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Contents

Thrice Monthly Volume 9 Number 28 October 6, 2021

REVIEW

- 8280** Transmission of severe acute respiratory syndrome coronavirus 2 *via* fecal-oral: Current knowledge
Silva FAFD, de Brito BB, Santos MLC, Marques HS, da Silva Júnior RT, de Carvalho LS, de Sousa Cruz S, Rocha GR, Santos GLC, de Souza KC, Maciel RGA, Lopes DS, Silva NOE, Oliveira MV, de Melo FF
- 8295** Nutrition, nutritional deficiencies, and schizophrenia: An association worthy of constant reassessment
Onaolapo OJ, Onaolapo AY

MINIREVIEWS

- 8312** Grounded theory qualitative approach from Foucault's ethical perspective: Deconstruction of patient self-determination in the clinical setting
Molina-Mula J
- 8327** Diabetes mellitus and COVID-19: Understanding the association in light of current evidence
Sen S, Chakraborty R, Kalita P, Pathak MP

ORIGINAL ARTICLE

Case Control Study

- 8340** Pregnancy complications effect on the nickel content in maternal blood, placenta blood and umbilical cord blood during pregnancy
Ding AL, Hu H, Xu FP, Liu LY, Peng J, Dong XD

Retrospective Study

- 8349** Clinical observation of Kuntai capsule combined with Fenmotong in treatment of decline of ovarian reserve function
Lin XM, Chen M, Wang QL, Ye XM, Chen HF
- 8358** Short-term effect and long-term prognosis of neuroendoscopic minimally invasive surgery for hypertensive intracerebral hemorrhage
Wei JH, Tian YN, Zhang YZ, Wang XJ, Guo H, Mao JH
- 8366** Ultrasonographic assessment of cardiac function and disease severity in coronary heart disease
Zhang JF, Du YH, Hu HY, Han XQ
- 8374** COVID-19 among African Americans and Hispanics: Does gastrointestinal symptoms impact the outcome?
Ashktorab H, Folake A, Pizuorno A, Oskrochi G, Oppong-Twene P, Tamanna N, Mehdipour Dalivand M, Umeh LN, Moon ES, Kone AM, Banson A, Federman C, Ramos E, Awoyemi EO, Wonni BJ, Otto E, Maskalo G, Velez AO, Rankine S, Thrift C, Ekwunazu C, Scholes D, Chirumamilla LG, Ibrahim ME, Mitchell B, Ross J, Curtis J, Kim R, Gilliard C, Mathew J, Laiyemo A, Kibreab A, Lee E, Sherif Z, Shokrani B, Aduli F, Brim H

Observational Study

- 8388** Validated tool for early prediction of intensive care unit admission in COVID-19 patients
Huang HF, Liu Y, Li JX, Dong H, Gao S, Huang ZY, Fu SZ, Yang LY, Lu HZ, Xia LY, Cao S, Gao Y, Yu XX
- 8404** Comparison of the impact of endoscopic retrograde cholangiopancreatography between pre-COVID-19 and current COVID-19 outbreaks in South Korea: Retrospective survey
Kim KH, Kim SB

Randomized Controlled Trial

- 8413** Effect of family caregiver nursing education on patients with rheumatoid arthritis and its impact factors: A randomized controlled trial
Li J, Zhang Y, Kang YJ, Ma N

SYSTEMATIC REVIEWS

- 8425** Dealing with hepatic artery traumas: A clinical literature review
Dilek ON, Atay A
- 8441** Clinical considerations for critically ill COVID-19 cancer patients: A systematic review
Ramasamy C, Mishra AK, John KJ, Lal A

CASE REPORT

- 8453** Atypical granular cell tumor of the urinary bladder: A case report
Wei MZ, Yan ZJ, Jiang JH, Jia XL
- 8461** Hepatocyte nuclear factor 1B mutation in a Chinese family with renal cysts and diabetes syndrome: A case report
Xiao TL, Zhang J, Liu L, Zhang B
- 8470** Ultrasound features of primary non-Hodgkin's lymphoma of the palatine tonsil: A case report
Jiang R, Zhang HM, Wang LY, Pian LP, Cui XW
- 8476** Percutaneous drainage in the treatment of intrahepatic pancreatic pseudocyst with Budd-Chiari syndrome: A case report
Zhu G, Peng YS, Fang C, Yang XL, Li B
- 8482** Postmenopausal women with hyperandrogenemia: Three case reports
Zhu XD, Zhou LY, Jiang J, Jiang TA
- 8492** Extremely high titer of hepatitis B surface antigen antibodies in a primary hepatocellular carcinoma patient: A case report
Han JJ, Chen Y, Nan YC, Yang YL
- 8498** Surgical treatment of liver metastasis with uveal melanoma: A case report
Kim YH, Choi NK

