Message from the Chief

By definition, “innovation” is the creation and implementation of new processes, products, services, and methods that result in improvements in outcomes, efficiency, effectiveness, or quality. We have the ability to improve our patients’ quality of life when we arm ourselves with the tools and know-how to better prevent, detect, and treat. Simply put, innovation means pushing beyond where we are to where we want to be.

Our faculty at UPMC have continued to dig deeper and, through their research and clinical work, have uncovered tools for better prevention, diagnosis, and treatment. Our goal is to give patients the opportunity for a better life. We have long been at the forefront of innovation and clinical excellence, but at this moment we concentrate on pushing ourselves even further, bringing not simply knowledge but new discovery to our bedside practice.

“Every article in this issue touches on innovative advancements as we hear from senior faculty, young investigators, and our outstanding fellows in training.”

This issue of Digest focuses on keeping people healthier by looking beyond what’s obvious to treat the entire person. We explore a large new study looking at screening intervals for colorectal cancer with Robert Schoen, MD, MPH, and Jeffrey Dueker, MD, MPH. This study has the ability to transform our traditional thinking on colon cancer prevention and diagnosis. We also take a closer look at the role of advanced endoscopy in the treatment of patients with liver disease with Harkirat Singh, MD. With the pandemic still at our heels, we also hear from the lab of Shari Rogal, MD, MPH, concerning COVID-cirrhosis interactions.

We make advances that matter to our patients, their loved ones, and the medical community. It is my pleasure to share our progress in this edition of Digest.

Sincerely,

Naudia L. Jonassaint, MD, MHS, MBA
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Tracking Cirrhosis Care During the COVID-19 Pandemic

Understanding how the COVID-19 pandemic has affected the delivery of preventative medicine is essential to restoring and improving care as the United States progresses through the pandemic. Shari Rogal, MD, MPH, and Adeyinka Adejumo, MD, PhD, MS, have been utilizing novel methodology to evaluate the impact of the COVID-19 pandemic on the implementation of high-value care among veterans with cirrhosis.

A healthy diet has long been lauded as an essential part of a healthy lifestyle conducive to disease prevention. While the nutrients and healthy fats digested in the stomach and small intestine are essential, the nondigestible fiber from plant foods that passes through the colon is crucial for good health as well.

**Dietary Switch Studies**

The United States Veterans Health Administration (VHA) provides care for over 9 million veterans at 146 VA Medical Centers (VAMCs) and 1,113 clinics nationwide. To maintain and improve their system, the VHA collects massive amounts of data reflecting which patients are seeking care, which patients are getting care, and the quality of care provided by each hospital in the system. Dr. Rogal, a staff transplant hepatologist and gastroenterologist in the VA Pittsburgh Healthcare System and associate professor of Medicine, Surgery, and Clinical and Translational Science in the Division of Gastroenterology, Hepatology and Nutrition, evaluates the programs offered by the VHA and was awarded a grant from the VHA to assess COVID-related disruptions to the care of patients with liver disease.1,2 Dr. Rogal hypothesized that utilization of preventative services would decline during the COVID pandemic even for critically ill patients, such as those with cirrhosis. Testing this hypothesis was possible due to VA databases that contain complex longitudinal data from the large population treated at VHA facilities, along with the expertise of Dr. Adejumo, a clinical and T32 research fellow in the Division, who proposed and applied an advanced computational analysis to the large data set under Dr. Rogal’s mentorship.

Approximately 80,000 veterans with cirrhosis receive care nationally at VAMCs. To examine the impact of the COVID-19 pandemic on the care of patients with advanced liver disease, all U.S. veterans with cirrhosis who were enrolled in VHA health care in October 2018 were identified using ICD-10-CM codes. This cohort was then followed for 12 quarters, through September 2021. Outcomes measured for each quarter included whether hepatocellular carcinoma (HCC) screening was performed and whether endoscopic variceal surveillance was conducted or treatment initiated with nonselective beta-blockers to prevent bleeding based on clinical findings suggestive of varices. Imaging to screen for HCC every six months and endoscopic surveillance of esophageal varices or initiation of beta-blocker treatment are considered the standard of care when monitoring patients with cirrhosis, and a VHA improvement initiative aimed to increase guideline-concordant utilization of these tests prior to the COVID pandemic.1,4,6 Additionally, all-cause hospitalizations and mortality were assessed by quarter.

