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***Observational Study***

**COVID-19 in the endoscopy unit: How likely is transmission of infection? Results from an international, multicenter study**

Papanikolaou IS *et al*. COVID-19 infection likelihood in the endoscopy unit

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**Abstract**

BACKGROUND

Coronavirus disease 2019 (COVID-19) significantly affected endoscopic practice, as gastrointestinal endoscopy is considered a risky procedure for transmission of infection to patients and personnel of endoscopy units (PEU).

AIM

To assess the impact of COVID-19 on endoscopy during the first European lockdown (March-May 2020).

METHODS

Patients undergoing endoscopy in nine endoscopy units across six European countries during the period of the first European lockdown for COVID-19 (March-May 2020) were included. Prior to endoscopy procedure, participants were stratified as low- or high- risk for potential COVID-19 infection, according to the ESGE/ESGENA joint statement and contacted 7-14 d later to assess COVID-19 infection status. PEU were questioned regarding COVID-19 symptoms and/or infection *via* questionnaire while information regarding hospitalizations, intensive care unit-admissions and COVID-19-related deaths were collected. The number of weekly endoscopies in each center during the lockdown period was also recorded.

RESULTS

One thousand two hundred sixty-seven endoscopies were performed in 1222 individuals, across 9 European endoscopic departments (6 countries). Of them, 87 (7%) were excluded due to initial positive testing.  Among the 1135 pre-endoscopically low risk or polymerase chain reaction negative for COVID-19, 254 (22.4%) were tested post-endoscopy and 8 were eventually found positive, resulting in an infection rate of 0.7% [95% confidence interval (CI): 0.2-0.12]. The majority (6 patients, *i.e.*, 75%) had undergone esophagogastroduodenoscopy. Data for all 163 PEU were recorded; five [*n* = 5/163, (3%); 95%CI: 0.4-5.7)] tested positive during the study period. A decrease of 68.7% (95%CI: 64.8-72.7) in the number of weekly endoscopies was recorded in all centers after March 2020. All centers implemented appropriate personal protective measures (PPM) from the initial phases of the lockdown.

CONCLUSION

COVID-19 transmission in endoscopic units is highly unlikely in a lockdown setting, provided endoscopies are reduced to emergency cases and PPM are implemented.

**Key Words:** COVID-19; SARS-CoV-2; Gastrointestinal endoscopy; Personal protection measures; Transmission; Lockdown

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**Core Tip:** Coronavirus disease 2019 (COVID-19) pandemic outbreak caused an unprecedented disruption in everyday endoscopic practice worldwide, with recent guidelines advocating suspension of non-emergency endoscopies, implementation of strict personal protection measures (PPM) and post-endoscopy patients’ evaluation, regarding their COVID-19 status. This was an international, multicenter, study seeking to evaluate the impact of COVID-19 on endoscopy during the first European lockdown (March-May 2020). COVID-19 transmission across endoscopic units proved to be highly unlikely in lockdown circumstances, as long as endoscopy performance is restricted to emergency cases and sufficient PPM are available.

**INTRODUCTION**

The pandemic of coronavirus disease 2019 (COVID-19) has spread throughout the world in a short period of time, rapidly affecting medical practice. Although the disease usually manifests with respiratory symptoms, gastrointestinal (GI) symptoms are not rare and, in some cases, constitute basic clinical manifestations[[1](#_ENREF_1),[2](#_ENREF_2)]. GI-endoscopy is considered a risky procedure for transmission of the infection: During endoscopy, close contact of the endoscopist with the patient takes place, respiratory droplets and aerosols are generated and contact with contaminated material, body fluids and faeces is likely to occur. Moreover, endoscopy involves also the assisting personnel of the endoscopy units (PEU), *i.e.*, not only the endoscopist, but also the assisting personnel including nurses and paramedical staff. In light of these considerations, specific protective measures and disinfection procedures have been recommended by scientific societies, as well as renowned experts[[3-5](#_ENREF_3)]. Endoscopic societies such as ESGE and ESGENA published timely a joint position statement for GI-endoscopy during the COVID-19 pandemic regarding safe endoscopies for patients and PEU[[3](#_ENREF_3)], suggesting minimization of non-emergency endoscopies, implementation of personal protection measures (PPM), and post-endoscopy calls to patients 7 d and 14 d after the endoscopy in order to check their COVID-19 status. In a study from the heavily affected Northern Italy, the number of post-endoscopy COVID-19 infections was negligible and the number of infected PEU was very small[[6](#_ENREF_6)]. The aim of this study was to evaluate the impact of endoscopic procedures on risk of transmission for patients and PEU on a European multicenter basis, using as tool the telephone contacts suggested by ESGE and ESGENA.

