

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE



PATRICK FRANK/MDEdge News

Dr. Reem Z. Sharaiha, of Weill Cornell Medical Center, presented results of the first long-term outcomes of this procedure.

Sustained weight loss 5 years after endoscopic sleeve gastroplasty

BY DOUG BRUNK
MDedge News

FROM DDW 2019

Five years after undergoing endoscopic sleeve gastroplasty (ESG), patients achieved a total body weight loss of about 15%, a retrospective study showed.

The finding comes from the first long-term analysis of outcomes following endoscopic sleeve gastroplasty, a relatively new, minimally invasive weight-loss procedure that offers patients an alternative to bariatric surgery.

“Endoscopic sleeve gastrectomy is a 1-day outpa-

tient procedure that uses a suturing device attached to an endoscope to create a series of sutures that cinch the stomach like an accordion down to roughly the size of a banana, and leaves no scars,” lead study author Reem Z. Sharaiha, MD, MSc, said during a media briefing in advance of the annual Digestive Disease Week.® “The procedure causes patients to eat less because they feel full faster. This results in weight loss.”

Digestive Disease Week is jointly sponsored by the American Association for the Study of Liver Diseases

See **Weight loss** • page 22

AGA CLINICAL PRACTICE UPDATE

Direct-acting antivirals and hepatocellular carcinoma

BY AMY KARON
MDedge News

Achieving sustained virologic response to direct-acting antiviral therapy for chronic hepatitis C virus infection cuts lifetime hepatocellular carcinoma risk by approximately 70%, even when patients have baseline cirrhosis, experts wrote in *Gastroenterology*.

When used after curative-intent treatment for hepatocellular carcinoma, direct-acting antiviral (DAA) therapy also does not appear to make recurrent cancer more probable or more aggressive, wrote

Amit G. Singal, MD, and associates in an American Gastroenterological Association clinical practice update. Studies that compared DAA therapy with either interferon-based therapy or no treatment have found “similar if not lower recurrence than the comparator groups,” they wrote. Rather, hepatocellular carcinoma is in itself highly recurrent: “While surgical resection and local ablative therapies are considered curative, [probability of] recurrence approaches 25%-35% within the first year, and 50%-60% within 2 years.”

Direct-acting antiviral
See **Antivirals** • page 15

Tenofovir disoproxil treated HBV with fewer future HCCs

BY MITCHEL L. ZOLER
MDedge News

VIENNA – Treatment of individuals chronically infected with hepatitis B virus (HBV) with the nucleotide analog tenofovir disoproxil

il fumarate significantly linked with a substantial cut in the incidence of hepatocellular carcinoma (HCC) compared with those who received the nucleoside analog entecavir, according to a review of more than

29,000 Hong Kong patients.

This is the second reported study to find that association. In January 2019, a study of more than 24,000 Korean residents chronically infected with HBV showed a

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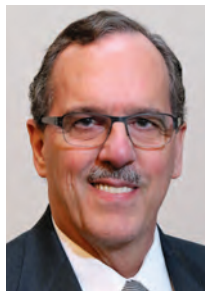
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LETTER FROM THE EDITOR: GI practice consolidation continues

Digestive Disease Week (DDW®) 2019 is now history. This was the 50th anniversary of DDW, and again, it lived up to its reputation as the world's foremost meeting dedicated to digestive diseases. GI & Hepatology News will publish multiple articles highlighting the best of DDW in the coming months.

The AGA Presidential Plenary session is an annual DDW highlight. This year's session did not disappoint and was attended by a large crowd. David Lieberman, MD, AGAF (outgoing AGA president), and Hashem B. El-Serag, MD, MPH, AGAF (incoming AGA president) moderated the session. Outstanding presentations about management of obesity, new findings in IBD, the use of virtual reality in the treatment of functional abdominal pain, and findings from a long-term colorectal cancer screening trial were some of the key presentations.

Recent behind-the-scenes work by the AGA is paying off for its members and the larger GI community. The AGA was again awarded an NIH-funded grant to advance its education and training of under-represented minorities. This is the second NIH grant given to the AGA, who now has become a leader in diversity and inclusive educa-



DR. ALLEN

The AGA was again awarded an NIH-funded grant to advance its education and training of under-represented minorities.

tion. The AGA has strengthened its close bond with the Crohn's and Colitis Foundation, adding to its portfolio of scientific and clinical offerings focused on IBD. The AGA

Center for Gut Microbiome Research and Education has emerged as one of the best sources of education and research about the microbiome's impact on digestive health.

On the business front, there are tectonic changes occurring. In 2018, three large GI practices were sold to private equity companies and each has completed multiple arbi-

trage plays (acquisition of smaller practices), growing to over 200 physicians. This year we will see 6-10 additional private equity acquisitions and will likely see one or more GI practices of 500-1,000 providers. This consolidation will have profound implications for the practice of gastroenterology and will provide some interesting opportunities to conduct population-based research for physicians who can capture that potential through academic-community partnerships.

John I. Allen, MD, MBA, AGAF
Editor in Chief



Q1. A 56-year-old female with a BMI of 42 (kg/m²), diabetes, and hyperlipidemia presents with a 5-cm hiatal hernia. She has symptoms of heartburn during the day and significant nocturnal regurgitation such that she is sleeping in a recliner at night.

What surgical option would be most effective in this patient?
A. Hiatal hernia repair with

Quick quiz

Nissen fundoplication
B. Hiatal hernia repair with Dor fundoplication
C. Magnetic sphincter augmentation
D. Hiatal hernia repair with gastric bypass
E. Gastric sleeve

Q2. A 64-year-old male with a recent history of acute pancreatitis has a dilated main pancreatic duct

with prominent side branch lesions seen on CT scan. Endoscopic evaluation reveals mucus extruding from a dilated ampulla.

What is the next best step in management of this patient?

A. EUS +/- FNA
B. ERCP with pancreatic stent
C. Surgical resection
D. Repeat MRI in 3 years
E. ERCP with Spyglass

The answers are on page 14.

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FROM THE AGA JOURNALS

Tailoring the Mediterranean diet for NAFLD

BY AMY KARON

MDedge News

Adults with nonalcoholic fatty liver disease (NAFLD) were more likely to implement the Mediterranean diet when they had greater nutritional knowledge and skills, family support, nutritional care, and positive reinforcement in the media, according to an in-depth study of 19 patients.

Barriers to adopting the diet included “an obesogenic environment, life stressors, and demand for convenience. Poor understanding of the causes and significance of NAFLD adversely affected readiness to change dietary habits,” wrote Laura Haigh of Newcastle University in Newcastle Upon Tyne, England, and associates. The study, which included both standard quantitative methods and semistructured interviews, was published in *Clinical Gastroenterology and Hepatology*.

The Mediterranean diet emphasizes vegetables, legumes, fish, fruits, whole grains, nuts, and olive oil in lieu of processed foods, sweets, saturated fats, and red meat. This diet has been definitively shown to improve insulin sensitivity and steatosis, even when patients do not lose weight. This has

sparked interest in its use for NAFLD disease, but keys to its successful adoption in Northern Europe are not well understood.

Therefore, the researchers recruited 19 NAFLD patients from a tertiary care center in the United Kingdom for a 12-week Mediterranean diet intervention. Most were female, white, in their late 50s, and obese, and had type 2 diabetes. “Participants were taught behavioral strategies through the provision of shopping lists, meal planners, and recipes. No advice was given on calorie allowances or physical activities,” the investigators noted.

By using a 14-point assessment tool, they found that dietary adherence rose significantly at 12 weeks, compared with baseline ($P = .006$). In all, 79% of patients lost weight (mean, 2.4 kg; $P = .001$ versus baseline), and 72% significantly increased their serum level of HDL cholesterol. Interviews linked successful adoption of the diet with diverse factors, such as believing that NAFLD is lifestyle associated, realizing that healthier nutrition can improve health outcomes, and having access to transportation and budget grocery stores. Patients generally saw the Mediterranean diet as flexible and



SNYFEROK/THINKSTOCK

affordable, but they struggled to adopt it if they worked irregular hours, experienced substantial life stress or were very busy, or tended to eat for self-reward or self-comfort.

Other cited barriers included “diet saboteurs” (including spouses), the plethora of unhealthy foods available in patients’ environments, low nutritional or medical knowledge, and cultural, social, or taste incompatibility, the researchers reported. Taken together, the findings underscore “the futility of a one-size-fits-all approach” when implementing the Mediterranean diet in this population, they concluded. Instead, their patients valued a collab-

orative, tailored approach – ideally one that incorporated in-person and group-based treatment, as well as online support.

Funders included the North East of England hub of the Allied Health Professions Research Network, the Elucidating Pathways of Steatohepatitis consortium, the Horizon 2020 Framework Program of the European Union, and the Newcastle NIHR Biomedical Research Centre. The researchers reported having no conflicts of interest.

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SOURCE: Haigh L et al. *Clin Gastroenterol Hepatol*. 2018 Oct 31. doi: 10.1016/j.cgh.2018.10.044.

Pancreatic cancers often contained targetable mutations

BY AMY KARON

MDedge News

Tumor specimens from 17% of patients with pancreatic ductal adenocarcinomas contained genomic alterations for which targeted therapies exist, researchers reported in *Gastroenterology*.

“We identified mutations in genes that could contribute to progression of intraductal papillary mucinous neoplasms into malignancies. These alterations might be used as biomarkers for early detection,” wrote Aatur D. Singhi, MD, PhD, of the University of Pittsburgh and associates.

The most common genomic mutations in pancreatic ductal adenocarcinoma (PDAC) involve KRAS, TP53, CDKN2A, and SMAD4, none of which can be treated by currently approved targeted agents. But PDACs are genomically very heterogeneous and contain low levels (less than 5%) of many other mutations, the researchers noted. In small studies, these low-prevalence mutations included kinase gene amplifications and rearrangements, which may be useful as

treatment targets or predictive biomarkers of response.

To further characterize PDAC mutations and their relative penetrance, the researchers performed targeted genomic profile analyses of 3,594 PDAC tumor specimens from an international cohort. The tests included capture-based targeted genomic profiling of up to 315 cancer-linked genes and the intron regions of 28 genes that are rearranged in cancer cells. The researchers classified genomic alterations based on published signaling pathways, including receptor tyrosine kinase/ras/mitogen-activated protein kinase (RTK/ras/MAPK) activation, DNA damage repair, cell cycle control, transforming growth factor beta signaling, histone modification, switching/sucrose nonfermenting complex, phosphoinositide 3-kinase/mammalian target of rapamycin signaling, Wnt/beta-catenin pathway, RNA splicing, Notch pathway, angiogenesis, and hedgehog signaling. In addition, they analyzed tumor mutation burden in 1,021 samples and microsatellite instability status in 2,563 samples.

In all, the samples contained 19,120 genomic

alterations of 317 genes. A total of 608 (17%) specimens harbored mutations considered actionable targets. These involved either the RTK/ras/MAPK signaling or DNA damage repair pathways. As expected, KRAS mutations were most common, but their penetrance (88%) was lower than in prior studies. This might be because the current study covered both resectable and nonresectable PDACs, while past studies tended to focus on resected PDACs only, the researchers said. Importantly, the 12% of KRAS wild-type PDACs often harbored other potentially targetable alterations of genes in the RTK/ras/MAPK pathway, such as kinase fusion, amplification, missense mutations, and intragenic-in-frame deletions.

