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Preface: Gastrointestinal, Hepatic, and Pancreatic Manifestations of COVID-19 Infection

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The Pathogenesis of Gastrointestinal, Hepatic, and Pancreatic Injury in Acute and Long Coronavirus Disease 2019 Infection

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Hadar Meringer, Andrew Wang, and Saurabh Mehandru

The gastrointestinal (GI) tract is targeted by severe acute respiratory syndrome coronavirus-2. The present review examines GI involvement in patients with long coronavirus disease and discusses the underlying pathophysiological mechanisms that include viral persistence, mucosal and systemic immune dysregulation, microbial dysbiosis, insulin resistance, and metabolic abnormalities. Due to the complex and potentially multifactorial nature of this syndrome, rigorous clinical definitions and pathophysiology-based therapeutic approaches are warranted.

Liver and Biliary Tract Disease in Patients with Coronavirus disease-2019 Infection Sirina Ekpanyapong and K. Rajender Reddy

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Coronavirus disease-2019 (COVID-19) had become a global pandemic since March 2020. Although, the most common presentation is of pulmonary involvement, hepatic abnormalities can be encountered in up to 50% of infected individuals, which may be associated with disease severity, and the mechanism of liver injury is thought to be multifactorial. Guidelines for management in patients with chronic liver disease during COVID-19 era are being regularly updated. Patients with chronic liver disease and cirrhosis, including liver transplant candidates and liver transplant recipients are strongly recommended to receive SARS-CoV-2 vaccination because it can reduce rate of COVID-19 infection, COVID-19—related hospitalization, and mortality.

The Pancreas in Coronavirus Disease 2019 Infection

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Tiago Correia de Sá and Mónica Rocha

An association between acute pancreatitis (AP) and coronavirus disease 2019 (COVID-19) has been proposed but the mechanisms of pancreatic injury of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) and the implicative role on the development of AP are not yet fully understood. COVID-19 also imposed major challenges on pancreatic cancer management. We conducted an analysis on the mechanisms of pancreatic injury by SARS-CoV-2 and reviewed published case reports of AP attributed to COVID-19. We also examined the pandemic effect on pancreatic cancer diagnosis and management, including pancreatic surgery.

A Surgical Perspective of Gastrointestinal Manifestations and Complications of COVID-19 Infection

Anthony Gebran, Ander Dorken-Gallastegi, and Haytham M.A. Kaafarani

The coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2, has quickly spread over the world since December 2019. COVID-19 is a systemic disease that can affect various organs throughout the body. Gastrointestinal (GI) symptoms have been reported in 16% to 33% of all patients with COVID-19 and in 75% of critically ill patients. This chapter reviews the GI manifestations of COVID-19 as well as their diagnostic and treatment modalities.

Diarrhea and Coronavirus Disease 2019 Infection

David M. Friedel and Mitchell S. Cappell

The global coronavirus disease-2019 (COVID-19) pandemic has caused significant morbidity and mortality, thoroughly affected daily living, and caused severe economic disruption throughout the world. Pulmonary symptoms predominate and account for most of the associated morbidity and mortality. However, extrapulmonary manifestations are common in COVID-19 infections, including gastrointestinal (GI) symptoms, such as diarrhea. Diarrhea affects approximately 10% to 20% of COVID-19 patients. Diarrhea can occasionally be the presenting and only COVID-19 symptom. Diarrhea in COVID-19 subjects is usually acute but is occasionally chronic. It is typically mild-to-moderate and nonbloody. It is usually much less clinically important than pulmonary or potential thrombotic disorders. Occasionally the diarrhea can be profuse and life-threatening. The entry receptor for COVID-19, angiotensin converting enzyme-2, is found throughout the GI tract, especially in the stomach and small intestine, which provides a pathophysiologic basis for local GI infection. COVID-19 virus has been documented in feces and in GI mucosa. Patients with preexisting diarrhea before contracting COVID-19 infection may have diarrhea exacerbation with COVID-19 infection, or alternatively the diarrhea may be incidental to COVID-19 infection. Treatment of COVID-19 infection, especially antibiotic therapy, is a common culprit, but secondary infections including bacteria, especially Clostridioides difficile, are sometimes implicated. Workup for diarrhea in hospitalized patients usually includes routine chemistries; basic metabolic panel; and a complete hemogram; sometimes stool studies. possibly including calprotectin or lactoferrin; and occasionally abdominal CT scan or colonoscopy. Treatment for the diarrhea is intravenous fluid infusion and electrolyte supplementation as necessary, and symptomatic antidiarrheal therapy, including Loperamide, kaolin-pectin, or possible alternatives. Superinfection with C difficile should be treated expeditiously. Diarrhea is prominent in post-COVID-19 (long COVID-19), and is occasionally noted after COVID-19 vaccination. The spectrum of diarrhea in COVID-19 patients is presently reviewed including the pathophysiology, clinical presentation, evaluation, and treatment.