**MATERIALS AND METHODS**

***Study design***

This was an international, multicenter study conducted during the period of the first European lockdown for COVID-19 (March-May 2020) in nine high-volume endoscopy departments across six European countries [Athens, Greece (two centers), Foggia/Verona, Italy (two centers), Brussels, Belgium, Skopje, Republic of North Macedonia, Zagreb/Rijeka, Croatia (two centers) and Belgrade, Serbia]. The centers were included, based on their high volume of endoscopic procedures prior to the COVID-19 outbreak and the fact that they represented regions with a high prevalence of the disease on the one side of the spectrum (Verona and Brussels) as well as regions with lower prevalences of COVID-19 (centers of the European South). This is analysis of retrospectively collected data within a prospectively built database.

***Inclusion criteria***

All consecutive patients undergoing any endoscopic procedure, including upper and lower GI endoscopy (colonoscopy or rectosigmoidoscopy), endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS) during the aforementioned period across each one of the abovementioned PEU were considered eligible for inclusion.

***Study population***

**Patients undergoing endoscopy:** According to each center’s triage protocol, the day of the endoscopy or the day before all patients were questioned by one of the predetermined local study’s coordinator for symptoms and contacts that could be linked to COVID-19 and then stratified as low- or high- risk for potential COVID-19 infection, according to the ESGE/ESGENA joint statement[[3](#_ENREF_3)]. Demographic data and procedural information regarding the endoscopy performed as well as previous performance of testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were also recorded. Following the ESGE/ESGENA joint statement recommendation regarding post-procedure risk management[[3](#_ENREF_3)], local study coordinators contacted the patients *via* telephone calls at  day 7 and day 14 after the endoscopy to inquire about any new COVID-19 diagnosis, or development of COVID-19 symptoms. This was carried out by a structured and identical across all centers questionnaire (Supplementary Table 1) filled out for each patient. Polymerase chain reaction (PCR) - testing *a posteriori* the endoscopic procedurewas possible at physician’s discretion on a case-by-case basis, taking into account each patient’s clinical status. For those tested positive after the endoscopic procedure, additional information regarding need for hospitalization, intensive care unit (ICU) - admission for COVID-19 and COVID-19-related deaths were also collected.

**PEU:** PEU were questioned regarding potential COVID-19 symptoms and/or SARS-CoV-2 infection with the use of a structured questionnaire (Supplementary Table 2). PEU included not only medical and nursing staff, but also assisting staff working in the PEU who could contact patients or material potentially infected by SARS-CoV-2, *i.e.*, cleaning personnel, transporters and secretarial staff of units. For those positive for SARS-CoV-2, information regarding hospitalizations, ICU-admissions and COVID-19-related deaths were collected. Additionally, the final part of the questionnaire recorded the total number of endoscopies conducted pre-, during and post- implementation of COVID-19 transmission preventative measures.

***Study endpoints***

The primary endpoint of the study was the incidence of infection among patients that underwent endoscopy during the established time period. Secondary endpoints comprised: (1) Incidence and outcome of hospitalization, ICU-admission for COVID-19 and COVID-19-related deaths, among patients who tested positive; (2) Prevalence of COVID-19 symptoms and/or positive SARS-CoV-2 testing among PEU; (3) Incidence and outcome of hospitalization, ICU-admission for COVID-19 and COVID-19-related deaths, among PEU tested positive; and (4) percentage of decrement in the overall number of endoscopies before and after lockdown measures implementation, as well as implementation of PPM in the study centers.

