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Gastrointestinal Endoscopy in COVID-19 Patients: Indications, Findings, and Safety

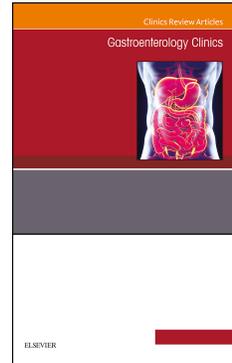
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Title: Gastrointestinal Endoscopy in COVID-19 Patients: Indications, Findings, and Safety

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Synopsis

The 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 how SARS-CoV2 was transmitted, limited testing capability, and resource constraints, especially availability of personal protective equipment (PPE). As 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. COVID-19 pandemic has taught us important lessons for the future of gastroenterology and endoscopy.

Key words: COVID-19, endoscopy, transmission risk, personal protective equipment, gastrointestinal manifestations

Key Points

1. SARS-CoV2 transmission appears to mainly occur via *respiratory particles* (respiratory droplets and smaller aerosols which are expelled from the respiratory tract during speaking, breathing and coughing) and **close contact** with infected persons
2. WHO and CDC advise using respirator masks, such as N95s when performing procedures that might pose higher risk for transmission if the patient has SARS-CoV-2 infection (e.g., that generate potentially infectious aerosols or involving anatomic regions where viral loads might be higher, such as the nose and throat, oropharynx, and respiratory tract).
3. Endoscopic findings in COVID-19 patients suggest that SARS-CoV-2 does not appear to behave as a highly invasive and injurious pathogen to gastrointestinal mucosa.

Introduction

The spread of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a pandemic by the World Health Organization (WHO) on the 11th of March 2020.¹ Since the outbreak was first identified in December 2019 in Wuhan, China, the public health and social impact of the disease and the cumulative morbidity and mortality across the world has been enormous. As with any new or emerging pathogen, early in the pandemic, there was limited evidence and understanding of how SARS-CoV2 was transmitted, limited testing capability, and resource constraints, especially in the availability of personal protective equipment (PPE).² Endoscopy centers shut down and the volume of endoscopic procedures plummeted save for only urgent, lifesaving or time-sensitive procedures. In line with international consensus statements and guidelines as well as local state and health system level policies, endoscopy centers slowly opened up and increased their volume of procedures with the paramount goal of reducing the potential risk of infection for patients and healthcare workers.³⁻⁶ Many studies showed drastic reductions in endoscopy volumes during the onset of the pandemic and persistent reductions in procedural volumes for sustained periods thereafter.⁷⁻⁹ This article summarizes the evolution of our understanding of SARS-CoV-2 infection, the performance of safe endoscopy, as well as indications and endoscopic findings in COVID-19 patients.

Understanding Modes of Transmission of Respiratory Viruses

A critical aspect of managing any pandemic from a respiratory virus requires a clear understanding of how an infectious pathogen is transmitted and the equipment or protection that is therefore needed to minimize transmission. Respiratory viruses are transmitted between individuals when the virus is released from the respiratory tract of an infected person and is transferred through the environment, to infect the respiratory tract of an exposed and susceptible person. The major modes of transmission of a respiratory virus from one person to another include: large droplets, aerosols, direct contact, or indirect contact (fomites).¹⁰ Often, the relative contributions of different modes to a successful transmission and the relative effects of each mode, as well as modifications of risk by viral, host and environmental factors, are unknown.¹⁰ See Table 1.

Table 1. Transmission Patters of Respiratory Viruses, such as Coronavirus

Definition	Key Attributes of Transmission
Large droplets originate in the upper respiratory system and vary in size between 5 and 60 microns	-contain epithelial cells from the lining of the airways, immune cells as well as electrolytes present in mucus and saliva, and infectious agents that reside in the upper respiratory systems (bacteria, fungi, and viruses). -large droplets are expelled from the mouth and the nose in multiple ways, including sneezing, coughing, talking, breathing, and singing.

