aga American Gastroenterological Association

Official newspaper of the AGA Institute

mdedge.com/gihepnews

GI&Hepatology News

January 2020

Volume 14 / Number 1

Courtesy Mayo Clinic

Dr. Edward Melnick and fellow researchers measured and quantified the link between EHRs and burnout.

Quantifying the EHR connection to burnout

BY GREGORY TWACHTMAN
MDedge News

While plenty of anecdotal and other evidence exists to connect the use of electronic health records to physician burnout, new research puts a more standard, quantifiable measure to it in an effort to help measure progress in improving the usability of EHRs.

Researchers used the System Usability Scale (SUS), "favored as an industry standard as a short, simple, and reliable measurement of technology usability with solid benchmarks to easily interpret its results, as the measure in this research, Edward Melnick, MD, of Yale University, New Haven, Conn., and colleagues wrote in Mayo Clinic Proceedings.

"The previous studies have definitely hinted at [the link between EHRs and burnout], but never really quantified it," Dr. Melnick said in an interview.

Among the 870 physicians evaluating their EHRs' usability, the mean score on a scale of 0-100 (higher being more usable) was 45.9. As a point of comparison, Microsoft Excel has an SUS score of

See **Burnout** · *page 25*

Five drugs show promise in NAFLD; Two additional agents fall short

BY ANDREW D. BOWSER
MDedge News

BOSTON – For treatment of nonalcoholic fatty liver disease, cotadutide, licogliflozin, tropifexor, saroglitazar, and PF-05221304 are just a few of the drugs with promising data, Kathleen E. Corey, MD, MPH, said at the annual meeting of the American Association for the Study of Liver Diseases.

By contrast, selonsertib and emricasan did not achieve their endpoints in studies described here at the meeting, "but we have a lot to learn from them," said Dr. Corey, director of the Mass General Fatty Liver Clinic and assistant professor at Harvard Medical School, Boston.

"This is an exciting time," Dr. Corey said in a special debriefing oral session held on the final day of the conference. "There are many novel mechanisms of action out there, as well as some known mechanisms of action, with a considerable amount of promise."

Cotadutide (MEDI0382)

Narha and coauthors (Abstract 35) described the effects of cotadutide, a GLP-1/glucagon receptor dual

See **NAFLD** · *page 19*

Disposable duodenoscope shows clinical potential – now FDA approved

BY WILL PASS
MDedge News

A single-use duodenoscope may reduce the risk of postendoscopic infections while maintaining a high level of user satisfaction, based on a recent multicenter case series study.

At six tertiary referral centers in the United States, seven expert endoscopists performed more than 70 procedures with disposable scopes, ultimately reporting a median satisfaction score of 9 out of 10, according to lead author Venkataraman Muthusamy, MD, of UCLA Health in Los

See **Scope** · *page 20*

INSIDE

FROM THE AGA JOURNALS
Early colonoscopy for acute GI bleeding
Timing does not improve diagnostics or stop rebleeding. • **7**

AGA CLINICAL PRACTICE UPDATE
Management of pancreatic necrosis
Endoscopic approaches have replaced surgery. • **21**

CAG PRACTICE GUIDELINE
Bile acid diarrhea
Guideline calls for more studies. • **22**

IBD AND INTESTINAL DISORDERS
High mortality for geriatric IBD hospitalization
New approaches needed. • **24**

GI & HEPATOLOGY NEWS
10255 W Higgins Road,
Suite 280
Rosemont, IL 60018

CHANGE SERVICE REQUESTED

PRSRT STD
U.S. POSTAGE
PAID
HARRISBURG PA
PERMIT 500

LETTER FROM THE EDITOR: *Tectonic shift*


Dr. Allen

Every community practice gastroenterologist knows that private equity is making an aggressive push into our specialty. This is a tectonic shift in GI practice and the implications for private practice, academic training programs, and our GI societies are substantial. Gastro Health (Florida), Atlanta Gastro (Georgia), and GI Alliance (Texas) all closed deals with private equity in 2018 and there are reported to be 16-20 deals completed or in process currently. The three "first movers" formed practice management companies that now have acquired numerous large and small practices around the country. We have one practice with more than 200 physicians, and we will see single groups of 500-1,000 in the near future.

Imagine what a digestive health multi-state practice of 500 physicians (gastroenterologists, pathologists, surgeons), 200 advance practice providers (APPs), plus other ancillary professionals (psychology, nutrition) could accomplish. Gross revenues could top $1 billion. All back-office operations would be consolidated and managed professionally. Each provider would work top of license so much routine care would be shifted away from MDs. Negotiating power with payers, vendors,

Continued on following page

CLINICAL CHALLENGES AND IMAGES

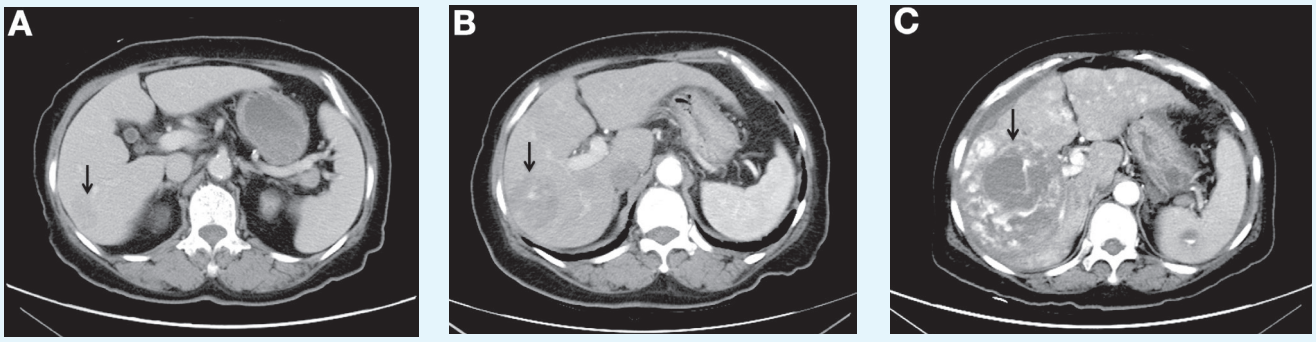
What is your diagnosis?

By Yang-Yuan Chen, MD, and Cheng-Che Chen. Published previously in Gastroenterology (2018;154[6]:1590-1).

A 72-year-old woman presented at the emergency department with diffuse abdominal tenderness. Her medical history revealed end-stage renal disease with hemodialysis for 10 years. She had previously undergone bilateral nephroureterectomy for left renal pelvis urothelial carcinoma and total thyroidectomy for papillary thyroidal cancer. She was regularly followed after bilateral nephroureterectomy. Abdominal computed tomography revealed a low-density liver nodule over segment 7 (Figure A). No interval size change was observed in the abdominal CT scan 3 months later.

An abdominal CT scan 13 months later revealed greater enlargement of the tumor with mild enhancement after contrast injection (Figure B). Physical examination was unremarkable. Findings of chronic hepatitis B or C were negative. Hepatic function tests revealed that aspartate aminotransferase, total bilirubin, and gamma-glutamyl transferase were within normal limits. The carcinoembryonic antigen level was 4 ng/mL, and the alpha-fetoprotein level was 3 ng/mL. A liver tumor biopsy was performed. She declined further resection of the liver tumor owing to a poor prognosis and body performance. She experienced sudden-onset diffuse abdominal rebounding pain and visited the emergency department. An emergency CT scan revealed a large right tumor with a considerable amount of contrast medium and much ascites (Figure C).

The diagnosis is on page 15.



aga American Gastroenterological Association
Official newspaper of the AGA Institute
mdedge.com/gihepnews
GI&Hepatology News

MDedge®

Editor in Chief, GI & Hepatology News
John I. Allen, MD, MBA, AGAF
Editor in Chief, The New Gastroenterologist
Vijaya L. Rao, MD

Associate Editors
Megan A. Adams, MD, JD, MSc
Ziad Gellad, MD, MPH, AGAF
Kim L. Isaacs, MD, PhD, AGAF
Charles J. Kahi, MD
Gyanprakash A. Ketwaroo, MD, MSc
Larry R. Kosinski, MD, MBA, AGAF
Sonia S. Kupfer, MD
Wajahat Mehal, MD, PhD

Editors Emeritus, GI & Hepatology News
Colin W. Howden, MD, AGAF
Charles J. Lightdale, MD, AGAF

Editor Emeritus, The New Gastroenterologist
Bryson Katona, MD, PhD

AGA Institute Staff
Managing Editor, GI & Hepatology News, Brook A. Simpson
Managing Editor, The New Gastroenterologist, Ryan A. Farrell
Senior Publications Coordinator Jillian L. Schweitzer
Director of Publications Lindsey M. Brounstein
Vice President of Publications Erin C. Landis

Officers of the AGA Institute
President Hashem B. El-Serag, MD, MPH, AGAF
President-Elect M. Bishr Omary, MD, PhD, AGAF
Vice President John M. Inadomi, MD, AGAF
Secretary/Treasurer Lawrence S. Kim, MD, AGAF

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

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

POSTMASTER Send changes of address (with old mailing label) to GI & Hepatology News, Subscription Service, 10255 W Higgins Road, Suite 280, Rosemont, IL 60018-9914.
RECIPIENT To change your address, contact Subscription Services at 1-800-430-5450. For paid subscriptions, single issue purchases, and missing issue claims, call Customer Service at 1-833-836-2705 or e-mail custsvc.gihep@fulcoinc.com
The AGA Institute headquarters is located at 4930 Del Ray Avenue, Bethesda, MD 20814, ginews@gastro.org.

