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***COVID-19 and GIT endoscopy Finding***



## **Introduction**

In the past 3 months, a new coronavirus of SARS-CoV-2, leading to coronavirus disease 2019 (COVID-19), has been rapidly disseminated throughout Asia. The World Health Organization (WHO) declared COVID-19 as pandemic on 11 March 2020, and by 24 March 2020 the number of confirmed COVID-19 cases had increased to more than 372 000 globally. A cohort study on 1099 patients with COVID-19 from Wuhan showed that typical clinical symptoms included cough and sputum, sore throat, fever, fatigue, and shortness of breath. More than 40% of patients had contact history and 56.2% had no raised temperature. Gastrointestinal symptoms are not uncommon and 5% of patients had nausea or vomiting and 3.8–10.1% had diarrhoea. The overall mortality was 1.4%, and for those with severe disease the mortality was 22.4%. Although there are no data on whether endoscopy is an aerosol-generating procedure, positive insufflation during endoscopic procedures could pose a risk of generating aerosol and increase the risk of SARS-CoV-2 transmission. Healthcare providers of endoscopy therefore are facing tremendous risk during the pandemic of COVID-19 as the spread is mainly through direct contact or aerosol droplets, and endoscopy procedures require a short physical distance between patients and personnel

A study performed during the SARS outbreak in 2003 showed that droplets from infected patients could reach people located two metres or more from the source. In addition, experience from the SARS epidemics demonstrated the presence of coronavirus in stool samples and intestinal biopsy samples. Recently, it has been confirmed that COVID-19 can be found in the oral cavity and faecal samples of infected individuals

To date, joint new guidance on the practice of endoscopy has been posted by the American College of Gastroenterology and the British Society of Gastroenterology.

Asia has already accumulated substantial experience in combating the COVID-19 outbreak; some regions have shown their ability to prevent outbreaks and maintain a high-quality endoscopy service without subjecting patients and staff to undue health hazards.

## **Guideline on Pre-Endoscopy Testing During the COVID-19 Pandemic**

As endoscopy centers have gradually reopened in the U.S., testing of asymptomatic patients for SARS-CoV-2 infection prior to their procedures has become more widespread. The AGA has issued recommendations on the role of pre-endoscopy testing based on asymptomatic disease prevalence, which was estimated as 10% of the local rate of positive cases.

## **Key Recommendations**

-Test for infection 48 to 72 hours prior to the procedure if asymptomatic prevalence is intermediate (0.5%–2%). This assumes good test performance characteristics and acceptable burden to patients. If these conditions are not met, centers may consider foregoing testing but

should use higher-level personal protective equipment (PPE) for all procedures (N95/N99 respirators, or powered air-purifying respirators PAPRs)

-Do not test for infection if asymptomatic prevalence is low (<0.5%) or high (>2%), given the unacceptably high rates of false-positives and false-negatives, respectively. Use N95/N99 or PAPR for all procedures in high-prevalence areas, and in most situations in low-prevalence areas.

-Reserve endoscopy for emergency or time-sensitive cases in settings where COVID-19 case surge has put a strain on hospital resources

-Do not use serologic testing for antibodies to check for past infection in patients or endoscopy staff.

#### **Key strategies to ensure continuity of endoscopy services and safe patient care include:**

-Endoscopy departments should be preserved as a priority and not requisitioned for COVID work, to allow cancer diagnostics and essential acute interventions such as ERCP and PEGs etc, to continue.

-Existing additional endoscopy facilities for service restoration should be maintained where possible, particularly where they are off site and "COVID-19 safe". Such capacity will be of great value when the current surge abates.

-Endoscopy teams should be preserved and not redeployed

-Ongoing senior clinician triage and prioritisation of patients at most pressing need is essential - to preserve already limited endoscopy capacity

The use of alternatives to endoscopy in keeping with recent guidance documents e.g. qFIT, radiological imaging, colon capsule endoscopy (CCE), Cytosponge etc.