	<ul style="list-style-type: none"> - once expelled, large droplets of over 5 μm can deposit by falling on surfaces (generally within 3 feet of their source) and cause propagation through fomites. -during normal breathing, aerosol particles smaller than 5 μm can disperse farther by airborne transmission -large droplets evaporate at rates dependent on temperature and relative humidity.
Aerosols are generated in a similar way as large droplets but are smaller	<ul style="list-style-type: none"> -aerosols also originate in the upper respiratory system and they have the same contents as large droplets -their small size, however, allows them to remain suspended in the air for longer periods of time and thus travel much farther than 3 feet.
Fomites , are the surfaces on which infectious particles cling once deposited	<ul style="list-style-type: none"> -droplets and aerosols expelled from the upper respiratory tract can survive for hours or days once attached to a fomite, depending upon the microbe and the environment -fomites facilitate indirect transmission from person to person

Understanding Modes of Transmission of SARS-CoV2

Our current understanding of SARS-CoV2 transmission has shifted and evolved since the beginning of the pandemic. According to the WHO, SARS-CoV2 transmission appears to occur mainly via *respiratory particles* and **close contact** with infected symptomatic cases.¹¹ These particles not only include respiratory droplets but also droplets as small as 5 microns (micrometers), and smaller aerosols which are expelled from the respiratory tract during speaking, breathing and coughing.¹²

The risk of transmission via aerosols is influenced by many factors including the concentration and mass of particles emitted, the viral load, the proximity and duration of exposure, and the circulation of air in the environment.¹⁰ The relative contribution according to particle size in virus transmission, however, is unknown. Epidemiological evidence suggests that the risk of transmission is predominantly from short range exposure from a person who generates significant amounts of virus. The SARS-CoV-2 virus has been detected in the air with a half-life of just over one hour and this evidence was offered as proof of “viable” virus that could be transmitted via aerosolization. However, this study was significantly limited in that it was conducted in a laboratory setting under an artificially created environment and not representative of real-world data.¹³ Human-to-human transmission can also occur from unknown infected persons (eg, asymptomatic carriers or individuals with mild symptoms), as well as individuals with virus shedding during the pre-incubation period before symptoms develop.¹⁴

A potentially compounding factor for transmission events is the contagiousness and transfer of SARS-CoV-2 infectious particles from fomites or contaminated surfaces (e.g., door handles). As other coronaviruses and respiratory viruses are known to be transmitted this way, spread through fomites may be an additional source of transmission. In early studies of hospitalized patients with COVID-19 positive SARS-CoV2 samples were identified

in various locations around patients' rooms, including the bed, sink, bathroom, light switches, and doors.¹⁵ In addition, positive samples were found on the shoes and stethoscopes of staff exiting patient rooms, but no contamination was found in the anteroom or corridor outside the room. These studies raised concerns about environmental contamination by patients with SARS-CoV-2 through respiratory droplets and fecal shedding.¹⁶ Despite the consistent evidence of SARS-CoV-2 contamination and survival of the virus on certain surfaces, there have been no specific reports demonstrating direct fomite transmission and the risk is generally thought to be small.¹⁷ People who come into contact with potentially infectious surfaces often also have close contact with the infectious person, thus making the distinction between respiratory droplet and fomite transmission difficult to differentiate.

Viral SARS-CoV2 particles have been isolated from various bodily fluids, including feces, urine, saliva, semen, and tears, raising concerns about possible transmission through these routes; however the presence of viral particles in these fluids has not been shown to correlate with clinical symptoms.^{18,19} The detection of viral particles in the stool was of particular importance because coronaviruses can have direct pathogenicity in the GI tract and cause enteric diseases. This raised concerns about fecal-oral spread as well as safety of endoscopy as aerosolization and increased exposure to fecal material may pose additional infectious risk. According to one systematic review of 35 studies that included 1,636 laboratory confirmed COVID-19 patients who received fecal, anal, and/or rectal swab SARS-CoV-2 RNA exams, the pooled prevalence of fecal SARS-CoV2 was 43% with about half of these patients demonstrating persistent shedding even after respiratory samples turned negative, and shedding was found more commonly in patients with GI symptoms.²⁰ Despite these data, no cases of direct fecal-oral transmission were reported thereby questioning the viability and infectivity of SARS-CoV2 virus found in fecal matter. Importantly, wastewater evaluation has been a useful surveillance strategy for tracking and predicting rates of prevalent COVID-19 for healthcare utilization.²¹