A total of 81% of samples contained alterations of TP53 or other genes involved in DNA damage repair. As with prior studies, the penetrance of individual DNA damage repair mutations was low – usually less than 5%. Most germline mutations involved the BRCA-FANCDNA repair pathway, and these may be targetable with agents such as poly (ADP-ribose) poly-

Continued on following page

FROM THE AGA JOURNALS

Infections within first year of life predicted IBD

BY AMY KARON

MDedge News

Infections during the first year of life were a significant risk factor for inflammatory bowel disease throughout the lifespan but especially prior to the age of 10 years, according to the findings of a large population-based study.

It remains unclear whether the risk reflects infections in themselves or the use of antibiotic ther-

Among neonatal events, the only significant risk factor was being in the highest versus the lowest socioeconomic quintile. This association persisted during the first year of life.

apy, wrote Charles N. Bernstein, MD, of the University of Manitoba, Winnipeg, and associates. Infections did not appear to be a proxy for immunodeficiency disorders, which were similarly infrequent among cases and controls, they noted. Limiting antibiotic usage, while desirable, would be difficult to do for infections as serious as many in the study. Hence, they suggested research to determine “exactly what antibiotic intake does to infant gut microflora or intestinal or systemic immune responses,” and whether giving probiotics or prebiotics after antibiotic therapy helps attenuate the risk of inflammatory bowel disease (IBD) and other autoimmune disorders. The findings were published in *Gastroenterology*.

IBD is probably multifactorial, but specific causal factors remain unclear. Based on mounting evidence for the role of gut dysbiosis,

the researchers explored whether IBD is associated with higher rates of infections and other critical events during the neonatal period and the first year of life by comparing 825 patients with IBD and 5,999 controls matched by age, sex, and area of residence. The data source was the University of Manitoba IBD Epidemiology Database, which includes all Manitobans diagnosed with IBD from 1984 to 2010. The researchers also compared patients with 1,740 unaffected siblings.

Gastrointestinal infections, gastrointestinal disease, and abdominal pain during the first year of life did not predict subsequent IBD. Maternal IBD was the strongest risk factor (odds ratio, 4.5; 95% confidence interval, 3.1-6.7). Among neonatal events, the only significant risk factor was being in the highest versus the lowest socioeconomic quintile (OR, 1.35; 95% CI, 1.01-1.79). This association persisted during the first year of life.

Infections during the first year of life were a significant risk factor for IBD before age 10 (OR, 3.1; 95% CI, 1.1-8.8) and age 20 years (OR, 1.6; 95% CI, 1.2-2.2) in the population-based analysis. In contrast, patients and their unaffected siblings had similar rates of infection during early life. The study may have missed differences in exposures between these groups, or perhaps patients lack certain protective genes possessed by healthy siblings, the researchers wrote.

Numbers of antibiotic prescriptions during the first year and the first decade of life did not significantly differ between 33 cases and 270 controls with available data. However, there was a trend toward more antibiotics prescribed to patients versus controls.

“Together with our past reports

Understanding and exploring factors that could impact inflammatory bowel disease (IBD) development is imperative. This study by Bernstein et al. evaluated whether environmental factors in the first year of life may impact subsequent diagnosis of IBD using population-based cohort data with robust and detailed health information. Maternal history of IBD was the most predictive factor in development of IBD, further evidence of a genetic component to disease pathogenesis. However, environmental factors such as high socioeconomic status within the first year of life were predictive of diagnosis of IBD later in life, possibly lending further support to the “hygiene hypothesis.” Also, significant infections identified in the clinical setting or requiring hospitalization were predictive of subsequent IBD diagnosis. This is particularly interesting as gut microbiome perturbations increasingly take the stage as a possible pathway of significance in IBD.



DR. HORST

Could infection within the first year of life or the subsequent antibiotic use required affect the gut microbiome so significantly and

perhaps permanently to affect development of later childhood or adult IBD?

While these are associations at a population-based level and not clear-cut causation, much can be considered for future research directions. Identifying high-risk patients ex-

tremely early in life may be key to further understand the complex interplay of genetic susceptibility and environmental influence. Whether any of these factors are modifiable will be a question that will only continue to gain importance as global rates of IBD continue to increase.

Sara Horst, MD, MPH, is an associate professor of medicine in the department of gastroenterology, hepatology, and medicine at Vanderbilt University, Nashville, Tenn. She has consulted for Janssen, UCB, and Boehringer Ingelheim.

that neither cesarean section birth nor antenatal or perinatal maternal use of antibiotics predict ultimate development of IBD, it seems that neonatal changes to the microbiome are subsumed by those occurring in the first year of life,” the investigators concluded. They recommended studying the infant gut microbiome before and for several months after infections and antibiotic exposure to determine which shifts in microbiota predict IBD onset.

The Manitoba Centre for Health

Policy provided access to the Population Health Research Data Repository. Dr. Bernstein is supported by the Bingham Chair in Gastroenterology. He reported ties to AbbVie Canada, Ferring Canada, Janssen Canada, Shire Canada, Takeda Canada, Pfizer Canada, Napo Pharmaceuticals, 4D Pharma, and Mylan.

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SOURCE: Bernstein CN et al. *Gastroenterology*. 2019 Feb 14. doi: 10.1053/j.gastro.2019.02.004.

Continued from previous page

merase inhibitors and DNA strand-damaging, platinum-based cytotoxic regimens, the investigators wrote.

Among 3,117 samples with clinicopathologic data, 51% were from the primary tumor and the rest were from distal metastases of the liver, lung, nonregional lymph nodes, peritoneum, omentum, and other sites. Not surprisingly, BRCA1 and BRCA2 mutations were more common in younger patients, but KRAS, SMAD4, DNMT3A, and AP mutations were

more common in older patients, and mutational frequencies also varied by sex, primary versus metastatic tumor status, and site of metastasis.

“The complex genomic heterogeneity in otherwise histologically similar PDACs suggests a one-size-fits-all approach to treating patients will not be successful,” they concluded. “Targeted genomic profiling of known genomic alterations across multiple tumor types highlights potentially targetable and predictive biomarkers for treatment in a significant subset of PDACs.”

Funders included the Pancreatic Cancer Action Network, the National Pancreas Foundation, and the Sky Foundation. Dr. Singhi and two coinvestigators reported receiving honoraria from Foundation Medicine, and seven other coinvestigators reported being employed by and having stock ownership in Foundation Medicine. No other financial disclosures were reported.

ginews@gastro.org

SOURCE: Singhi AD et al. *Gastroenterology*. 2019 Mar 2. doi: 10.1053/j.gastro.2019.02.037.

FROM THE AGA JOURNALS

Zoster vaccination is underused but looks effective in IBD

BY AMY KARON

MDedge News

For men with inflammatory bowel disease (IBD), herpes zoster vaccination was associated with about a 46% decrease in risk of associated infection, according to the results of a retrospective study from the national Veterans Affairs Health-care System.

Crude rates of herpes zoster infection were 4.09 cases per 1,000 person-years among vaccinated patients versus 6.97 cases per 1,000 person-years among unvaccinated patients, for an adjusted hazard ratio of 0.54 (95% confidence interval, 0.44-0.68), reported Nabeel Khan, MD, of the University of Pennsylvania, Philadelphia, and associates. "This vaccine is therefore effective in patients with IBD, but underused," they wrote in *Clinical Gastroenterology and Hepatology*.

Studies have linked IBD with a 1.2- to 1.8-fold increased risk of herpes zoster infection, the researchers noted. Relevant risk factors include older age, disease flare, recent use or high cumulative use of prednisone, and use of thiopurines, either alone or in combination with a tumor necrosis factor (TNF) inhibitor. Although the American College of Gastroenterology recommends that all patients with IBD receive the herpes zoster vaccine by age 50 years, the efficacy of the vaccine in these patients remains unclear.

For their study, Dr. Khan and associates analyzed International Classification of Diseases (ICD) codes and other medical record data from 39,983 veterans with IBD who had not received the herpes zoster vac-

cine by age 60 years. In all, 97% of patients were male, and 94% were white. Most patients had high rates of health care utilization: Approximately half visited VA clinics or hospitals at least 13 times per year, and another third made 6-12 annual visits.

Despite their many contacts with VA health care systems, only 7,170 (17.9%) patients received the herpes zoster vaccine during 2000-2016, the researchers found. Vaccination rates varied substantially by region – they were highest in the Midwest (35%) and North Atlantic states (29%) but reached only 9% in Arkansas, Colorado, Louisiana, Montana, Oklahoma, Texas, Utah, and Wyoming, collectively.

The crude rate of herpes zoster infection among unvaccinated patients with IBD resembled the incidence reported in prior studies, the researchers said. After researchers accounted for differences in geography, demographics, and health care utilization between vaccinated and unvaccinated veterans with IBD, they found that vaccination was associated with an approximately 46% decrease in the risk of herpes zoster infection.

Very few patients were vaccinated for herpes zoster while on a TNF inhibitor, precluding the ability to study this subgroup. However, the vaccine showed a protective effect (adjusted HR, 0.63) among patients who received thiopurines without a TNF inhibitor. This effect did not reach statistical significance, perhaps because of lack of power, the researchers noted. "Among the 315 patients who were [vaccinated while] on thiopurines, none developed a documented painful or

Preventive care is an under-emphasized component of IBD management because the primary focus tends to be control of active symptoms. However, as patients are treated with immunosuppression, particularly combinations of therapies and newer mechanisms of action such as the Janus kinase inhibitors, the risk of infections increases, including those that are vaccine preventable including shingles and its related complications. This study by Khan et al. highlights several important messages for patients and providers. First, in this large older IBD cohort, the vaccination rates were very low at 18% even though more than 80% of patients had more than six annual visits to the VA Health Systems during the study period. These represent multiple missed opportunities to discuss and administer vaccinations. Second, the authors highlighted the vaccine's efficacy: Persons receiving herpes zoster vaccination had a clearly decreased risk of subsequent infection. While the number of vaccinated patients on immunosuppression was too small to

draw conclusions about efficacy, the live attenuated vaccination is contraindicated for immunosuppressed patients. However, the newer recombinant shingles vaccine offers the opportunity to extend the reach of shingles vaccination to include those on immunosuppression. As utilization of the newer vaccine series increases, we will be able to evaluate the efficacy for immunosuppressed IBD patients, although studies from other disease states suggest efficacy. However, vaccinations will never work if they aren't administered. Counseling patients and providers regarding the importance of vaccinations is a low-risk, efficacious means to decrease infection and associated morbidity.

Christina Ha, MD, AGAF, associate professor of medicine, Inflammatory Bowel Disease Center, division of digestive diseases, Cedars-Sinai Medical Center, Los Angeles. She is a speaker, consultant, or on the advisory board for AbbVie, Janssen, Genentech, Samsung Bioepis, Pfizer, and Takeda. She also received grant funding from Pfizer.

painless vesicular rash within 42 days of herpes zoster vaccination," they added. One patient developed a painful blister 20 days post vaccination without vesicles or long-term sequelae.