GI & Hepatology News (ISSN 1934-3450) is published monthly for $230.00 per year by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609.
Phone 973-206-3434, fax 973-206-9378

Scan this QR Code to visit mdedge.com/gihepnews

Frontline Medical Communications Society Partners
VP/Group Publisher; Director, FMC Society Partners Mark Branca
Executive Editors Denise Fulton, Kathy Scarbeck
Editor Lora T. McGlade
Creative Director Louise A. Koenig
Director, Production/Manufacturing Rebecca Slebodnik
National Account Manager Artie Krivopal, 973-290-8218, cell 973-202-5402, akrivopal@mdedge.com
Digital Account Manager Rey Valdivia, 973-206-8094, rvaldivia@mdedge.com
Senior Director of Classified Sales Tim LaPella, 484-921-5001, tlapella@mdedge.com
Advertising Offices 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609 973-206-3434, fax 973-206-9378
Editorial Offices 2275 Research Blvd, Suite 400, Rockville, MD 20850, 240-221-2400, fax 240-221-2548

FRONTLINE MEDICAL COMMUNICATIONS

Corporate
SVP, Finance Steven J. Resnick
VP, Sales Mike Guire
VP, Society Partners Mark Branca
VP, Digital Content & Strategy Amy Pfeiffer
President, Custom Solutions JoAnn Wahl
VP, Custom Solutions Wendy Raupers
VP, Human Resources & Facility Operations Carolyn Caccavelli
Data Management Director Mike Fritz
Circulation Director Jared Sonners
Corporate Director, Research & Comms. Lori Raskin
Director, Custom Programs Patrick Finnegan

In affiliation with Global Academy for Medical Education, LLC
President David J. Small, MBA

Fibrosis scoring systems have 'modest' predictive value

BY ANDREW D. BOWSER
MDedge News

Currently available fibrosis scoring systems appear to have only a modest predictive ability for development of severe liver disease in the general population, according to authors of a large, retrospective cohort study.

Of five noninvasive scoring systems evaluated, all did have high negative predictive value in the general population, according to authors of the study, which included data on more than 800,000 individuals in Sweden. However, their sensitivities were low, with most of the individuals who developed severe liver disease over a 10-year follow-up period initially classified as being at low risk for advanced fibrosis, according to the study authors, led by Hannes Hagström, MD, PhD, of the division of hepatology, Karolinska University Hospital, Stockholm, and reported in Gastroenterology.

The population-based cohort study by Dr. Hagström and colleagues was based on data from 812,073 patients enrolled in the Swedish Apolipoprotein Mortality Risk (AMORIS) cohort between 1985 and 1996. Investigators said they excluded patients under 35 and over 79 years of age, patients with severe liver disease at baseline, and those with a prior diagnosis of alcohol or drug abuse.

Investigators used available data to calculate five scores, including the AST to Platelet Ratio Index (APRI); the body mass index, AST/ALT ratio, and diabetes (BARD) score; the Fibrosis-4 (FIB-4) score; Forns Index; and NAFLD Fibrosis Score (NFS).

At baseline, 0.5%-8.0% of patients were considered to be at high risk for advanced fibrosis, depending on the test used, investigators said. With up to 10 years of follow-up, the proportion of individuals who developed severe liver diseases (cirrhosis, liver failure, hepatocellular carcinoma, liver transplantation, or decompensated liver disease) was 0.3%-0.6%, and with the maximum 27 years of follow-up, the incidence ranged from 1.0% to 1.4%.

There was a "strong association" between baseline risk of fibrosis and development of severe liver diseases; however, the majority of cases occurred in patients deemed low risk at baseline, Dr. Hagström and colleagues noted in their report.

For example, 12.4% of individuals classified as high risk by APRI developed severe liver diseases over 10 years, compared to just 0.4% of the low-risk group, yet out of 723 cases, 502 (69%) occurred in the low-risk patients, the data show.

Hazard ratios did increase with risk level, and at the high-risk level, adjusted hazard ratios ranged from 1.7 (95% confidence interval, 1.1-2.5) for the high-risk BARD patients to 45.9 (95% CI, 36.1-58.3) for the high-risk APRI patients, investigators reported.

Of all tests, APRI was least likely to falsely classify patients who never developed severe liver diseases and had an intermediate-risk group of 4%, the lowest of any test, which are findings that may have implications for routine primary care, according to investigators.

The study was supported by an independent grant from AstraZeneca. Dr. Hagström reported disclosures related to that company, as well as Novo Nordisk, Gilead Sciences, IQVIA, Intercept, and Bristol Myers-Squibb.

ginews@gastro.org

SOURCE: Hagström H et al. Gastroenterology. 2019 Sep 26. doi: 10.1053/j.gastro.2019.09.008.

Continued from previous page

hospital systems, and referring providers would be immense (care would be taken to avoid the appearance of a monopoly, but Department of Justice scrutiny has already been evident). Referral sources (CVS, Optum, health systems, and a few remaining independent practices) would be secured by contract or favored reimbursement rates. Academic health systems will find competition challenging save for high tertiary and quaternary care, but even these complex procedures often will have been consolidated (and contained within risk bundles) to a half dozen health systems by direct-to-employer contracting. Current society offerings such as meetings, journals, and clinical guidelines will become obsolete because of practice-distributed virtual education, open publishing, and internal outcomes measurement. The vast provider network will be on a single data platform so it can generate true outcomes based on a payer's patient base (not guideline-restricted process measures), and these outcomes will be used for negotiating restricted networks.

I hope these trends will be a clarion call for our societies and training programs to awaken to a new world order and adapt their efforts to meet demands from our patients and the critical (and changing) needs of current and future digestive health professionals.

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

Early colonoscopy for acute lower GI bleeding fails to reduce rebleeding

BY ANDREW D. BOWSER
MDedge News

While generally recommended for diagnosis and treatment of severe bleeding, early colonoscopy did not improve stigmata identification or reduce rebleeding rates in patients admitted for acute lower gastrointestinal bleeding in a relatively large, multicenter randomized trial, investigators report.

The proportion of patients with identified stigmata of recent hemorrhage (SRH) was not significantly different between groups of patients who had early colonoscopy versus those who had a procedure 24 hours or more after admission, according to results of the 170-patient randomized study.

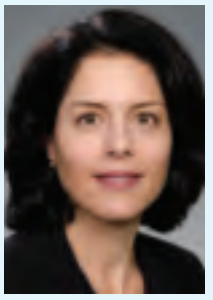
Although rebleeding rate was a secondary endpoint, a larger study would be "unlikely to show a benefit" of the urgent approach, said investigators led by Ryota Niikura, MD, PhD, of the department of gastroenterology in the graduate school of medicine at the University of Tokyo.

"Our results for rebleeding sug-

Continued on following page

When to perform colonoscopy for the evaluation of acute lower gastrointestinal bleeding (LGIB) is controversial. Multiple studies have produced mixed results. Therefore, a large, multicenter trial is of high priority.

This study by Niikura et al. is the largest and first multicenter trial on this topic. The authors found no difference between the early vs. elective colonoscopy arms in the primary outcome, identification of SRH. SRH is a surrogate outcome; however, previous studies have found SRH to be predictive of rebleeding, and any decrease in rebleeding would likely be due to endoscopic treatment of these lesions. Furthermore, although the study was not powered to detect differences in clinical outcomes such as rebleeding, the 95% confidence interval suggests at most a 1.4% decrease in rebleeding with early colonoscopy. It is possible that early colonoscopy is beneficial in certain patient populations or in expert hands. However, in subgroup analyses there was no benefit for early colonoscopy in patients with severe bleeding, a diverticular source, or a colonoscopy performed by an expert.


Dr. Strate

Overall, the results suggest that, in most patients presenting with acute LGIB, we do not need to perform colonoscopy within 24 hours of admission. However, the mean time to colonoscopy in the elective group was 41 hours from presentation. Therefore, colonoscopy should be performed on a next available basis. Further delays add unnecessary hospital days and increase cost of care.

Lisa L. Strate, MD, AGAF, is professor of medicine, University of Washington, and section chief, gastroenterology, Harborview Medical Center, Seattle. She has written on lower GI bleeding for UpToDate.

Loss of pancreatic E-cadherin contributes to carcinogenesis

BY WILL PASS
MDedge News

Loss of pancreatic E-cadherin may interfere with normal growth and maintenance of the pancreas while contributing to multiple pathological processes, based on evidence from mouse models.

In the presence of an oncogene, E-cadherin may play a pivotal role in pancreatic tumor formation, according to lead author Yoshihiro Kaneta, of Yokohama (Japan) City University, and colleagues. These findings could lead to new treatment strategies for patients with pancreatic cancer who lack E-cadherin, they noted.

Previous studies have shown that E-cadherin is involved in tissue homeostasis, although exact mechanisms vary by organ, and have remained unclear in the pancreas, the investigators explained in Cellular and Molecular Gastroenterology and Hepatology.

According to the investigators, E-cadherin expression is up-regulated in chemically induced acute pancreatitis, while in chronic pancreatitis, which is associated with an increased risk of pancreatic adenocarcinoma, E-cadherin expression is either low or absent. Other research has pointed to a link between dysregulated E-cadherin expression and cancer progression, with a loss of E-cadherin implicated in development of diffuse-type gastric cancer; however, evidence of a similar process in pancreatic cancer has not been reported.

To determine the role of E-cadherin in pancreatic function and tumor development, the investigators conducted experiments with knockout mice lacking pancreatic E-cadherin.

For the first 2 days after birth, knockout mice were similar both phenotypically and histologically to control mice. But over time, differences became apparent. Starting at day 3, control mice were comparatively larger than knockout mice, and by day 12, knockout mice began to die, with none surviving beyond day 28. Starting at day 6, histologic changes were observed in the pancreatic tissue of knockout mice, specifically, with aberrant epithelial tubules that resembled acinar-to-ductal metaplasia (ADM). Moreover, acinar cells were dilated and lacked surface expression of E-cadherin.

"These results suggested that E-cadherin was not required for pancreatic development at the embryonic stage but was required for growth and maintenance of the pancreas in the postnatal stage," the investigators wrote.

Additional analyses revealed further differences between pancreatic tissue from knockout mice and control mice. A variety of aberrant processes were observed in knockout mice, including replacement of acini with alpha-smooth muscle actin–positive fibrotic cells, an increased number of ductal-like structures, a reduced number of amylase-positive cells, and an increased number of cytokeratin-19–positive and CD45-positive cells. Messenger RNA expression levels were also abnormal in pancreatic tissue of knockout mice, with shifts across a variety of cytokines and chemokines. These trends toward inflammation and fibrosis were described by the investigators as pancreatitis-like changes, although they observed no pancreatic intraepithelial neoplasia (PanIN), which is a precursor of pancreatic ductal adenocarcinoma.