Dr. Adejumo applied joinpoint regression analysis to identify inflection points in the data reflecting increased or decreased health care use.12 This analysis used data to select important timepoints rather than the investigators selecting timepoints based on a priori perceptions.

Using joinpoint regression, Dr. Adejumo found that screening for HCC dropped precipitously in early 2020. Guideline-concordant screening for HCC began to recover in late 2020, although as of September 2021, it had not returned to 2019 levels. (Figure 1A) Screening or treatment for suspected esophageal varices also dropped precipitously at the beginning of the pandemic and was still decreasing at nearly the same rate when the study period ended in September 2021. (Figure 1B) Dr. Adejumo and Dr. Rogal are currently continuing the analyses through 2022.

When the cohort was stratified by gender, race, proximity to a VAMC, or socioeconomic factors, there were no differences in the observed trends in the subgroups assessed. Dr. Rogal had hypothesized that people with limited access or other barriers to care would be disproportionately affected by the COVID pandemic, resulting in decreases in preventative screenings necessitated by their severe liver disease. Reassuringly, the study indicated that many disparities in health care that were exacerbated by the COVID pandemic were not exacerbated in patients with cirrhosis treated by the VA Healthcare System. However, the decreases observed in preventative care across all veterans with cirrhosis are concerning and are being actively addressed by the VHA leadership.

Dr. Adejumo presented this work in May 2022 at Digestive Diseases Week, a large, multisociety meeting for physicians, researchers, and industry partners in the fields of gastroenterology, hepatology, endoscopy, and gastrointestinal surgery, where it was well-received.

The study provides information that will help guide policies for the VHA at a national level and suggests potential areas for improvement to other health care systems as well. The VHA is offering support for VAMCs with barriers to care. Understanding trends in the utilization of preventative medical care is necessary to ensure a full recovery of services as the country progresses through the COVID pandemic.

**References/Recommended Reading**

Endo-Hepatology: Advanced Endoscopy in the Management of Liver Disease

Esophago-gastro-duodenoendoscopy (EGD) has long been used in patients with liver disease to assess and treat esophageal varices and gastric antral vascular ectasias. New techniques guided by endoscopic ultrasound (EUS) have broadened the scope of care that endoscopists can provide for patients with liver disease. EUS allows evaluation of the liver parenchyma and hepatic vessels from a close proximity, which has led to development of advanced interventions, aptly termed endo-hepatology. We’ll discuss how this subspecialty of advanced endoscopy can essentially offer comprehensive evaluation during a single procedure when multiple assessments are deemed necessary for patients with suspected or established chronic liver disease.

EUS-guided liver biopsy (EUS-LB) is technically easy due to the location of the left liver lobe adjacent to the stomach and excellent visualization of any intervening blood vessels, which minimizes bleeding complications. Although liver biopsies have been traditionally done via a percutaneous or transangular route, published data shows that the samples obtained using EUS-LB meet or exceed the criteria set by the American Association for the Study of Liver Diseases for an adequate liver biopsy specimen in >95% of biopsies. Anecdotally, we have achieved adequate sampling in almost 100% of EUS-guided liver biopsies at our center. EUS-LB has several advantages as compared with percutaneous or transangular biopsy. Because no skin is punctured, there is less postprocedural pain. With the ability to perform both right and left lobe biopsies, sampling error due to patchy distribution of liver disease is minimized. The recovery time is shorter. The sedation used for EUS makes EUS-LB an appealing option for patients here at UPMC.