Pfizer provided funding. Dr. Khan disclosed research funding from Pfizer, Luitpold, and Takeda Pharmaceuticals. One coinvestigator dis-

closed ties to Pfizer, Gilead, Merck, AbbVie, Lilly, Janssen, Johnson & Johnson, UCB, and Nestle Health Science. The remaining researchers disclosed no conflicts.

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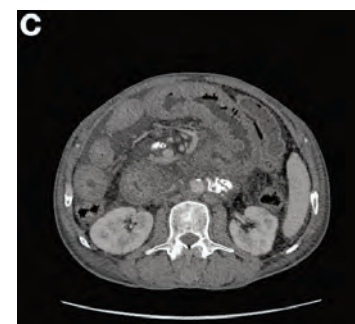
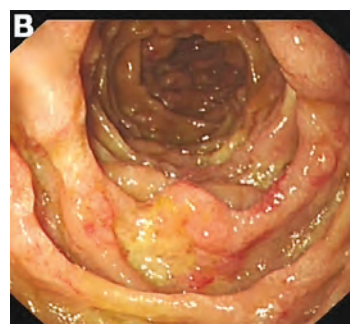
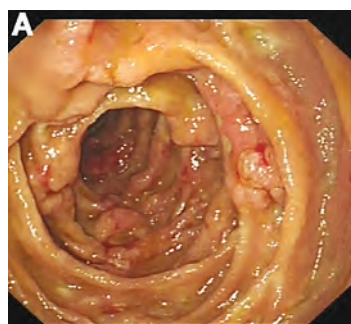
SOURCE: Khan N et al. *Clin Gastroenterol Hepatol*. 2018 Oct 13. doi: 10.1016/j.cgh.2018.10.016.

CLINICAL CHALLENGES AND IMAGES

What is your diagnosis?

By Lei Miao, MD, XiangRong Chen, MD, and ZhiMing Huang MD. Published previously in *Gastroenterology* (2018;154[4]:812-3).

A 60-year-old man complaining of recurrent melena for more than 2 months, accompanied by fatigue and anemia, was admitted to our gastroenterology ward. He denied experiencing hematemesis, abdominal pain, fever, osteodynia, or arthralgia. His medical history included a 6-year history of alcoholic hepatocirrhosis and type 2 diabetes mellitus. Colonoscopy found no evidence of hemorrhage.



However, gastroduodenoscopy showed multiple polypoid lesions in the duodenum (Figures A, B). An abdominal computed tomography (CT) scan was performed (Figure C).

What is the underlying condition leading to the endoscopic and CT findings?

The diagnosis is on page 23.

A doctor in the House: Rep. Raul Ruiz is fighting for GIs and our patients

Rep. Raul Ruiz, MD, was a virtually unknown candidate and defeated then incumbent Mary Bono, R-CA, for the seat that represents Coachella Valley and Palm Springs. Rep. Ruiz is the son of migrant farmers from Mexico; he went on to medical school and became the first Latino to receive three graduate degrees from Harvard – a medical degree, a masters of public policy, and a masters of public health. Rep. Ruiz is an emergency physician by training and AGA got to know him early in his congressional career and provided support for his initiatives that aligned with our policy priorities and support through AGA PAC.

When Rep. Ruiz was elected to Congress, the Democrats were in the minority in the House, and as a freshman member in the minority, he did not yield a lot of power and influence. However, AGA continued to work with Rep. Ruiz in garnering his support for repealing the Independent Payment Advisory Board (IPAB) that was created under the Affordable Care Act (ACA) – it was charged with making budgetary decisions for the Medicare program that would have disproportionately impacted physicians. Rep. Ruiz was willing to work with Republicans to support legislation to repeal IPAB; Congress eventual-



REP. RAUL RUIZ

ly repealed it in the last Congress.

AGA also worked with Rep. Ruiz in support of increasing access to colorectal cancer screening especially for underrepresented minorities, and he has been a strong supporter of the Removing Barriers to Colorectal Cancer Screening Act that would fix the current Medicare screening colonoscopy coinsurance problem that disproportionately impacts poorer Medicare beneficiaries who lack supplemental coverage.

Recently, AGA has been working closely with Rep. Ruiz as he champions an issue that impacts GI patients with inflammatory bowel disease and their ability to

access the treatment that their doctor recommends. Rep. Ruiz has introduced H.R. 2279, the Safe Step Act, legislation that would provide a clear, transparent, and easily accessible appeals process for physicians and their patients when subject to step-therapy protocols. Step therapy, also known as “fail first,” requires patients to try and fail one or more medications before the insurer will provide coverage for the therapy that their doctor thinks is the best to manage their condition. The Safe Step Act would not eliminate step therapy but would provide some common sense guardrails for patients and reasonable exceptions for patients who would be harmed if subjected to such a policy.

Because of AGA PAC’s and other physician organizations’ PAC support for Rep. Ruiz, he was able to secure a seat on the highly coveted Energy and Commerce Committee and its Health Subcommittee. The Committee has jurisdiction over all public health programs such as NIH, CDC, FDA, and Medicare Part B which is all physician services. Given Rep. Ruiz’s background and the committee position he holds, he is well suited to continue to help champion AGA’s policy priorities and those of all organized medicine.

Over the years, Rep. Ruiz has spoken to AGA members at our annual Advocacy Day on the importance of physicians being involved politically and also in advocacy. He has also met with AGA Government Affairs Committee member Gaurav Singhvi, MD, in the district on issues important to the gastroenterology community and our patients.

AGA looks forward to working with Rep. Ruiz to continue to ensure that patients have access to specialty care, that the administrative burdens that physicians face like prior authorization are reduced, that we continue to invest in research, and that we continue to train the next generation of GIs.

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Scope-associated infection still a concern in U.S.

On April 12, FDA issued a safety communication releasing new information on the duodenoscope contamination rate from postmarket surveillance studies and medical device reports. While the outlook has improved significantly since this issue first arose in 2015, we are not yet at our goal of zero device-associated infections.

AGA encourages all members to stay vigilant when it comes to duodenoscope reprocessing and strictly adhere to the manufacturer’s reprocessing and maintenance instructions.

In the safety communication, FDA reports:

- In the past 6 months, three people died and 45 people developed infections from contaminated endoscopes.

- Results from sampling studies show up to 5.4% of all properly collected samples tested positive for “high concern” organisms. “High concern” bacteria are more often associated with disease, such as *E. coli* or *Staphylococcus aureus*.

- Additionally, up to 3.6% of properly collected samples tested positive for low to moderate concern organisms; while these

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*Use as directed. Take 1 pill in the morning for 14 days. May take
1 to 4 days for full effect.

†Based on a post hoc analysis of 2-week data from 2 previously
published identical phase IV, multicenter, randomized, double-
blind, placebo-controlled trials that demonstrated efficacy
and safety of esomeprazole 20 mg once daily in the morning
in subjects with sleep disturbances due to reflux and frequent
nighttime heartburn.

References: **1.** National Sleep Foundation. Ease heartburn at bedtime. <https://sleep.org/articles/ease-heartburn-bedtime/>. Accessed
August 6, 2018. **2.** Johnson DA, Le Moigne A, Hugo V, Nagy P. Rapid resolution of sleep disturbances related to frequent reflux: effect
of esomeprazole 20 mg in two randomized, double-blind, controlled trials. *Curr Med Res Opin.* 2015;31(2):243-250.

Food the focus of gut health at 2019 Freston Conference

Recognition is increasing among GI practitioners about the influence of nutrition and diet on patient outcomes. From irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), celiac, mast cell activation syndrome, and other maladies, what patients consume plays a role in how well they combat these diseases. Increasingly, clinicians are working with allied health professionals including allergists, nutritionists, and dietitians to forge partnerships to promote sound gut health. In response to this growing trend, the 2019 James W. Freston Conference – Food at the Intersection of Gut Health and Disease, Aug. 9-10, 2019, in Chicago, will examine how nutrition management therapies can combat GI disorders and how diet supports improvement across the care continuum.

Since 2008, Freston has focused on single-issue topics where experts gather to address practitioner challenges and solutions

as well as gastroenterological science.

Following this year's Freston, attendees will leave with a deep understanding about:

- How to recognize and differentiate food-induced GI disorders.
- Diets which promote sound gut health care.
- How nutrient-gene interactions may alter gastrointestinal conditions.
- How nutrition can help patients with gastroesophageal reflux disease, IBS, IBD, FGIDs and mast cell activation syndrome.
- Implement nutrition management therapies.

Join like-minded practitioners and industry counterparts in Freston's intimate environment designed to foster learning, networking, and engagement. Registration is open and early bird rates are in effect through June 5. Learn more by visiting freston.gastro.org.

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Top AGA Community patient cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community (<https://community.gastro.org/discussions>) to seek advice from colleagues about therapy and disease management options, best practices, and diagnoses.

In case you missed it, here are the most popular clinical discussions shared in the forum recently:



1. Perianal fistula found in UC patient (<http://ow.ly/BhnG30oSnTS>)

A 20-year-old male patient with no previous medical history was seen and treated last year for pancolitis. His physician solicits drug therapy preferences from the GI community, given the age of the patient and a newly discovered perianal fistula.

2. IBD patient with risk of cancer (<http://ow.ly/KoGz30oHdjG>)

A 62-year-old female patient with a long history of Crohn's disease developed acute hepatitis. She had a colectomy in 2011 where a one-stage ileo rectal anastomosis was performed instead of a J-pouch. She was in remission under surveillance and mesalamine, until recently. She also has primary sclerosing cholangitis (PSC) and multifocal dysplasia, a combination that raised concern

among the GI community about the patient's risk of cancer.

3. Significant daily pain in Crohn's patient (<http://ow.ly/FHUI30oHdl8>)

A recent colonoscopy for a 39-year-old man with Crohn's disease revealed active disease in the ileum and sigmoid colon with narrowing at the recto-sigmoid colon. The MRE

revealed active inflammation at the ileo-colonic anastomosis and of the sigmoid and descending colon, with no noted fistulas. His physician solicits advice in the forum on next steps for the patient, who was experiencing significant pain daily, despite being on a low-residue diet and consistent drug therapy.

Another popular clinical discussions:

• WATS imaging in Barrett's esophagus (<http://ow.ly/PrJ330oHdCN>)

Members share their opinions and experiences with Wide-Area Transepithelial Sampling (WATS) in Barrett's esophagus (BE) after mention of recent data demonstrating its promising potential for surveillance in BE patients, despite not yet being approved by the FDA.

More clinical cases and discussions are at <https://community.gastro.org/discussions>.



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organisms don't usually lead to dangerous infections, they are indicative of a reprocessing failure.

Jeff Shuren, MD, director of the Center for Devices and Radiological Health at FDA, also issued a communication on continued efforts to assess duodenoscope contamination risk. Dr. Shuren puts this new data into perspective: "While the current contamination rates we're seeing in the post-market studies show the need for improvement, I want to emphasize that an individual patient's risk of acquiring infection from an inadequately reprocessed medical device remains relatively low given the large number of such devices in use."

The AGA Center for GI Innovation and Technology (CGIT) continuously monitors this issue and engages with industry and FDA on efforts that will help us reach our goal of zero device-transmitted infections to our patients.