In the presence of an oncogene, however, loss of pancreatic E-cadherin did contribute to the development of pancreatic cancer. In the presence of a Kras mutation, knockout mice began to develop PanINs and ADMs as soon as day 4. By day 7, PanINs stained partially positive for E-cadherin, showed structural abnormalities, and exhibited decreased amylase and increased cytokeratin-19. Within a similar time

Continued on following page

E-cadherins have remained an enigma in cancer biology. Initially thought to be modulators of organism growth, studies in the past several years have established their role in tumor growth and metastasis. Cadherins are a large family of glycoproteins that mediate specific cell-cell adhesion in a calcium-dependent manner. Among this family, E-cadherins were among the first ones to be discovered almost 50 years back. During embryonic development, the spatiotemporal regulation of E-cadherin regulates cell migration and morphogenesis. In malignant cells, loss of E-cadherin leads to metastasis.

This has spurred studying of E-cadherin as a tumor suppressor. Loss of E-cadherin–mediated cell adhesion often correlates with loss of epithelial morphology and acquisition of metastatic properties. In the pancreas specific context as described by Kaneta et al, loss of E-cadherin leads to loss of acinar cells, elevated serum amylase accompanied with increased inflammation, showing a pancreatitis like phenotype. In the presence of activated oncogenic K-Ras, however, deletion of E-cadherin showed abundant desmoplasia resembling aggressive tumors in the early postnatal stage.

This is also reflected in the patient population. Studies have shown that 43% of the pancreatic adenocarcinomas analyzed had partial or complete loss of E-cadherin expression. Patients with a complete loss of this protein showed ~5.5 months median survival whereas those with partial loss had a survival of 12.7 months, indicating that loss of E-cadherin had a trend toward correlating with poor outcome (Modern Pathol. 2011;24:1237-47). Similarly, Epithelial-mesenchymal transition orchestrated by loss of E-cadherin has been shown to be a driver of tumor initiation (Nat Rev Cancer. 2013;13:97-110). Thus, the study by Kaneta et al. demonstrating the loss of E-cadherin is a step forward in understanding the role of this protein in light of not only pancreatic carcinogenesis but pancreatic pathology in general.

Sulagna Banerjee, PhD is associate professor, department of surgery, University of Miami. She is a consultant with Minneamrita Therapeutics LLC.

Continued from previous page

gested that early colonoscopy does not improve rebleeding outcomes, even if we chose rebleeding as the primary outcome," Dr. Niikura and colleagues said in Gastroenterology.

Leading up to this trial, there was "controversy" over whether early colonoscopy could improve significant clinical outcomes such as rebleeding, transfusion need, and mortality, according to the authors, who said this is the largest of four randomized, controlled trials reported on the subject to date, and the first multicenter trial.

Two of three of the previous randomized trials also showed no improvement in diagnostic yield with early colonoscopy, though "some meta-analyses" do suggest such a benefit, Dr. Niikura and coauthors said.

The trial by Dr. Niikura and coinvestigators included patients 20 years of age or older who had moderate to severe hematochezia or melena within 24 hours of admission. A total of 162 adult patients at 15 hospitals in Japan were randomized to undergo early colonoscopy within 24 hours, or elective colonoscopy between 24 and 72 hours.

The primary outcome, identification of SRH, was not significantly different for the early versus later colonoscopy. Investigators said SRH was observed in 17 of 79 (21.5%) patients undergoing early colonoscopy, and in 17 of 80 (21.3%) patients in the elective colonoscopy group ($P = .967$).

Similar rates of SRH between early and elective colonoscopy is "in line" with the two of three previous randomized trials that found no increase in diagnostic yield, Dr. Niikura and coworkers noted.

Rebleeding within 30 days, the "key secondary outcome" of the study according to investigators, was seen in 11 of 72 patients in the early colonoscopy group, and in 5 of 75 patients in the elective colonoscopy group, for a difference of 8.6 percentage points (95% confidence interval, –1.4 to 18.7).

Taken together, these findings suggest that early colonoscopy did not improve the SRH identification rate and that the 30-day rebleeding rate was not different, the authors said.

"Guidelines and prior studies often recommend that early colonoscopy be performed within 8-24 hours of admission to increase diagnostic yield and the likelihood of a therapeutic intervention," they added in their discussion.

Dr. Niikura and coauthors acknowledged receiving grant funding from the Japanese Gastroenterological Association. One study coauthor reported disclosures related to Takeda, AstraZeneca, Zeria, Daiichi-Sankyo, and EA Pharma. The remaining authors declared no competing interests.

ginews@gastro.org

SOURCE: Niikura R et al. Gastroenterology. 2019. doi: 10.1053/j.gastro.2019.09.010.

In UC patients, tofacitinib tied to modest, reversible lipid increases, infrequent cardiovascular events

BY ANDREW D. BOWSER
MDedge News

Serum lipid increases seen after 8-61 weeks of tofacitinib treatment for ulcerative colitis (UC) are modest, reversible, and correlated with reduced systemic inflammation, according to results of an analysis including more than 1,000 patients.

Major adverse cardiac events (MACEs) were "infrequent" following treatment, according to the authors of the analysis, with an incidence rate similar to what has been reported for tofacitinib in rheumatoid arthritis and for other agents in UC.

The period of observation in the analysis is "relatively short," and so may not provide an accurate risk estimate for MACEs, noted the investigators, led by Bruce E. Sands, MD, AGAF, of the division of gastroenterology at the Icahn School of Medicine at Mount Sinai, New York.

"Longer-term studies, involving a larger number of patients, will be needed to further assess MACE risk in patients with ulcerative colitis," Dr. Sands and coinvestigators wrote in their report on the observational analysis, which appears in Clinical Gastroenterology and Hepatology.

"It is noteworthy that no increase in MACE risk and no dose relationship with tofacitinib have been observed in a larger rheumatoid arthritis cohort with over 8.5 years of observation and more than 19,000 patient-years of collective exposure," they continued.

The present analysis included 1,157 patients with UC who participated in 8-week phase 2 and 3 tofacitinib induction studies, a phase 3 maintenance study, and a long-term extension study that is ongoing.

Reversible and dose-dependent increases in both LDL cholesterol and HDL cholesterol were observed after 8 weeks of treatment with tofacitinib at the recommended induction dose of 10 mg twice daily, the investigators found.

Increases in LDL cholesterol, HDL cholesterol, and total cholesterol correlated with decreases in high-sensitivity C-reactive protein, suggesting any potential impact of lipid increases on cardiovascular events might be offset by reduced inflammation, according to the investigators.

"Previous studies in RA and inflammatory bowel disease have shown an inverse relationship between active inflammation and serum lipid profiles, suggesting that inflammation lowers lipid concentrations, and that treatment of the underlying inflammatory disease may, therefore, increase them," Dr. Sands and colleagues wrote.

The lipid changes also correlated with increases in body mass index, possibly because of better nutrition, reduced protein loss, and less catabolism following tofacitinib treatment, along with the corticosteroid taper required in these studies of the drug, they added.

Lipid increases generally stayed elevated through 61 weeks of treatment, while in patients randomized to placebo after 8 weeks of tofacitinib treatment, lipid levels fell back toward baseline, which suggests a reversal of the increases after tofacitinib withdrawal, the investigators wrote.

Four MACEs were seen among the 1,157 patients in the analysis, for an incidence rate of 0.24 (95% confidence interval, 0.07-0.62), according to the report. Those events included an acute coronary syndrome, an MI, an aortic dissection, and a hemorrhagic stroke. All four occurred in tofacitinib-treated patients, though the investigators noted that the aortic dissection and hemorrhagic stroke are events typically associated with genetics or other nonlipid factors.

In any case, that MACE incidence rate was "similar" to infliximab (Remicade) for what has been observed in tumor necrosis factor antagonist treatment of UC within a U.S. claims database study. In that analysis, including patients treated with infliximab, golimumab, and adalimumab, the incidence rate was 0.51 (95% CI, 0.31-0.79), the investigators noted.

These findings support recommendations in tofacitinib prescribing information that call for monitoring of lipid concentrations 4-8 weeks after treatment is started, according to Dr. Sands and coauthors.

Funding for the study came from Pfizer. The study authors disclosed potential conflicts of interest related to Pfizer, AbbVie, Bristol-Myers Squibb, Celgene, Janssen, MedImmune (AstraZeneca), Takeda, and 4D Pharma, among others.

ginews@gastro.org

SOURCE: Sands BE et al. Clin Gastroenterol Hepatol. 2019 May 8. doi: 10.1016/j.cgh.2019.04.059.

Tofacitinib has several well-described effects on lipid metabolism, increasing levels of LDL cholesterol, HDL cholesterol, and total cholesterol. The clinical consequences of these lipid changes remains uncertain in ulcerative colitis (UC), for which there may be an increased risk of cardiovascular events.


Dr. Scott

In this study, Sands and colleagues used the largest cohort to date to quantify the effect of tofacitinib-associated lipid profile changes, their association with inflammatory markers, and the risk of major adverse cardiovascular events (MACEs). Using pooled data from multiple controlled, open-label studies of tofacitinib in UC, the authors appreciated a significant association between the rise in HDL cholesterol, LDL cholesterol, and total cholesterol levels and declines in C-reactive protein. They noted only four MACEs, an incidence rate similar to that seen in prior anti–tumor necrosis factor trials, and no change in a commonly used risk score for cardiovascular events.

These results are an important initial step in quantifying the cardiovascular risk associated with tofacitinib, but should be interpreted with caution. A significant proportion of individuals evaluated were from induction studies, with only 8 weeks of exposure. Only one dose of tofacitinib was required for inclusion. The median age in the OCTAVE trials, which contributed the majority of the data for this cohort, was only 41 years, and the baseline cardiovascular risk was low. While these data and rheumatologic literature are reassuring, further research with longitudinal follow-up, the assessment of time-varying exposures, and stratification by baseline cardiovascular risk will be required to better understand the association between tofacitinib and MACEs.