A 58-year-old male presented with recurrent ascites. Evaluation at an outside institution showed no cirrhosis on imaging or liver biopsies and no portal hypertension on transjugular HVPG measurement. After evaluation, our hepatology team was still concerned about portal hypertension, and EGD and EUS exams were performed. EGD showed portal hypertensive gastropathy and small esophageal varices. The EUS-HVPG was 15 mm Hg, consistent with clinically significant portal hypertension. Liver biopsy showed obliterator portal venopathy without cirrhosis. So, a diagnosis of noncirrhotic portal hypertension was made to explain the etiology of the patient’s recurrent ascites. He underwent a TIPS procedure for management of his condition. This efficient “one-stop-shop” comprehensive assessment using advanced endoscopy yielded an actionable diagnosis, which truly benefited this patient.

References
In February 2022, the first patient was enrolled in a multicenter, National Cancer Institute-funded clinical trial that could reduce the number of surveillance colonoscopy exams performed, freeing up resources to better serve public health. Robert E. Schoen, MD, MPH, and Jeffrey M. Duinker, MD, MPH, in the UPMC Division of Gastroenterology are national primary investigators of the FORTE (Five or Ten Year Colonoscopy for 1-2 Non-Advanced Adenomatous Polyps) trial, which will determine the best timing for a repeat colonoscopy in patients with nonadvanced adenomas found and removed at colonoscopy.

Screening with colonoscopy reduces colorectal cancer (CRC) incidence and mortality and is recommended for individuals over 45 years of age. Approximately 50% of individuals who undergo screening colonoscopy will be found to have adenomatous polyps, benign growths that can be a precursor to CRC. After adenomas are excised, patients are advised to return for surveillance colonoscopy exams to ensure that future malignant or premalignant lesions are detected in a timely fashion.

CRC Risk and Adenomatous Polyps

Adenomatous polyps are common. Most are small and nonadvanced and are unlikely to evolve into cancer. Since 2012, patients found to have one to two nonadvanced polyps removed during screening colonoscopy have been advised to return for surveillance colonoscopy in five to 10 years. Patients with no polyps detected during screening colonoscopy were advised to repeat colonoscopy in 10 years. However, in recent years, several large studies demonstrated a similar long-term cancer incidence for individuals with one to two small, nonadvanced adenomatous polyps removed as compared with individuals with no polyps detected.1 In one study, Dr. Schoen and his colleagues examined the colonoscopy findings of over 16,000 patients enrolled in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, which included patients treated at UPMC. At the outset, approximately 50% had no adenomas, 31% had nonadvanced adenomas, and 18% had an advanced adenoma. They were followed for a median of 12.9 years. There was no significant difference in colorectal cancer incidence between participants with nonadvanced adenoma as compared with participants with no adenoma (rate ratio [RR], 1.1 [95% CI, 0.8-1.7]; P = .30) and no significant difference in CRC (RR, 1.2 [95% CI, 0.5-2.7]; P = .68). In contrast, patients with advanced adenomas were significantly more likely to develop CRC (RR, 2.7 [95% CI, 1.9-3.7]; P < .001) and had an increased mortality risk (RR, 2.6 [95% CI, 1.2-5.7]; P = .01) as compared with patients with no adenomas.1 As a result of these and similar findings, the U.S. Multi-Society Task Force on Colorectal Cancer modified its recommendations in 2020, extending the interval for repeat colonoscopy after the detection and removal of one to two small (<10 mm) adenomatous polyps to seven to 10 years, from the previous recommendation of five to 10 years.2

However, there was concern in concluding that the patients with nonadvanced adenomas in the aforementioned studies had the same cancer risk as patients with no adenomas. The individuals with nonadvanced adenomas had much higher rates of surveillance colonoscopy, during which adenomatous polyps, and even advanced adenomatous polyps, were more likely to have been removed during the follow-up period. The reason for the similar cancer incidence observed was not that the underlying risk was the same but rather that surveillance colonoscopy with polypectomy drove down the cancer incidence in patients with nonadvanced adenomas. So, rather than demonstrating that surveillance was not necessary, on the contrary, the findings may provide evidence that surveillance was effective and necessary. Only a randomized trial could answer the question of whether the recommended surveillance was beneficial—hence the rationale for FORTE.