For the purposes of the current study, only PCR - testing was deemed adequately accurate for confirmation of infection`s diagnosis, while rapid tests, when performed needed to be confirmed *via* PCR.

***Statistical analyses***

Categorical data are presented as number (%) with respective 95% confidence intervals (CI). Distribution of quantitative data was evaluated for normality after Kolmogorov–Smirnov’s statistic and expressed as mean (± SD) or mean (IQR) according to their distribution. A *P* value < 0.05 was considered significant. The statistical review of the study was performed by a biomedical statistician (IP).

***Ethical approval***

The protocol of this study was reviewed and approved by the local Institutional Review Board (BΠΠΚ EBΔ 320/10-6-20). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and in compliance with good clinical practice.

**RESULTS**

Overall, 1267 endoscopies were performed in 1222 patients during the study’s time period. Of them, 87 (7%) were excluded due to initial positive testing, thus 1135 patients were enrolled in the study (Figure 1). Patients’ baseline characteristics and recruitment rate per center are presented in Table 1.

***Primary endpoint***

Among the 1135 enrolled patients, 254 (22.4%) were retested the days following endoscopy due to new symptoms onset that could indicate a potential COVID-19 infection and eight (*n* = 8) were eventually found positive. Thus, the incidence of infection among patients undergoing endoscopy was 0.7% (95%CI: 0.2-0.12). Of these eight patients, the majority had undergone upper GI-endoscopy (*n* = 6/8, 75%), while a negative pre-endoscopy PCR testing was available in only one case. A detailed overview of the infected patients’ characteristics is presented in Table 2.

***Secondary endpoints***

Of the eight SARS-CoV-2 positive cases, 2 (25%) presented with a very mild illness and did not require hospitalization at all; the other 6 (75%) were hospitalized at some point, with 2 (33.3%) of them finally dying due to COVID-19. Another 2 (33.3%) patients died, but the cause of death was considered their underlying cancer while the rest 2 (33.3%) were discharged to home and to a nursing residency, respectively.

Overall, data regarding COVID-19 infection status of 163 PEU from the nine PEU were recorded. These included 84/163 (51.5%) physicians (attendings as well as trainees), 62/163 (38%) nurses and 17/163 (10.4%) assisting staff working exclusively (or mostly) in the PEU (*i.e.*, cleaning personnel, transporters and secretarial staff of the units). Overall, 5/163 of the total PEU tested positive during the study period (2 physicians, 3 nurses), giving an incidence of infection of 3% (95%CI: 0.4-5.7). In the majority of them (*n* = 4, 80%), the infection was considered to be associated to their work environment. These cases represent 2.3% (4/163) of the total PEU of our study and 7% and 16.6% of the PEU of their own units, respectively.

None (0/5) of the infected PEU developed severe disease, none required hospitalization and no COVID-19 related death of the PEU that were included in our study occurred.

Preventative measures in accordance with the ESGE/ESGENA position statement (reduction of cases to focus on emergency therapies, use of PPM *i.e.*, gowns, goggles and masks) were implemented and adhered in all participating centers during the initial phase of the study (spanning from the 9 March, 2020 to the 23 March, 2020). Overall, a significant reduction in the number of endoscopies was evident throughout all participating centers after March 2020 (Figure 2). In detail, one week before implementation of the ESGE/ESGENA position statement the total number of endoscopies across all centers was 534 (246 upper GI-endoscopies, 209 colonoscopies/rectosigmoidoscopies, 56 ERCPs and 23 EUS). During the 6 following weeks this number gradually dropped, reaching a plateau phase with a mean of 167 ± 14 endoscopies per week, estimating a 68.7% (95%CI: 64.8-72.7) decrease in endoscopic procedures performance.

**DISCUSSION**

Endoscopic procedures were deemed as risky procedures for bidirectional COVID-19 infection transmission[[1](#_ENREF_1),[2](#_ENREF_2),[7](#_ENREF_7),[8](#_ENREF_8)]. In this analysis of retrospectively collected data within a prospectively built database conducted across nine European endoscopic facilities, we showed that risk of COVID-19 infection for patients undergoing GI endoscopy is extremely low in a lockdown setting, underlining the value of following ESGE/ESGENA recommendations to address the danger of COVID-19 infection in everyday, real-world clinical practice.