Frank I. Scott, MD, MSCE, assistant professor of medicine, Crohn's and Colitis Center, codirector of clinical research/DART, director of GI fellowship research, division of gastroenterology and hepatology, University of Colorado at Denver, Aurora. He has received research funding and consulting fees from Takeda, and Janssen, and consulting fees from Merck.

Continued from previous page

frame, pancreatic tissue began to adhere to the intestine, resulting in ascites and death. No metastases to other organs were observed.

Further testing showed that pancreatic stroma contained tumor cells. While DNA double-strand breaks were scarce, the investigators pointed out that chemotherapy and radiotherapy are typically responsible for DNA damage. Based on previous research linking stem cell conversion with Kras-acquired resistance, the investigators tested markers of stem cells in pancreatic tissue of knockout mice, finding that CD44, KLF4, and KLF5 were increased.

"These observations suggested that loss of E-cadherin provided tumorigenic activity to pancreatic cells and contributed to PanIN formation," the investigators wrote.

Additional experiments with cell lines supported the above results and added further insight. Of clinical relevance, the investigators suggested that targeting Hdac1 with histone deacetylase inhibitors may be a viable treatment strategy for patients lacking pancreatic E-cadherin.

The study was funded by the Japan Society for the Promotion of Science KAKENHI grant JP17K09465 and the Yokohama City University Kamome project. The investigators declared no conflicts of interest.

ginews@gastro.org

SOURCE: Kaneta Y et al. Cell Mol Gastroenterol Hepatol. 2019 Sep 14. doi: 10.1016/j.jcmgh.2019.09.001.

No clear-cut evidence of vedolizumab effect in retrospective study of primary sclerosing cholangitis

BY ANDREW D. BOWSER
MDedge News

While initial case reports and series provided preliminarily encouraging results, a larger retrospective study has provided no clear-cut evidence of biochemical response to vedolizumab in patients with primary sclerosing cholangitis and inflammatory bowel disease, investigators report.

A subset of patients in the retrospective analysis did experience a substantial drop in alkaline phosphatase, according to investigators with the International Primary Sclerosing Cholangitis Study Group.

Overall, however, levels of that cholestasis marker rose by a small but statistically significant amount in this study, which included more than 100 patients with primary sclerosing cholangitis (PSC) and inflammatory bowel disease.

Responses were more likely in patients with cirrhosis and in those with elevated ALP at baseline, both of which are indicators of more aggressive disease, according to investigator Kate D. Lynch, MD, PhD, of the University of Oxford (England) and her coauthors.

The rate of liver outcomes was in line with the natural history of the disease, according to Dr. Lynch and coinvestigators, who added that most patients had an endoscopic inflammatory bowel disease response, as might be expected based on studies of inflammatory bowel disease–only patients treated with vedolizumab.

'It is possible that vedolizumab may play a role in reducing lymphocyte infiltration into the liver in patients with PSC and thereby in reducing hepatic and biliary inflammation.'

"Despite the disappointment with lack of a uniform response, further evaluation of vedolizumab as a beneficial treatment in PSC may be warranted in a subset of patients via a stratified randomized clinical trial," Dr. Lynch and coauthors said in their report, which was published in Clinical Gastroenterology and Hepatology.

Vedolizumab, a monoclonal antibody against integrin alpha4-beta7, is effective in Crohn's disease and ulcerative colitis, according to investigators, who added that the "gut-homing pathway" it targets has also been implicated in the pathophysiology of primary sclerosing cholangitis.

"It is possible that vedolizumab may play a role in reducing lymphocyte infiltration into the liver in patients with PSC and thereby in reducing hepatic and biliary inflammation," authors of the retrospective analysis said.

Their analysis included 102 patients with primary sclerosing cholangitis and inflammatory bow-

el disease at 20 centers in Europe and North America. All patients had received at least three doses of vedolizumab for their inflammatory bowel disease, given according to the usual dosing schedule. Most of the patients were male (64 patients, or 62.8%) and about 90% had classical large-duct primary sclerosing cholangitis. About one-fifth had cirrhosis, and the majority (about 65%) had ulcerative colitis. Patients were followed until death, liver transplant, or 56 days after the last vedolizumab dose.

The median ALP increased from 1.53 times the upper limit of normal at baseline to 1.64 times the upper limit of normal by the last follow-up, an increase that was statistically significant ($P = .018$) but not clinically significant, according to investigators. Likewise, they said, statistically significant increases were seen overall in median alanine transaminase and aspartate aminotransferase levels.

However, 21 patients (20.6%) had a drop in ALP of at least 20% from baseline to last follow-up, and another 39 patients (38.2%) had stable ALP over that period, data show, while the remaining 42 (41.2%) had an increase of 20% or more.

Cirrhosis was associated with a near fivefold odds of a 20% or greater ALP drop from baseline to follow-up (odds ratio, 4.70; 95% confidence interval, 1.61-13.76), according to results of univariate analysis, which investigators said were "reproduced" in multivariate analysis.

While no other variables were so clearly linked to a 20% or greater drop in ALP, Dr. Lynch and colleagues said there was a "trend toward an association" in patients with ALP raised at baseline, and in those who had Crohn's disease or inflammatory bowel disease–unspecified instead of ulcerative colitis.

Endoscopic inflammatory bowel disease responses were seen in 42 out of 74 patients (56.8%) for whom those data were available, investigators added.

A total of 22 patients (20.9%) had a liver-related outcome over median follow-up of 561 days; however, that outcome may be "slightly overrepresented" by an incidence of cholangitis in 8.8%, which in and of itself is not necessarily an indicator of advanced liver disease, said Dr. Lynch and coauthors in their report.

"This proportion of liver-related outcomes is consistent with the natural history of PSC and does not by itself indicate that vedolizumab treatment is harmful in PSC," they said, adding that the findings were similar to a study of simtuzumab, a monoclonal antibody directed against lysyl oxidase-like 2, in patients with primary sclerosing cholangitis, of whom 20.1% had a primary sclerosing cholangitis–related event and the incidence of cholangitis was 13.2%.

The retrospective study was supported by the Birmingham National Institute for Health Research (NIHR) Biomedical Research Centre in the United Kingdom. Authors of the report provided disclosures related to Takeda, AbbVie, Dr. Falk Pharma, Intercept, MSD, Janssen, Vifor, Gilead, and Novartis, among others.

ginews@gastro.org

SOURCE: Lynch KD et al. Clin Gastroenterol Hepatol. 2019 May 14. doi: 10.1016/j.cgh.2019.05.013.

GI societies advise FDA on duodenoscope reprocessing

AGA, ACG, ASGE and SAGES were represented by three physicians who made oral remarks to the panel: Michael Kochman, MD, AGAF, Wilmott Professor of Medicine and Surgery at the University of Pennsylvania; Bret Petersen, MD, FASGE, professor of medicine and advanced

COURTESY AGA

endoscopist at the Mayo Clinic in Rochester, Minn. and Danielle Walsh, MD, associate professor of surgery at East Carolina University.

The GI societies over-arching goal is to ensure patient safety and ready access to clinically indicated procedures employing duodenoscopes and other elevator-channel endoscopes.

The panel discussed the adequacy/margin of safety for high-level disinfection, as well as the challenges and benefits of sterilization for routine for duodenoscope reprocessing. The panel's consensus was that cleaning is the most important step in duodenoscope reprocessing. The panel noted that in properly cleaned duodenoscopes, high-level disinfection is appropriate; however, panel members acknowledged that reports indicate that duodenoscopes are not properly cleaned. The panel also discussed the challenges of implementing sterilization of duodenoscopes, such as potential decreased patient access to endoscopic retrograde cholangiopancreatography (ERCP) and increased costs.

On behalf of the GI societies, Dr. Kochman and Dr. Petersen proposed several overarching principles for the future evolution of our clinical practices focusing on patient safety and outcomes:

We encourage embracing multiple solutions, using a measured step-wise approach to the transition with both iterative and novel devices and processes.

We encourage data-based solutions addressing real-world efficacy while incorporating ongoing surveillance of processes and performance to ensure that early trouble signals are detected.

We believe that device or reprocessing transitions can be incorporated over the lifecycle of current instrumentation, to eliminate the potential for gaps in accessibility of care and to ensure that there is adequate efficacy and safety data to support the adoption of new technology.

We accept minimizing extensive premarket studies, while expecting vigilant post-market surveillance, for technologies or device changes made exclusively with intent to convert to conceptually more safe designs without significant changes in mechanism or function.

We support the addition of durability testing for devices undergoing both standard reprocessing and, in particular, those undergoing sterilization.

Our societies are prepared to support and participate in continued discussion regarding:

Mandatory servicing and inspections.

Mandatory device retirement for reusable devices.

Assessment of the role and standards for third-party inspection and repair.

Our societies strongly support the importance and oversight of succinct, practical, reproducible, user-friendly guidance in manufacturers' instructions for use (IFUs), which should incorporate post-market validation studies and updates.

We recommend that devices that incorporate programmable features (AERs, washers, sterilizers) should have lock-down mechanisms in place to prevent both user and manufacturer from deviating from the FDA-cleared IFU parameters for the device.

Our societies, as well as numerous guidelines, include high-level disinfection as a currently acceptable option for endoscope reprocessing, assuming use of enhanced washing and drying standards of practice.

Finally, we support the FDA in its efforts to convey to companies the necessary endpoints and goals for performance and expectations relative to post-market review and development of new data to ensure efficacy in the community.

Our societies appreciated this opportunity to comment on the complex and critical topic at hand. Our over-arching goal as physicians remains that of ensuring patient safety and ready access to clinically indicated procedures employing duodenoscopes and other elevator-channel endoscopes.

ginews@gastro.org

Step therapy national day of advocacy

AGA and 17 other specialty physician and patient advocacy organizations partnered with the Digestive Disease National Coalition (DDNC) on an advocacy day focused on the need for step therapy reform.