The role of personal protective equipment (PPE) in minimizing risk of infection from SARS-CoV2

Personal protective equipment (PPE) includes gowns gloves, eye protection (e.g. face shield or goggles), and surgical/medical or respirator masks. **Surgical masks** (also known as medical masks) are fluid resistant and often used for droplet precautions, because they are designed to block large particles, but are less effective in blocking small particle aerosols (<5 µm). Surgical masks provide a barrier to prevent droplets reaching the wearer's nose, mouth, and respiratory tract. Most masks are not designed to fit closely to the face which means that airborne particles (aerosols <100 microns) could potentially pass through the gap between the mask and the face. In contrast, **respirator masks** are designed to block aerosols. Respiratory protection for airborne precautions in health care commonly follows 2 filtering device paths, **N95 or N99 masks/respirators** or filtering facepiece respirators (such as FFP2 or FFP3) and **powered air-purifying respirators (PAPRs)**. The N95 masks filter at least 95% of aerosols (<5 µm) and droplet-size (5–50 µm) particles and are not resistant to oil. Lightweight, no-hose, PAPRs are a highly

effective alternative to face masks that force air through a large, multilayer filter housed in the helmet and provide positive pressure within the face-shield compartment. These devices are approved by US National Institute for Occupational Safety and Hazard (NIOSH) and can provide high-level protection from common airborne viruses that exceed that for N95 face masks without the need for “fit-testing” and also have the advantage of providing head and neck protection.²² Maximum protection is achieved only with proper donning and doffing techniques.

Requirements for PPE During Endoscopy

Due to the high-risk of human-to-human transmission and the potential for transmission of infection with SARS-CoV2 during routine performance of endoscopy, there was a lack of clarity regarding the necessity of PPE.²³ Since the initial severe acute respiratory syndrome (SARS) infection in the early 2000s, there was ongoing recognition that certain medical interventions, labelled aerosol generating procedures, increased the risk of potential infection due to aerosol generation.²⁴ According to the World Health Organization, an AGP is any medical or patient care procedure that results in the production of airborne particles, or aerosols which are ‘associated with an increased risk of pathogen transmission’ and therefore require enhanced precautions.²⁵ Per the WHO, the following procedures were considered AGPs: open airway suction, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation such as bilevel positive airway pressure and continuous positive airway pressure, bronchoscopy, and manual ventilation. The quantitative evidence to support this categorization was, however, limited to retrospective cohort/case control studies that were all deemed as very low-quality.²⁶

The gastroenterology community had a significant controversy as to whether upper or lower endoscopy qualified as AGPs.²⁷ AGG classification was critical in informing infection prevention and control policies, specifically the requirements for respiratory protective devices, such as N95 or N99 masks/respirators or filtering facepiece respirators (such as FFP2 or FFP3) or masks at endoscopy.²⁸ In the context of COVID-19, a classification of a procedure as an AGP necessitated a higher grade of PPE to protect against aerosolized virus and potential airborne transmission risk. While certain interventions such as intubation and bronchoscopy were acknowledged as high risk, there was a lot more uncertainty about endoscopic procedures. Possible sources of aerosolization during endoscopy include: intubation and removal of the endoscope, coughing, belching during endoscopy, heavy breathing from sedation, patient expulsion of gas and liquid, and dispersion of contaminated fluid during insertion and removal of tools through the working channel of the endoscope, adjustment of the air/water button, retrieval of tissue from a biopsy channel, and during pre-cleaning of the endoscope.²⁹ Our knowledge of the role of aerosol generation during endoscopy has expanded during the course of the pandemic. A number of authors, using various techniques, have studied this phenomenon to help us better understand the degree and quantity of aerosolization that is generated during routine endoscopy. These newer studies are summarized in Table 2.

Table 2: Recent studies that have aimed to assess the possibility and quantity of aerosol generation during upper and lower gastrointestinal endoscopy.