"We continually meet with industry partners, just as recently as last week at the AGA Tech Summit, to understand how they are innovating to reduce the risk of potential infection. We are also in close communication with FDA and other key stakeholders. We all have a role in preventing device-transmitted infections, and we don't take our role lightly," added V. Raman Muthusamy, MD, AGAF, FACC, FASGE, chair of the AGA CGIT.

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References: **1.** Schiller LR, Emmett M, Santa Ana CA, Fordtran JS. Osmotic effects of polyethylene glycol. *Gastroenterology*. 1988;94(4):933-941. **2.** Hammer HF, Santa Ana CA, Schiller LR, Fordtran JS. Studies of osmotic diarrhea induced in normal subjects by ingestion of polyethylene glycol and lactulose. *J Clin Invest*. 1989;84(4):1056-1062. **3.** Survey of 672 consumers, August 2017, Bayer Consumer Health. **4.** Bharucha AE, Dorn SD, Lembo A, Pressman A; American Gastroenterological Association. American Gastroenterological Association medical position statement on constipation. *Gastroenterology*. 2013;144(1):211-217.



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What are the risk factors for IBS?



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Massachusetts General Hospital, Boston

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FND19-6

The AGA Research Foundation funds 52 promising research projects

The American Gastroenterological Association is thrilled to announce the 52 researchers selected to receive funding through the AGA Research Foundation Awards Program. The AGA Research Foundation will provide more than \$3 million in research funding in the 2019 award year.

“The 2019 class of AGA Research Foundation awardees represents some of the most innovative and promising early-stage investigators working in the field of gastroenterology,” said Robert S. Sandler, MD, MPH, AGAF, chair, AGA Research Foundation. “We’re proud to support these individuals as they continue on their ultimate mission to improve the treatment and care of digestive disease patients through their discoveries.”

Of the 2019 class of awardees, 40% are performing clinical research and 58% hold MD, MD/PhD, or equivalent degrees. Forty-four percent of awardees are female and 8% are from racial or ethnic groups underrepresented in medicine. In line with the AGA Research Foundation’s mission to support the next generation

of researchers in digestive diseases, 88% of the 2019 awardees are early-career investigators.

The AGA Research Foundation Awards Program recruits, retains, and supports the most promising investigators in gastroenterology and hepatology. With AGA Research Foundation funding, recipients have protected time for research that will enhance the diagnosis, management, treatment, and potentially cure of digestive disorders. AGA grants have launched the careers of investigators doing important work that translates to new patient care tools for clinicians and better outcomes for patients.

To view the full list of recipients, go to <https://www.gastro.org/press-release/the-aga-research-foundation-funds-52-promising-research-projects>.

The awards program is made possible thanks to generous donors and funders contributing to the AGA Research Foundation. Learn more at www.gastro.org/foundation.

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Q1: Correct Answer: D

Rationale

The severe reflux may be due to the hiatal hernia and worsened by the obesity. This patient has medically complicated obesity and thus bariatric surgery is an option. A gastric bypass in this situation offers the best anti-reflux procedure for this patient. A fundoplication in the setting of obesity has a higher rate of recurrence of symptoms (Answers A, B). While a gastric sleeve is an option for the obesity, a gastric sleeve (Answer E) may cause de novo reflux or worsen pre-existing symptoms. Magnetic sphincter augmentation (Answer C) has demonstrated promising results in patients with a BMI less than 35 and hiatal hernia less than 3 cm. Data are not available for patients with higher BMIs.

References

1. Abdelrahman T, Latif A, Chan DS, et al. Outcomes after laparoscopic anti-reflux surgery related

Answers

to obesity: A systematic review and meta-analysis. *Int J Surg*. 2018 Mar;51:76-82.

2. Stenard F, Iannelli A. Laparoscopic sleeve gastrectomy and gastroesophageal reflux. *World J Gastroenterol*. 2015 Sep 28;21(36):10348-57.

Q2: Correct Answer: C

Rationale

This patient has a main duct IPMN, which has a high potential for malignant transformation and should be resected if possible. Resection is also indicated for branch-duct IPMN’s, which are symptomatic (e.g. pancreatitis), associated with obstructive jaundice or main duct involvement, have a solid component within the cyst, or have concerning features on EUS-FNA.

Reference

1. Elta GH, et al, ACG Clinical Guideline: Diagnosis and Management of Pancreatic Cysts. *Am J Gastroenterol*. 2018;113:464-79.

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Treat the cancer first

Antivirals from page 1

therapy for chronic hepatitis C infection improves several aspects of liver health, but experts have debated whether and how these benefits affect the risk and behavior of hepatocellular carcinoma. To explore the issue, Dr. Singal, medical director of the liver tumor program and clinical chief of hepatology at UT Southwestern Medical Center in Dallas and associates reviewed published clinical trials, observational studies, and systematic reviews. Among 11 studies of more than 3,000 patients in five countries, sustained virologic response (SVR) to DAA therapy was associated with about a 70% reduction in the risk of liver cancer, even after adjustment for clinical and demographic variables. "The relative reduction is similar in patients with and without cirrhosis," the experts wrote.

Since patients with fibrosis (F3) or cirrhosis are at highest risk for hepatocellular carcinoma, they should undergo baseline imaging

and remain under indefinite post-SVR surveillance as long as they are eligible for potentially curative treatment, the practice update states. The experts recommended twice-yearly



DR. SINGAL

ultrasound, with or without serum alpha-fetoprotein, noting that current evidence supports neither shorter surveillance intervals nor alternative imaging modalities. "The presence of active hepatocellular carcinoma is associated with a small but statistically significant decrease in SVR with DAA therapy," the experts confirmed, based on the results of three studies. They recommended that, when possible, patients with hepatocellular carcinoma first receive curative-intent treatment,

such as with liver resection or ablation. Direct-acting antiviral therapy can begin 4-6 months later, once there has been time to confirm response to hepatocellular carcinoma treatment.

For patients who are listed for liver transplantation, timing of DAA therapy "should be determined on a case-by-case basis with consideration of median wait times for the region, availability of HCV-positive organs, and degree of liver dysfunction," they added. "For example, DAA therapy may be beneficial pretransplant for patients in regions with long wait times or limited hepatitis C virus-positive donor organ availability, whereas therapy may be delayed until posttransplant in regions with shorter wait times or a high proportion of hepatitis C virus-positive donor organs that would otherwise go unused."

For patients with active intermediate or advanced liver cancer, it remains unclear whether DAA therapy is usually worth the costs and risks, they noted. This is because the likelihood of complete response

is lower and the competing risk of death is higher than in patients with earlier-stage hepatocellular carcinoma. Pending further data, they recommend basing the decision on patients' preferences, tumor burden, degree of liver dysfunction, and life expectancy. At their institutions, the researchers do not treat patients with DAA therapy unless their life expectancy exceeds 2 years.

The experts disclosed research funding from the National Cancer Institute, U.S. Veterans Administration, and the National Institute of Diabetes and Digestive and Kidney Diseases. Dr. Singal reported personal fees or research funding from AbbVie, Bayer, Bristol-Myers Squibb, Eisai, Exact Sciences, Exelixis, Gilead, Glycotest, Roche, and Wako Diagnostics. His coauthors disclosed ties to AbbVie, Allergan, Bristol-Myers Squibb, Conatus, Genfit, Gilead, Intercept, and Merck.

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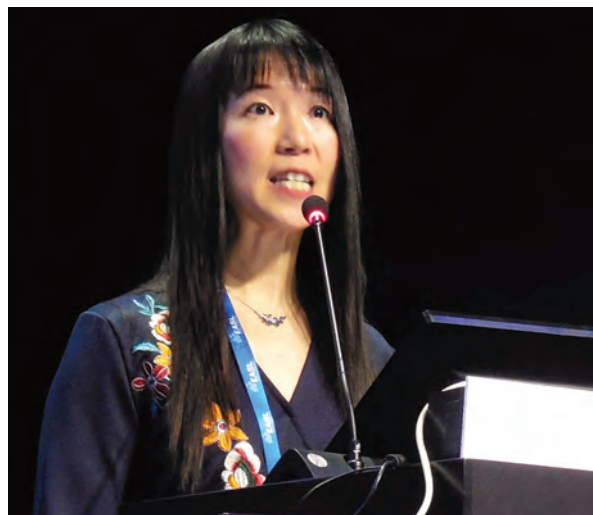
SOURCE: Singal AG et al. *Gastroenterology*. 2019 Mar 13. doi: 10.1053/j.gastro.2019.02.046.

The tenofovir difference

HBV from page 1

similar, statistically significant link between treatment with tenofovir disoproxil fumarate (Viread) and a lower incidence of HCC compared with patients treated with entecavir (Baraclude) (*JAMA Oncol*. 2019 Jan;5[1]:30-6), Grace L.H. Wong, MD, said at the meeting, sponsored by the European Association for the Study of the Liver (EASL).

However, another report published just a few days before Dr. Wong spoke failed to find an association between tenofovir disoproxil treatment of HBV and the subsequent rate of HCC compared with patients treated with entecavir. That study comprised nearly 2,900 HBV patients treated at any of four Korean medical centers (*J Hepatol*. 2019 Apr. doi: 10.1016/j.jhep.2019.03.028).



MITCHELL L. ZOLER/MDEDGE NEWS

Dr. Grace L.H. Wong of the Chinese University of Hong Kong suggested that tenofovir disoproxil may have subtly different effects than entecavir.

Dr. Wong noted that, although current guidelines from EASL cite both tenofovir disoproxil and entecavir (as well as tenofovir alafenamide [Vemlidy]) as first-line treatments for chronic HBV infection (*J Hepatol*. 2017 Aug;67[2]:370-98), some evidence suggests that tenofovir disoproxil might produce effects subtly different from those of entecavir.

At the meeting in Vienna, for example, a report on 176 Japanese patients with chronic HBV showed that those who were treated with a nucleotide analog such as tenofovir disoproxil produced higher serum levels of interferon-lambda3 compared with patients treated with entecavir, and increased levels of this interferon could improve clearance of HBV surface antigen (*J Hepatol*. 2019 April;70[1]:e477). The most recent EASL guidelines for treatment of chronic hepatitis B infection also list tenofovir disoproxil, entecavir, and tenofovir alafenamide as preferred agents (*Hepatology*. 2018 Apr;67[4]:1560-99).

The data Dr. Wong and her associates analyzed came from health records kept for about 80% of Hong Kong's population in the Clinical Data Analysis and Recording System of the Hospital Authority of Hong Kong. From January 2010 to June 2018, this database included 28,041 consecutive patients chronically infected with HBV and treated with entecavir, and 1,309 consecutive patients treated with tenofovir disoproxil. These numbers excluded patients treated for less than 6 months, patients coinfecting with hepatitis C or D virus, patients with cancer diagnosed or a liver transplanted before or during their first 6 months on treatment, and patients previously treated with an interferon or nucleos(t)ide.

During an average follow-up of 2.8 years of tenofovir disoproxil treatment, 8 patients developed HCC, and during an average follow-up of 3.7 years of entecavir treatment, 1,386 patients developed

HCC, reported Dr. Wong, a hepatologist and professor of medicine at the Chinese University of Hong Kong.