Gastrointestinal Bleeding in COVID-19-Infected Patients

Mitchell S. Cappell and David M. Friedel

COVID-19 infection is an ongoing catastrophic global pandemic with significant morbidity and mortality that affects most of the world population.

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Respiratory manifestations predominate and largely determine patient prognosis, but gastrointestinal (GI) manifestations also frequently contribute to patient morbidity and occasionally affect mortality. GI bleeding is usually noted after hospital admission and is often one aspect of this multisystem infectious disease. Although the theoretical risk of contracting COVID-19 from GI endoscopy performed on COVID-19-infected patients remains, the actual risk does not seem to be high. The literature concerning GI bleeding in COVID-19 patients is presently reviewed.

COVID-19 and Inflammatory Bowel Disease

Keith C. Summa and Stephen B. Hanauer

The COVID-19 pandemic caused by the SARS-CoV-2 virus represents an unprecedented global health crisis. Safe and effective vaccines were rapidly developed and deployed that reduced COVID-19-related severe disease, hospitalization, and death. Patients with inflammatory bowel disease are not at increased risk of severe disease or death from COVID-19, and data from large cohorts of patients with inflammatory bowel disease demonstrate that COVID-19 vaccination is safe and effective. Ongoing research is clarifying the long-term impact of SARS-CoV-2 infection on patients with inflammatory bowel disease, long-term immune responses to COVID-19 vaccination, and optimal timing for repeated COVID-19 vaccination doses.

The Impact of COVID-19 Infection on Miscellaneous Inflammatory Disorders of the Gastrointestinal Tract

Mitchell S. Cappell, Martin Tobi, and David M. Friedel

The novel coronavirus pandemic of COVID-19 has emerged as a highly significant recent threat to global health with about 600,000,000 known infections and more than 6,450,000 deaths worldwide since its emergence in late 2019. COVID-19 symptoms are predominantly respiratory, with mortality largely related to pulmonary manifestations, but the virus also potentially infects all parts of the gastrointestinal tract with related symptoms and manifestations that affect patient treatment and outcome. COVID-19 can directly infect the gastrointestinal tract because of the presence of widespread angiotensin-converting enzyme 2 receptors in the stomach and small intestine that can cause local COVID-19 infection and associated inflammation. This work reviews the pathopysiology, clinical manifestations, workup, and treatment of miscellaneous inflammatory disorders of the gastrointestinal tract other than inflammatory bowel disease.

Gastrointestinal and Hepatobiliary Symptoms and Disorders with Long (Chronic) COVID Infection

Anam Rizvi, Yonatan Ziv, James M. Crawford, and Arvind J. Trindade

Long COVID is a novel syndrome characterizing new or persistent symptoms weeks after COVID-19 infection and involving multiple organ systems. This review summarizes the gastrointestinal and hepatobiliary sequelae of long COVID syndrome. It describes potential biomolecular mechanisms, prevalence, preventative measures, potential therapies, and health care and economic impact of long COVID syndrome, particularly of its gastrointestinal (GI) and hepatobiliary manifestations.