Particle-counting approach: <i>aerosols from patients undergoing upper gastrointestinal endoscopy were measured by a handheld optical particle counter before, during, and after the procedure. Particle sizes were reported to be in the range of 0.3 to 10 μm.10-12</i>	
Sagami et al. ³⁰	-a significant increase in the number of particles during and after the procedure was noted in the upper endoscopy group with conscious sedation compared to the non-endoscopy control group
Chan et al. ³¹	-a significant increase in particles of all sizes was noted during upper gastrointestinal endoscopy when measured at 10 cm from the patient's mouth
Air-sampling approach: <i>aerosols were measured in a sample of air</i>	
Gregson et al. ³²	<ul style="list-style-type: none"> -an uneventful upper endoscopy (without coughing or burping) does not generate aerosol above that associated with tidal breathing -insertion and removal of an endoscope for EGD does not generate an increase in aerosol concentration. -high aerosol concentrations were noted when endoscopy triggered coughing or belching by the patient
Phillips et al. ³³	<ul style="list-style-type: none"> -upper endoscopy (per oral and trans-nasal) as well as lower endoscopy generate aerosols (increased over background levels). -lower endoscopy generates less aerosols than upper endoscopy, thus upper endoscopy should be classified as an AGP whereas lower endoscopy depends on the definition of AGP used. -most significant contributing events for aerosol particle generation: local anesthetic throat spray application followed by extubation which is the second-most particle-generating event (but the particles generated were in the droplet range with less propensity for airborne transmission) and then coughing or gagging -for lower endoscopy the absolute number of particles produced was higher (because of longer procedure duration) but the risk from lower procedures is likely to be considerably lower than equivalent aerosols generated by upper procedures. -no statistically significant particle production from rectal insufflation or injection of water through the scope

A major criticism of this approach to categorizing AGPs into discrete dichotomous categories (AGP versus non-AGP and high risk versus low risk AGPs) is that this categorization does not consider the continuum of procedure-related aerosol generation and the different levels of transmission risks. Thus, there is likely a hierarchy of AGPs with each intervention conveying a different degree of transmission risk.³⁴ Further complicating this issue is that numerous studies have shown that certain respiratory events, such as coughing, can generate vastly greater numbers of droplets and aerosols, considerably more aerosol particles than aerosols generated from currently classified AGPs.³⁵⁻³⁹ Additionally, some studies have found that traditional AGPs pose no greater risk than talking or

breathing.⁴⁰ It is difficult to infer risk of infection from these studies because aerosols may not necessarily contain viable virus material, and the amount and quantity of aerosol generation does not equate to infectivity from endoscopy.

In summary, aerosol generation occurs as a continuum and endoscopy is associated with variable degrees of aerosolization. Risk of infection from aerosolized viral particles is, however, not only associated with the degree of aerosolization but also other factors such as quantity of infective virus, proximity to source, and room ventilation. Based on these studies, however, there is increasing consensus that upper gastrointestinal endoscopy should be classified as an AGP and periprocedural management including PPE recommendations, should follow the AGP protocols to minimize transmission.

Current recommendations by the WHO and CDC (Centers for Disease Control) advise the use of respirator masks, such as N95s or N99s, when performing surgical procedures that might pose higher risk for transmission if the patient has SARS-CoV-2 infection. These procedures generate potentially infectious aerosols or involve anatomic regions where viral loads might be higher, such as the nose and throat, oropharynx, or respiratory tract. Respirator masks are warranted in caring for individuals with COVID-19 or when community transmission levels increase but standard surgical masks are adequate for routine care not involving aerosol-generating procedures.^{25, 41} A systematic review of 172 observational studies on COVID-19, SARS-CoV-1, and MERS-CoV indicated that people, including healthcare workers, are strongly protected by wearing surgical face masks (adjusted Odds Ratio 0.15, 95% CI 0.07 to 0.34), with eye protection potentially conferring additional benefit.⁴²

Early Impact of the COVID-19 Pandemic on Endoscopy Units

In March 2020 when the COVID-19 outbreak was declared a global pandemic all endoscopy services came to a virtual halt.¹ Considering the escalating rates of hospitalizations and deaths, limited PPE availability, limited COVID-19 test availability, and the burden on the healthcare system, routine elective endoscopy services were temporarily discontinued. HCWs, physicians and nursing staff were redeployed, and protocols were developed for triaging of endoscopies to identify and perform only endoscopic procedures for urgent or emergent indications. While there were variations in how procedures were prioritized, many centers limited procedures for the following indications: active gastrointestinal bleeding, acute cholangitis, food impactions, gastrointestinal obstructions, and cancer diagnosis/staging/treatment. This strategy was aimed to reduce the risk of spreading infection, reducing use of limited PPE supplies, and reducing use of hospital resources.