In a multivariate analysis that adjusted for demographic and clinical differences, treatment with tenofovir disoproxil linked with a statistically significant 68% reduced rate of HCC development compared with the entecavir-treated patients, she said. In a propensity score-weighted analysis, tenofovir disoproxil linked with a statistically significant 64% reduced rate of incident HCC, and in a propensity score-matched analysis tenofovir disoproxil linked with a 58% reduced rate of HCC, although in this analysis, which excluded many of the entecavir-treated patients and hence had less statistical power, the difference just missed statistical significance.

As an additional step to try to rule out the possible effect of unadjusted confounders, Dr. Wong and associates analyzed the links between tenofovir disoproxil and entecavir treatment and two negative-control outcomes, the incidence of lung cancer and the incidence of acute myocardial infarction. Neither of these outcomes showed a statistically significant link with one of the HBV treatments, suggesting that the link between treatment and HCC incidence did not appear because of an unadjusted confounding bias, Dr. Wong said. The Hong Kong database did not include enough patients treated with tenofovir alafenamide to allow assessment of this drug, she added.

Dr. Wong has been an adviser to Gilead and a speaker for Abbott, AbbVie, Bristol-Myers Squibb, Gilead, Janssen, and Roche. Tenofovir disoproxil fumarate is marketed by Gilead, and entecavir is marketed by Bristol-Myers Squibb.

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SOURCE: Wong GLH et al. *J Hepatol*. 2019 Apr;70(1):e128.

Palliative care blocked in end-stage liver disease

BY ANDREW D. BOWSER

MDedge News

Hepatologists and gastroenterologists see multiple and substantial barriers to the use of palliative care in patients with end-stage liver disease, results of a recent survey show.

Cultural factors, unrealistic expectations of the patient, lack of reimbursement, and competing demands for physicians' time were some of the barriers to palliative care cited most frequently in the survey, said the researchers, in their report on the survey results that appears in *Clinical Gastroenterology and Hepatology*.

Moreover, most responding physicians said they felt end-of-life advance care planning discussions take place too late in the course of illness, according to Nneka N. Ufere, MD, of the Gastrointestinal Unit,

Department of Medicine, Massachusetts General Hospital, Boston, and co-authors of the report.

"Multiple interventions targeted at patients, caregivers, institutions, and clinicians are needed to overcome barriers to improve the delivery of high-quality palliative and end-of-life care for patients with end-stage liver disease," the researchers said.

Specialty palliative care can improve quality of life for patients with life-limiting conditions such as end-stage liver disease, which is associated with poor quality of life and a median survival of just two years without liver transplant, the authors said.

Advance care planning, in which patients discuss goals and care preferences in light of the expected course of illness, was a "critical component" of palliative care that can im-

prove the quality of end-of-life care, Dr. Ufere and co-authors said.

Unfortunately, palliative care planning services are underutilized in end-stage liver disease, studies show, while rates of timely advance care planning discussions are low.

To find out why, Dr. Ufere and colleagues asked 1,238 physicians to fill out a web-based questionnaire designed to assess their perceptions of barriers to use of palliative care and to timely advance care planning discussions. A total of 396 physicians (32%) completed the survey between February and April 2018.

Sixty percent were transplant hepatologists, and 79% of the survey participants said they worked in a teaching hospital, according to Dr. Ufere and co-authors, who added that no respondents had formal palliative care training.

Almost all respondents (95%)

agreed that centers providing care for end-stage liver disease patients should have palliative care services, and most (86%) said they thought such patients would benefit from palliative care earlier in the disease course.

While most (84%) agreed that a hepatologist was the best provider to discuss advance care planning with the patient, only about one-quarter (27%) said the hepatologist was best suited to provide palliative care, while most (88%) said the palliative care specialist was best for that role.

When asked about patient and caregiver barriers, nearly all respondents (95%) agreed that cultural factors that influenced palliative care perception was an issue, while 93% said patients' unrealistic expectations was an issue.

Care Continued on following page

FMT shows promise for hepatic encephalopathy

BY MITCHEL L. ZOLER

MDedge News

VIENNA – A single, oral treatment with fecal microbiota transplant (FMT) was safe and well tolerated, and showed suggestive evidence of clinical improvement in patients with cirrhosis and recurrent hepatic encephalopathy in a phase 1 randomized study with 20 patients.

The oral fecal microbiota transplant (FMT), modeled on guideline-directed treatment for *Clostridium difficile* (Clin Infect Dis. 2018 Apr 1;66[7]:e1-48), was linked with a cut in hospitalizations and serious adverse events, as well as a clinically meaningful improvement in a cognitive measure specific for hepatic encephalopathy, Jasmohan S. Bajaj, MD, AGAF, said at the meeting sponsored

by the European Association for the Study of the Liver. Given the preliminary scope of the study, the next step is to assess the treatment in more patients and to evaluate delivery of the FMT specifically to the upper or lower gastrointestinal tract, said Dr. Bajaj, a hepatologist at Virginia Commonwealth University and McGuire VA Medical Center, both in Richmond.

The study included 20 patients



MITCHEL L. ZOLER/MDEDGE NEWS

Dr. Jasmohan S. Bajaj noted some signs of clinical improvement with FMT.

with recurrent hepatic encephalopathy (RHE) and a history of at least two encephalopathy episodes despite treatment with lactulose and rifaximin (Xifaxan). After a baseline assessment, 10 patients received a single, oral dose of FMT contained in 15 capsules and composed of fecal material from the OpenBiome collection, and 10 patients received placebo capsules. All of the FMT material came from a single donor and contained a high level of beneficial microbial types, specifically Lachnospiraceae and Ruminococcaceae species. Patients averaged 64 years of age.

During 5 months of follow-up, 6 of the 10 placebo patients had a serious adverse event versus 1 of the 10 patients treated with an active FMT; altogether, there were 11 serious adverse events in the placebo

Promise Continued on following page



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MEM19-9

Care

Continued from previous page

Clinician barriers that respondents perceived included competing demands for clinicians' time, cited by 91%; fear that palliative care might destroy the patient's hope, cited by 82%; and the misperception that palliative care starts when active treatment ends, cited by 81%.

One potential solution to the competing demands on clinicians' time would be development of "collaborative care models" between palliative care and hepatology services, according to Dr. Ufere and co-authors.

"Outpatient specialty palliative care visits, ideally temporally coordinated with the hepatology visits, can play a role not only in attending to symptom assessment and ACP, but also in addressing important psychosocial aspects of care, such as patient coping and well-being," they said in their report on the survey.

Promise

Continued from previous page

patients versus only 1 event in the FMT patients, Dr. Bajaj reported. Three patients in the control arm had a total of seven hepatic encephalopathy events, compared with a single patient with one event in the intervention arm.

Enrolled patients also underwent two cognitive tests at baseline and during follow-up. Using a Stroop smartphone app (EncephalApp) designed to assess patients with RHE (Hepatology. 2013 Sept;58[3]:1122-32), the researchers found an average 51-second improvement in OffTime+OnTime, a statistically significant and clinically meaningful improvement in the patients treated with FMT, whereas the control patients showed no significant change in this parameter. The second cognitive measure was the average performance by patients using the Psychometric Hepatic Encephalopathy Score (Curr Gastroenterol Rep. 2014 Jan;16[1]:362), which showed no significant change after treatment in either study arm. The actively treated patients also showed favorable changes in the microbial composition of their stool and mucosa, as well as an enhanced small intestinal barrier following treatment, Dr. Bajaj said.

Dr. Bajaj had no relevant disclosures.

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SOURCE: Bajaj JS et al. J Hepatol. 2019 April;70(1):e55.

Institutional barriers of note included limited reimbursement for time spent providing palliative care, cited by 76% and lack of a palliative care service, cited by nearly half (46%).

Some of the most commonly affirmed barriers to timely advance care planning discussions included

insufficient training in end-of-life communication issues, and insufficient training in cultural competency issues related to the discussions.

In terms of timeliness, only 17% said advance care planning discussions happen at the right time, while 81% said they happen too late, investigators found.

Funding for the research came from the National Institutes of Health. The authors had no disclosures related to the report.

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SOURCE: Ufere NN et al. Clin Gastroenterol Hepatol. 2019 Mar 15. doi: 10.1016/j.cgh.2019.03.022.



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Aspirin did not improve sensitivity of fecal immunochemical test

BY HEIDI SPLETE

MDedge News

A single oral dose of aspirin did not improve the sensitivity of the fecal immunochemical test to identify advanced colorectal neoplasms in a randomized trial of 2,134 adults.

The study was inspired by an observational study in which the sensitivity of the fecal immunochemical test (FIT) was enhanced in adults taking aspirin for cardiovascular disease prevention.

It was surmised that “aspirin predisposes to subclinical bleeding and, hence, increased detection of advanced adenomas by FIT. This suggests that administration of aspirin prior to fecal sampling might be a practical intervention to increase FIT sensitivity,” wrote Hermann Brenner, MD, of the German Cancer Research Center, Heidelberg, and colleagues.

In a study published in JAMA, the researchers analyzed 2,134 adults aged 40-80 years who were scheduled for colonoscopy. The study participants, who had no recent use of aspirin or other drugs with antithrombotic effects, were randomized to a 300-mg aspirin tablet or a placebo tablet 2 days before stool samples were obtained. The average age of the participants was 60 years, and 78% of the colonoscopies were for primary screening.

Overall, 224 of the study participants had advanced neoplasms, including 216 individuals with advanced adenoma and 8 with colorectal cancer.

Sensitivity was not significantly different between the aspirin and placebo groups at either of two predefined cutoffs of 10.2-mcg Hb/g stool (40.2% and 30.4%, respectively) and 17-mcg Hb/g stool (28.6% and 22.5%, respectively).

Although the results do not support the findings from previous observational studies, they suggest the need for more research of the potential impact of aspirin on FIT sensitivity.

Two serious adverse events occurred in the aspirin group but were not considered related to aspirin. No serious adverse events were reported in the placebo group.

Although the results do not support the findings from previous observational studies, they suggest the need for more research of the potential impact of aspirin on FIT sensitivity, the researchers said.

“This trial was designed to detect a 24% absolute increase in sensitivity and was not adequately

Key clinical point: Sensitivity of the FIT test was 40% in the aspirin group and 30% in the placebo group, a nonsignificant difference.

powered to detect small differences that may nevertheless be clinically meaningful given the low morbidity observed, the low cost of a single dose of aspirin, and the ease of implementation of this intervention across health systems,” they explained.

Additional limitations of the study included lack of adjustment for multiple testing in secondary analyses, inability to analyze subtypes of advanced neoplasms, and the inclusion of only one round of screening. FIT programs usually include multiple rounds, the researchers said. Therefore, “potential effects on detection of advanced neoplasms and reduction of CRC incidence and mortality in the long run are yet to be determined.”

Lead author Dr. Brenner disclosed grants from the German Federal Ministry of Education and Research, which funded the study, German Cancer Aid, the European Commission, the U.S. National Institutes of Health, Applied Proteomics, Roche Diagnostics, Volition, and Goodgut during the study period.

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SOURCE: Brenner H et al. JAMA. 2019;321(17):1686-92.

ctDNA predicts recurrence in nonmetastatic CRC

BY WILL PASS

MDedge News

Circulating tumor DNA (ctDNA) could be used to predict disease recurrence in patients with nonmetastatic colorectal cancer (CRC), according to investigators following an observational study.