We met with congressional offices to seek support for patient protection guardrails in step therapy and to encourage co-sponsorship of the Safe Step Act. This bipartisan legislation would create a clear process for a patient or physician to request an exception to a step therapy protocol. It also would require insurers to grant exemptions to step therapy in the following situations:

- Patient already tried and failed on a required treatment
- Delayed treatment will cause irreversible damage
- Required treatment will cause harm to the patient
- Required treatment will prevent a patient from working or fulfilling daily activities
- Patient is stable on their current treatment

AGA representatives and patient advocates met with the congressional offices of these legislators who serve on key committees that have jurisdiction over this issue.

Sen. Chris Van Hollen, D-Md.
Sen. Tim Scott, R-S.C.
Sen. Thom Tillis, R-N.C.
Sen. Lamar Alexander, R-N.C.
Rep. Alma Adams, D-N.C.
Rep. Mark Walker, R-N.C.
Rep. Tim Walberg, R-Mich.

A special thanks to AGA members who contacted your legislators online. A combination of 344 tweets and emails were sent urging federal legislators to support the Safe Step Act.

Sharing is caring

Legislators and their staff are always asking us for real-life examples from constituents about step therapy burdens to humanize the issue. Contact AGA staff at agaadvocacy@gastro.org to share your story.

ginews@gastro.org

Simple ways to create your legacy

Creating a legacy of giving is easier than you think. As the New Year begins, take some time to start creating your legacy while supporting the AGA Research Foundation. Gifts to charitable organizations, such as the AGA Research Foundation, in your future plans ensure your support for our mission continues even after your lifetime.

Here are two ideas to help you get started.

Name the AGA Research Foundation as a beneficiary. This arrangement is one of the most tax-smart ways to support the AGA Research Foundation after your lifetime. When you leave retirement plan assets to us, we bypass any taxes and receive the full amount.

Include the AGA Research Foundation in your will or living trust. This gift can be made by including as little as one sentence in your will or living trust. Plus, your gift can be modified throughout your lifetime as circumstances change.

Want to learn more about including a gift to the AGA Research Foundation in your future plans? Visit our website at https://gastro.planmylegacy.org or contact Harmony Excellent at 301-272-1602 or hexcellent@gastro.org.

ginews@gastro.org

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

Top AGA Community patient cases

Physicians with difficult patient scenarios regularly bring their questions to the AGA Community (https://community.gastro.org) 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. Possible congestive heart failure, tuberculosis (http://ow.ly/QdmG30pZqqo) – Join the GI community in discussing the echocardiogram results of a Holocaust survivor with a history of diabetes, hypothyroidism, benign prostate hyperplasia and hypercholesterolemia, and whose daughter was recently found to be QuantiFERON Gold positive.

2. Recurrent diarrhea in Behçet's disease patient (http://ow.ly/YX6L30pZqws) – A 42-year-old patient diagnosed with Behçet's disease at age 13 presented with recurrent diarrhea; a colonoscopy revealed terminal ileal and cecal ulcerations.

3. Gastroparesis patient unable to take anti-emetics (http://ow.ly/E5jD30pZqw4) – Help your colleague address a tricky patient with prolonged QT and gastroparesis.

Access these clinical cases and more discussions at https://community.gastro.org/discussions.

ginews@gastro.org

Talk to your patients about the current state of prebiotics

Bridgette Wilson, PhD, RD, postdoctoral research associate in nutritional sciences, and Kevin Whelan, PhD, RD, professor of dietetics, King's College London, England, share talking points to help your patients understand what is currently known about the use of prebiotics for GI disorders.

MLADENOVIC/ISTOCK/GETTY IMAGES

Explaining prebiotics for GI disorders

Different prebiotic supplements have different effects on gut symptoms. For example, lower doses of noninulin type fructans (e.g., beta-galacto-oligosaccharides [GOS], pectin, partially hydrolyzed guar gum) are likely to be better tolerated in patients with functional gut symptoms, including irritable bowel syndrome (IBS).

Though prebiotic-containing foods are thought to benefit gut health in general, some prebiotics are FODMAPs that have been associated with symptoms in IBS patients. Individual patients on restrictive diets should systematically introduce prebiotic foods to identify the type and quantity they can tolerate.

Prebiotic supplementation of more than 10 g/d may soften stools and increase bowel movements in patients with defecation difficulty or constipation.

Prebiotic supplementation may worsen symptoms in Crohn's disease but is well tolerated in ulcerative colitis, although there is no effect on disease activity.

These tips are from "The current state of prebiotics," the third article of a four-part CME series on prebiotics. This activity is supported by an educational grant from GlaxoSmithKline. Part one, "Prebiotics 101," and part two, "Diet vs. Prebiotics," are available through AGA University (agau.gastro.org).

AGA also has educational materials for patients on probiotics, which can be accessed at www.gastro.org/probiotics in English and Spanish.

ginews@gastro.org

CLINICAL CHALLENGES AND IMAGES

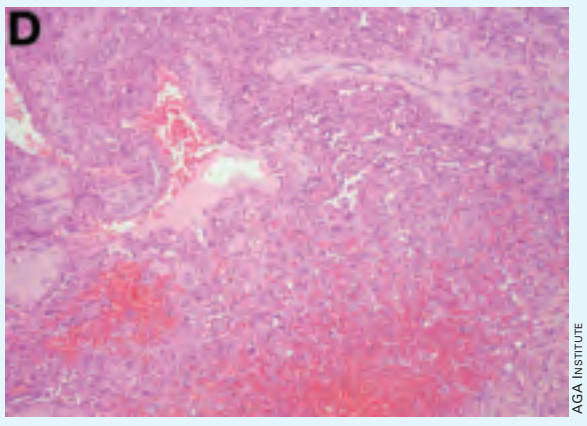
The diagnosis

Answer to: "What is your diagnosis?" on page 6: Natural course of primary hepatic angiosarcoma with rupture

The pathology demonstrated slitlike vascular channels lined by spindle-shaped endothelial cells with large and hyperchromatic nuclei (Figure D). Primary hepatic angiosarcoma (PHA) was diagnosed. The patient declined operation because of poor prognosis and body performance. Ascites tapping was performed, and the fluid was bloody. The patient received a blood transfusion and died 2 days later.

PHA is an aggressive malignant tumor that originates from the endothelium of liver blood vessels. It is a rare condition and accounts for 0.6%-2.0% of all primary liver tumors and less than 5% of all angiosarcomas.[1]

Most PHAs exhibit no obvious symptoms and signs, particularly when they are small. As the disease progresses, symptoms and signs including abdominal pain, weakness, fatigue, weight loss, hepatomegaly, and ascites occur. The spontaneous rupture of PHA was reported in 15%-27% of patients in a previous study.[2] As in our case, no obvious symptoms were noted in the early stage, and spontaneous rupture was observed in the later stage.



AGA INSTITUTE

A CT scan of PHA reveals multiple nodules or a dominant mass and a diffusely infiltrating lesion. The tumor is composed of low-density lesions with small heterogeneous hypervascular foci.[3] In our patient, a CT scan revealed a hepatic tumor that had a low density when it was small and multiple heterogeneous hypervascular foci when it grew large.

PHAs are very aggressive tumors, and most cases are diagnosed at an advanced stage. The median survival was reported to be 6 months without treatment. Complete resection with clear margins is the choice of treatment; however, the prognosis is poor even after complete resection.[2] In our case, operation after diagnosis was declined because of the patient's poor prognosis and body performance. She lived for 18 months after the diagnosis. The entire natural course of PHA from initial diagnosis to rupture was well presented in our case.

References

1. Zheng YW, Zhang XW, Zhang JL, et al. Primary hepatic angiosarcoma and potential treatment options. J Gastroenterol Hepatol. 2014;29:906-11.

2. Cawich SO, Ramjit C. Herald bleeding from a ruptured primary hepatic angiosarcoma: a case report. Mol Clin Oncol. 2015;3:1063-6.

3. Huang IH, Wu YY, Huang TC, et al. Statistics and outlook of primary hepatic angiosarcoma based on clinical stage. Oncol Lett. 2016;11:3218-22.

ginews@gastro.org

WWW.GIHEPNEWS.COM

GI & HEPATOLOGY NEWS

THE OFFICIAL NEWSPAPER OF THE AGA INSTITUTE

HVPG predicts clinical benefit after SVR

BY WILL PASS
MDedge News

BOSTON – For patients with hepatitis C virus infection who achieve sustained virologic response to interferon-free therapy, changes in hepatic venous pressure gradient (HVPG) predict clinical benefit, according to investigators.

This finding will allow investigators to use HVPG as a surrogate endpoint for etiologic therapies, which could accelerate future research, reported lead author Mattias Mandorfer, MD, PhD, of the Medical University of Vienna and colleagues.

"Sustained virologic response to interferon-free therapies ameliorates portal hypertension," Dr. Mandorfer said during a presentation at the annual meeting of the American Association for the Study of Liver Diseases. "[Previous research has shown that] nearly two-thirds of patients with pretreatment clinically significant portal hypertension had an HVPG decrease above or equal to 10%, which denotes a clinically meaningful change according to current recommendations. However, evidence is limited to studies evaluating the impact of HVPG response to nonselective beta-blockers, and nonselective beta-blockers have a completely different mode of action than etiological therapies. Accordingly, it is unclear whether a decrease in HVPG after the cure of hepatitis C translates into the same clinical benefit."

Will Pass/MDedge News

Dr. Mattias Mandorfer presented data showing that HVPG predicts clinical benefit.

To find out, the investigators enrolled 90 patients with HCV who had an elevated HVPG of 6 mm Hg or higher before SVR. Before and after interferon-free therapy, patients underwent paired HVPG measurement. In addition, to evaluate noninvasive methods of HVPG assessment, the researchers performed transient elastography and von Willebrand factor to platelet count ratio testing.

