Thailand. I am also proud to be part of one of the first few centers worldwide performing the combination of injectable semaglutide and endoscopic sleeve gastroplasty, resulting in a remarkable weight reduction of 44%, comparable to surgical gastric bypass.

In addition, Bumrungrad International Hospital, where I practice, sees over 1.1 million visits annually from patients from more than 190 countries. This offers a unique opportunity to engage with a global patient base and learn from diverse cultures. Over time, although the hospital has professional interpreters for all languages, I have become able to communicate basic sentences with international patients in their preferred languages, including Chinese, Japanese, and Arabic, which has enriched my practice.

What's your favorite thing to do when you're not practicing GI?

I enjoy traveling, exploring new cuisines, and spending quality time with family and friends. These activities help me recharge and offer fresh perspectives on life. ■

‘A First- or Second-Line Biologic’

Guselkumab *from page 1*

by the Food and Drug Administration (FDA) for moderately to severely active CD. In September, guselkumab (Tremfya, Johnson & Johnson) was approved for use in moderately to severely active ulcerative colitis.

GALAXI 2 and 3 Pooled Dataset

In the two independent, identically designed GALAXI 2 and 3 studies, patients were randomized to guselkumab treatment at either 200 mg intravenous (IV) induction at weeks 0, 4, and 8, followed by 200 mg subcutaneous maintenance every 4 weeks, starting at week 12, or 200 mg IV induction at weeks 0, 4, and 8, followed by 100 mg subcutaneous maintenance every 8 weeks, starting at week 16; or to ustekinumab; or to placebo.

Participants were required to remain on their treatment of initial randomization for a long-term extension study (up to 5 years) looking at clinical, endoscopic, and safety outcomes, except for participants on placebo who were allowed to switch to ustekinumab if clinical response was not met at week 12.

Inclusion criteria for the studies comprised a Crohn’s Disease Activity Index score between 220 and 450, a mean daily stool frequency count > 3 or an abdominal pain score > 1, and a simple endoscopic score for CD score ≥ 6. Participants were also required to have shown an inadequate response or intolerance to oral corticosteroids, 6-mercaptopurine/azathioprine/methotrexate, or biologic therapies.

The pooled dataset included patients on either dose of guselkumab and patients on placebo (total n = 730). Of these, 52% of participants had shown a prior inadequate response to a biologic, 42% were biologic naive, and 6% had prior exposure to biologics but no documented failure. Patients on ustekinumab were not included in this analysis.

These latest results add to the primary results of the studies reported earlier in 2024 that guselkumab was shown to be superior to both placebo and ustekinumab in the same patient population with moderately to severely active CD.

Almost all patients (97%) in the biologic-inadequate response group had previously received at least one anti–tumor necrosis factor agent, and around 15% had received vedolizumab. As expected, the biologic-inadequate responders were a lot sicker than the biologic-naive patients, Sands reported.

The composite co–primary endpoints for each guselkumab regimen vs placebo were clinical response at week 12 plus clinical remission at week 48, and clinical response at week 12 plus endoscopic response at week 48.

The major secondary endpoints comprised clinical remission at week 12 and endoscopic response also at week 12.

Short- and Long-Term Endpoints in Both Subgroups

In the biologic-naive subgroup, 54.7% of patients receiving the 200-mg dose regimen of guselkumab and 51.7% of those receiving the 100-mg dose regimen showed a clinical response at week 12 plus clinical remission at week 48, compared with 11.5% in the placebo group ($P < .001$ for both compared with placebo).

In the biologic-inadequate response group, 49.7% of those receiving the 200-mg dose regimen of guselkumab and 45.8% on the 100-mg dose regimen reached the composite endpoint, compared with the placebo response of 12.8% ($P < .001$ for both compared with placebo).

“You can see a slight decrease in response in the biologic-inadequate responders, but on the whole, the confidence intervals are highly overlapping,” said Sands.

As for major secondary endpoints at week 12, clinical remission was reached by 49.6% of the biologic-naive group on the 200-mg guselkumab regimen vs 16.4% on placebo, and by 46.0% of the biologic-inadequate group on the 200-mg regimen vs 19.2% on placebo ($P < .001$ for both subgroups). Endoscopic response was achieved by 46.3% of patients in the biologic-naive group and 29.0% in the biologic-inadequate group on the 200-mg regimen vs 18.0% and 6.4%, respectively, on placebo ($P < .001$ for both subgroups).

Sands noted that the drug has an excellent safety profile.