About three out of four patients with a positive ctDNA test went on to have disease recurrence, reported lead author Yuxuan Wang, MD, PhD, of Johns Hopkins University School of Medicine in Baltimore, and her colleagues. On average, positive tests preceded clinical and radiologic evidence of recurrence by 3 months.

“[T]he optimal protocol for surveillance of resected colorectal cancer remains uncertain,” the investigators wrote in JAMA Oncology.

“The only recommended blood marker for CRC surveillance is serum [carcinoembryonic antigen (CEA)], an oncofetal protein that is elevated in the serum of patients with a variety of disease conditions, including CRC. Unfortunately, its utility is limited by the lack of sensitivity and specificity.” Although

computed tomography and magnetic resonance imaging can improve disease detection, these techniques also have their own shortcomings, the investigators noted, setting the stage for the present study.

The investigators recruited 63 patients with stage I, II, or III CRC

‘Because ctDNA measurements can be obtained from blood samples collected during routine follow-up, they may be easily incorporated into routine follow-up.’

who underwent surgical resection in Sweden between 2007 and 2013. Blood samples for ctDNA testing were collected 1 month after surgery, then every 3-6 months. CT was performed every 6-12 months. During this process, 5 patients were excluded, leaving 58 patients in the final dataset, 18 (31%) of whom received adjuvant chemotherapy. Patients were followed until metas-

tasis or a median of 49 months.

Among all patients, 13 tested positive for ctDNA, and 10 of these relapsed (77%), with a median time of 3 months between ctDNA positivity and CT or clinical evidence of recurrence. Three of the 48 patients (6%) who did not relapse had a positive ctDNA result that later dropped to an undetectable level. Of the 45 patients who tested negative for ctDNA, none had recurrence, although 1 was positive for CEA.

Results were also divided into patients who received or did not receive adjuvant chemotherapy. Among the 40 patients who did not receive chemotherapy, 8 had disease recurrence after a positive ctDNA test, although only 5 tested positive for CEA. Among the 18 patients who did receive chemotherapy, 2 tested positive for ctDNA and later relapsed, although only 1 tested positive for CEA. These figures translated to a ctDNA sensitivity for recurrence of 100%, compared with 60% for CEA testing.

“Serial ctDNA levels during follow-up can precede disease recurrence prior to routine radiographic imaging,” the investigators con-

Key clinical point: Circulating tumor DNA could be used to predict disease recurrence in patients with nonmetastatic colorectal cancer; the sensitivity of ctDNA testing was 100%.

cluded. “Because ctDNA measurements can be obtained from blood samples collected during routine follow-up, they may be easily incorporated into routine follow-up to complement a CEA test, radiographic imaging, and other conventional modalities to help stratify patients on the basis of the risk of disease recurrence. Such a personalized surveillance strategy may allow for earlier detection of relapse and minimize unnecessary testing.”

The study was funded by the Virginia and D.K. Ludwig Fund for Cancer Research, the Commonwealth Foundation, the John Templeton Foundation, and others. The investigators reported financial relationships with PapGene, Sysmex, Eisai, and others.

ginews@gastro.org

SOURCE: Wang Y et al. JAMA Onc. 2019 May 9. doi: 10.1001/jamaoncol.2019.0512.

Canagliflozin after metabolic surgery may aid weight loss, reduce glucose levels

BY DOUG BRUNK

MDedge News

LOS ANGELES – Patients who took the sodium-glucose cotransporter-2 inhibitor canagliflozin after undergoing metabolic surgery experienced reductions in blood glucose, body mass index, and truncal body

fat, results from a small pilot study have shown.

“We hypothesized that canagliflozin would be a good choice for these patients, because these drugs work independently of insulin,” the study’s principal investigator, Sangeeta R. Kashyap, MD, said in an interview at the annual scientific and

clinical congress of the American Association of Clinical Endocrinologists. “They help promote weight loss and improve blood pressure. [After] bariatric surgery, patients have an issue with weight regain, and sometimes their diabetes comes back.”

In what she said is the first prospective, randomized, controlled trial of its kind, Dr. Kashyap, an endocrinologist at the Cleveland Clinic, and her colleagues enrolled 11 women and 5 men with type 2 diabetes who had undergone Roux-en-Y gastric bypass or sleeve

gastrectomy to study the effects of canagliflozin on clinical parameters over a period of 6 months. At baseline, the patients’ mean body mass index was 39.2 kg/m² and their mean hemoglobin A_{1c} level was 7.4%. The researchers used maximum likelihood estimation in a linear mixed-effect model to deduce differences between the treatment and placebo groups. Patients randomized to the study drug were assigned a 6-month course of canagliflozin, starting on 100 mg for 2 weeks titrated up to 300 mg daily.

Continued on following page



DOUG BRUNK/MDEDGE NEWS

Dr. Sangeeta R. Kashyap reported on her study of canagliflozin at the scientific and clinical congress of the American Association of Clinical Endocrinologists.

Simpler, safer procedure

Weight loss from page 1

(AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT).

While previous studies have tracked ESG results for 1-2 years, her research team followed 203 patients who underwent the procedure between August 2013 and October 2018. “We felt that a longer-term study was needed to make sure weight loss was sustainable with this method of treatment, because research shows that, if you keep weight loss for an extended period of time, you’re more likely to keep it off permanently, which is ultimately what we want for these patients,” said Dr. Sharaiha, who is an attending physician at New York-Presbyterian/Weill Cornell Medical Center, New York.

At baseline, the mean age of the 203 patients was 46 years, 67% were female, and their mean body mass index was 39 kg/m². Dr. Sharaiha and colleagues observed that maximum weight loss was generally achieved by 24 months after the procedure, after which patients tended to regain a small amount of their lost weight. For example, at 1 year, the mean weight loss was 18.1 kg, with a total body weight loss of 15.2% (*P* less than .0001 for both associations). At 2 years, the mean weight loss was 17.3 kg, with a total body weight loss of 14.5% (*P* less than .0001 for both associations). At 3 years, the mean weight loss was 20.8 kg, with a total body weight

loss of 14.5% (*P* less than .0001 for both associations). At 5 years, the mean weight loss was 18.7 kg (*P* = .0003) and the total body weight loss was 14.5% (*P* = .0002).

Overall, patients gained an average 2.4 kg of weight after achieving their minimum weight after ESG until the end of follow-up. The researchers also found that failure to lose at least 10% of total body weight within the first 3 months after ESG decreased the chance of subsequent significant weight loss by 80%. Fewer than 1% of patients experienced complications, an improvement over surgical procedures.

“Our study showed very sustainable, significant weight loss for our patients between the 1 and 5 year mark,” Dr. Sharaiha said. “Out to 5 years, there was an average 15% total body weight loss. This is significant, because studies have shown that, when people lose at least 10% of their body weight, they see improvement in blood pressure, diabetes, and heart outcomes, which are the comorbidities associated with obesity. We hope these findings will help persuade insurance companies that ESG is not experimental, but has value over patients’ lifespans.”

Dr. Sharaiha and colleagues plan to follow the current cohort for the next 10-20 years. “We’re also part of a randomized study that’s currently under way looking at ESG in combination with diet and exercise.”

She reported having no financial disclosures.

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Continued from previous page

At 6 months, fasting glucose was significantly reduced in the canagliflozin group, compared with baseline (from 163 to 122 mg/dL; $P = .007$), but it rose in the placebo group (from 164 to

Canagliflozin also improved abdominal fat levels after bariatric surgery, and in this way might even lower cardiovascular disease risk in these patients.

192 mg/dL), a between-group difference that fell short of statistical significance ($P = .12$). In addition, C-reactive protein in the treatment group fell from 8.9 mg/L to 3.9 mg/L, but rose from 1.6 mg/L to 4.7 mg/L in the placebo group, a between-group difference that trended toward significance ($P = .07$).

During the 6-month study period, the mean BMI fell from 39.6 kg/m² to 38 kg/m² in the canagliflozin group but increased

from 38 to 41 in the placebo group, a between-group difference that reached statistical significance ($P = .014$). Mean changes in body fat (a reduction of 1.82%), truncal fat (a reduction of 2.67%), and android fat (a reduction of 3%) also reached statistical significance in the treatment group, compared with the placebo group. Reductions in adiponectin, leptin, and high-molecular weight adiponectin did not reach statistical significance.

"I think these drugs have a place in post-bariatric surgery care," Dr. Kashyap said. "Canagliflozin after metabolic surgery improved weight-loss outcomes and blood sugar levels. It also improved abdominal fat levels, and in this way might even lower cardiovascular disease risk in these patients."

She acknowledged the study's small sample size and single-center design as limitations. "It was very difficult to recruit patients for this study," she said. "Not many patients have recurrent diabetes after bariatric surgery."

Janssen provided funding to Dr. Kashyap for the trial.

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Adding meds to gastric balloons increases weight loss

BY LORA T. MCGLADE

FROM DDW 2019

SAN DIEGO – In a multicenter study involving four academic medical centers, the addition of weight-loss drugs to intragastric balloons resulted in better weight loss 12 months after balloon placement.

In a video interview (go to www.mdedge.com/gihepnews) at the annual Digestive Disease Week,[®] study



Dr. Reem Z. Sharaiha

investigator Reem Z. Sharaiha, MD, explained that one of the drawbacks of intragastric balloons is that, although they produce weight loss for the 6 or 12 months that they are in place, patients tend to regain that weight after they are removed. The study, involving 111 patients, was designed to determine whether the addition of weight-loss drugs could mitigate this effect and improve weight loss, said Dr. Sharaiha of Weill Cornell Medical Center, New York.

Adding drugs such as metformin or weight-loss drugs tailored to patients' particular weight issues (cravings, anxiety, or fast gastric emptying) at the 3- or 6-month mark while the intragastric balloon was in place helped patients continue losing weight after balloon removal. At 12 months, the percentage of total body weight lost was significantly greater in the intragastric balloon group with concurrent pharmacotherapy (21.4% vs. 13.1%).

lmcglade@mdedge.com

SOURCE: Shah SL et al. DDW 2019, Abstract 1105.