Although COVID-19 infection and its potential implications have been at the focal point of ongoing research worldwide, evidence regarding this risk for professional and patient infection post-endoscopy remain scarce[[9](#_ENREF_9)]. In one of the few studies, Repici *et al*[[6](#_ENREF_6)] analyzed retrospectively data from 802 patients and 968 PEU across 41 hospitals in Northern Italy. Their results suggested that the number of post-endoscopy patient infections is negligible (namely 1 infection out of 802 patients - proven infection rate of 0.12%). Similarly in a much smaller multicenter, retrospective study, patients that underwent stent placement for upper GI obstruction were evaluated[[10](#_ENREF_10)]; only one out of 29 (*n* = 1/29, 3.4%) was tested positive for SARS-CoV-2 after the procedure, while all medical staff involved in stenting procedures remained COVID-19 free 14 d later. Results of our multicenter study are also in the same direction, as only 8 out of the 1135 patients who were deemed pre-endoscopically SARS-CoV-2 Low risk or negative, became positive. Indeed, these results are further corroborated by the findings of a recent cross-sectional study. In a high-volume Japanese endoscopic facility, not a single positive result was detected among 783 PCR-analyzed saliva samples from patients undergoing endoscopic procedures[[11](#_ENREF_11)].

Regarding PEU infection after endoscopy, our study also concurs to that of Repici *et al*[[6](#_ENREF_6)], showing a very low risk for PEU contamination. Indeed, the Italian study demonstrated  a very small number of infected PEU (42 cases, which represents a mere 4.3% of the total PEU of their study, with 85.7% of infections occurring before PPM were introduced); moreover, even for those PEU who were infected, less than 1% needed hospitalization and none required admission in ICU or died[[6](#_ENREF_6)]. Outside Europe, the risk of COVID-19 infection for PEU may be even higher reaching up to 23.9%, especially among endoscopy technicians[[12](#_ENREF_12)]. Our study showed even more impressive results with only 5 PEU testing positive during the study period, representing a 3% of the total PEU involved in the endoscopies that were performed in the study and in only 4 of the total PEU included in our study (1 physician, 3 nurses) was the infection considered to be linked to their work. As in the Italian study, none of the infected PEU of our study group developed severe disease, neither required hospitalization nor died, compared to 2 COVID-19-related deaths that occurred among the 8 patients that became positive post-endoscopy. Whether this was merely a random association, or a result of the younger age and better health status of the PEU compared to that of our patient population -who were severely ill individuals undergoing emergency endoscopies- remains unclear. Published data suggest that PEU, when affected, suffer a relatively mild disease, but as the numbers are extremely small, we cannot provide further insights[[5](#_ENREF_5),[6](#_ENREF_6)]. Notably, a case-by-case analysis revealed a clustering of infections, as all PEU found positive worked in a unit performing almost exclusively ERCPs. A possible explanation could be speculated based on the longer duration of these particular examinations compared to standard upper GI-endoscopies, resulting in increased risk for transmission.

Pre-endoscopic testing for COVID-19 was available only for one fourth of the patients of our study (326/1222, 26.7%). One might consider this percentage low; however, it should be underlined that this policy is in accordance with the ESGE/ESGENA recommendations that do not advocate SARS-CoV-2 tests as a prerequisite for GI-endoscopy. Contrariwise, they put a spotlight on appropriate triaging of non-emergency endoscopies and PPM. Our low post-endoscopy infection rates for both patients and PEU seem to justify these suggestions.