“These data show the drug works for naive patients who have failed conventional therapies, as well as for those who have failed biologic therapies,” so it could be used as a first- or second-line biologic, he added.

Sands reported potential conflicts of interest with AbbVie, Abivax, Adiso Therapeutics, Agomab, Alimentiv, Amgen, AnaptysBio, Arena Pharmaceuticals, Artugen Therapeutics, AstraZeneca, Biora Therapeutics, Boehringer Ingelheim, Boston Pharmaceuticals, Bristol-Myers Squibb, Calibr, Celgene, Celltrion, ClostraBio, Equillium, Enthera, Evommune, Ferring, Fresenius Kabi, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Index Pharmaceuticals, Innovation Pharmaceuticals, Inotrem, Janssen, Kaleido, Kallyope, Lilly, Merck, Microbiotica, Mobius Care, Morphic Therapeutic, MRM Health, Pfizer, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Progenity, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Pharma, Reistone Biopharma, Sun Pharma, Surrozen, Target RWE, Takeda, Teva, Theravance Biopharma, TLL Pharmaceutical, Tr1X, UNION Therapeutics, and Ventyx Biosciences. ■

No Increased Risk for MACE Seen for JAK Inhibitors vs Anti-TNF

BY CAROLYN CRIST

FROM ACG 2024

PHILADELPHIA — Patients with inflammatory bowel disease (IBD) don’t appear to face an increased risk of major adverse cardiovascular events (MACE) or venous thromboembolism (VTE) when taking Janus kinase inhibitors (JAKi), compared with anti–tumor necrosis factor (TNF) agents, according to a study presented at the American College of Gastroenterology (ACG) 2024 Annual Scientific Meeting.

In particular, 1.76% of patients taking JAKi and 1.94% of patients taking anti-TNF developed MACE. There also weren’t significant differences when comparing ulcerative colitis with Crohn’s disease, upadacitinib with tofacitinib, or JAKi with infliximab.

“IBD is associated with an increased risk of cardiovascular diseases, and with the emergence of JAK inhibitors and anti-TNF therapies, there is a concern about the increased risk of MACE,” said lead author Saqr Alsakarneh, MD, an internal medicine resident at the University of Missouri–Kansas City School of Medicine.

Previous randomized controlled trials have indicated increased risks of MACE with JAKi and anti-TNF agents, compared with placebo, but researchers haven’t conducted a head-to-head comparison, he said.

“A potential explanation for previous associations could be linked to immune modulation and inflammation that can increase coagulation risk, as well as fluctuation in disease severity while patients are on the medications, which can impact cardiovascular risk factors,” he added.

Alsakarneh and colleagues conducted a retrospective cohort study using the TriNetX database to identify adult patients with IBD who were treated with JAKi or anti-TNF therapy after diagnosis. After matching patients in the JAKi cohort with patients in the anti-TNF cohort, the research team looked for MACE and VTE within a year of medication initiation, as well as associations by age, sex, and IBD type.

Overall, 3740 patients in the JAKi cohort had a mean age of 43.1 and were 48.9% women and 75.3% White individuals, while 3740 patients in the anti-TNF cohort had a mean age of 43 and were 48.9% women and 75.3% White individuals.

After exclusion of those with a history of a prior cardiovascular event, 57 patients (1.76%) in the JAKi cohort developed MACE, compared with 63 patients (1.94%) in the anti-TNF cohort. There weren’t significant differences between the groups in MACE (adjusted hazard ratio [aHR], 0.99) or VTE (aHR, 0.9).

Among patients aged ≥ 65, 25 patients (5.3%) in the JAKi cohort developed MACE, as compared with 30 patients (6.4%) in the anti-TNF cohort. There weren’t significant differences between the groups in MACE (aHR, 0.83) or VTE (aHR, 0.77).

In addition, there were no differences when comparing Crohn’s disease with ulcerative colitis for MACE (aHR, 1.69) or VTE (aHR, 0.85); upadacitinib with tofacitinib for MACE (aHR, 1.1) or VTE (aHR, 1.13); or JAKi medications with infliximab

Continued on following page

Noninvasive Microbiome Test May Specifically Identify Crohn's and Ulcerative Colitis

BY DIANA SWIFT

International researchers have uncovered potentially diagnostic gut microbiome signatures and metabolic pathways associated specifically with ulcerative colitis (UC) and Crohn's disease (CD).