-Communication to reassure GPs and patients that endoscopy units are open and that urgent referrals e.g. those on 2WW (USoC) pathways, AND FIT+ve bowel screening patients should continue

-Reassurance to patients that it is safe to come into hospitals for endoscopic procedures and that these can be performed safely with minimal risk of infection

-Assuring patient safety by creation and maintenance of 'green pathways' with patient testing 3-days pre-procedure in keeping with established guidance and by regular testing of all patient facing endoscopy staff

-Use of enhanced ('level 2') PPE when performing any endoscopic procedures if no 'green pathway' exists or if negative test results pre-procedure cannot be confirmed, while community infection rates remain high

-Risk assessment of all endoscopy staff to protect those who are clinically extremely vulnerable (CEV), and prioritising them for early vaccination

-Vaccination of all other patient-facing endoscopy staff

-Current COVID-19 measures for pre-procedural testing and PPE must continue to be observed

-Patients and staff who have been vaccinated should continue to observe social distancing, hygiene, and PPE use.

## **Screening for COVID-19 before endoscopy**

### **1-Symptomatology and FTOCC**

All patients entering the endoscopy unit should be screened for COVID-19. This should include a mandatory questionnaire for respiratory symptoms such as cough, runny nose, and/or shortness of breath; and also gastrointestinal symptoms such as nausea, vomiting and diarrhea as these may be the only symptoms present in some cases. This should be coupled together with questionnaires on fever, travel history, occupation, contact, and clustering (FTOCC). Some experts also recommend including screening questions on alterations of taste and smell. Endoscopy will only proceed for patients who screen negative unless for life-threatening indications.

### **2-Polymerase chain reaction testing\_**

The most widely advocated method of pre-endoscopy testing for COVID-19 is by reverse transcriptase-polymerase chain reaction (RT-PCR). An economic analysis has shown that performing nucleic acid amplification tests for SARS-CoV-2 on all patients is an effective strategy, though this is subject to the availability of local resources. Recently, recommendations from the AGA suggest that a pre-testing strategy will likely work best for regions with intermediate prevalence of asymptomatic carriers (0.5%-2%). Real world data from the United Kingdom during the recovery phase of the pandemic found that only 0.11% of asymptomatic patients tested positive for SARS-CoV-2 on nasopharyngeal swab testing pre-endoscopy.

### **3-Serology**

Some authors have recommended testing for immunoglobulins against SARS-CoV-2, as a screening test. However, this strategy may only indicate a past infection and has no role in diagnosing active COVID-19 in asymptomatic individuals prior to endoscopy

### **4-CT of the chest**

Chest CT has also been suggested as a potential screening strategy where it was widely utilized by centers in China. It is thought that CT findings may precede a positive RT-PCR SARS-CoV-2 test, though later studies showed that almost 18% of nonsevere COVID-19 patients displayed no radiographic or CT abnormality limiting its usefulness. In Mainland China, a negative chest CT together with a negative nucleic acid amplification tests for SARS-CoV-2 are usually required prior to proceeding with endoscopy to improve safety for both patients and healthcare staff during the COVID-19 pandemic. However, this strategy may be difficult to be implemented more widely due to issues relating to generalizability, accessibility and cost

### **5-Point of-care testing**

The rationale behind point-of-care testing is that these rapid and easy-to-use devices can provide COVID-19 testing outside of laboratory settings using various techniques and allow for more accurate risk stratification. However, despite some promising results many of these tests have yet to be validated. At present, the WHO advises that these should only be used in research settings until further evidence is made available.

## **DURING ENDOSCOPY**

### **Personal protection equipment**

All organizations concur that for all procedures, all members of the endoscopy team should wear appropriate personal protection equipment (PPE) – usually consisting of N95 or surgical mask, eye shield/goggles, face shield, water-resistant gown and gloves. AGA and ASGE advise the use of N95 mask for all procedures. In contrast, ESGE, CAG and GESA limit the use of N95 mask for high-risk procedures only. AGA also specifies that 2 sets of gloves (rather than 1 set) should be used in all procedures, whereas CAG and ESGE suggest that 2 sets of gloves be used in high-risk procedures only. This minimizes contamination by reducing risk of transferring viral organisms from PPE to clothes or the rest of the body during removal of PPE. These differences probably reflect variable availability and practical rationing to conserve limited PPE resources amidst competing needs. Endoscopy staff should be trained in donning and removing PPE, and hand hygiene practices must be observed strictly. In our center, we have enhanced our universal precautions, to N95 mask, eye goggles, water resistant gown and gloves for endoscopy in all patients. In addition, for confirmed or suspected COVID-19 cases, the endoscopist and assisting nurses wear all PPE with the addition of powered air-purifying respirators (PAPR) as an additional barrier. All confirmed or suspected COVID-19 cases should have been admitted to hospital. Suspected cases are defined as per guidance from our Ministry of Health[12] – usually suspected if they have clinical signs and symptoms suggestive of acute respiratory illness, and COVID-19 cases are confirmed with syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction test of respiratory or nasopharyngeal swabs.