FORTE: A Randomized Clinical Trial Comparing Five or Ten Year Surveillance Colonoscopy

FORTE is a clinical trial sponsored by the National Cancer Institute Community Oncology Research Program (NCORP), a national network of investigators and cancer providers, which is funded by NCI Oncology, a participating organization of the NCI National Clinical Trials Network (NCTN) program. NCORP conducts multi-site cancer clinical trials in prevention, screening, symptom management, and cancer care delivery. Dr. Schoen, Dr. Duinker, and their colleagues nationwide are recruiting 9,500 individuals to participate in the FORTE trial. Candidates must be between the ages of 50 and 70 and have undergone a qualifying colonoscopy with a first-time diagnosis and complete removal of one or two adenomas. A history of adenomatous polyps, a genetic predisposition to CRC, or a high-risk family history of CRC exclude participation. Patients will be randomized to either surveillance colonoscopy at 5 and 10 years or at 10 years. Participants in either arm may undergo an undersampled colonoscopy if medically indicated. (Figure 1)

The primary endpoint of the FORTE trial is the incidence of CRC at 10 years; the two surveillance protocols — 10 vs. 5 and 10 years — will be compared. Secondary endpoints are the incidence of advanced adenomas, the incidence of advanced CRC, and mortality due to CRC. A cost-benefit analysis is also planned. Additionally, blood and stool samples will be collected from this large study cohort and will provide a resource to study the relationships between genetics, stool microbial content, and outcomes.

If the FORTE trial finds that surveillance colonoscopy every 10 years is noninferior to 5- and 10-year surveillance, as observational studies have suggested, millions of individuals will avoid the inconvenience, costs, and medical risks incurred for a colonoscopy that does not add significant benefit. Additionally, if millions fewer surveillance colonoscopies are performed, personnel and facility resources could be reallocated to better serve public health, for example, by increasing screening to underserved populations. The American College of Gastroenterology (ACG), the American Society for Gastrointestinal Endoscopy (ASGE), and the American Gastroenterological Association (AGA) have formally expressed their support for the conduct of the trial and encourage participation by endoscopists and eligible patients.

Because ~15 million colonoscopies are performed every year, and small, benign adenomas are found in a third of patients undergoing screening colonoscopy, there are numerous potential participants for the FORTE trial. Additionally, eligibility is not limited to patients with colonoscopy performed after a site launches the FORTE trial. Patients with a qualifying colonoscopy up to four years prior may be eligible. The FORTE team is applying innovative approaches to enhance patient recruitment for the trial. For example, they have contracted with Peces, a healthcare artificial intelligence company with expertise in natural language processing (NLP). Using NLP, colonoscopy and pathology reports in the electronic medical record can be analyzed in bulk.3 A participating institution may be performing 30,000–40,000 colonoscopies per year, and NLP will provide a more efficient and automated way to identify eligible participants.

The FORTE trial is open to a great start! Centers that launched the study are enrolling well. For example, UPMC has enrolled ~50 patients in the first six months. New study locations are being added. For more, visit FORTE’s trial portal with the potential to definitively inform subsequent clinical practice.

References:

What Is This?

A 46-year-old female with a history of hypothyroidism was transferred from an outside hospital for respiratory and cardiac failure and extensive clot burden with concern for malignancy. She was found to have a large right-sided pleural effusion, multifocal pneumonia, a new decrease in her left ventricular ejection fraction which is 15%, and extensive clots bilaterally from her wrist to her internal jugular vein and left popliteal artery. At the outside hospital, she was intubated, and was started on norepinephrine, ejection fraction which is 15%, and extensive clots bilaterally from her wrist to her internal jugular vein.

What Is This?

The pleural effusion was found to be an extensive venous and arterial clot burden, she underwent a thorough work-up and extensive venous and arterial clot burden, she underwent a thorough work-up and extensive thrombi and reported hemorrhoidal bleeding. She was discharged on life-long anticoagulation.

Patient’s Outcome (turn over to read)

The findings were consistent with porcelain gallbladder (PGB).