Targeted droplet digital polymerase chain reaction (ddPCR)–based quantification of bacterial species led to convenient inflammatory bowel disease (IBD) diagnostic assays that "are sufficiently robust, sensitive and cost-effective for clinical application," the investigators wrote in a recent study published in *Nature Medicine*.

"Although traditional modalities used for diagnosis of IBD, including colonoscopy and cross-sectional imaging, are well established, the inconvenience of bowel preparation and radiation represents relevant concerns," senior author Siew C. Ng, MBBS, PhD, a professor in the Department of Medicine and Therapeutics at the Chinese University of Hong Kong, said in an interview. "Furthermore, existing serological and fecal markers indicate inflammation but lack specificity for IBD."

Identifying reproducible bacterial biomarkers specific to CD and IBD should enable precise and personalized approaches to detection and management.

As a starting point, the researchers hypothesized that changes in the gut microbiome of IBD patients may reflect underlying functional associations, if not causes, of the disease, said Ng, who is also director of Hong Kong's Microbiota I-Center (MagIC). "Unlike inflammation, which is a manifestation of the disease, the gut microbiome may serve as a more reliable biomarker less affected by the disease's fluctuating cycle."

The study findings showed that bacterial markers remain consistent even during the inactive disease phase. Additionally, the results are reproducible across different populations, suggesting that these markers are true indicators of IBD, she added. "With a better performance than the commonly used noninvasive test, fecal calprotectin, we believe the test will be a valuable addition to clinician's toolbox and a strong option for first-line diagnostics."

The Study

The group used metagenomic data from 5979 fecal samples from persons with and without IBD from different regions (including the United States) and of different ethnicities. Identifying several microbiota alterations in IBD, they selected bacterial species to construct diagnostic models for UC (n = 10) and CD (n = 9). Some species were deleted and some were enriched in IBD.

Metagenomic findings confirmed, for example, enrichments of *Escherichia coli* and *Bacteroides fragilis* in the guts of CD patients, with adherent invasive *E coli* present in more than half of these. This pathogen has been linked to mucosal dysbiosis and functional alteration, and has been associated with disease activity and endoscopic recurrence following surgery. *B fragilis* may induce intestinal inflammation through toxin production.

The researchers also identified a new oral bacterium, *Actinomyces* species oral taxon 181, which was significantly enriched in stool samples with both CD and UC.

The diagnostic models achieved areas under the curve of > 0.90 for distinguishing IBD patients from controls in the discovery cohort and maintained satisfactory performance in transethnic validation cohorts from eight populations.

Ng's group further developed a multiplex droplet digital PCR test targeting selected IBD-associated bacterial species. Models based on this test showed numerically higher performance than fecal calprotectin in discriminating UC and CD samples from controls. These universally IBD-associated bacteria suggest the potential applicability of a biomarker panel for noninvasive diagnosis.

Commenting on the paper but not involved in it, Ashwin N. Ananthakrishnan, MBBS, MPH, AGAF, director of the Crohn's and Colitis Center at Massachusetts General Hospital and associate professor of medicine at Harvard Medical School, both in Boston, called it "a very important study that highlights the potential role of a microbiome-based diagnostic for screening. It could have application in a wide variety of settings and is very promising."

More work, however, is necessary to clarify such testing's role. "The study's validation in independent cohorts is an important strength, but the sizes of those cohorts are still quite small," he said in an interview. "It's important to understand its accuracy across a spectrum of IBD phenotypes and severity."

Furthermore, endoscopic evaluation at diagnosis is important to establish severity and extent of disease. "It's not clear this diagnostic biomarker can help supplant that role. But I see potential value to it for patients for whom we may not be considering endoscopy yet but who would like to risk-stratify."

The Test's Future

"We expect to see a real shift in clinical practice," Ng said. "As a cost-effective test, it will help millions of people dealing with nonspecific gastrointestinal symptoms get the diagnoses they need." Because the bacterial test can identify IBD at an inactive stage, it has the potential for early diagnosis. "This capability allows clinicians to initiate treatment sooner, helping to prevent progression from subclinical to clinical stages of the disease."

The next research steps involve prospective studies with a larger and more diverse group of patients with various gastrointestinal symptoms. "This will enable a comprehensive evaluation of bacterial biomarkers in real-world populations," she said. In vivo and in vitro experiments are expected to provide mechanistic insights into the causal role of these bacteria and metabolic dysregulations in the pathogenesis of IBD, as well as their future clinical utility in disease monitoring and predicting treatment response.

