

Endoscopic Ultrasound at Crossroads in COVID - 19 era: a Multi-Center Global Study.

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Background and study aim: During COVID-19 pandemic most of non-emergency endoscopic procedures has been suspended. Endoscopic ultrasound (EUS) is important diagnostic and therapeutic procedure. This survey aimed to provide a rapid assessment of status of EUS during COVID-19 pandemic in different leading units of the world.

Patients and Methods: Senior endoscopists from 10 different countries were invited to participate. Patient demographics, COVID-19 status, EUS indications as well as laboratory and radiology findings were reported. Pre-procedural preparation and post procedure complications were reported. Data were analyzed to reveal the effect of SARS-CoV-2 pandemic on different perspectives

of EUS practice in the collaborating endoscopy units. Descriptive analysis was done by calculating percentages for categorical variables and mean± standard deviation for quantitative variables.

Results: data of 316 patients from 11 countries were accrued. The mean (± SD) age of the patients in this study was 55.57±13.94 years. In this analysis 62.3% were laboratory confirmed SARS-Cov-2 negative while 8 patients were suspected and only 1 patient was laboratory confirmed positive for COVID -19. Daily performance of EUS was similar in before and during COVID-19 pandemic with an insignificant decrease of -1.1%. Emergent and urgent EUS was needed in 58 (14.4%) and 91 (28.8%) patients respectively. Pancreatic mass (27.8%),

biliary dilatation (10.4%) formed major chunk of indications for procedure. Therapeutic outcomes were achieved with majority (40.8%).

Conclusion: our data underscores the point of efforts of clinicians to provide the same level of care provided by EUS units despite the negative impact of COVID-19 pandemic.

INTRODUCTION

Coronavirus disease 2019 (COVID -19) emanated in China in late 2019 and soon became rapidly progressive pandemic. Covid-19 crisis is an overwhelming challenge affecting world and has forced nations to make hard choices on how to respond. Brutality of Covid-19 pandemic forced centers to double down their efforts on patient care and safety [1,2]. Scientifically robust and ethically sound clinical research has finally led to availability of vaccines against COVID -19, but real-time decision-making implementation is paramount for navigating vaccination challenges especially in time and resource constraint setting.

Aerosol generating nature of gastrointestinal (GI) endoscopy has made it high risk procedure for COVID-19 transmissions. Endoscopy personnel are at risk of transmission during various exposures from person-to-person via direct or prolonged contact and also exposure to infected aerosols or droplets generated during endoscopic procedures that are likely to trigger cough and retching during the procedure. Besides that, handling of contaminated endoscopic equipment, accessories and body fluids also increases the risk of exposure [3,4]. However, transmission of virus to uninfected patients via contaminated endoscopes has not been reported so far under the circumstances where the current disinfection and reprocessing guidelines that has been advocated by American Society for Gastrointestinal Endoscopy and European Society of Gastrointestinal Endoscopy have been practiced strictly [5-7].

Endoscopic ultrasound (EUS) is an important diagnostic and therapeutic procedure that is required for several critical and emergent causes such as biliary drainage, gallstone pancreatitis, EUS guided drainage of walled off pancreatic necrosis, symptomatic pancreatic pseudocysts, management of bleeding gastric varices with coils, histological diagnosis for cancers and gallbladder in acute cholecystitis in a surgically unfit patient [4,8,9]. Furthermore, EUS

procedures are thought to generate more droplets due to its larger diameter of the endoscopes leading to higher possibility of cough, increased use of accessories for interventions, relatively longer procedural time, and more leakage of body fluids like GI secretions and bile through the working channel during procedures [10,11].

Responsible stewardship is need of hour for safely restarting GI endoscopy in the era of COVID-19. There is limited information about how the pandemic has influenced EUS performance so far [12,13]. The impact of different recommendations released by GI societies needs to be continuously evaluated to confirm their effectiveness in preventing spread of infection and to report its overall impact on services provided by different endoscopy unit. This survey is designed to provide a rapid and robust assessment of status of EUS during COVID-19 pandemic in different leading units of the world, and also to elucidate patient and procedure characteristics during this period.