Numerous studies from the United States, United Kingdom, The Netherlands, Canada, China, Spain, Japan, and Taiwan reporting on endoscopy volumes during the initial 3–4 months of the pandemic demonstrated reductions in total number of upper endoscopies and colonoscopies of 51%–72% and 59%–85%, respectively (compared with the same time period from prior years).⁴³⁻⁴⁹ After the initial phase, many centers resumed limited endoscopy services

with the implementation of stringent infection prevention and control policies and worked to reduce the backlog of colonoscopies by offering patients noninvasive stool-based tests for colorectal cancer screening.^{50,51}

Resumption of Endoscopy with a Focus on Safety During the COVID-19 Pandemic

An important framework for managing health and safety interventions used by the CDC to develop infection control policies, was the Hierarchy of Controls which recommended using strategies to reduce risks of exposure to the virus in addition to the use of PPE.⁵² Such strategies included **eliminating hazards** by avoiding admission/treatment of people with active infection and using COVID-19 testing to segregate patients with the infection. **Engineering controls** such as physical barriers, and **administrative controls** to facilitate physical distancing, were also included in the hierarchy. And finally given the physical proximity required to deliver many elements of care, the use of **PPE** was also a required control measure within the healthcare environment.

Following the hierarchy of controls framework, various operational changes were implemented across endoscopy suites and centers to safely re-open endoscopy units while mitigating the risk of infection.⁵³ These changes were implemented based on local factors such as availability of resources, local prevalence of COVID-19, patient demographics, procedure indication, and hospital/endoscopy unit policies. The common goals of these changes were to maintain endoscopic volume and efficiency, while minimizing risk of transmission and infection to patients, staff, and HCWs. Sources of human-to-human transmission could occur from unknown infected persons (eg, asymptomatic carriers or individuals with mild symptoms), as well as individuals with virus shedding during the pre-symptomatic incubation period. Sources of risk during endoscopy included aerosols generated during endoscopy which could increase the potential for subsequent airborne transmission, infection from respiratory secretions from patients, and potential contamination from other sources of bodily fluid (stool and patient saliva). Many authorities issued guidance on how to safely restart routine endoscopy and advocated for stringent infection control policies that included universal masking of patients, symptom screening before endoscopy, COVID testing before endoscopy, and use of high-level PPE.⁵⁴⁻⁶⁰ See Table 3.

Table 3. Overview of Modifications Implemented Across Various Endoscopy Centers During Various Stages of the Pandemic Prior to the Availability of Vaccines

Pre-Procedure Modifications
Triage and risk stratification used a screening questionnaire for 1) symptoms of COVID-19 (such as cough, shortness of breath, and persistent fever), 2) known history of contact with a COVID-19 patient, 3) travel to high risk areas. These were performed in all cases at least 24 to 72 hours prior to endoscopy
Pre-procedure SARS-CoV2 testing- individualized protocols for outpatient pre-procedural testing of patients 24-72 hours prior to the scheduled appointment depending on local prevalence rates and institutional policies