- 8504** Intermittent appearance of right coronary fistula and collateral circulation: A case report
Long WJ, Huang X, Lu YH, Huang HM, Li GW, Wang X, He ZL
- 8509** Synchronous concomitant pancreatic acinar cell carcin and gastric adenocarcinoma: A case report and review of literature
Fang T, Liang TT, Wang YZ, Wu HT, Liu SH, Wang C
- 8518** Spontaneous resolution of gallbladder hematoma in blunt traumatic injury: A case report
Jang H, Park CH, Park Y, Jeong E, Lee N, Kim J, Jo Y
- 8524** Rupture of ovarian endometriotic cyst complicated with endometriosis: A case report
Wang L, Jiang YJ
- 8531** Rotarex mechanical thrombectomy in renal artery thrombosis: A case report
Li WR, Liu MY, Chen XM, Zhang ZW
- 8537** Necrotizing fasciitis of cryptoglandular infection treated with multiple incisions and thread-dragging therapy: A case report
Tao XC, Hu DC, Yin LX, Wang C, Lu JG
- 8545** Endoscopic joint capsule and articular process excision to treat lumbar facet joint syndrome: A case report
Yuan HJ, Wang CY, Wang YF
- 8552** Spinocerebellar ataxia type 3 with dopamine-responsive dystonia: A case report
Zhang XL, Li XB, Cheng FF, Liu SL, Ni WC, Tang FF, Wang QG, Wang XQ
- 8557** Disseminated soft tissue diffuse large B-cell lymphoma involving multiple abdominal wall muscles: A case report
Lee CH, Jeon SY, Yhim HY, Kwak JY
- 8563** Genetic characteristics of a patient with multiple primary cancers: A case report
Ouyang WW, Li QY, Yang WG, Su SF, Wu LJ, Yang Y, Lu B
- 8571** Hypereosinophilia with cerebral venous sinus thrombosis and intracerebral hemorrhage: A case report and review of the literature
Song XH, Xu T, Zhao GH
- 8579** Itraconazole therapy for infant hemangioma: Two case reports
Liu Z, Lv S, Wang S, Qu SM, Zhang GY, Lin YT, Yang L, Li FQ
- 8587** One-stage total hip arthroplasty for advanced hip tuberculosis combined with developmental dysplasia of the hip: A case report
Zhu RT, Shen LP, Chen LL, Jin G, Jiang HT
- 8595** *Pneumocystis jirovecii* and *Legionella pneumophila* coinfection in a patient with diffuse large B-cell lymphoma: A case report
Wu WH, Hui TC, Wu QQ, Xu CA, Zhou ZW, Wang SH, Zheng W, Yin QQ, Li X, Pan HY

- 8602** Delayed massive cerebral infarction after perioperative period of anterior cervical discectomy and fusion: A case report
Jia F, Du CC, Liu XG
- 8609** Cortical bone trajectory fixation in cemented vertebrae in lumbar degenerative disease: A case report
Chen MM, Jia P, Tang H
- 8616** Primary intramedullary melanocytoma presenting with lower limbs, defecation, and erectile dysfunction: A case report and review of the literature
Liu ZQ, Liu C, Fu JX, He YQ, Wang Y, Huang TX

ABOUT COVER

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WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

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Observational Study

Comparison of the impact of endoscopic retrograde cholangiopancreatography between pre-COVID-19 and current COVID-19 outbreaks in South Korea: Retrospective survey

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Abstract

BACKGROUND

The coronavirus disease 2019 (COVID-19) outbreak has markedly influenced the endoscopic patterns. Endoscopic retrograde cholangiopancreatography (ERCP) is an essential technique for pancreatobiliary disease but increases the risk of exposure to the virus-containing body fluid; however, the impact of COVID-19 on ERCP is unknown.