METHODS

Study Design and Oversight: the primary objectives of this study were to measure the percentage change in performed EUS inside GI endoscopy units in response to COVID-19 in different countries. The study was conducted as a survey in June 2020. Senior endoscopists (who were directly involved in doing EUS) representing high throughput endoscopy units in different countries were invited by email to complete questionnaire. The structured questionnaire was available on the Redcap platform (Supplementary material) covering all aspects regarding COVID-19-related changes in endoscopic activities, demographics, COVID-19 status, EUS indications, routine or urgent status, laboratory findings, radiology findings, procedural details, endoscopic findings, other procedures, and post procedure complications. Participation was voluntary and no incentive was offered for participation.

Data Collection and Analysis: All responses were collected in the online platform and transferred to SPSS version 24 (IBM SPSS Inc, Chicago, IL) for analysis. Descriptive analysis was done by calculating percentages for categorical variables and mean \pm standard deviation for quantitative variables. Comparative analysis was done by using the chi-square test or

the Student t test where appropriate. All differences were considered significant at a 2-sided P value of <.05.

RESULTS

A total of 45 high volume endoscopy units from different parts of world participated and 316 patients were enlisted during the period of study (**Table 1**).

Demographic, clinical and laboratory characteristics of study population:

The mean (\pm SD) age of the patients in this study was 55.57 ± 13.94 years and 42.7 % were females. A history of smoking was present in 14.6% of the patients and about 4 % were alcoholics. In this analysis 62.3% were lab confirmed SARS-Cov-2 negative while 8 patients were suspected and only 1 patient was lab confirmed positive for COVID -19 (**Table 2**). The remaining patients (34.8 %) were presumed SARS-Cov-2 negative (on basis of clinical and radiological features) though PCR confirmation was not available.

Daily performance of EUS was similar in before and during COVID-19 pandemic with an insignificant decrease of -1.1% Emergent and urgent EUS was needed in 58 (14.4%) and 91 (28.8%) patients respectively. Half of procedures done were routine. Few patients (6.6 %) had history of previous EUS. About half of patients didn't receive antibiotic and most patient didn't

receive any NSAIDS either prior to or after procedure. Almost half of the patients s (n=164, 51.9 %) underwent CT prior to EUS. The median AST, ALT and Alkaline phosphatase were 80, 97 and 295 IU/L.

Indications of EUS:

Pancreatic mass (27.8%), biliary dilatation (10.4%) and pancreatic cyst (7.3%) formed major chunk of indications for procedure. Other important indications were possible subepithelial lesion, luminal GI cancer staging, pancreatic duct dilation, evaluation for CBD stones, abdominal/mediastinal lymphadenopathy and abdominal pain. Fifty-five patients (17.4%) were referred to EUS after ERCP (**Table 3**).

Final diagnosis, outcomes and complications of EUS:

Most patients (93.4%) underwent examination by linear EUS with only 1 patient needing both linear and radial EUS. Complete detailed examination was done in almost all patients (n = 314, 99.4 %) (**Table 4**).

Therapeutic outcomes were achieved with majority (40.8%) undergoing fine needle aspiration/ biopsy (FNA / FNB). Seven patients needed celiac plexus block/ neurolysis, while 4 patients underwent EUS guided coil and cyanoacrylate injection. Few of them needed pseudocyst drainage. Few of these patients (17.4%) were referred for surgery and 2 patients needed interventional radiology procedures.

Table (1): Number of procedures per country.

Country	Frequency (n)
Brazil	33
China	55
Croatia	30
Egypt	145
India	25
Malaysia	19
Morocco	5
Philippines	3
Turkey	1
Total	316

Table (2): Demographic, clinical and laboratory characteristics of study population (n=316).

Variables	Mean \pm SD or n(%)
Age of patients (in years)	55.57 \pm 13.94 (range 9-87)
Gender	
Male	181(57.3)
Female	135(42.7)
Special habits	
Smoking	46(14.6)
Alcohol	12(3.8)
Others	5(1.6)
Does the patient have covid-19?	
Yes	1(0.3)
Suspected	8(2.5)
No	197(62.3)
No reply	110(34.8)
History of previous EUS (Yes)	21(6.6)
According to patient's clinical profile, the procedure is considered as	
Routine	167(52.8)
Urgent	91 (28.8)
Emergent	58(14.4)
AST (range) IU/L	80 (11-550)
ALT(range) IU/L	97(12-935)
Alkaline phosphatase (range) IU/L	295(32-5717)
Diagnostic Imaging Modality	
Ultrasound	34(10.8)
CT scan	164(51.9)
MRCP	61(5.1)
EUS	17(5.4)
Findings on image	
CBD size (in mm)	10.76 \pm 4.93
IHBR dilated (present)	45(14.2)
Antibiotic	
It was given before the procedure	77(24.4)
It was given after the procedure	5(1.6)
It was not given at all	173(54.7)
No reply	61(19.3)
NSAIDs	
It was given before the procedure	8(2.5)
It was given after the procedure	1(0.3)
It was not given at all	243(76.9)
No reply	64(20.3)