The finding that COVID-19 pandemic led to significant reduction in the volume of endoscopic procedures is not novel. Beyond patients’ stratification as low- or high- risk for potential COVID-19 infection, the position statement for GI-endoscopy during the COVID-19 pandemic by ESGE/ESGENA, also clearly lists which endoscopic procedures should be definitely performed and which can be postponed, policy uniformly applied all participating centers of our study, as well. Thus, all the endoscopies performed in our series, if not emergency were nevertheless completely necessary and none were pure elective. Still, the optimal policy, when resumption of endoscopy services comes into question remains to be elucidated. In this regard, a stepwise approach taking into account: (1) The regional prevalence of COVID-19 with stricter guidelines in endoscopy and use of PPE in high-prevalence (> 2%) areas[[13](#_ENREF_13)]; (2) Patient stratification to procedures that should be performed immediately or postponed as well as low or high risk for infection[[3](#_ENREF_3)]; and (3) modifications in PEU working schedule to prevent hospital-based transmission, seems the most appropriate[[14](#_ENREF_14),[15](#_ENREF_15)].

A number of strengths related to our study could be cited. First, this iteration is one of the few studies addressing the question of safety of endoscopy during COVID-19 pandemic. Second, we enrolled patients from different countries, giving a more representative overview of the impact of COVID-19 outbreak on endoscopy units. Third, our questionnaire was guided by the ESGE/ESGENA position statement. Finally, our population was homogenous, including patients who underwent endoscopic procedures involving both the upper and lower GI tract as well as the respective participating PEU.

On the other hand, there are also limitations that merit attention. Absence of testing for SARS-CoV-2 among patients presenting for endoscopy without COVID-19 symptoms and a heterogeneity on PEU testing could initially be seen as such; however, this practice is followed in accordance to endoscopic societies’ recommendations (including those by ESGE/ESGENA) and should therefore be considered unavoidable, although it undoubtedly has in impact on our epidemiological data, as the rate of asymptomatic patients in our group remains unknown, hindering the complete tracking of the infection. Another shortcoming is the possibility of recall bias, given that study’s data was acquired by asking patients to recall their symptoms. Again, this was unavoidable, as it complied with the ESGE/ESGENA directive, stating that patients should be contacted 7-d and 14-d post endoscopy. Finally, the small number of positive cases and study design are factors preventing a definitive causal relationship to be established; however, aim of this study was not to address issues related to potential route of infection transmission, rather than investigate the actual possibility of COVID-19 transmission in endoscopic units, when established guidelines are implemented.

**CONCLUSION**

In conclusion, COVID-19 transmission in endoscopic units is a highly unlikely event for both patients and PEU in a lockdown setting, provided endoscopies are effectively reduced to emergency cases and appropriate, stringent PPM are implemented. In the extremely rare cases that PEU infection occurred in our series, the disease was relatively mild, with no hospitalizations or COVID-19 related deaths.

**ARTICLE HIGHLIGHTS**

***Research background***

Coronavirus disease 2019 (COVID-19) outbreak significantly affected endoscopic practice, as gastrointestinal endoscopy is considered a risky procedure for transmission of infection. Endoscopic societies such as ESGE and ESGENA published a position statement for endoscopy during the COVID-19 pandemic regarding safe endoscopies for patients and personnel of endoscopy units (PEU). However, the incidence and outcome of infection among patients undergoing endoscopy and PEU remains to be determined.

***Research motivation***

Currently, there is insufficient data investigating the incidence and outcome of COVID-19 infection among patients undergoing endoscopy and PEU.

***Research objectives***

We aimed to evaluate the impact of endoscopic procedures on risk of transmission for patients and PEU on a European multicenter basis, using as tool the telephone contacts suggested by ESGE and ESGENA.

***Research methods***

Patients undergoing endoscopy in nine endoscopy departments across six European countries during the period of the first European lockdown for COVID-19 (March-May 2020) were included. Participants were stratified as low- or high- risk for potential COVID-19 infection, according to the ESGE/ESGENA joint statement and contacted 7-14 d later to assess COVID-19 infection status. PEU were questioned regarding COVID-19 symptoms and/or infection *via* questionnaire while information regarding hospitalizations, ICU-admissions and COVID-19-related deaths were collected. The number of weekly endoscopies during the lockdown period was also recorded.