Analysis showed that HVPG measurements after, but not before, interferon-free therapy predicted liver decompensation. HVPG was associated with an 18% increased risk of hepatic decompensation per mm Hg. After 3 years, 40.1% of patients with posttherapy HVPG measurements of 16 mm Hg or more developed hepatic decompensation, an event that occurred in none of the patients with a posttherapy HVPG of 9 mm Hg or less. Among patients who had a baseline HVPG of 10 mm Hg or more, which is considered a clinically significant level of portal hypertension, a decrease in HVPG of least 10% after therapy was associated with a similar level of protection against decompensation, compared with those who had no such decrease (2.5% vs. 31.8%).

While the two noninvasive methods were able to detect clinically significant portal hypertension (at least 10 mm Hg), they were not accurate enough to detect the protective 10% drop in HVPG.

"These results support the concept of applying HVPG as a surrogate endpoint for interventions that primarily aim at decreasing intrahepatic resistance," the investigators concluded.

The study was funded by the Medical Scientific Fund of the city of Vienna. The investigators disclosed relationships with AbbVie, Bristol-Myers Squibb, Gilead, and others.

ginews@gastro.org

SOURCE: Mandorfer M et al. The Liver Meeting 2019, Abstract 146.

Pipeline drugs show promise

NAFLD *from page 1*

agonist on biomarkers of nonalcoholic steatohepatitis (NASH) at 26 weeks in overweight or obese patients with type 2 diabetes mellitus. In the randomized, phase 2b study, cotadutide produced superior reductions versus liraglutide, the GLP-1 receptor agonist, in alanine aminotransferase and aspartate aminotransferase, and body weight, which investigators said supported prospective trials of the drug for a potential indication in NASH.

"The adverse events were fairly typical for what we see with the GLP-1s – GI side effects that usually over 8 weeks improve," Dr. Corey told attendees at the debrief session.

Andrew D. Bowser/MDedge News

Dr. Kathleen E. Corey presented a panel of pipeline drugs for NASH and NAFLD at the Liver Meeting.

Licogliflozin (LIK066)

Interim analysis of a 12-week, randomized, placebo-controlled, phase 2a study showed that this SGLT1/2 inhibitor produced "robust" decreases in ALT and improvements in markers of hepatic and metabolic health in patients with NASH, according to Zhang and coauthors (Abstract L07).

Some 67% of those who received licogliflozin had at least a 30% decrease in their liver fat, while decreases in weight and hemoglobin A_{1c} were also reported, according to Dr. Corey. "It was associated with diarrhea in about 97%, but this was considered mild, and certainly, we're seeing good metabolic effects overall," she said.

Tropifexor

Treatment for 12 weeks with this potent FXR agonist resulted in robust, dose-dependent reductions in hepatic fat and serum ALT in patients with fibrotic NASH, according to investigators in a phase 2 randomized, placebo-controlled trial known as FLIGHT-FXR (Abstract L04).

A total of 65% of patients achieved a 30% or greater reduction in liver fat, and decreases in weight and insulin resistance were reported. "Similar to other FXRs, they did have this concerning although potentially manageable increase in low-density lipoprotein-cholesterol, and the adverse event of pruritis," said Dr. Corey.

Saroglitazar

Gawrieh and coauthors presented results from EVIDENCES IV, a phase 2, double-blind, randomized, placebo-controlled study of saroglitazar, a novel dual peroxisome proliferator activated receptor (PPAR) alpha/gamma agonist, in patients with NAFLD or NASH (Abstract LO10).

The investigators found that 41% of patients achieved a 30% or greater relative reduction in liver fat, as well as reductions in hemoglobin A_{1c} and lipids, but the treatment was "weight neutral," Dr. Corey said, adding that no serious adverse events were reported.

PF-05221304

This liver-targeted acetyl-CoA carboxylase inhibitor (ACCI) demonstrated robust reduction in liver fat and ALT in a 16-week phase 2a, dose-ranging study in adults with NAFLD, according to Amin and coinvestigators (Abstract 31).

There was a "dramatic" decrease in liver fat in this study, said Dr. Corey, with 90% of treated patients experiencing a 30% or greater decrease. Side effects included a "significant" increase in triglycerides, she added, as well as transient increases in ALT and AST.

Selonsertib and emricasan

One agent not meeting study endpoints was selonsertib, an apoptosis signal–regulating kinase 1 (ASK1) inhibitor. While safe and well tolerated, the drug was nevertheless not effective as monotherapy in phase 3 double-blind, placebo-controlled trials including patients with advanced fibrosis due to NASH, investigators said (Abstract 64). Currently, the agent is being evaluated in combination with firsocostat – an ACCI – in a phase 2 study called ATLAS, according to the authors.

Emricasan, an oral pan-caspase inhibitor that suppresses apoptosis, did not improve fibrosis or resolve NASH in a multicenter, double-blind, placebo-controlled randomized trial, and may have even worsened histology, according to Dr. Corey. Investigators said further evaluation of the mechanisms underlying findings could provide insights into the role of necro-apoptosis in NASH pathophysiology (Abstract 61).

Dr. Corey provided disclosures related to BMS, Novo Nordisk, Boehringer Ingelheim, and Gilead.

ginews@gastro.org

Single use may be the answer

Scope *from page 1*

Angeles, and colleagues.

Writing for Clinical Gastroenterology and Hepatology, the investigators noted that duodenoscope-related infections represent a serious threat to public health, particularly when considered in the context of antibiotic resistance and the high number of endoscopic procedures performed annually.

According to the investigators, routine culture surveillance and field investigations following suspected duodenoscope-related infections may fail to detect culprit bacteria or shortcomings in equipment reprocessing; and even when performed correctly, standard reprocessing can be insufficient.

To determine if a single-use endoscope could overcome such risks, the investigators first conducted preclinical testing with animal laboratories and simulations, finding that a single-use duodenoscope was comparable with three reusable scope models. The present study, which included 73 patients with normal pancreaticobiliary anatomy, evaluated clinical feasibility, safety, and performance. The single-use duodenoscope was a first-generation device by Boston Scientific named EXALT Model D.

Of the 73 patients, 13 underwent roll-in maneuvers and 60 underwent endoscopic retrograde cholangiopancreatography (ERCP). The most common cause for ERCP was exchange or removal of biliary stent (55.0%), followed by evaluation of biliary defect or stricture (26.7%), then bile duct stone clearance (18.3%). The majority of ERCPs had an American Society for Gastrointestinal Endoscopy (ASGE) procedural complexity grade of 2 (43.3%) or 3 (43.3%), while a minority were graded 1 (11.7%) or, most severe, 4 (1.7%).

Two ERCPs required crossover to a reusable duodenoscope for completion. In the first instance, crossover was needed because dilation of a biliary stricture was unsuccessful, with the endoscopist reporting difficulties maneuvering the disposable scope, possibly because of shaft stiffness. In the second case, crossover was elected because cannulation was unsuccessful with standard access techniques; however, cannulation also was not possible with the reusable scope, necessitating an alternative approach.

According to the investigators, safety signals were comparable with standard practice. No serious, scope-related adverse events were reported. Serious adverse events of any kind were relatively uncommon; three patients developed post-ERCP pancreatitis within 7 days of ERCP, one developed a postsphincterotomy bleed, and one had worsening of a preexisting infection that required hospitalization.

The endoscopists reported a median overall satisfaction score of 9 out of 10. Specifically, 17 out of 23 scored ERCP maneuvers (73.9%) received a median 5 out of 5 performance rating. Out of 1,289 total ratings, almost all (98.1%) received a performance rating of at least 3 out of 5. Low-scoring performance characteristics (receiving at least one "1" rating), included elevator function; aspects of positioning; visualization; image quality, brightness, or appearance; and ease and ability of passing ancillary devices through the channel of the single-use duodenoscope and into the papilla.

"The new device provides an alternative to reusable duodenoscopes that may harbor residual contamination despite appropriately implemented reprocessing," the investigators concluded.

"The single-use duodenoscope is a timely and innovative option to improve exogenous infection control, and must be used with awareness of the continued risk of endogenous infection, with standard infection control precautions and continued diligence in the use of existing reusable devices," they wrote.

The study was funded by Boston Scientific. The investigators reported additional relationships with Medtronic, Ethicon/Torax, CapsoVision, and others.

ginews@gastro.org

SOURCE: Muthusamy V et al. Clin Gastroenterol Hepatol. 2019 Oct 11. doi: 10.1016/j.cgh.2019.10.052.

FDA clears first fully disposable duodenoscope

BY M. ALEXANDER OTTO
MDedge News

The Food and Drug Administration on Dec. 13 cleared Boston Scientific's single-use duodenoscope, the Exalt Model D, for endoscopic retrograde cholangiopancreatography (ERCP).

It's the first disposable duodenoscope to hit the market in the wake of the agency's August call for manufacturers and health care facilities to move to partially or fully disposable duodenoscopes. The goal is to eliminate the risk of spreading infections between patients from incomplete sterilization of traditional, multi-use scopes. The FDA also recently approved a Pentax duodenoscope with a disposable elevator, the most difficult part to clean.

The agency reported in April that 5.4% of samples from multi-use scopes test postive for *Escherichia coli*, *Pseudomonas aeruginosa,* or other "high-concern" organisms.

Boston Scientific spokesperson Kate Haranis said the Exalt Model D will be available in the first quarter of 2020, but the company is still working out how much it will charge.

"The feel is a little different," said Gyanprakash A. Ketwaroo, MD, MSc, an interventional endoscopist and assistant professor of gastroenterology at Baylor University, Houston, who's tried the new device, but "it's pretty functional and probably okay to use in almost all endoscopic procedures that require ERCP."

AGA is working with FDA to ensure physicians continue to have access to ERCP as new devices are introduced to the market. Review the GI societies' guiding principles for continued scope evolution at https://www.gastr.org/news/gi-societies-advise-fda-on-duodenoscope-reprocessing.

Dr. Ketwaroo had no relevant financial disclosures. He is an associate editor for GI and Hepatology News.

aotto@mdedge.com

AGA CPU: Management of pancreatic necrosis

BY WILL PASS
MDedge News

The American Gastroenterological Association recently issued a clinical practice update for the management of pancreatic necrosis, including 15 recommendations based on a comprehensive literature review and the experiences of leading experts.