### **Members of endoscopy team**

In our center, endoscopy staff are assessed daily for symptoms and signs suggestive of COVID-19 infection—temperature is checked twice a day. Staff are grouped into teams of 2-3 which are segregated into separate endoscopy rooms and remain together for the whole day. This is to minimize concomitant exposure to infection and prevent potential spread of infection between teams. The number of endoscopy staff should be curbed with only essential staff (senior endoscopist +/- trainee, maximum of 2-3 assisting nurses) allowed in the room during procedures. Particular mention should be made of different perspectives of the involvement of trainees in procedures. AGA and BSG have recommended to review and consider limiting their participation in procedures in view of constraints in PPE supply and concerns of increased procedural time. GESA has adopted a more nuanced approach and suggested that trainees should be restricted from participating in procedures involving confirmed COVID-19 cases or cases at high risk of COVID-19 but should be allowed to do procedures involving cases at low risk of

**COVID-19.** Our center adopts this stance, valuing trainee participation in standard endoscopy but limiting their exposure to COVID-19 confirmed or suspected cases.

### **Procedure logistics**

In our center, for confirmed or suspected patients with COVID-19, endoscopic procedures should be done in negative pressure rooms if fluoroscopy is not required, or in a designated operating theatre with negative pressure if fluoroscopy is required. In limited resource settings where negative pressure rooms are not available, AGA advises portable industrial-grade high-efficiency particulate air filters as an alternative, in line with Centers for Disease Control and Prevention guidelines. Our center has a total of 6 available endoscopy rooms-all inpatient cases are consolidated in 1-2 specified rooms, and outpatient cases are done in other available rooms. This ensures no cross-contamination between Patients.

### **What are the findings?**

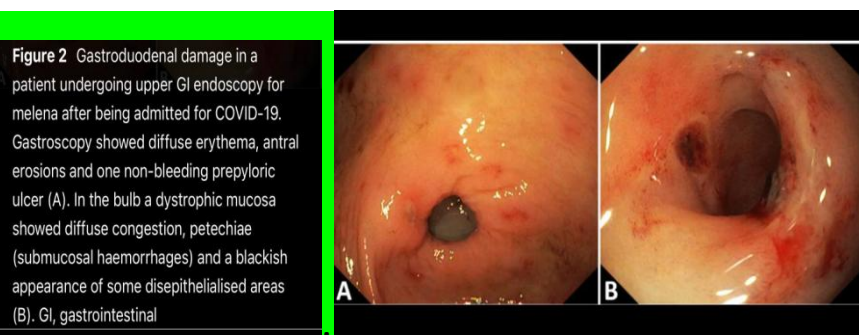
-In an international prospective endoscopy registry of patients with COVID-19 requiring urgent endoscopy, almost half were found to have an acute major GI mucosal injury.

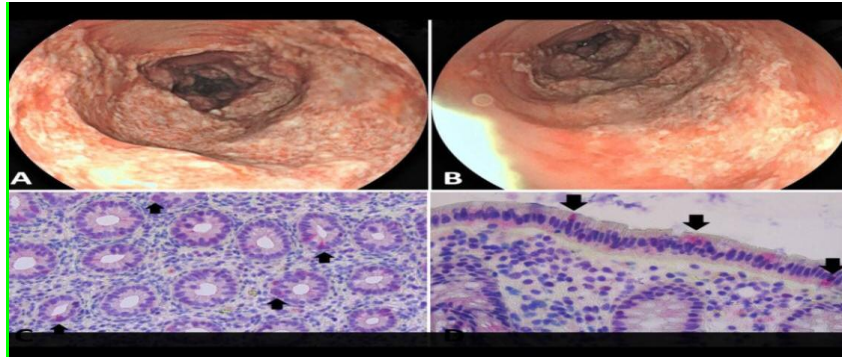
-In this highly selected population, erosive/ulcerative damage was the most prevalent endoscopic abnormality and an ischaemic-like colopathy was commonly (33.3%) observed.