The rate of gallbladder carcinoma in PGB is about 0% to 5% based on recent studies.1 Of the two types of PGB, selective mucosal calcification holds a higher malignancy risk. Gallbladder carcinoma is usually adenocarcinoma. In selective mucosal calcification, some glands are still present and have the potential to transform into malignant cells.2-3 Gallbladder carcinoma has a five-year survival of <5%4 with median survival of nine months.5 Should we recommend cholecystectomy for every PGB case? There are no guidelines to answer this question currently, but published expert opinion recommends cholecystectomy if the patient is symptomatic or has concurrent gallbladder disease, complications, or selective mucosal calcification type.1,4,5,9,10

Patient’s Outcome (turn over to read)

Milestones

The Division of Gastroenterology, Hepatology and Nutrition honors the service of Dr. David Whitcomb, MD, PhD, previous chief and chair of the section of gastroenterology. Dr. Whitcomb will retire in December 2022. We also recognize the outstanding leadership of Robert (Rocky) Schoen, MD, MPH, who served as Division chief from 2016 through the summer of 2022. After his support and success as chief, Dr. Schoen will return to his robust clinical practice and to the rigorous study associated with his three NIH grants.

We welcome interim chief Naulia L. Jonassaint, MD, MPH, MBA. You met Dr. Jonassaint on the front cover of the Division’s Clinical and Research Communities. We are saddened by the passing of colleagues, friend, and outstanding physician Kim Works, MD. Dr. Works served as faculty with the Division of Gastroenterology, Hepatology, and Nutrition in Greenville, PA.

UPMC Total Care-IBD: Accepting Referrals

As the nation’s first patient-centered, multidisciplinary program for people with IBD, UPMC Total Care-IBD provides UPMC Health Plan members with enhanced access to an IBD gastroenterologist, specialized health care professionals (including a dietitian, behavioral health counselor, etc.), and a full spectrum of support services to develop personalized treatment plans. Patients who prefer to remain with their existing gastroenterologist can still enroll and take advantage of the program’s offerings.

• To enroll a patient or ask medical questions, call 412-647-2183
• To request an in-person or virtual educational Grand Rounds or a discussion with our team, email jol2@pitt.edu

References/ Recommended Reading

When Constipation Is Not Just Constipation

A 29-year-old female with a history of asthma presented with abdominal pain and constipation for over a week. She had tried lactulose, magnesium citrate, and bisacodyl without success. She usually takes Miralax™ daily and has one to two bowel movements every other day. She had a colonoscopy the year prior for constipation, which showed two hyperplastic polyps but otherwise no mucosal abnormalities.

Her exam was notable for a distended and tympanic abdomen without rebound or rigidity. Blood work was unremarkable. Computed tomography (CT) of the abdomen and pelvis showed an extremely distended colon with fluid, suggesting colonic obstruction. (Figure 1a) In addition, an ill-defined mass was seen in the rectum, raising suspicion for a malignant lesion. (Figure 1b)

The patient underwent decompressive colonoscopy the following day, where an obstructing mass was identified about 10 cm from the anal verge. (Figure 2) The mucosa overlying the mass appeared only mildly congested but was otherwise similar in morphology to the surrounding healthy rectal mucosa. Biopsies of the mass showed colonic mucosa with focal active colitis, which was negative for malignancy. Tumor markers (CEA and CA-19-9) were negative. Rebiopsy was recommended. Her abdominal pain and distension improved in the subsequent days, and she started to have bowel movements. She was discharged with an aggressive bowel regimen and planned to pursue a rectal EUS for tissue sampling.

However, the patient returned to the hospital 10 days later with recurrent constipation and abdominal distension despite implementation of scheduled laxatives. A rectal EUS showed congested mucosa causing narrowing and tortuosity in the rectum, and diffuse wall thickening with surrounding ill-defined inflammatory response. Increased thickness of the intramural wall was also visualized endoscopically, but the wall layers could not be fully defined due to the inability to pass the echoendoscope beyond the tortuous region. A few benign-appearing lymph nodes were biopsied in the perirectal region. There was limited tissue for evaluation, but an equally mixed population of T and B cells was believed to be benign lymphoid tissue. A second decompression tube was placed at that time, which unfortunately dislodged a few days later and she developed obstruction again.