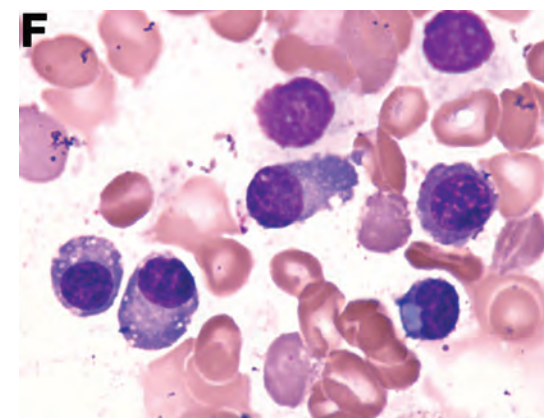
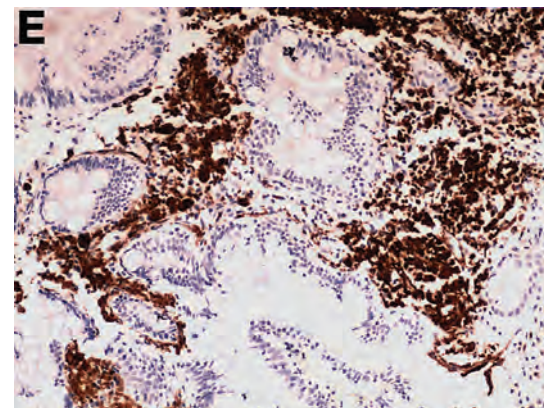
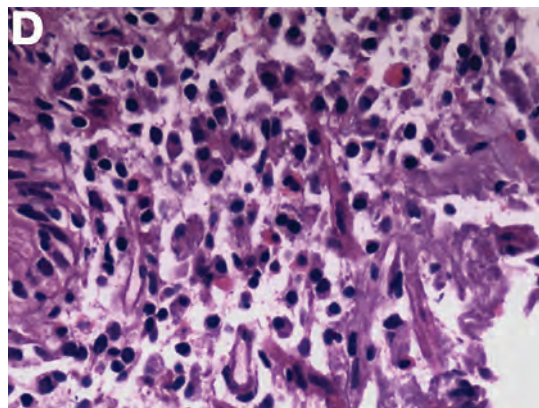
CLINICAL CHALLENGES AND IMAGES

The diagnosis

Answer to "What is your diagnosis?" on page 9: Multiple myeloma

An abdominal CT scan showed gastric and whole intestinal wall thickening of up to 2 cm. Pathology (Figures D,E) demonstrated that diffuse plasmacytoid cells, eosinophilic granulocytes, and lymphocytes infiltrated into the lamina propria. Immunohistochemically, the plasmacytoid cells were positive for the common plasma cell marker CD38, and in situ hybridization indicated that they were kappa-Ig light-chain restricted (Figure F). Results of the subsequent bone marrow aspirate revealed 27.5% atypical plasma cells. Serum electrophoresis and immunofixation showed an M spike of IgA-kappa. Together, these findings confirmed a final diagnosis of a multiple myeloma (MM) involving the whole gastrointestinal duct, which was the cause of his melena.

MM is a malignant hematologic neoplasm, primarily involving the bone marrow, and has a potent tendency to involve other organs and to present with various clinical manifestations.¹ The clinical features of MM with GI involvement are uncommon. Patients may present with nausea, vomiting, diarrhea, protein loss, malabsorption, intestinal obstruction, and hemorrhage. Endo-



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scopic findings can manifest as four types: a discrete ulcer, ulcerating mass, thickening of the mucosal fold, and mucosal polyp.² However, GI bleeding in MM has been reported in only a few patients. A biopsy reaching the submucosal layer and bone marrow biopsy is essential. Diagnosis of MM as a cause of the GI duct wall edema and multiple small intestinal polypoid ulcers is challenging. An interdisciplinary approach is mandatory to establish such a diagnosis.

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Ustekinumab trough levels predicted Crohn's response

BY AMY KARON

MDedge News

For patients with Crohn's disease, therapeutic drug monitoring helped identify early primary nonresponders to induction with ustekinumab, according to researchers. The report is in *Clinical Gastroenterology and Hepatology*.

At week 8, median trough levels of ustekinumab were 6.0 mcg/mL (interquartile range, 3.1-8.0) among patients who achieved a primary response to induction at week 16, versus 1.3 mcg/mL (IQR, 0.9-5.6) among primary nonresponders ($P = .03$). An 8-week ustekinumab trough level cutoff of 2.0 mcg/mL distinguished week 16 responders from nonresponders with an area under the receiver operating curve of 0.75, wrote Ninon Soufflet, MD, of University Claude Bernard Lyon 1 in France, and associates. The researchers recommended "dedicated studies" to assess whether escalating the dose

of ustekinumab can benefit patients with lower trough levels at week 8.

Few studies have explored biomarkers for response to ustekinumab induction therapy. Hence, the researchers assessed the relative utility of ustekinumab trough levels, C-reactive protein (CRP) levels, and fecal calprotectin levels for predicting early primary nonresponse. All 51 study participants had active luminal Crohn's disease and received body weight-based intravenous infusions of ustekinumab at baseline, followed by subcutaneous injections of 90 mg. Primary nonresponders did not achieve steroid-free clinical and biochemical remission at week 16, defined as a Harvey-Bradshaw Index of 4 points or less, a CRP level under 5 mg/L, and a fecal calprotectin level under 250 mcg/g. Week 16 was chosen to account for any delayed responders, the researchers noted.

A total of 32 patients (63%) achieved remission to ustekinumab induction therapy by week 16. An

8-week trough level of 2.0 mcg/mL was found to be optimal and distinguished primary nonresponders from responders with a sensitivity of 87%, a specificity of 66%, a positive predictive value of 82%, and a negative predictive value of 75%. In prior studies, optimal thresholds exceeded 3.3 mcg/mL for achieving remission and 4.5 mcg/mL at week 26 for achieving endoscopic response, the researchers noted. They said that this discrepancy might reflect different time points for evaluation, assays for measuring ustekinumab, patient populations, and a lack of endoscopic data in their study. "The relatively small sample size and the short period of follow-up evaluation [were] substantial limitations" they acknowledged.

In this study, levels of CRP did not change significantly between weeks 0 and 16 in either responders or nonresponders. In contrast, fecal calprotectin levels dropped rapidly and significantly over time only in responders. Median fecal calprotectin

AGA Resource

Learn more about therapeutic drug monitoring in IBD by reviewing the AGA Institute guideline at [www.gastrojournal.org/article/S0016-5085\(17\)35963-2/fulltext](http://www.gastrojournal.org/article/S0016-5085(17)35963-2/fulltext).

levels were 1,612 mcg/g of stools at week 0 versus 374 mcg/g at week 4 and 339 mcg/g at week 8. The finding "confirms the value of this biomarker," the researchers wrote.

The investigators did not acknowledge external funding sources. Dr. Soufflet reported having no conflicts of interest. The senior author and three coinvestigators disclosed ties to MSD, AbbVie, Tillots, and several other pharmaceutical companies.

ginews@gastro.org

SOURCE: Soufflet N et al. *Clin Gastroenterol Hepatol*. 2019 Mar 6. doi: 10.1016/j.cgh.2019.02.042.

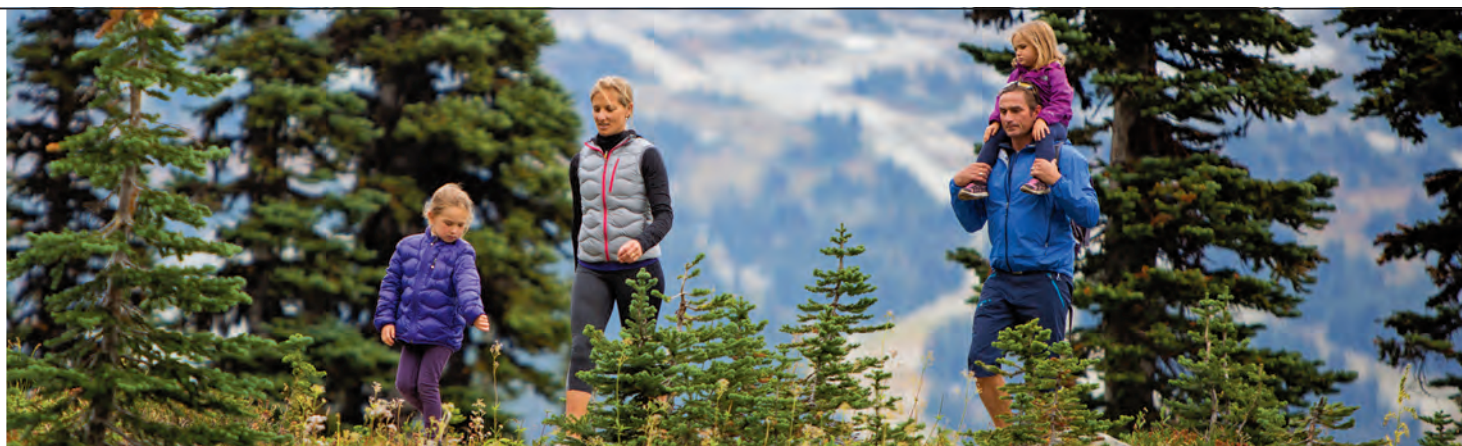
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PRACTICE MANAGEMENT TOOLBOX:

Teamwork makes the dream work – maximizing the relationship between physicians and advanced practice providers

BY KRISTIN BURKE, MD, MPH, AND
ANDREA THURLER, DNP, FNP-BC

Advanced practice providers (APPs: physician assistants and nurse practitioners) play a vital role in the success of an academic or private gastroenterology practice. Partnership with APPs in the clinical setting can improve inpatient and outpatient workflow and complex chronic care management, optimizing downstream revenue from endoscopy, radiology, and motility studies and enhancing physician productivity in research or academic affairs. In an informal AGA Community survey of physicians throughout the United States, 86% of respondents worked with advanced practice providers, 61% of whom had done so for over 5 years. While APPs may fill diverse roles in gastroenterology practice, there are common principles that may help optimize the physician-APP relationship. We surveyed both APPs and physicians to gain their perspective and present a tool kit to optimize the relationship among APPs and physicians.

The APP perspective

In qualitative interviews with 12 APPs practicing gastroenterology in a variety of specialties in Massachusetts, we aimed to understand 1) what APPs felt they brought to GI practice and 2) how APPs can be best utilized and integrated into GI practice and flow.

All interviewees independently noted that improving patient access to care and providing continuity of care were key benefits they brought to their practice, resulting in the possible downstream prevention of unnecessary emergency room admissions. Additionally, APPs felt that they brought significant value by having the time to listen to patient concerns to allow the team to prioritize care (83%), and provide patient education on their disease or medications (92%).

Though APPs are often utilized based on the individual needs of the practice, physician understanding of the APP skillset (83%) and a clear job description with set expectations up front (75%) were two critical elements of practice integration and job satisfaction on qualitative APP surveys. Additionally, APPs felt that

strong mentorship with opportunities for career growth could enhance career satisfaction and improve the overall retention of the APP (100%).

The physician perspective

Informed by themes identified from the qualitative APP survey, we posted an informal, anonymous online survey to physicians on the AGA Community Forum. Nearly all physicians that worked with an APP felt that they were beneficial to their practice. Ninety-seven percent of respondents found that APPs improved patient access to the clinic, while 47% found that APPs decreased phone calls and 43% found that APPs improved administrative burden. Other less commonly cited benefits of APPs included increased practice revenue, improved efficiency of inpatient care, and assistance with procedures.

In building relationships and developing trust with their APPs, respondents valued communication (94%), observed or measured competency through orientation or standardized training (55%), and increased time managing patients (48%). However, 52% of respondents were concerned regarding the time required to train an APP to their standards, 45% were concerned regarding knowledge deficits, and 48% were concerned regarding risk of turnover and burnout. Though patient satisfaction was noted as a possible benefit of a physician/APP team approach, physicians also noted a potential concern that it may compromise the existing physician/patient relationship.

Despite concerns regarding training and knowledge deficits, only 29% of respondents had a standard orientation for APPs, 26% had a clearly defined job description, and 32% had formal teaching in their specialty content area.