IHBR; Intrahepatic biliary radical, CBD; Common bile duct, NSAID; Non-steroidal anti-inflammatory drugs

Table (3): Indication of EUS.

Indications	N (%)
Pancreatic Mass	88(27.8)
Biliary dilation	33(10.4)
Pancreatic Cyst	23(7.3)
Mediastinal mass	3(0.9)
Rule out Chronic Pancreatitis	3(0.9)
Pancreatic Duct Dilation	10(3.2)
Possible subepithelial lesion	22(7.0)
Luminal GI cancer staging	13(4.1)
Evaluate for CBD stones	12(3.8)
Abdominal/Mediastinal lymphadenopathy)	13(4.1)
Abdominal pain	14(4.4)
Others	49(15.5)
Did the patient was referred to EUS after ERCP? (yes)	55(17.4)

Table (4): Final diagnosis, outcomes and complications of EUS (n=316).

Variables	N (%)
Type of EUS used	
Linear	295(93.4)
Radial	20(6.3)
Both	1(0.3)
Outcome of EUS	
Achieve FNA/FNB	129(40.8)
Achieve celiac plexus block/ neurolysis)	7(2.2)
Others	28(8.9)
EUS guided coil + cyanoacrylate	4 (0.01)
Referred for ERCP	4 (0.01)
Gastric varices injection of 2 ampule of histoacryl	1 (0.003)
Successful drainage with 8 cm PCSEMS	1 (0.003)
EUS pseudocyst drainage	1 (0.003)
No intervention	2 (0.006)
EUS completed *	315(99.6)

* No adverse events were reported.

DISCUSSION

The COVID-19 outbreak significantly disrupted routine health care standards all over the world. In the meantime, it is clear that multiple waves of the pandemic are expected and similar patterns are being noticed in many countries. It is important to depict the status and the practice of EUS from the start of the pandemic till now. Real life observations should be highlighted and reported to help improving the practice during the second wave. This will help better allocation of resources and avoid deferring patients in need for immediate intervention.

The nature of EUS as mostly a diagnostic and sometimes therapeutic procedure makes it difficult to defer patients according to indications. Except in the follow up of previously diagnosed benign conditions as chronic pancreatitis and benign cysts, patients are referred for either the diagnosis, exclusion or staging of malignant conditions. Worldwide endoscopy units are under enormous pressure to help patients while doing no harm. During peak of pandemic there was continued delay in diagnostic endoscopic services. Centers radically modified for containment of virus to overcome this terrible limbo and prioritized resources to resume services to near normal (pre COVID-19) levels.

In the beginning of the pandemic, most of the centers if not all experienced deferment of elective or semi-elective procedures to accommodate on the rising need of health care worker (HCW) being deployed to the respective

units to care for COVID-19 patients. By now, majority centers have started resuming most if not all of the endoscopic procedures in a staggered manner depending on the status of COVID -19 in their region and the availability of personal protective equipment (PPE).

This study is sufficiently powered and designed to provide a rapid and robust assessment of EUS during covid pandemic. EUS has paramount role in patient care affecting diagnosis and treatment of patients. Despite the disparaging effect of pandemic, the proportion of patients undergoing EUS was not diminished as highlighted by our study. Reliable testing and triage helped units to maintain commitment for maximizing benefits to patients. Half of patients underwent routine EUS which speaks volumes of tenacious nature of clinicians to overcome detrimental effects [14]. As more data accrue on responses to COVID-19 pandemic, our study helps to clarify the effect of factors affecting advance endoscopy.

One more clearly imminent result of this survey is the fundamental value of EUS in management of gastrointestinal malignancies. Despite the detrimental effect of pandemic, all centers kept on performing EUS with resolute as highlighted by the significant number of FNA/FNB done. Findings in this study suggest that mostly linear EUS was used and majority patients underwent one or other therapeutic procedure. Reliable evidence provided by this study elucidates the indications and outcomes of EUS in multiple high-volume centers around the world. Interplay of ERCP with EUS is also highlighted as

significant number were referred for EUS after ERCP.