***Research results***

One thousand two hundred sixty-seven endoscopies were performed in 1222 individuals. 87 (7%) were excluded due to initial positive PCR testing. Among the 1135 pre-endoscopically low risk or PCR negative for COVID-19, 254 (22.4%) were tested post-endoscopy and 8 were eventually found positive, resulting in an infection rate of 0.7% [95% confidence interval (CI): 0.2-0.12]. The majority (6 patients, *i.e.*, 75%) had undergone esophagogastroduodenoscopy. Data regarding for a total number of 163 PEU was recorded; five [*n* = 5/163, (3%); 95%CI: 0.4-5.7)] tested positive during the study period. In four of them (*n* = 4/163, 2% of the total), the infection was deemed relevant to their work environment. A decrease of 68.7% (95%CI: 64.8-72.7) in the number of endoscopies was recorded.

***Research conclusions***

This study showed that COVID-19 transmission in endoscopic units is highly unlikely during a lockdown setting, provided endoscopies are reduced to emergency cases and PPM are implemented.

***Research perspectives***

More robust data are definitely warranted to identify various clinical factors that contributes to higher risk for endoscopy-related COVID-19 infection risk.

**REFERENCES**

1 **Gu J**, Han B, Wang J. COVID-19: Gastrointestinal Manifestations and Potential Fecal-Oral Transmission. *Gastroenterology* 2020; **158**: 1518-1519 [PMID: 32142785 DOI: 10.1053/j.gastro.2020.02.054]

2 **Song Y**, Liu P, Shi XL, Chu YL, Zhang J, Xia J, Gao XZ, Qu T, Wang MY. SARS-CoV-2 induced diarrhoea as onset symptom in patient with COVID-19. *Gut* 2020; **69**: 1143-1144 [PMID: 32139552 DOI: 10.1136/gutjnl-2020-320891]

3 **Gralnek IM**, Hassan C, Beilenhoff U, Antonelli G, Ebigbo A, Pellisè M, Arvanitakis M, Bhandari P, Bisschops R, Van Hooft JE, Kaminski MF, Triantafyllou K, Webster G, Pohl H, Dunkley I, Fehrke B, Gazic M, Gjergek T, Maasen S, Waagenes W, de Pater M, Ponchon T, Siersema PD, Messmann H, Dinis-Ribeiro M. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic. *Endoscopy* 2020; **52**: 483-490 [PMID: 32303090 DOI: 10.1055/a-1155-6229]

4 **Repici A**, Maselli R, Colombo M, Gabbiadini R, Spadaccini M, Anderloni A, Carrara S, Fugazza A, Di Leo M, Galtieri PA, Pellegatta G, Ferrara EC, Azzolini E, Lagioia M. Coronavirus (COVID-19) outbreak: what the department of endoscopy should know. *Gastrointest Endosc* 2020; **92**: 192-197 [PMID: 32179106 DOI: 10.1016/j.gie.2020.03.019]

5 **Lui RN**. Safety in Endoscopy for Patients and Healthcare Workers During the COVID-19 Pandemic. *Tech Innov Gastrointest Endosc* 2021; **23**: 170-178 [PMID: 33103130 DOI: 10.1016/j.tige.2020.10.004]

6 **Repici A**, Aragona G, Cengia G, Cantù P, Spadaccini M, Maselli R, Carrara S, Anderloni A, Fugazza A, Pace F, Rösch T; ITALIAN GI-COVID19 Working Group. Low risk of COVID-19 transmission in GI endoscopy. *Gut* 2020; **69**: 1925-1927 [PMID: 32321857 DOI: 10.1136/gutjnl-2020-321341]

7 **Ang TL**. Gastrointestinal endoscopy during COVID-19 pandemic. *J Gastroenterol Hepatol* 2020; **35**: 701-702 [PMID: 32216110 DOI: 10.1111/jgh.15048]

8 **Tian Y**, Rong L, Nian W, He Y. Review article: gastrointestinal features in COVID-19 and the possibility of faecal transmission. *Aliment Pharmacol Ther* 2020; **51**: 843-851 [PMID: 32222988 DOI: 10.1111/apt.15731]