Evidence on endoscopic findings in patients with COVID-19 is limited to sporadic case report or series,<sup>17</sup> describing non-specific findings, and suggesting that the virus directly damages GI mucosal surfaces.<sup>18</sup>

In addition, increasing evidence has been suggesting that vascular changes might be a distinctive feature of COVID-19 and that systemic endothelial damage and consequent disseminated microvascular thrombosis might act as a primer for many organs' damage, including the pulmonary one (the 'microvascular thromboinflammatory syndrome' theory).<sup>19, 20</sup> It is therefore tempting to hypothesise that such ischaemic damage might also occur in the GI tract

The present multicentre study was therefore aimed at (1) systematically describing GI findings during endoscopic examination of patients with SARS-CoV-2 infection and (2) investigating factors associated with GI injury to gain more knowledge on its pathogenesis





**Figure 6** A middle-age patient, with a history of dyslipidaemia, was admitted following an episode of abdominal discomfort, rectal blood loss and a vasovagal syncope. On admission COVID-19-screening came back positive. Subsequent flexible sigmoidoscopy revealed unilateral ulcerations in the left colon with rectal sparing (A, B). Histopathology showed patchy atrophic changes, mucus depletion, signs of regeneration and infiltration by polymorphonuclear neutrophils, typical for an ischaemia-type colitis. COVID-19-antibody-staining was positive on various enterocytes (C, D arrows).

In the majority of patients (22, 91.7%), the endoscopist deemed the endoscopic findings to be more likely related to prolonged hospitalization or critical illness rather than COVID-19. Only 1 patient (4.2%) had an endoscopic finding thought to be related to the virus itself: erosive gastritis. A second patient had a normal colonoscopy but on cross-sectional imaging was noted to have pneumatosis intestinalis. No major procedure-related adverse events were reported. There were 2 reported cases (8.3%) mucosal trauma from OGT placement.

## Discussion

This case series highlights the GI endoscopic and histologic findings in 38 COVID-19 patients. Endoscopic examination was abnormal in a high proportion of cases, and there was a wide heterogeneity in the endoscopic findings. Peptic ulcers and esophagitis were detected in most upper GI endoscopies, and colitis, ranging from mild to more severe ulcerative lesions, was the most common finding during colonoscopy. Most patients required endoscopy because of GI bleeding, which could be related to the concomitant low molecular weight heparin therapy (76% of patients), bleeding predisposition in patients with severe infection, and/or disseminated intravascular coagulation, which is one of the major causes of organ dysfunction in sepsis.<sup>7</sup> Moreover, the high proportion of ulcerative colonic lesions observed in our series, with pictures superimposed on either segmental colitis associated with diverticulosis or colonic ischemia, could suggest an ischemic injury possibly due to a thrombotic dysfunction attributable to excessive inflammation, platelet activation, and endothelial dysfunction.<sup>8</sup> On the other hand, colonic ischemia can be caused by hypoperfusion state that is due to transient hypotension or shock related to sepsis itself. Furthermore, a direct inflammatory effect on the GI mucosa can be hypothesized, because SARS-CoV-2 binds to the angiotensin-converting enzyme-2 receptors, which are also constitutively expressed in the GI tract.<sup>2</sup>

The limits of our study are the relatively small sample size and the retrospective nature of the study. However, this study highlights the heterogeneous and wide spectrum of GI manifestation in COVID-19, of which gastroenterologists and endoscopists should be aware. More research is needed to elucidate the extent to which some of the endoscopic and histologic findings are

attributable to the virus. Last, the fact that none of the endoscopists was infected is reassuring for endoscopists as they begin to reopen practices

### **Endoscopic Transmission**

Among the endoscopy procedures, duodenoscopes and echoendoscopes carry a high risk of nosocomial infections . While single-use duodenoscopes might be of value in COVID-19-positive patients, they are not universally available and have cost-related constraints . Multiple societies have recommended using negative pressure rooms, especially for patients who are suspected of COVID-19 or when the endoscopy is being performed emergently without COVID-19 testing results Intraprocedural changes such as minimal verbal communication, avoiding spill of GI contents via biopsy channel, and avoiding procedures in patients with inadequate bowel preparation should be done . Franzini et al. reported the use of a “double gauze technique” where the endoscopists use one gauze and the other by the technician in a controlled fashion to avoid the “whip” effect of accessories and spillage of GI secretions . Institutional policies have been developed for minimal personnel to be present for the procedure . This is to minimize the risk of exposure among the endoscopy staff. Procedures performed with moderate sedation without the need for anesthesia providers (endoscopist guided sedation) can further minimize the risk of transmission. However, for procedures requiring general anesthesia, societies currently recommend using ETI to reduce the risk of aerosolization with suspected or confirmed COVID-19.