A decompensive sigmoidoscopy as well as a repeat rectal EUS were performed that again demonstrated diffuse wall thickening at the site of strictureing, but with no definitive mass discerned. The rectal wall layers were distorted and appeared tethered with heterogenous changes extrinsic to the rectal wall. Fine needle aspiration (FNA) showed gastrointestinal epithelial contaminants and fragments of bland smooth muscle. These findings were nonspecific and nondiagnostic overall, with differential including spindle cell neoplasm, endometriosis, and leiomyoma. Upon further investigation of her history, the patient noted that constipation was worsened by the onset of menses. A pelvic MRI showed a mass-like circumferential submucosal thickening of midrectum with adjacent stranding extending posteriorly to the right pelvic sidewall. Multiple prominent perirectal lymph nodes and uterus with tiny fibroids were also seen. The ovaries appeared unremarkable without evidence of endometriomas. Gynecology was consulted, and it was believed that rectal endometriosis, though possible, was atypical due to lack of evidence of disease in the other parts of the pelvis. Her symptoms improved, and she was discharged with gynecology follow-up for further evaluation.

Unfortunately, she presented again four days later with constipation and distension, and underwent repeat flexible sigmoidoscopy for decompression. Given the persistence of symptoms and recurrent hospitalizations and procedures within one month, a decision was made to pursue diagnostic laparoscopy and exam under anesthesia with Colorectal Surgery. As soon as the pelvis was visualized on laparoscopy, extensive adhesions and implants were detected in the uterus, right ovary, right fallopian tube, and right uterosacral region, extending circumferentially to involve the middle third of the rectum. These findings were concerning for stage IV endometriosis, and gynecology was consulted intraoperatively. Given the extent of disease, right salpingo-oophorectomy and hysterectomy, as well as enterolysis along the perirectal spaces, were pursued in efforts to free up the area of endometrial implants. After further dissection and evaluation however, the fibrosis around the rectum could not be released. Therefore, a diverting sigmoid loop colostomy was created with plans to pursue a low anterior resection later on. The patient did well post-surgery. Biopsy of the uterosacral adhesions showed fibrous and smooth muscle tissue with endometriosis, present also in the biopsies of the right fallopian tube and right ovary.

Endometriosis affects the bowel in approximately 5% to 12% of all cases, with 90% involving the rectum or sigmoid colon. Disease often presents as a mass or luminal stenosis, and mainly involves the muscularis propria and serosa. As a result, endoscopic biopsies are frequently not sufficient because mucosal involvement is sparse, leading to a high proportion of falsely negative evaluations.1 The average time from onset of symptoms to achieving a diagnosis of endometriosis can be prolonged. Therefore, high clinical suspicion is warranted to ensure prompt recognition.

References


Figure 1b. Dilated loops of bowel with fluid suggesting colonic obstruction.

Figure 1a. Dilated loops of bowel with fluid suggesting colonic obstruction.
UPMC Pittsburgh Gut Club (Virtual Program)

Why and When Should I Use Pre-emptive TPS?
Presented by Juan Carlos García-Pagán, MD, PhD

Tuesday, Jan. 24, 2023
7:30 to 9 a.m. ET
Register at cce.upmc.com/content/pittsburgh-gut-club-2022/2023

Save the Date: IBD U.N.I.T.E. 2023
Free patient education event

Saturday, March 4, 2023
9 a.m.
Contact: joj2@pitt.edu
Registration opens in early 2023.

UPMC/IBDUNITE
This event is open to patients, family members, and loved ones, and it is an accredited symposia for nurses and dietitians.

Topics will include:

• The history of IBD and the impact of medical advancements on treatment strategies
• Case studies
• Education for new patients
• Fertility, nutrition, and behavioral health concerns
• Caregiver support
• Ostomy decisions
• Long-term patient care

Save the Date: PancreasFest 2023
July 27 to 28, 2023
Pittsburgh, Pa.
PancreasFest.com

To learn more about the UPMC Division of Gastroenterology, Hepatology and Nutrition, please visit UPMCPhysicianResources.com/GI.