Reverse transcription PCR testing was performed in all asymptomatic patients before endoscopic procedures to risk stratify and determine PPE needs (see section below).	
- Patient reassurance about safety precautions taken to decrease transmission from patient to patient	
Procedural modifications for patients	
All patients required to wear surgical masks and keep at least 1 to 2 m of distance from others.	
Arrangements made in advance to reduce patient congestion in the waiting area. Chairs and beds spaced to avoid the transmission of viral particles to non-infected patients.	
Informed consent includes informing individuals about the possible risk of nosocomial infection (COVID-19 infection) during endoscopy Patients informed to report back if experiencing any <i>de novo</i> symptoms post-procedure.	
Triage and screening questionnaire- at the time of presentation to the endoscopy, questions asked again re: 1) symptoms of COVID-19 (such as cough, shortness of breath, and persistent fever), 2) known history of contact with a COVID-19 patient, 3) travel to high risk areas performed in all cases at least 24 to 72 hours prior to endoscopy High-risk patients classified by the presence of respiratory tract symptoms, previous travel to COVID-19 locations in the past 14 days, and close contact with COVID-19 positive patients, prompted procedure cancellation and self-quarantine	
Temperature measurements prior to entering the endoscopy unit	
Patient's relative/caregiver or driver required to wait offsite and return after the procedure is completed. If this is not feasible, the waiting area should be appropriately distanced.	
Procedural modifications for HCWs	
Barriers such as glass or plastic to walls/shields set up in check in areas	
Safe distancing in the pre-operative area as well as decreased numbers of patients that nursing staff can receive for pre-procedure care. Endoscopy staff with pre-existing conditions at higher risk of contracting COVID-19 have been assigned non-clinical duties	
Use of PPE mandated by all healthcare systems to minimize the risk of transmission All endoscopy team members required to wear surgical masks, gloves, hair coverings, face shields or goggles, water-proof disposable gowns, and shoe covers or boots.	
Initially use of highest level of PPE mandated by all healthcare systems to minimize the risk of transmission Eventually PPE for endoscopy personnel adjusted according to patient risk stratification with full PPE required for high-risk or confirmed COVID-19-positive patients. In low-resource settings, reusable respirators, face shields, goggles, and boots deemed acceptable after appropriate sterilization and decontamination methods	

Training and adherence to strict precautions of properly donning and doffing
Staff required to complete questionnaire about symptoms before their daily work. Similar distances should be maintained between individuals.
Staff required to keep at least 1 to 2 m of distance from staff and patients
For COVID-19 positive (or suspected) cases, procedures performed in a negative-pressure endoscopic unit, if available or portable industrial-grade high-efficiency particulate air filters placed in endoscopy rooms In low-resource situations, adequate ventilation of the room was acceptable
As much as possible, all required documentation should be performed outside the endoscopy room.
Minimal number of workers should be in procedure room to minimize risk Team switching during procedures discouraged to minimize PPE usage and decrease contamination risks
Post-procedure Modifications
Procedural downtime and Room turnover- time needed to allow for dispersion of potential virus-laden aerosols dependent on rate of air changes/hour (ACH). The precise time needed for closure of the room is dependent on the use of negative pressure and air-exchange rate COVID-19 patient- some centers used only negative pressure rooms (room maintained under negative pressure for at least 30 minutes, and in the absence of negative pressure, for 60 minutes, before the next patient)
Initially patients are monitored in the recovery area, with no family available in the waiting room Eventually limited family available in the waiting room with adequate spacing between seats and requirement of face masks
Post-procedure telephone follow-ups with patients utilized to inquire about developing any new COVID-19 related symptoms (traced and contacted after 7 and 14 days)

Endoscopy Room and Endoscope Cleaning

Enhanced cleaning procedures with cleaning of all horizontal surfaces, especially frequently touched surfaces, with particular emphasis on areas within a few feet of the patient (using standard hospital-grade disinfectant solution with viricidal agents) were implemented by most endoscopy units.^{6,53,61} Endoscope cleaning and decontamination processes remained unchanged; as per guidelines, mechanical and detergent cleaning followed by high-level disinfection (a process that eliminates or kills all vegetative bacteria, mycobacteria, fungi, and viruses, except for small numbers of bacterial spores and reduces the number of microorganisms and organic debris by 4 logs, or 99.99% .⁶²

Pre-Procedure Testing-Changing Recommendations Through the Course of the Pandemic

The use of pre-procedure testing in asymptomatic individuals became a common path to triage for risk stratification. A critical aspect of resuming endoscopy services included providing reassurance to patients and importantly to reassure HCWs, including endoscopists, nurses, and staff. At the pandemic onset, in the absence of available diagnostic tests and knowledge of treatments for COVID-19, one of the earliest evidence-based guidelines was developed by the American Gastroenterological Association (AGA); the guideline panel members made a strong recommendation to use N95 (or N99 or PAPR) masks (along with gowns, shoe covers, goggles, and face shields) instead of surgical masks for all HCWs performing upper endoscopies. Recommendations also included wearing double gloves and using negative pressure rooms, placing a high value on minimizing risks to HCWs, despite having low or very low certainty of evidence for risk of transmission of infection, because of documented community spread during a pandemic. In addition to limited resources for testing, limitations of PPE availability necessitated re-use or prolonged use of N95 masks. Finally, the decision to extend the recommendation to lower GI procedures was based on limited evidence of possible aerosolization during colonoscopy and the uncertain risks associated with evidence of the presence of SARS-CoV-2 RNA in fecal samples. These recommendations assumed the absence of widespread reliable testing for the diagnosis of COVID-19 infection or immunity and unclear data on prevalence.