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Gastrointestinal Endoscopy in Patients with Coronavirus Disease 2019: Indications, Findings, and Safety

Shahnaz Sultan

The coronavirus disease 2019 (COVID-19) pandemic has changed the practice of gastroenterology and how we perform endoscopy. As with any new or emerging pathogen, early in the pandemic, there was limited evidence and understanding of disease transmission, limited testing capability, and resource constraints, especially availability of personal protective equipment (PPE). As the COVID-19 pandemic progressed, enhanced protocols with particular emphasis on assessing the risk status of patients and proper use of PPE have been incorporated into routine patient care. The COVID-19 pandemic has taught us important lessons for the future of gastroenterology and endoscopy.

Surgical Implications of Coronavirus Disease-19

Ander Dorken-Gallastegi, Dias Argandykov, Anthony Gebran, and Haytham M.A. Kaafarani

As the coronavirus disease-19 (COVID-19) pandemic continues to evolve in 2022 with the surge of novel viral variants, it is important for physicians to understand and appreciate the surgical implications of the pandemic. This review provides an overview of the implications of the ongoing COVID-19 pandemic on surgical care and provides recommendations for perioperative management. Most observational studies suggest a higher risk for patients undergoing surgery with COVID-19 compared with risk-adjusted non-COVID-19 patients.

Diagnostic and Therapeutic Radiology of the GI Tract, Liver, and Pancreas in Patients with COVID

Piero Boraschi, Francescamaria Donati, Ilaria Ambrosini, Luciana Bruni, Maria Letizia Mazzeo, Rachele Tintori, Michele Tonerini, and Emanuele Neri

Coronavirus disease 2019 (COVID-19) pulmonary involvement has been extensively reported in the literature. Current data highlight how COVID-19 is a systemic disease, affecting many other organs, including the gastrointestinal, hepatobiliary, and pancreatic organs. Recently, these organs have been investigated using imaging modalities of ultrasound and particularly computed tomography. Radiological findings of the gastrointestinal, hepatic, and pancreatic involvement in patients with COVID-19 are generally nonspecific but are nonetheless helpful to evaluate and manage COVID-19 patients with involvement of these organs.

Pathologic Characteristics of Digestive Tract and Liver in Patients with Coronavirus Disease 2019

Chunxiu Yang, Lijun Cai, and Shu-Yuan Xiao

With the high prevalence of coronavirus disease-2019 (COVID-19), there has been increasing understanding of the pathologic changes associated with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This review summarizes the pathologic changes in the digestive system and liver associated with COVID-19, including the injuries induced by

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SARS-CoV2 infection of GI epithelial cells and the systemic immune responses. The common digestive manifestations associated with COVID-19 include anorexia, nausea, vomiting, and diarrhea; the clearance of the viruses in COVID-19 patients with digestive symptoms is usually delayed. COVID-19-associated gastrointestinal histopathology is characterized by mucosal damage and lymphocytic infiltration. The most common hepatic changes are steatosis, mild lobular and portal inflammation, congestion/sinusoidal dilatation, lobular necrosis, and cholestasis.

Special Critical Review Articles

Critical Review Two-Years Thereafter of the Effectiveness of the Revolutionary Changes in a Gastroenterology Division at A Medical School Teaching Hospital in Response to the COVID-19 Pandemic Medical School, Residency, and Gastrointestinal Fellowship Education and Clinical Practice of Gastroenterology Attendings and Gastrointestinal Endoscopy