### **Limitations**

Due to the rapidly evolving nature of the COVID-19 pandemic, endoscopy units continue to adapt, and the above recommendation can change. Due to the heterogeneity of the published literature, we could not perform a systematic review. Pre-procedural testing, triaging, and trainee involvement in the procedures are dependent on infection risk, local endoscopy unit, and hospital policies. As countries are starting the recovery phase of the COVID-19 pandemic, these measures are constantly being updated

### **Future Outlook of Endoscopy Units**

In the future, endoscopy units will likely incorporate some of the changes during the pandemic for increased safety of the patients and endoscopy staff. It remains speculative to predict the end of this pandemic, but localized outbreaks may continue to occur even when we see a pandemic downtrend .Important questions remain open if endoscopy staff and patients should continue to be screened and tested regularly. It is only presumptive to say about the effect of cancer burden due to delayed screening, surveillance, and handling the increased backlog cases. Multiple strategies can be adopted to decrease or ease endoscopy demand. Patients who are eligible for the screening should be provided with options of CRC screening, including stool-based testing, which do not need patients to present to the healthcare facilities. Home-based stool testing has



the advantage of testing without contact with hospitals or clinics . For patients who test positive, there is a significant risk of advanced adenomas on the endoscopy, and hence a triage system should be developed to prioritize the procedures . Because of these, there will be increased demand in the recovery phase that likely needs to be phased appropriately to avoid significant waiting times for procedures that need to happen in a timely fashion. It involves careful evaluation of patient demographics (comorbidities) and environmental factors (staff availability, local resources, community spread, and infection rate) . As the recovery phase starts, the real effect on the delay in cancer screening will emerge.

Patients should be communicated about the importance of screenings in the recovery phase to avoid delays and to keep the appointments. There should be an effective use of electronic health record communication strategies to provide updates to patients about COVID-19-related changes in endoscopy units. Virtual tools such as increased telehealth visits to discuss and engage patients about cancer screening programs will increase the endoscopy show rates . A triage system to review all the posted case by qualified medical personnel and reschedule the procedures in a tiered fashion can make this process less stressful . Furthermore, endoscopy staff should communicate with schedulers about the patient's concerns, which can be directly addressed. Finally, a higher threshold should be adopted for endoscopy procedures, which will less likely change the outcomes in patients . Despite these changes, as this pandemic unfolds with localized outbreaks, endoscopy units remain at a threat of temporary closures and need for enhanced disinfection protocols. Preparing for future pandemics should be a part of the operation of the endoscopy units' stress response. Nevertheless, endoscopy units should continue to adapt and navigate to provide high-quality patient care with equal emphasis on patient and staff safety.

### **POST ENDOSCOPY**

Standard cleaning and disinfection of endoscopy rooms and endoscopy equipment should continue. Endoscopes and endoscopic accessories are reprocessed with standardized reprocessing procedures. Our center's practice is in line with the United States multi-society guidelines. Endoscopes are cleaned manually—endoscope components are disassembled, and endoscope and their components are immersed in detergent which is compatible with the endoscope. All available channels are flushed and brushed to remove any residue. Endoscopes and their components are subsequently subjected to high-level disinfection with an automated .endoscope reprocessing unit

For confirmed or suspected COVID-19 cases, used endoscopes and endoscopic equipment will be cleaned on site with disinfectant. Used scopes will then be placed in biohazard bags (double bagged) into a container and transported back to the endoscopy centre for further cleaning and reprocessing, which will be done separately from other endoscopic equipment. All endoscopy staff involved in disinfection and reprocessing of endoscopes and endoscopic equipment should be wearing PPE.