As the number of COVID tests that received Emergency Use Authorization approval increased, pre-procedure testing became more readily available, and questions arose regarding the role of routine pre-procedure testing of all individuals to minimize risk for patients and HCWs. At the individual patient level, testing in symptomatic patients helped identify individuals who could be isolated to prevent the spread of disease. At the population level, widespread testing of individuals (symptomatic and asymptomatic) was critical to determine the true prevalence of disease and the provision of health care services, and to reintroduce endoscopy across health care systems and ambulatory care centers. Recommendations developed by the AGA provided a framework for routine pre-procedure testing prior to endoscopy (for all asymptomatic persons) that accounted for local contextual factors such as the local prevalence of SARS-CoV2 and availability of PPE and weighed the pros and cons of a pretesting strategy. Based on a systematic review and meta-analysis of the tests (available at that time), the authors of this guideline conducted and made conditional recommendations against endoscopy centers adopting routine pre-procedural testing to triage patients into low and high prevalence settings because of concerns about the accuracy of test results and the potential downsides for individuals with false positive or false negative test results. They suggested that all HCWs wear N95s (or higher) masks, if available, and forego testing. For endoscopy centers where the prevalence of asymptomatic SARS-CoV-2 infection was intermediate (0.5%–2%), the AGA suggested implementing a pretesting strategy, if tests were available, to determine the type of PPE (such as use of surgical masks in individuals who tested negative). Alternatively, in settings where the logistics of testing were challenging and the downsides outweighed the benefits, HCWs could choose to wear N95 (or higher) masks and again forego testing. The changing prevalence of COVID-19 was an important factor as new variants emerged and created documented new waves of infection.

The rapid development of vaccines and the widespread implementation of vaccination programs worldwide helped decrease morbidity and mortality from COVID-19. Another important positive change was the availability of

relatively effective treatments. Furthermore, within the GI community, as our understanding of disease transmission increased and data on infection rates from endoscopy and universal screening and testing became available, and PPE became widely available, many endoscopy centers again revised their testing policies. In contrast to early reports of high rates of HCW infections early in the pandemic (in the setting of limited PPE) accumulating evidence demonstrated low rates of COVID-19 infections among HCWs performing endoscopy.⁶⁰ This evidence along with data demonstrating the relative effectiveness of vaccines in decreasing rates of transmission of infection prompted a recommendation against routine pre-procedure testing emphasizing the downsides of testing at the patient level (of burden, cost, and access) and at the population level (low rates of screening and surveillance endoscopies leading to lower rates of screening, surveillance and diagnosis of various GI cancers).

Endoscopic Indications and Findings

In patients with COVID-19, a number of systematic reviews and meta-analyses have described the prevalence of gastrointestinal symptoms including diarrhea (8–17%), nausea or vomiting (4–20%), loss of appetite (2–21%), abdominal pain (3–20%), anorexia (8–10%), abdominal distension (1%) and loss of taste (1–3%).⁶³⁻⁷⁰ Most gastrointestinal symptoms associated with COVID-19 are mild. Diarrhea caused by SARS-CoV-2 may be the initial symptom in patients with COVID-19. A small subset of patients with COVID-19, may develop isolated gastrointestinal symptoms throughout the disease (2.9–16%).⁷¹

Our understanding of the endoscopic findings in COVID-19 is limited. A number of case series, retrospective and prospective cohort studies have helped us to understand the direct and indirect effects of COVID-19 on the GI tract.⁷²⁻⁷⁵ Gastrointestinal endoscopy for GI bleeding in COVID-19 patients is reviewed in a chapter by Cappell and Friedel in this issue. Mechanistically, viruses in the gastrointestinal tract, including coronaviruses, can contribute to disease by interacting with the mucus layer, epithelial cells, and potentially lamina propria immune cells. SARS-CoV-2 infection can disrupt the tight and adherent junctions of the endothelium and intestinal epithelium, which may lead to a leaky gut, local and systemic invasion of normal microbiota, and consequent immune activation.⁷⁶