Mitchell S. Cappell

AIM: Critically review two-years afterwards effectiveness of revolutionary changes in academic-gastroenterologydivision due to COVID-19 pandemic.HOSPITAL-SETTING: William-Beaumont-Hospital-Royal-Oak, primary teachinghospital, Oakland-University-Medical-School, 6 GI fellows, 36 GI attendings (reduced to 29 with resignations). COVID-19 epicenter, metropolitan Detroit (daily hospital census: 0-patients, March-2020, increased to 300-patients, April-2020). Review based on expert opinion: (GI chief/Program Director >14 years, >320 publications). ADVANAGEOUS-CHANGES: 1- Temporarily pulled GI fellows to supervise exclusively COVID-19 wards; 2- performed only emergency/urgent endoscopy during pandemic peak (reduction from 100 to 4 endoscopies/day at nadir); 3-Changed "live" to "virtual" lectures, conferences, interviews, and graduations; 4-initially used "canned" video talks which worked poorly, eventually changed to Google- Zoom/Microsoft-Teams which performed superbly; 5-medical students/GI fellows graduated on-time despite missing minor requirements due to pandemic; 6-GI clinic reduced 50%; 7-GI-fellowship-program-director contacted fellows twice weekly to monitor pandemic-induced emotional stress; 8-ACGME cancelled annual fellowship survey in 2020. DISADVANTAGEOU-SCHANGES: Huge hospital revenue shortfall exacerbated by Hospital's \$84.5-milion governmental fine for Stark-Law/antikickback violations. Employee terminations during pandemic: reduced GI-fellowship support staff and endoscopy nurses. Severe personnel shortages from changing long-term academic anesthesiology group to low-cost anesthesiology group and many nurse resignations (after hospital prevented nursing unionization) caused 50% reduction in endoscopies and long endoscopy delays. Hospital terminated without cause numerous, most senior, highly respected, and elderly hospital leaders (e.g., chief medical officer, multiple department chairs).CONCLUSION: Profound, pervasive, GI-Divisional changes maximized clinical resources devoted to pandemic and minimized risk of infection transmission. Massive cost-cutting degraded academic quality of hospital while offering hospital to about 100 hospital systems, until hospital eventually "sold" to Spectrum Health, without faculty input.

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A Critical Review from the Perspective of 2 Years Thereafter of the Effectiveness of Revolutionary Changes in a Gastroenterology Division at a Medical School Teaching Hospital due to the Coronavirus Disease-2019 Pandemic Gastrointestinal Physician Clinical Practice and Emotional Stresses, Gastrointestinal Graduate Medical Education, Gastrointestinal Professional Societies, and Pandemic Control

Mitchell S. Cappell

AIM: Critically review two-years afterward effectiveness of revolutionary changes in academic-gastroenterologydivision due to COVID-19 pandemic.HOSPITAL-SETTING: William-Beaumont-Hospital-Royal-Oak, primary teachinghospital, Oakland-University-Medical-School, 6 GI fellows, 36 GI attendings (reduced to 29 with resignations). COVID-19 epicenter, metropolitan Detroit (daily hospital census: 0-patients, March-2020, increased to 300-patients, April-2020). Review based on expert opinion: (GI chief/Program Director >14 years. >320 publications).ADVANAGEOUS-CHANGES: 1- Temporarily pulled GI fellows to supervise exclusively COVID-19 wards; 2- performed only emergency/urgent endoscopy during pandemic peak (reduction from 100 to 4 endoscopies/day at nadir); 3-Changed "live" to "virtual" lectures, conferences, interviews, and graduations; 4-initially used "canned" video talks which worked poorly, eventually changed to Google-Zoom/Microsoft-Teams which performed superbly; 5-medical students/Gl fellows graduated on-time despite missing minor requirements due to pandemic: 6-GI clinic reduced 50%; 7-GI-fellowship-program-director contacted fellows twice weekly to monitor pandemic-induced emotional stress; 8-ACGME cancelled annual fellowship survey in 2020, DISADVANTAGEOU-SCHANGES: Huge hospital revenue shortfall exacerbated by Hospital's \$84.5-milion governmental fine for Stark-Law/antikickback violations. Employee terminations during pandemic: reduced GI-fellowship support staff and endoscopy nurses. Severe personnel shortages from changing long-term academic anesthesiology group to low-cost anesthesiology group and many nurse resignations (after hospital prevented nursing unionization) caused 50% reduction in endoscopies and long endoscopy delays. Hospital terminated without cause numerous, most senior, highly respected, and elderly hospital leaders (e.g., chief medical officer, multiple department chairs).CONCLUSION: Profound, pervasive, GI-Divisional changes maximized clinical resources devoted to pandemic and minimized risk of infection transmission. Massive cost-cutting degraded academic quality of hospital while offering hospital to about 100 hospital systems, until hospital eventually "sold" to Spectrum Health, without faculty input.