Her group plans to work with the biotech industry and regulatory agencies to transform these biomarkers into an approved test kit. "The rollout is likely to be gradual, but we're optimistic that supportive international and national guidelines will be developed and will pave the way for widespread implementation."

This study was supported by various academic, charitable, and governmental research-funding bodies, including the governments of Hong Kong and the People's Republic of China. Ng has served as an advisory board member or speaker for Pfizer, Ferring, Janssen, AbbVie, Tillotts, Menarini, and Takeda. She has received research grants through her institutions from Olympus, Ferring, and AbbVie and is a founding member and shareholder of GenieBiome. She receives patent royalties through her institutions, including MagIC, which holds patents on the therapeutic and diagnostic use of the microbiome in IBD. Several co-authors reported various relationships, including patent holding, with private-sector companies. Ananthakrishnan had no relevant competing interests.

Dr. Regueiro

Continued from previous page

for MACE (aHR, 0.85) or VTE (aHR, 0.8).

Patients in the JAKi group were more likely to undergo intestinal resection surgery (aHR, 1.32), but there wasn't a statistically significant difference in systematic corticosteroid use (aHR, 0.99).

The study limitations included the inability to assess for disease severity, dose-dependent risk for MACE or VTE, or long-term outcomes among the two cohorts, Alsakarneh said. Prospective controlled trials are needed to confirm findings.

"This is a wonderful study and nice to see. We presented the same thing at Digestive Disease Week that's being confirmed in this data," said Miguel Regueiro, MD, AGAF, chief of Cleveland Clinic's Digestive Disease Institute in Ohio. Regueiro, who wasn't involved with the study, attended the conference session.

"Looking ahead, all of us are wondering if the regulatory guidance by the FDA [Food and Drug Administration] is going to change the label so we don't need to step through a TNF," he said. "I think we're seeing study after study showing safety or at least not an increased risk with JAK."

The study was awarded an ACG Noteworthy Abstract. Alsakarneh and Regueiro reported no relevant disclosures.

AI-Aided Colonoscopy's 'Intelligent' Module Ups Polyp Detection

BY DIANA SWIFT

Results from the British COLO-DETECT trial add to the growing body of evidence supporting the use of artificial intelligence (AI)–aided colonoscopy to increase premalignant colorectal polyp detection in routine colonoscopy practice.

Colin J. Rees, MBBS, a professor of gastroenterology in the Faculty of Medical Sciences at Newcastle University in Newcastle Upon Tyne, England, and colleagues compared the real-world clinical effectiveness of computer-aided detection (CADe)–assisted colonoscopy using an "intelligent" module with that of standard colonoscopy in a study in *The Lancet Gastroenterology & Hepatology* (2024 Aug 14. doi: 10.1016/S2468-1253[24]00161-4).

They found the GI Genius Intelligent Endoscopy Module (Medtronic) increased the mean number of adenomas detected per procedure and the adenoma detection rate, especially for small, flat (type 0-IIa) polyps, and sessile serrated lesions, which are more likely to be missed.

"Missed sessile serrated lesions disproportionately increase the risk of post-colonoscopy colorectal cancer, thus the adoption of GI Genius into routine colonoscopy practice could not only increase polyp detection but also reduce the incidence of post-colonoscopy colorectal cancer," the investigators wrote.

"AI is going to have a major impact upon most aspects of healthcare. Some areas of medical practice are now well established, and some are still in evolution," Rees, who is also president of the British Society of Gastroenterology, said in an interview.

'Most studies, particularly randomized controlled trials have shown significant improvements with CADe in detection both in terms of adenomas per colonoscopy and reductions in adenoma miss rate.'

"Within gastroenterology, the role of AI in endoscopic diagnostics is also evolving. The COLO-DETECT trial demonstrates that AI increases detection of lesions, and work is ongoing to see how AI might help with characterization and other elements of endoscopic practice."

Study Details

The multicenter, open-label, parallel-arm, pragmatic randomized controlled trial was conducted at 12 National Health Service hospitals in England. The study cohort consisted of adults ≥ 18 years undergoing colorectal cancer (CRC) screening or colonoscopy for gastrointestinal symptom surveillance owing to personal or family history.

Recruiting staff, participants, and colonoscopists were unmasked to allocation, whereas histopathologists, cochief investigators, and trial statisticians were masked.

CADe-assisted colonoscopy consisted of standard colonoscopy plus the GI Genius module active for at least the entire inspection phase of colonoscope withdrawal.