In one retrospective, single-center study of 95 laboratory-confirmed cases of SARS-CoV-2 infection from Zhuhai, China, 6 patients with GI symptoms underwent upper endoscopy and two underwent proctoscopy. Biopsies were taken from the esophagus, stomach, duodenum and rectum for viral RNA detection. One severe patient (case 1) exhibited symptoms of GI bleeding localized to the esophagus and attributed to multiple round herpetic erosions and ulcers, each with a diameter of 4–6 mm. SARS-CoV-2 RNA was detected in the esophageal erosions and bleeding site, as well as in the stomach, duodenum, and rectum. In the other five patients (cases 2–6) no erosions, ulcers or bleeding were noted. SARS-CoV-2 RNA could also be detected in the esophagus, stomach, duodenum, and rectum of another patient with severe COVID-19 infection (case 2). In contrast, the virus was only detected in the duodenum of the non-severe case 3 and could not be detected in any GI specimens of the non-severe cases 4–6.⁷³

In a case report of a patient with COVID-19 who underwent endoscopy, biopsies revealed no damage to the epithelium of the esophagus, stomach, duodenum, and rectum but infiltrates of occasional lymphocytes were observed in esophageal squamous epithelium and numerous infiltrating plasma cells and lymphocytes with interstitial edema were observed in the lamina propria of the stomach, duodenum, and rectum.⁷⁵

In a retrospective study from Lombardy, Italy, 38 patients with confirmed SARS-CoV-2 underwent endoscopic evaluation (24 EGDs, 20 colonoscopies). Endoscopic lesions were observed in 18 of 24 EGDs (75%) and in 14 of 20 colonoscopies (70%). The main findings were esophagitis (20.8%), bulbar ulcer (20.8%), erosive gastritis (16.6%), neoplasm (8.3%), and Mallory-Weiss tear (4.1%). Colonoscopy revealed segmental colitis associated with diverticulosis (25%), colonic ischemia (20%), diffuse hemorrhagic colitis (5%), and colonic neoplasms (5%).⁷⁴

Finally, in a multicenter cohort of ~2000 hospitalized COVID-19 patients across a geographically diverse network of medical centers in North America, only 1.2% of patients (n=24) underwent endoscopy despite a high prevalence of gastrointestinal symptoms and substantial burden of critical or prolonged illness. The majority of endoscopic procedures were performed for either emergency cases (e.g. ongoing GI bleeding or biliary obstruction) or for placement of enteral access tubes. Among those who underwent endoscopy, the indications and findings were judged more likely to reflect overall systemic illness or related to prolonged hospitalization rather than direct viral injury from COVID-19. The authors did not observe inflammatory pathology and concluded that SARS-CoV-2 did not appear to behave as a highly invasive and injurious pathogen to gastrointestinal mucosa.⁷²

Summary

In summary, the unprecedented COVID-19 pandemic led to significant disruptions in gastroenterology practice necessitating endoscopy centers to be adaptive, reactive, and innovative. With the emergence of new variants and the ever-present threat of new pandemics, lessons learned during these past few years will help maintain the safe practice of endoscopy and prepare for new and emerging pathogens. While mechanistically SARS-CoV2 may contribute to enteric disease, endoscopic findings in COVID-19 patients are likely to reflect the underlying critical illness rather than the direct effect of the virus.

Clinical Care Points

- Aerosolization during upper and lower endoscopy occurs along a continuum and respirator masks, such as N95s along with eye protection, gowns, and gloves are an important strategy to minimize risk of viral transmission
- Endoscopy centers should incorporate a number of strategies based on the Hierarchy of Controls Model to reduce the risk of viral transmission

- The role of pre-procedure testing should be based on local prevalence, testing availability, PPE availability, and patient burden
- While SARS-CoV2 can be detected in stool, there have been no reports of infection via the fecal-oral route
- Endoscopic and histologic findings in COVID-19 patients are more consistent with prolonged and severe systemic illness and suggest no direct viral or inflammatory pathogenic effects

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