### **Follow-up**

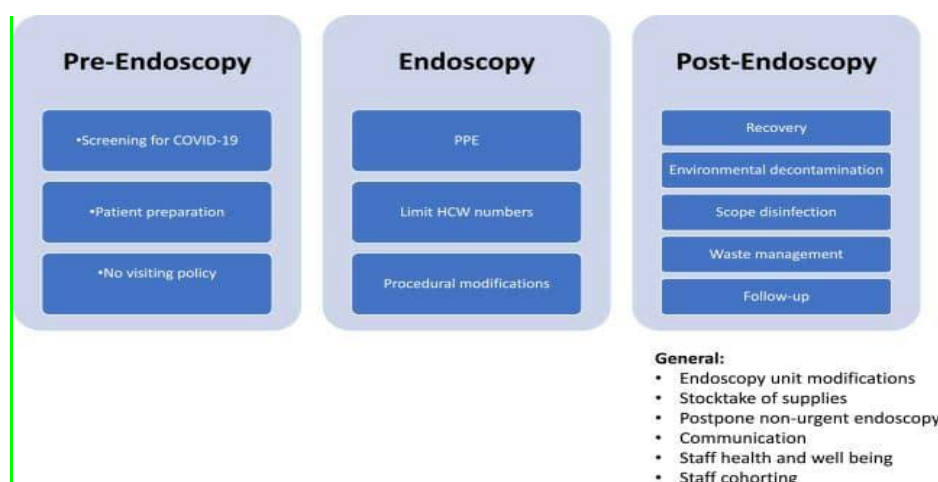
Patients can be contacted at 7-d and 14-d post-procedure to ask about new diagnosis of COVID-19 or development of symptoms of COVID-19 infection. This is suggested by the United States

Joint GI Society and ESGE but not routinely practiced elsewhere. Our center conducts routine follow-up calls as per our patient feedback process but not specifically for COVID-19.

## **RESUMING ENDOSCOPY AFTER CORONAVIRUS DISEASE PANDEMIC**

With numerous countries employing strategies such as social distancing to decrease rates of SARS-CoV-2 infection, the peak of the COVID-19 pandemic may have passed and attention now turns to how best to re-introduce normal activities and services safely. AGA and Digestive Health Physicians Association (DHPA), ASGE, and BSG have recently published guidelines on resumption of endoscopy during the COVID-19 pandemic-. Timing of resuming elective procedures should be guided by incidence of COVID-19 cases in the local community, and availability of equipment and manpower. AGA/DHPA propose to resume elective endoscopic procedures when there is a sustained decrease in rate of new COVID-19 cases in the community for at least 14 d, and the decision to resume should also take into consideration availability of resources required to ensure the safety of both healthcare staff and patients.

Resumption of elective endoscopic procedures should be done cautiously and gradually in a phased manner. Both AGA/DHPA and ASGE recommend additional measures for pre-procedure patient screening. AGA/DHPA suggest conducting SARS-CoV-2 PCR testing within 48 h before procedure; if unable to do so, to consider asking patients to keep daily temperature logs for 10 d before procedure. On the day of procedure, a symptom questionnaire will be administered to patients and their temperatures will be checked. ASGE suggests doing pre-screening with a questionnaire on symptoms, contact history, travel history, and occupational exposure within 72 h before procedure. Responses to the questionnaire should be updated on the day of procedure. The rest of the infection prevention and control measures discussed above should continue to be implemented and observed. Additionally, ASGE mentions that patients should be followed up and surveyed 1-2 wk post-procedure – they are advised to inform the endoscopy centre if they develop symptoms or are diagnosed with COVID-19 within 14 d of procedure.



## **CONCLUSION**

In contrast to the Severe Acute Respiratory Syndrome (SARS) outbreak in 2003 which was contained within 8 months, the COVID-19 pandemic is exhibiting a vastly different epidemic trajectory. Despite encouraging studies showing that some drugs such as interferon-based

combination therapy, remdesivir, and steroids may be effective against SARS-CoV-2, the future will likely depend on the development of safe and effective vaccines. In the meantime, strict adherence to personal hygiene measures and social distancing will be of utmost importance. As COVID-19 rages on further issues relating to complacency and response fatigue will also need to be addressed. The safety of endoscopy for both patients and healthcare workers is paramount as endoscopy units adapt to the ongoing outbreak and start resuming regular service. Stringent measures taken before, during, and after endoscopy can hopefully mitigate the risk of infection. The silver lining is that this is an opportunity to introduce new care models and enhance our preparedness for future pandemics.

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