A model for success

Based on the results of these surveys and our practice experience, we present seven recommendations to optimize the APP/physician relationship:

1. Create a clear job description that ensures your APP works to the top of their license and training. This key principle can have a great impact on practice revenue and

APP job satisfaction.

2. Develop a plan to train the APP to your standards, whether it be through a dedicated content curriculum or a mentored preceptorship. Most APPs finish formal training with very little gastroenterology specialty expertise, and would benefit from content-based learning in the area of gastroenterology

Physician understanding of the APP skillset (83%) and a clear job description with set expectations up front (75%) were two critical elements of practice integration and job satisfaction on qualitative APP surveys.

in which they will work. The AGA publishes on-demand webcasts in different content areas, geared toward advanced practice providers (<https://www.gastro.org/aga-leadership/initiatives-and-programs/nurse-practitioner-and-physician-assistant-resource-center>). The AGA also hosts an annual conference to review GI content and prepare APPs to deliver optimal patient care (<https://nppa.gastro.org/>).

3. Designate objective criteria by which you will measure competency. Share this model with your APP up front to establish transparent expectations, and meet to review competencies and plans for further training at least annually. This structure presents a model for clinical growth and transparent expectations may enhance APP retention.
4. Establish APP mentorship. Just as for physicians, both clinical and career mentorship are an important part of job satisfaction and retention for APPs.

- Meet regularly. We recommend that mentors schedule weekly meetings with their APPs to review cases, questions/concerns, outstanding clinical work, quality-improvement initiatives, and/or research. These regular meetings will keep lines of communication open and may enhance APP retention.

- Provide feedback. Both APPs and physicians benefit from constructive feedback. An annual review should not bring any surprises. Keeping feedback honest

and constructive will further strengthen the relationship.

5. Introduce the APP as an integral member of the care team during the initial patient encounter. Whether working in a dedicated subspecialty team (inflammatory bowel disease, hepatology, motility, or hepatobiliary) or as part of a general gastroenterology practice, APPs should be introduced during the initial encounter as a key member of the team to establish rapport. The APP's name should also be listed in the after-visit summary, on business cards, and on stationery to strengthen the team image. Once a patient is established with an APP and a therapeutic relationship is built, patients often report positive outcomes and maintain follow-up with the APP/physician team. We recommend that the physician see the patient at least every other visit (alternating with the APP) to reinforce the team dynamic and dedication of all members of the team to the patient's health.

6. Provide a sense of community. Depending on the size of your practice, you can connect APPs within your practice, institution, or at a professional organization level. Belonging to a larger group that understands APP practice provides strong support and APP career satisfaction.
7. Create growth opportunities. In addition to clinical growth, APPs can provide value in leading quality-improvement and research initiatives. Establish goals and timelines for achieving goals up front, and be prepared to protect the APP's time to achieve these goals. Successful APP growth and development may enhance job satisfaction and lead to reduced turnover. In addition, establishment of APP leaders provides candidates to help design and implement an effective APP program as a practice grows.

The authors wish to recognize research coordinators Casey Silvernale and April Mendez, and Kyle Staller, MD, MPH, who assisted with the coordination of the surveys that contributed to this work. Dr. Burke is a gastroenterologist affiliated with Massachusetts General Hospital, Boston; Ms. Thurler is staff member of the Neurointestinal Health Center at Massachusetts General Hospital. The authors had no disclosures.

Treatment-resistant GERD reported by 54%

GERD is more common in women than men.

BY LORA T. MCGLADE
MDedge News
FROM DDW 2019

SAN DIEGO – Gastroesophageal reflux disease (GERD) refractory to proton pump inhibitors may affect nearly half of those treated, according to the findings of a population-based sample of more than 70,000 Americans.



Dr. Sean Delshad described results of a national questionnaire about symptoms of GERD and heartburn.

As part of the National Institutes of Health GI Patient Reported Outcomes Measurement Information System (NIH GI-PROMIS) questionnaire, respondents could download a free app called “My GI Health,” which led them through a series of questions about GI diseases. Sean Delshad, MD, MBA, of Cedars-Sinai Medical Center Los Angeles, and his colleagues examined data on symptom responses about GERD and heartburn. Their somewhat surprising findings were that 44% of respondents had ever had GERD and that 70% of

those respondents had symptoms in the past week. GERD seemed to be more common in women than in men, and in non-Hispanic whites

more than other demographic groups. The rate of proton pump inhibitor–refractory GERD was reported at 54%. Dr. Delshad discussed the implications of the study results for

treatment and research in a video interview (www.mdedge.com/gihepnews) at the annual Digestive Disease Week®.

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IMPORTANT SAFETY INFORMATION

SUPREP® Bowel Prep Kit (sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution is an osmotic laxative indicated for cleansing of the colon as a preparation for colonoscopy in adults. Most common adverse reactions (>2%) are overall discomfort, abdominal distention, abdominal pain, nausea, vomiting and headache. Use is contraindicated in the following conditions: gastrointestinal (GI) obstruction, bowel perforation, toxic colitis and toxic megacolon, gastric retention, ileus, known allergies to components of the kit. Use caution when prescribing for patients with a history of seizures, arrhythmias, impaired gag reflex, regurgitation or aspiration, severe active ulcerative colitis, impaired renal function or patients taking medications that may affect renal function or electrolytes. Use can cause temporary elevations in uric acid. Uric acid fluctuations in patients with gout may precipitate an acute flare. Administration of osmotic laxative products may produce mucosal aphthous ulcerations, and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Patients with impaired water handling who experience severe vomiting should be closely monitored including measurement of electrolytes. Advise all patients to hydrate adequately before, during, and after use. Each bottle must be diluted with water to a final volume of 16 ounces and ingestion of additional water as recommended is important to patient tolerance.

BRIEF SUMMARY: Before prescribing, please see Full Prescribing Information and Medication Guide for SUPREP® Bowel Prep Kit (sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution. **INDICATIONS AND USAGE:** An osmotic laxative indicated for cleansing of the colon as a preparation for colonoscopy in adults. **CONTRAINDICATIONS:** Use is contraindicated in the following conditions: gastrointestinal (GI) obstruction, bowel perforation, toxic colitis and toxic megacolon, gastric retention, ileus, known allergies to components of the kit. **WARNINGS AND PRECAUTIONS:** SUPREP Bowel Prep Kit is an osmotic laxative indicated for cleansing of the colon as a preparation for colonoscopy in adults. Use is contraindicated in the following conditions: gastrointestinal (GI) obstruction, bowel perforation, toxic colitis and toxic megacolon, gastric retention, ileus, known allergies to components of the kit. Use caution when prescribing for patients with a history of seizures, arrhythmias, impaired gag reflex, regurgitation or aspiration, severe active ulcerative colitis, impaired renal function or patients taking medications that may affect renal function or electrolytes. Pre-dose and post-colonoscopy ECGs should be considered in patients at increased risk of serious cardiac arrhythmias. Use can cause temporary elevations in uric acid. Uric acid fluctuations in patients with gout may precipitate an acute flare. Administration of osmotic laxative products may produce mucosal aphthous ulcerations, and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Patients with impaired water handling who experience severe vomiting should be closely monitored including measurement of electrolytes. Advise all patients to hydrate adequately before, during, and after use. Each bottle must be diluted with water to a final volume of 16 ounces and ingestion of additional water as recommended is important to patient tolerance. **Pregnancy:** Pregnancy Category C. Animal reproduction studies have not been conducted. It is not known whether this product can cause fetal harm or can affect reproductive capacity. **Pediatric Use:** Safety and effectiveness in pediatric patients has not been established. **Geriatric Use:** Of the 375 patients who took SUPREP Bowel Prep Kit in clinical trials, 94 (25%) were 65 years of age or older, while 25 (7%) were 75 years of age or older. No overall differences in safety or effectiveness of SUPREP Bowel Prep Kit administered as a split-dose (2-day) regimen were observed between geriatric patients and younger patients. **DRUG INTERACTIONS:** Oral medication administered within one hour of the start of administration of SUPREP may not be absorbed completely. **ADVERSE REACTIONS:** Most common adverse reactions (>2%) are overall discomfort, abdominal distention, abdominal pain, nausea, vomiting and headache. **Oral Administration:** Split-Dose (Two-Day) Regimen: **Early in the evening prior to the colonoscopy:** Pour the contents of one bottle of SUPREP Bowel Prep Kit into the mixing container provided. Fill the container with water to the 16 ounce fill line, and drink the entire amount. Drink two additional containers filled to the 16 ounce line with water over the next hour. Consume only a light breakfast or have only clear liquids on the day before colonoscopy. **Day of Colonoscopy (10 to 12 hours after the evening dose):** Pour the contents of the second SUPREP Bowel Prep Kit into the mixing container provided. Fill the container with water to the 16 ounce fill line, and drink the entire amount. Drink two additional containers filled to the 16 ounce line with water over the next hour. Complete all SUPREP Bowel Prep Kit and required water at least two hours prior to colonoscopy. Consume only clear liquids until after the colonoscopy. **STORAGE:** Store at 20°-25°C (68°-77°F). Excursions permitted between 15°-30°C (59°-86°F). **Rx only.** Distributed by Braintree Laboratories, Inc. Braintree, MA 02185.

SUPREP®
BOWEL PREP KIT
(sodium sulfate, potassium sulfate and magnesium sulfate)
Oral Solution
(17.5g/3.13g/1.6g) per 6 ounces

For additional information, please call 1-800-874-6756 or visit www.suprepkit.com



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THE ORIGINAL 1 LITER PRESCRIPTION BOWEL PREP SOLUTION



**#1 MOST PRESCRIBED,
BRANDED BOWEL PREP KIT¹**

WITH MORE THAN 15 MILLION KITS DISPENSED SINCE 2010¹



FIVE-STAR EFF¹CACY WITH SUPREP[®]

Distinctive results in all colon segments

- SUPREP Bowel Prep Kit has been FDA-approved as a split-dose oral regimen³
- 98% of patients receiving SUPREP Bowel Prep Kit had “good” or “excellent” bowel cleansing^{2*†}
- >90% of patients had no residual stool in all colon segments^{2*†}
 - These cleansing results for the cecum included 91% of patients^{2*†}

Aligned with Gastrointestinal Quality Improvement Consortium (GIQulC) performance target of ≥85% quality cleansing for outpatient colonoscopies.⁴

**SUPREP[®]
BOWEL PREP KIT**
(sodium sulfate, potassium
sulfate and magnesium sulfate)
Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

*This clinical trial was not included in the product labeling. †Based on investigator grading.

References: 1. IQVIA. National Prescription Audit Report. September 2018. 2. Rex DK, DiPalma JA, Rodriguez R, McGowan J, Cleveland M. A randomized clinical study comparing reduced-volume oral sulfate solution with standard 4-liter sulfate-free electrolyte lavage solution as preparation for colonoscopy. *Gastrointest Endosc.* 2010;72(2):328-336. 3. SUPREP Bowel Prep Kit [package insert]. Braintree, MA: Braintree Laboratories, Inc; 2017. 4. Rex DK, Schoenfeld PS, Cohen J, et al. Quality indicators for colonoscopy. *Gastrointest Endosc.* 2015;81(1):31-53.