The primary outcome was mean adenomas per procedure (total number of adenomas detected divided by total number of procedures). The key secondary outcome was adenoma detection rate (proportion of colonoscopies with at least one adenoma).

From March 2021 to April 2023, the investigators recruited 2032 participants, 55.7% men, with a mean cohort age of 62.4 years and randomly assigned them to CADe-assisted colonoscopy (n = 1015) or to standard colonoscopy (n = 1017). Of these, 60.6% were undergoing screening and 39.4% had symptomatic indications.

Mean adenomas per procedure were 1.56 (SD, 2.82; n = 1001 participants with data) in the CADe-assisted group vs 1.21 (n = 1009) in the standard group, for an adjusted mean difference of 0.36 (95% CI, 0.14-0.57; adjusted incidence rate ratio, 1.30; 95% CI, 1.15-1.47; $P < .0001$).

Adenomas were detected in 555 (56.6%) of 980 participants in the CADe-assisted group vs 477 (48.4%) of 986 in the standard group, representing a proportion difference of 8.3% (95% CI, 3.9%-12.7%; adjusted odds ratio, 1.47; 95% CI, 1.21-1.78; $P < .0001$).

Dr. Mansour

As to safety, adverse events were numerically comparable in both the intervention and control groups, with overall events 25 vs 19 and serious events 4 vs 6. On independent review, no adverse events in the CADe-assisted colonoscopy group were related to GI Genius.

Offering a US perspective on the study, Nabil M. Mansour, MD, an associate professor and director of the McNair General GI Clinic at Baylor College of Medicine in Houston, Texas, said GI Genius and other CADe systems represent a significant advance over standard colonoscopy for identifying premalignant polyps.

"While the data have been mixed, most studies, particularly randomized controlled trials have shown significant improvements with CADe in detection both in terms of adenomas per colonoscopy and reductions in adenoma miss rate," he said in an interview.

He added that the main utility of CADe is for asymptomatic patients undergoing average-risk screening and surveillance colonoscopy for CRC screening and prevention, as well as for those with positive stool-based screening tests, "though there is no downside to using it in symptomatic patients as well." Though AI colonoscopy likely still stands at < 50% of endoscopy

Continued on following page

When It Comes to Polyp Diagnosis With CADx, Location Matters

BY BECKY MCCALL

FROM UEG 2024

VIENNA — The effectiveness of computer-aided diagnosis (CADx) in differentiating neoplastic from non-neoplastic polyps depends on the region of the colon examined, according to a systematic review and meta-analysis.

In particular, the diagnostic performance of CADx for polyps showed significantly lower specificity in the proximal colon than in the distal colon.

"While current CADx systems are suitable for use in the distal colon, they should not be employed for diagnosing polyps in the proximal colon until new, higher performing systems are developed specifically for these lesions," said study lead Tommy Rizkala, MD, Endoscopy Unit, IRCCS Humanitas Clinical and Research Center, Rozzano, Italy.

The "main strength" of the review is that the researchers contacted each study author for more specific information and were therefore able to divide the data into the proximal colon and the rectosigmoid colon, he explained.

"This is the first paper that has really collected these data. Most papers provide data for the entire colon or just for the rectosigmoid colon," said Rizkala, who presented the findings at the United European Gastroenterology (UEG) Week 2024.

The study was also recently published in *Clinical Gastroenterology and Hepatology* (2024 Aug. doi: 10.1016/j.cgh.2024.08.021).

Optical diagnosis enables real-time histologic predictions of polyps 5 mm or smaller during colonoscopy, offering potential clinical and cost-saving benefits. Two optical diagnostic strategies are used for polyps in this size range based on location: a leave-in-situ strategy (applied only in the rectosigmoid colon when there is high confidence of non-neoplastic polyps) and a resect-and-discard strategy (applied only in the whole colon when there is high confidence of neoplastic polyps upon optical diagnosis).

Rizkala carried out a review of studies that evaluated the performance of real-time CADx alone — independent of endoscopist judgment — for predicting the histology of colorectal polyps 5 mm or smaller. The primary endpoints were CADx sensitivity and specificity in the proximal colon (the portion extending from the descending colon to the cecum) and the distal colon (limited to the rectosigmoid region). Secondary outcomes were the negative predictive value (NPV), positive predictive value (PPV), and accuracy of the CADx alone in the proximal colon and the distal colon.