Recommendations range from the general, such as the need for a multidisciplinary approach, to the specific, such as the superiority of metal over plastic stents for endoscopic transmural drainage.

The expert review, which was conducted by lead author Todd H. Baron, MD, of the University of North Carolina in Chapel Hill and three other colleagues, was vetted by the AGA Institute Clinical Practice Updates Committee (CPUC) and the AGA Governing Board. In addition, the update underwent external peer review prior to publication in Gastroenterology.

'Successful management of these patients requires expert multidisciplinary care by gastroenterologists, surgeons, interventional radiologists, and specialists in critical care medicine, infectious disease, and nutrition.'

In the update, the authors outlined the clinical landscape for pancreatic necrosis, including challenges posed by complex cases and a mortality rate as high as 30%.

"Successful management of these patients requires expert multidisciplinary care by gastroenterologists, surgeons, interventional radiologists, and specialists in critical care medicine, infectious disease, and nutrition," the investigators wrote.

They went on to explain how management has evolved over the past 10 years.

"Whereby major surgical intervention and debridement was once the mainstay of therapy for patients with symptomatic necrotic collections, a minimally invasive approach focusing on percutaneous drainage and/or endoscopic drainage or debridement is now favored," they wrote. They added that debridement is still generally agreed to be the best choice for cases of infected necrosis or patients with sterile necrosis "marked by abdominal pain, nausea, vomiting, and nutritional failure or with associated complications including gastrointestinal luminal obstruction, biliary obstruction, recurrent acute pancreatitis, fistulas, or persistent systemic inflammatory response syndrome (SIRS)."

Other elements of care, however, remain debated, the investigators noted, which has led to variations in multiple aspects of care, such as interventional timing, intravenous fluids, antibiotics, and nutrition.

Continued on following page

Continued from previous page

Within this framework, the present practice update is aimed at offering "concise best practice advice for the optimal management of patients with this highly morbid condition."

Among these pieces of advice, the authors emphasized that routine prophylactic antibiotics and/or antifungals to prevent infected necrosis are unsupported by multiple clinical trials. When infection is suspected, the update recommends broad-spectrum intravenous antibiotics, noting that, in most cases, it is unnecessary to perform CT-guided fine-needle aspiration for cultures and Gram stain.

Regarding nutrition, the update recommends against "pancreatic rest"; instead, it calls for early oral intake and, if this is not possible, then initiation of total enteral nutrition. Although the authors deemed multiple routes of enteral feeding acceptable, they favored nasogastric or nasoduodenal tubes, when appropriate, because of ease of placement and maintenance. For prolonged total enteral nutrition or patients unable to tolerate nasoenteric feeding, the authors recommended endoscopic feeding tube placement with a percutaneous endoscopic gastrostomy tube for those who can tolerate gastric feeding or a percutaneous endoscopic jejunostomy tube for those who cannot or have a high risk of aspiration.

As described above, the update recommends debridement for cases of infected pancreatic necrosis. Ideally, this should be performed at least 4 weeks after onset, and avoided altogether within the first 2 weeks, because of associated risks of morbidity and mortality; instead, during this acute phase, percutaneous drainage may be considered.

For walled-off pancreatic necrosis, the authors recommended transmural drainage via endoscopic therapy because this mitigates risk of pancreatocutaneous fistula. Percutaneous drainage may be considered in addition to, or in absence of, endoscopic drainage, depending on clinical status.

The remainder of the update covers decisions related to stents, other minimally invasive techniques, open operative debridement, and disconnected left pancreatic remnants, along with discussions of key supporting clinical trials.

Review the Gastroenterology clinical guideline collection for AGA Institute statements detailing preferred approaches to specfic medical problems or issues based on the most current available data at https://www.gastrojournal.org/content/agai.

The investigators disclosed relationships with Cook Endoscopy, Boston Scientific, Olympus, and others.

ginews@gastro.org

SOURCE: Baron TH et al. Gastroenterology. 2019 Aug 31. doi: 10.1053/j.gastro.2019.07.064.

Bile acid diarrhea guideline highlights data shortage

BY WILL PASS
MDedge News

The Canadian Association of Gastroenterology (CAG) recently co-published a clinical practice guideline for the management of bile acid diarrhea (BAD) in Clinical Gastroenterology and Hepatology and the Journal of the Canadian Association of Gastroenterology.

Given a minimal evidence base, 16 out of the 17 guideline recommendations are conditional, according to lead author Daniel C. Sadowski, MD, of Royal Alexandra Hospital, Edmonton, Alta., and colleagues. Considering the shortage of high-quality evidence, the panel called for more randomized clinical trials to address current knowledge gaps.

"BAD is an understudied, often underappreciated condition, and questions remain regarding its diagnosis and treatment," the panelists wrote in Clinical Gastroenterology and Hepatology. "There have been guidelines on the management of chronic diarrhea from the American Gastroenterological Association, and the British Society of Gastroenterology, but diagnosis and management of BAD was not assessed extensively in these publications. The British Society of Gastroenterology updated guidelines on the investigation of chronic diarrhea in adults, published after the consensus meeting, addressed some issues related to BAD."

For the current guideline, using available evidence and clinical experience, expert panelists from Canada, the United States, and the United Kingdom aimed to "provide a reasonable and practical approach to care for specialists." The guideline was further reviewed by the CAG Practice Affairs and Clinical Affairs Committees and the CAG Board of Directors.

The guideline first puts BAD in clinical context, noting a chronic diarrhea prevalence rate of approximately 5%. According to the guideline, approximately one out of four of these patients with chronic diarrhea may have BAD and prevalence of BAD is likely higher among those with other conditions, such as terminal ileal disease.

While BAD may be relatively common, it isn't necessarily easy to diagnose, the panelists noted.

"The diagnosis of BAD continues to be a challenge, although this may be improved in the future with the general availability of screening serologic tests and other diagnostic tests," the panelists wrote. "Although a treatment trial with bile acid sequestrants therapy (BAST) often is used, this approach has not been studied adequately, and likely is imprecise, and may lead to both undertreatment and overtreatment."

'The diagnosis of BAD continues to be a challenge, although this may be improved in the future with the general availability of screening serologic tests and other diagnostic tests.' The panelists recommended testing for BAD with 75-selenium homocholic acid taurine or 7-alpha-hydroxy-4-cholesten-3-one.

Instead, the panelists recommended testing for BAD with 75-selenium homocholic acid taurine (SeHCAT) or 7-alpha-hydroxy-4-cholesten-3-one.

After addressing treatable causes of BAD, the guideline recommends initial therapy with cholestyramine or, if this is poorly tolerated, switching to BAST. However, the panelists advised against BAST for patients with resection or ileal Crohn's disease, for whom other antidiarrheal agents are more suitable. When appropriate, BAST should be given at the lowest effective dose, with periodic trials of on-demand, intermittent administration, the panelists recommended. When BAST is ineffective, the guideline recommends that clinicians review concurrent medications as a possible cause of BAD or reinvestigate.

Concluding the guideline, the panelists emphasized the need for more high-quality research.

"The group recognized that specific, high-certainty evidence was lacking in many areas and recommended further studies that would improve the data available in future methodologic evaluations," the panelists wrote.

While improving diagnostic accuracy of BAD should be a major goal of such research, progress is currently limited by an integral shortcoming of diagnostic test accuracy (DTA) studies, the panelists wrote.

"The main challenge in conducting DTA studies for BAD is the lack of a widely accepted or universally agreed-upon reference standard because the condition is defined and classified based on pathophysiologic mechanisms and its response to treatment (BAST)," the panelists wrote. "In addition, the index tests (SeHCAT, C4, FGF19, fecal bile acid assay) provide a continuous measure of metabolic function. Hence, DTA studies are not the most appropriate study design."

"Therefore, one of the research priorities in BAD is for the scientific and clinical communities to agree on a reference standard that best represents BAD (e.g., response to BAST), with full understanding that the reference standard is and likely will be imperfect."

Review the AGA clinical practice guideline on the laboratory evaluation of functional diarrhea and diarrhea-prodominant irritable bowel syndrome in adults at https://www.gastrojournal.org/article/S0016-5085(19)41083-4/fulltext.

The guideline was funded by unrestricted grants from Pendopharm and GE Healthcare Canada. The panelists disclosed relationships with AstraZeneca, AbbVie, Merck, Pfizer, and others.

ginews@gastro.org

SOURCE: Sadowski DC et al. Clin Gastroenterol Hepatol. 2019 Sep 14. doi: 10.1016/j.cgh.2019.08.062.

CLASSIFIEDS

Also available at MedJobNetwork.com

PROFESSIONAL OPPORTUNITIES

Geriatric IBD hospitalization carries steep inpatient mortality

BY BRUCE JANCIN
MDedge News

SAN ANTONIO – Patients aged over 75 years who are hospitalized for management of inflammatory bowel disease (IBD) have a four to five times greater risk of inpatient mortality than those who are younger, Jeffrey Schwartz, MD, reported at the annual meeting of the American College of Gastroenterology.

The magnitude of the age-related increased risk highlighted in this large national study was strikingly larger than the differential inpatient mortality between geriatric and nongeriatric patients hospitalized for conditions other than IBD. It's a finding that reveals a major unmet need for improved systems of care for elderly hospitalized IBD patients, according to Dr. Schwartz, an internal medicine resident at Beth Israel Deaconess Medical Center, Boston.

"Given the high prevalence of IBD patients that require inpatient admission, as well as the rapidly aging nature of the U.S. population, it's our hope that this study will provide some insight to drive efforts to improve standardized guideline-directed therapy and propose interventions to help close what I think is a very important gap in clinical care," he said.

It's well established that a second peak of IBD diagnoses occurs in 50- to 70-year-olds. At present, roughly 30% of all individuals carrying the diagnosis of IBD are over age 65, and with the graying of the baby-boomer population, this proportion is climbing.

Dr. Schwartz presented a study of the National Inpatient Sample for 2016, which is a representative sample comprising 20% of all U.S. hospital discharges for that year, the most recent year for which the data are available. The study population included all 71,040 patients hospitalized for acute management of Crohn's disease or its immediate complications, of whom 10,095 were aged over age 75 years, as well as the 35,950 patients hospitalized for ulcerative colitis (UC), 8,285 of whom were over 75.