The limitation of this study includes that, the heterogeneity of cases and distribution of the participating centers and their contribution. However, the large number of patients and the prospective nature of the study would help neutralizing these effects.

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Ethical consideration: this study was approved by the Institutional review board of the National Liver Institute, Menoufia University, Egypt (NLI IRB 00003413, 00203/2020).

HIGHLIGHTS

- Despite of pandemic all centers kept on performing EUS in these critical times.
- Reliable testing and triage helped units to maintain commitment for maximizing benefits to patients.

REFERENCES

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J et al; China Novel Coronavirus Investigating and Research Team. A Novel Coronavirus from Patients with Pneumonia in China, 2019. *N Engl J Med*. 2020 Feb 20;382(8):727-733.
2. WHO. Pneumonia of unknown cause – China. Available at: <http://www.who.int/csr/don/05-january-2020-pneumonia-of-unknown-cause-china/en/>. Accessed September 1, 2020
3. Mohandas K M, Gopalakrishnan G. Mucocutaneous exposure to body fluids during digestive endoscopy: the need for universal precautions. *Indian J Gastroenterol*. 1999;18(03):109–111.
4. Johnston E R, Habib-Bein N, Dueker J M, Quiroz B, Corsaro E, Ambrogio M et al. Risk of bacterial exposure to the endoscopist's face during endoscopy. *Gastrointest Endosc*. 2019;89(04):818–824.
5. Chiu P WY, Ng S C, Inoue H, Reddy DN, Hu El, Cho JY et al. Practice of endoscopy during COVID-19 pandemic: position statements of the Asian Pacific Society for Digestive Endoscopy (APSDE-COVID statements) *Gut*. 2020;gutjnl-2020-321185
6. Calderwood A H, Day L W, Muthusamy V R, Collins J, Hambrick R D, Brock A S et al. ASGE Quality Assurance in Endoscopy Committee. ASGE guideline for infection control during GI endoscopy. *Gastrointest Endosc*. 2018;87(05):1167–1179.
7. Beilenhoff U, Biering H, Blum R, Brijak J, Cibro M, Dumonceau J et al. Reprocessing of flexible endoscopes and endoscopic accessories used in gastrointestinal endoscopy: Position Statement of the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Gastroenterology Nurses and Associates (ESGENA) - Update 2018. *Endoscopy*. 2018;50(12):1205–1234.
8. Choudry N, Fuller R, Anderson N, Karlsson J. Separation of cough and reflex bronchoconstriction by inhaled local anaesthetics. *Eur Respir J*. 1990; 3:579–583.
9. Sinonquel P, Roelandt P, Demedts I, Gerven L, Vandenbrielle C, Wilmer A et al. COVID-19 and gastrointestinal endoscopy: What should be taken into account? *Digestive endoscopy : official journal of the Japan Gastroenterological Endoscopy Society*. 2020.
10. Machicado JD, Papachristou GI, Cote GA, Wani S, Groce J R, Conwell D L et al. Pancreaticobiliary Endoscopy in the COVID-19 Pandemic Era. *Pancreas*. 2020;49(6):729-732.
11. Rana SS. Risk of COVID-19 Transmission During Gastrointestinal Endoscopy. *Journal of Digestive Endoscopy*. 2020 Mar;11(1):27-30.
12. Gralnek IM, Hassan C, Beilenhoff U, Antonelli G, Ebigbo A, Pellise M, et al. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic. *Endoscopy*. 2020; 52: 483-90.
13. Amato A, Rondonotti E, Radaelli F. Lay-off of Endoscopy services for the COVID-19 pandemic: how can we resume the practice of routine cases? [published online ahead of print, 2020 Apr 26]. *Gastroenterology*. 2020; S0016-5085(20)30568-0.
14. Elshaarawy O, Lashen SA, Makhlof NA, Abdeltawab D, Zaghoul MS, Ahmed RM et al. Barriers for resuming endoscopy service in the context of COVID-19 pandemic: A multicenter survey from Egypt. *World J Gastroenterol*. 2020;26(43):6880-6890. doi:10.3748/wjg.v26.i43.6880.