Lower Specificity in the Proximal Colon

An analysis of data based on 7782 polyps ≤ 5 mm from 11 studies found specificity values of 0.62 (95% CI, 0.52-0.71) and 0.85 (95% CI, 0.75-0.92) for the proximal and distal regions of the colon, respectively, with a risk ratio (RR) of 0.74 (95% CI, 0.72-0.84), meaning that CADx accuracy was significantly lower in the proximal colon than in the distal colon.

'Recent insights in the molecular and morphological features of hyperplastic polyps indicates that there are different classes with more goblet cell–rich hyperplastic polyps in the right colon, and more microvesicular hyperplastic polyps in the left.'

"According to the optical diagnosis strategy, we can use the leave-in-situ approach for the distal colon because the performance is adequate, but for the rest of the colon, CADx requires further enhancement," Rizkala said.

Sensitivity values were 0.89 (95% CI, 0.83-0.93) and 0.87 (95% CI, 0.80-0.92) for the proximal and distal regions, respectively, with an RR of 1.00 (95% CI, 0.97-1.03).

Regarding the secondary outcomes, the NPV was 0.64 vs 0.93 for the proximal vs distal colon, with an RR of 0.71 (95% CI, 0.64-0.79), and accuracy was 0.81 vs 0.86, with an RR of 0.95 (95% CI, 0.91-0.99).

With the higher prevalence of neoplastic lesions in the proximal colon than in the distal colon, a lower NPV was observed in the proximal colon, Rizkala noted.

The PPV was 0.87 vs 0.76 for the proximal vs distal colon, with an RR of 1.11 (95% CI, 1.06-1.17), so the two parts of the colon were comparable, he reported.

In the future, CADx systems should focus on using lesions from the proximal colon to train more accurately because currently CADx systems are trained on the available endoscopic data in which most of those polyps are from the rectosigmoid colon, Rizkala said.

We would also "like manufacturers of CADx systems to provide public access to data balanced between the proximal and distal regions of the colon," he added.

Diagnosis More Challenging Than Detection With CADx

Commenting on the study, comoderator David G. Graham, MD, consultant gastroenterologist at University College London Hospital in England, remarked: "The key questions here relate to why are these systems underperforming in the proximal colon, and how can we improve this?"

Are these results "due to the very different appearance of adenomas in the distal colon vs the proximal colon on CADx (which is not what we see as endoscopists but seems to be what the systems are seeing), or is it due to a different characterization of polyps," that is, more sessile serrated lesions in the proximal colon than in the distal colon, he asked.

Also commenting on the study was Raf Bisschops, MD, head of endoscopy at KU Leuven in Belgium. He remarked that the review underscores the fact that optical diagnosis by artificial intelligence is a more challenging task than detection.

It is "not entirely clear" what would explain the difference in performance of CADx between the distal colon and proximal colon, he said. It can't be excluded that the inclusion of different CADx systems, some of which clearly underperformed, may account for the difference.

He went on to suggest that the differences might be down to location beyond proximal and distal.

"The difference in performance between the right and left colon is also interesting, since recent insights in the molecular and morphological features of hyperplastic polyps indicates that there are different classes with more goblet cell–rich hyperplastic polyps in the right colon, and more microvesicular hyperplastic polyps in the left."

These have "distinct microscopic and endoscopic appearances" that could account for a difference in performance of a CADx system if not included in the training and validation sets, he explained.

Rizkala and Graham reported no relevant disclosures. Bisschops reported receiving research grants and speaker fees from Medtronic, Fujifilm, and Pentax. ■

Continued from previous page

centers overall, and is used mainly at academic centers, his clinic has been using it for the past year.

The main question, Mansour cautioned, is whether increased detection of small polyps will actually reduce CRC incidence or mortality, and it will likely be several years before clear, concrete data can answer that.

"Most studies have shown the improvement in adenoma detection is mainly for diminutive polyps < 5 mm in diameter, but whether that will actually translate to substantive improvements in hard outcomes is as yet unknown," he said. "But if gastroenterologists are interested in doing everything they can today to help improve detection rates and lower miss rates of premalignant polyps, serious consideration should be given to adopting the use of CADe in practice."

This study was supported by Medtronic. Rees reported receiving grant funding from ARC Medical, Norgine, Medtronic, 3-D Matrix, and Olympus Medical, and has been an expert witness for ARC Medical. Other authors disclosed receiving research funding, honoraria, or travel expenses from Medtronic or other private companies. Mansour had no competing interests to declare. ■

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