Inpatient mortality occurred in 1.5% of the geriatric admissions, compared with 0.2% of nongeriatric admissions for Crohn's disease. Similarly, the inpatient mortality rate in geriatric patients with UC was 1.0% versus 0.1% in patients under age 75 hospitalized for UC.

There are lots of reasons why the management of geriatric patients with IBD is particularly challenging, Dr. Schwartz noted. They have a higher burden of comorbid conditions, poorer nutritional status, and increased risks of infection and cancer. In a regression analysis that attempted to control for such confounders using the Elixhauser mortality index, the nongeriatric Crohn's disease patients were an adjusted 75% less likely to die in the hospital than those who were older. Nongeriatric UC patients were 81% less likely to die than geriatric patients with the disease. In contrast, nongeriatric patients admitted for reasons other than IBD had only an adjusted 50% lower risk of inpatient mortality than those who were older than 75.

Asked if he could shed light on any specific complications that drove the age-related disparity in inpatient mortality in the IBD population, Dr. Schwartz replied that he and his coinvestigators were thwarted in their efforts because the inpatient mortality of 1.0%-1.5% was so low that further breakdown as to causes of death would have been statistically unreliable. It's reasonable to hypothesize that cardiovascular complications are an important contributor, he added.

Dr. Schwartz reported having no financial conflicts regarding his study, conducted free of commercial support.

bjancin@mdedge.com

Usability is measurable

Burnout *from page 1*

57, digital video recorders score 74, Amazon scores 82, microwave ovens score 87, and Google search scores 93.

"A score of 45.9 is in the bottom 9% of usability scores across studies in other industries and is categorized as in the 'not acceptable' range with a grade of F," the authors wrote. "In aggregate, 733 of 870 (84.2%) of respondents rated their EHR less than 68 on the SUS, the average score across industries."

In tying the SUS results to burnout, which was measured using the Maslach Burnout Inventory, the authors noted that the scores "were strongly and independently associated with physician burnout in a dose-response relationship.

'So, if you bring in something new and say this is going to be better, how do you know it is going to be better? Well maybe you measure it using the System Usability Scale' to give it a quantifiable measure of improvement.

The odds of burnout were lower for each 1-point more favorable SUS score, a finding that persisted after adjusting for an extensive array of other personal and professional characteristics. The relationship between SUS score and burnout also persisted when emotional exhaustion and depersonalization were treated as continuous variables."

The authors did note that, despite the strong relationship, they could not determine a causation given the cross-sectional nature of the data.

"I'm hoping that this paper will spark conversation and drive change and be a way of tracking improvements," Dr. Melnick said. "So, if you bring in something new and say this is going to be better, how do you know it is going to be better? Well maybe you measure it using the System Usability Scale" to give it a quantifiable measure of improvement. He said it is an advantage "of having a metric that has been standardized and used in other industries," allowing EHR stakeholders to measure improvement. "Once you can measure it, you can manage it and make improvements faster."

The findings "will not come as a surprise to anyone who practices medicine," Patrice Harris, MD, president of the American Medical Association, said in a statement. "It is a national imperative to overhaul the design and use of EHRs and reframe the technology to focus primarily on its most critical function: helping physicians care for patients."

"Significantly enhancing EHR usability is key and the AMA is working to ensure a new generation of EHRs are designed to prioritize time with patients, rather than overload physicians with type-and-click tasks," she said.

Funding for the study was provided by the Stanford Medicine WebMD Center, the American Medical Association, and the Mayo Clinic Department of Medicine Program on Physician Well-Being. No relevant financial conflicts of interest were reported by the authors.

gtwachtman@mdedge.com

SOURCE: Melnick E et al. Mayo Clinic Proceedings. 2019 Nov 14. doi: 10.1016/j.mayocp.2019.09.024.

PRACTICE MANAGEMENT TOOLBOX

New Year's resolutions for your GI practice in 2020

BY JAMES A. TURNER, JR., MBA, MHA

I know that many have already started the planning process for next year's business priorities and therefore I remain hopeful that time was taken to reflect on the success stories already achieved to provide the foundation for next year's business goals.

What is key, is that one recognizes that the planning process must begin this year to kickstart next year's work soon after the holidays are over. This planning process should lay out the framework from which to assign the work so it's part of the business operations wherein goals can be established and ultimately achieved.

As we move into a new decade the evolution of medicine and specifically gastroenterology hasn't stopped. The question is, have you set yourself (and your practice) up for success in 2020? In the ever-changing world of the gastroenterology practice you don't want to be left behind this year. Here are the top things you need to know for a productive and successful new year!

1 Use the new Medicare Beneficiary Identifier (MBI). Starting January 1, 2020, if you want to get paid by Medicare you must use the MBI when billing Medicare regardless of the date of service. Claims submitted without MBIs will be rejected, with some exceptions. The MBI replaces the social security number–based Health Insurance Claim Numbers (HICNs) from Medicare cards and is now used for Medicare transactions like billing, eligibility status, and claim status.

2 Prepare for Evaluation and Management (E/M) changes. Did you know that E/M coding and guidelines are about to undergo the most significant changes since their implementation? The changes to guidelines and coding for new and established office/outpatient visits (CPT codes 99202-99205, 99211-99215) won't officially take place until January 1, 2021, but they are so significant that the American Medical Association has already released a preview of the CPT 2021 changes. Don't miss out on the preview – https://www.ama-assn.org/system/files/2019-06/cpt-office-prolonged-svs-code-changes.pdf. Sit down with your coders or contact your medical billing company and create a plan for training physicians and staff for the changes for a smooth transition on Jan. 1, 2021. With changes this big, you may find you need all of 2020 to prepare.

3 Review your quality reporting under the Merit-Based Payment Incentive System (MIPS). There have been several changes to the weights of quality and cost performance categories under MIPS for the 2020 performance year. These will go into effect January 1st and will impact your 2022 Medicare payments.

4 Evaluate your clinician participation level if you're reporting under MIPS as a group. During the 2020 performance year, the threshold for clinician participation is increasing. At least 50% of clinicians from the group must participate in or perform an activity for the same continuous 90-day period to earn credit for that improvement activity.

5 Don't forget to report under MIPS for 2019. Those not in an Advanced Alternative Payment Model (APM), a Medicare Accountable Care Organization (ACO), or other MIPS alternative must report the required data under the program or face payment cuts in 2021. The submission window for your 2019 data opens on January 2, 2020, and closes on March 31!

6 Review your commercial contracts. With reimbursement decreasing each year, protect yourself by renegotiating multi-year contract rates now with payers based on the 2019 fee schedule. Review all your commercial contracts and focus on the ones with the lowest rates first. Prepare a case to justify higher rates by creating a value proposition and don't forget to involve your coders; they are often aware of payer-specific reimbursement problems. Not comfortable negotiating with payers? Be open to looking for outside help, like a contract attorney.

Stress to your team that proper planning is the norm and not the exception, and that seeking improvement in all facets of your medical practice is critical to achieving long-term success. Be sure to write your plans in the future tense and to include timelines in your final work product.

7 Mark your calendars! Here's a list of dates that you will want to put on your calendar for 2020!

January 2020
- January 1 - MIPS Performance Year 2019 Begins
- January 2 - Submission Window Opens for MIPS Performance Year 2019

March 2020
- March 31 - Submission Window Closes for MIPS Performance Year 2019

July 2020
- CMS publishes proposed reimbursement values for the E/M codes in the 2021 Medicare Physician Fee Schedule proposed rule
- CMS "Targeted Review" opens once CMS makes your MIPS payment adjustment available
- July 1 - MIPS Performance Feedback Available. CMS will provide you with performance feedback based on the data you submitted for Performance Year 2019. You can use this feedback to improve your care and optimize the payments you receive from CMS.

August 2020
- August 31 - Targeted Review period closes (appeals process)

September 2020
- AMA releases CPT 2021 book with new E/M coding guidelines and new coding for new patient office/outpatient visits (99202-99205)

October 2020
- October 1, 2020 – Final day to start QPP activities to meet 90-day minimum.

November 2020
- CMS finalizes reimbursement values for the E/M codes in the MPFS final rule

December 2020
- December 31, 2020 - Quality Payment Program Exception Applications Window Closes
- December 31, 2020 – MIPS Performance year 2020 ends

Stress to your team that proper planning is the norm and not the exception, and that seeking improvement in all facets of your medical practice is critical to achieving long-term success. Be sure to write your plans in the future tense and to include timelines in your final work product, as well as delegate accountability to accomplish those goals.

Use the planning process as an opportunity to build your team so that everyone is focused on the future and stress that their participation is important to achieve the success required to remain an independent medical group.

Mr. Turner is chief executive officer, Indianapolis Gastroenterology and Hepatology. jturner@indygastro.com

INDEX OF ADVERTISERS

Braintree Laboratories, Inc.
Suprep 27-28

Shionogi Inc.
Mulpleta 13-14

Takeda Pharmaceuticals U.S.A., Inc.
Entyvio 2-5
Motegrity 16-18

THE ORIGINAL 1 LITER PRESCRIPTION BOWEL PREP SOLUTION

#1 MOST PRESCRIBED, BRANDED BOWEL PREP KIT[1]

WITH MORE THAN 15 MILLION KITS DISPENSED SINCE 2010[1]

A CLEAN SWEEP

EFFECTIVE RESULTS IN ALL COLON SEGMENTS[2]

- SUPREP® Bowel Prep Kit has been FDA-approved as a split-dose oral regimen[3]
- >90% of patients had no residual stool in all colon segments[2*†]
  - These cleansing results for the cecum included 91% of patients[2*†]
  - SUPREP Bowel Prep Kit also achieved ≥64% no residual fluid in 4 out of 5 colon segments (ascending, transverse, descending, and sigmoid/rectum)[2*†]

Aligned with Gastrointestinal Quality Improvement Consortium (GIQuIC) 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.

Braintree
A PART OF SEBELA PHARMACEUTICALS®

HH27314B September 2018