9 **Ginès À**, Fernández-Esparrach G, Pellisé M, Sendino O, Balaguer F, Llach J, González-Suárez B, Saló S. Critical importance of early introduction of prevention measures for SARS-CoV-2 infection in endoscopy units. *Gastrointest Endosc* 2020; **92**: 936-937 [PMID: 32553570 DOI: 10.1016/j.gie.2020.06.023]

10 **Rodrigues-Pinto E**, Ferreira-Silva J, Fugazza A, Capogreco A, Repici A, Everett S, Albers D, Schumacher B, Gines A, Siersema PD, Macedo G. Upper gastrointestinal stenting during the SARS-CoV-2 outbreak: impact of mitigation measures and risk of contamination for patients and staff. *Endosc Int Open* 2021; **9**: E76-E86 [PMID: 33403239 DOI: 10.1055/a-1319-1201]

11 **Miyake S**, Ashikari K, Kato S, Takatsu T, Kuwashima H, Kaneko H, Nagai K, Watari I, Sato T, Yamaoka Y, Yamamoto T, Ryo A, Maeda S, Nakajima A, Higurashi T. Severe acute respiratory syndrome coronavirus 2 prevalence in saliva and gastric and intestinal fluid in patients undergoing gastrointestinal endoscopy in coronavirus disease 2019 endemic areas: Prospective cross-sectional study in Japan. *Dig Endosc* 2021 epub ahead of print [PMID: 33548095 DOI: 10.1111/den.13945]

12 **Kumar Goenka M**, Bharat Shah B, Goenka U, Das SS, Afzalpurkar S, Mukherjee M, Patil VU, Jajodia S, Ashokrao Rodge G, Khan U, Bandopadhyay S. COVID-19 prevalence among health-care workers of Gastroenterology department: An audit from a tertiary-care hospital in India. *JGH Open* 2021; **5**: 56-63 [PMID: 33490614 DOI: 10.1002/jgh3.12447]

13 **Bhandari P**, Subramaniam S, Bourke MJ, Alkandari A, Chiu PWY, Brown JF, Keswani RN, Bisschops R, Hassan C, Raju GS, Muthusamy VR, Sethi A, May GR, Albéniz E, Bruno M, Kaminski MF, Alkhatry M, Almadi M, Ibrahim M, Emura F, Moura E, Navarrete C, Wulfson A, Khor C, Ponnudurai R, Inoue H, Saito Y, Yahagi N, Kashin S, Nikonov E, Yu H, Maydeo AP, Reddy DN, Wallace MB, Pochapin MB, Rösch T, Sharma P, Repici A. Recovery of endoscopy services in the era of COVID-19: recommendations from an international Delphi consensus. *Gut* 2020; **69**: 1915-1924 [PMID: 32816921 DOI: 10.1136/gutjnl-2020-322329]

14 **1 Gupta S**, Shahidi N, Gilroy N, Rex DK, Burgess NG, Bourke MJ. Proposal for the return to routine endoscopy during the COVID-19 pandemic. *Gastrointest Endosc* 2020; **92**: 735-742 [PMID: 32360301 DOI: 10.1016/j.gie.2020.04.050]

15 **Hennessy B**, Vicari J, Bernstein B, Chapman F, Khaykis I, Littenberg G, Robbins D. Guidance for resuming GI endoscopy and practice operations after the COVID-19 pandemic. *Gastrointest Endosc* 2020; **92**: 743-747 [PMID: 32437712 DOI: 10.1016/j.gie.2020.05.006]

**Footnotes**

**Institutional review board statement:** The protocol of this study was reviewed and approved by the local Institutional Review Board (BΠΠΚ EBΔ 320/10-6-20). The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and in compliance with good clinical practice.

**Informed consent statement:** All study participants, or their legal guardian, provided informed written consent prior to study enrollment.

**Conflict-of-interest statement:** The authors of this manuscript have no conflicts of interest to disclose.

**Data sharing statement:** No additional data are available.

**STROBE statement:** The authors have read the STROBE statement, and the manuscript was prepared and revised according to the STROBE statement.

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**Figure Legends**



**Figure 1 Study flowchart.** PCR: Polymerase chain reaction; SARS-CoV2: Severe acute respiratory syndrome coronavirus 2.

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**Figure 2 Overall endoscopies one week before and the weeks during lockdown.**

**Table 1 Baseline characteristics of patients, *n* (%)**

|  |  |
| --- | --- |
| **Patients’ characteristics** |  |
| Male/femaleAge (mean ± SD), yrInpatientOutpatient Referral | 678 (59.7)/457 (40.3)63.4 ± 14.5506 (44.6)598 (52.7)31 (2.7) |
| Recruitment per center |  |
| "Attikon" Hospital, Athens, Greece | 236 (20.8) |
| Aretaieio Hospital, Athens, Greece | 42 (3.7) |
| Foggia, Italy | 215 (18.9) |
| Verona, Italy | 235 (20.7) |
| Belgrade, Serbia | 19 (1.7) |
| Brussels, Belgium | 143 (12.6) |
| Skopje, Republic of North Macedonia | 149 (13.1) |
| Zagreb/Rijeka, Croatia | 96 (8.5) |
| Type of endoscopy1 |  |
| Upper GI-endoscopies Colonoscopies/rectosigmoidoscopiesERCPEUS | 587 (46.3)444 (35.1)178 (14.1)57 (4.5) |

1Sums up to 1266 endoscopies. SD: Standard deviation; GI: Gastrointestinal; ERCP: Endoscopic retrograde cholangiopancreatography; EUS: Endoscopic ultrasonography.

**Table 2 Baseline characteristics and outcomes of patients positive for severe acute respiratory syndrome coronavirus 2 after endoscopy**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Patient, age** | **Endoscopy** | **Date of endoscopy** | **COVID PCR test before endoscopy** | **Contact of suspected or confirmed COVID 19 case after endoscopy** | **Symptoms** | **COVID PCR test after endoscopy** | **Outcome of those hospitalized** | **Case related to endoscopy** |
| 1 | Female, 66 yr | Upper GI | March 12, 2020 | No | No | Fever and cough | Tested positive March 18, 2020 | Death/deceased due to COVID-19 | Cannot reasonably exclude |
| 2 | Male, 81 yr | Upper GI | April 8, 2020 | No | No | Fever, cough and sore throat since April 17 for 42 d | Hospital admission April 12, 2020, tested positive and had Pneumonia | Death May 4/deceased due to COVID-19 | Cannot reasonably exclude |
| 3 | Male, 66 yr, head/neck cancer and arterial disease | Upper GI | March 18, 2020 | No | Yes with Suspected Case | Fever and Diarrhea since March 27, 2020 | Tested positive March 28, 2020 | Death May 7 due to cancer | Cannot reasonably exclude |
| 4 | Male, 55 yr, cancer esophagus | Upper GI | March 18, 2020 | No | Yes with Suspected Case | Cough since March 16, 2020 | Tested positive March 24, 2020 | Discharge | No |
| 5 | Male, 76 yr, cancer stomach, 2, COPD | EUS | March 24, 2020 | No | Yes with suspected case | Cough since March 19, 2020 | Tested positive Apirl 23, 2020 | Became negative/remained at nursing home | No |
| 6 | Female, 66 yr, AML | Lower GI | Apirl 1, 2020 | Yes March 30, 2020negative | Yes with suspected case | Fever since April 3, 2020 for 6 d | Tested positive Apirl 10, 2020 | Death May 4 due to cancer/at home | Cannot reasonably exclude |
| 7 | Male, 48 yr | Upper GI | March 27, 2020 | No | No | Fever and cough since April 8, 2020 for 4 d | Tested positive Apirl 12, 2020 | Not hospitalized | No |
| 8 | Male, 63 yr, diabetes, lung siseas, IBD | Upper GI | March 30, 2020 | No | Yes with Suspected Case | Fever and cough since April 22, 2020 for 2 d | Tested positive Apirl 22, 2020 | Not hospitalized | No |

PCR; Polymerase chain reaction; GI: Gastrointestinal; COPD; Chronic obstructive pulmonary disease; EUS: Endoscopic ultrasonography; AML: Acute myeloid leukemia; IBD: Inflammatory bowel disease.