AIM

To compare the number of endoscopic activities and to analyze the clinical outcomes of ERCPs before and during the COVID-19 outbreak in Daegu, South Korea.

METHODS

This retrospective cohort study included patients aged ≥ 18 years who underwent ERCP between February 18 and March 28, 2020, at a tertiary hospital. ERCP indications and endoscopic details were compared with those from the same period in 2018 and 2019 as control groups.

RESULTS

Of the 269 ERCP procedures, 113 (42.0%) cases were performed as emergency procedures. The number of ERCP procedures in 2018 and 2019 decreased by 20.2% and 56.6%, respectively, compared with that in 2020 ($P < 0.01$); among the 113 emergency ERCPs, the observed numbers in 2018 ($n = 42$) and 2019 ($n = 55$) dramatically dropped by 61.9% and 70.9%, respectively, compared with that in 2020 ($n = 16$). Of the 16 cases in 2020, stone removal was performed in five, biliary stenting in five, sphincterotomy in five, and nasobiliary drainage in one. No case of ERCP-related infection in medical workers or other patients has been reported.

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CONCLUSION

The COVID-19 outbreak significantly reduced the number of ERCPs; however, there is no difference in the indications and endoscopic interventions before and during the COVID-19 outbreak.

Key Words: Coronavirus disease 2019; Coronavirus; Endoscopic retrograde cholangiopancreatography; Emergency endoscopic retrograde cholangiopancreatography; Endoscopy

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Core Tip: The advent of the coronavirus disease 2019 (COVID-19) outbreak has transformed the patterns of endoscopic activities. However, little is known about the clinical impact associated with COVID-19 on endoscopic retrograde cholangiopancreatography (ERCP). We compared the change in the number of ERCP procedures, causes, and clinical outcomes of emergency ERCP before (2018, 2019) and during the COVID-19 (2020) outbreak at a tertiary referral hospital in South Korea.

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INTRODUCTION

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), has infected approximately 100 million people worldwide, with more than 2 million mortalities as of February 2021. The catastrophic viral transmission led to a pandemic in March 2020[1]. The advent of COVID-19 outbreak has revolutionized the pattern of endoscopies. However, little is known about the clinical changes associated with COVID-19 on endoscopic retrograde cholangiopancreatography (ERCP). SARS-CoV-2 infection is usually transmitted *via* aerosol droplets; however, there are emerging reports that SARS-CoV-2 can be spread *via* the gastrointestinal route[2-5]. Following the first identification of SARS-CoV-2 positivity on February 18, there was an alarming surge of COVID-19 at the end of February in Daegu, the third most densely populated city in South Korea. Statistics show that the cumulative number of COVID-19 cases had rapidly risen to 6600 within 1 mo[6].

Recently, endoscopic manipulation has been regarded as a potentially dormant reservoir for viral spread and aerosol formation during procedures[7-9]. Both protecting healthcare providers (HCPs) and limiting viral shedding in patients are of great importance in the endoscopy center[10]. Very recently, it has been reported that the sophisticated parts of the side-view scope can be a culprit of lethal bacterial colonization throughout procedures, thus requiring a series of laborious cleaning and disinfection processes[11]. Compared with other endoscopies such as colonoscopy and upper endoscopy, ERCPs are relatively time-sensitive procedures[12]. Most patients with pancreatobiliary disorders are referred to the emergency room (ER) from the clinics or medium-volume hospitals, mainly due to fever, abdominal pain, or jaundice. Most elective endoscopies were canceled or postponed due to the reinforced disease and infection control in our hospital, between February 18 and March 28, 2020, resulting in a substantial decrease in the number of endoscopic procedures, including ERCP[13]. The goal of this study was to compare and to analyze the change in the number of ERCP procedures, causes, and clinical outcomes of emergency ERCP before and during the COVID-19 outbreak in Daegu, the hardest-hit city in South Korea.

MATERIALS AND METHODS

Study population and design

This was a retrospective cohort study of patients aged ≥ 18 years who underwent ERCPs between February 18 and March 28, 2020, at a single tertiary referral hospital during the COVID-19 outbreak. These specific intervals are chosen based on the first SARS-CoV-2 confirmed date and the plateau date of the cumulative curve of the COVID-19 outbreak, in Daegu, South Korea. Baseline demographics, causes of ER visits, blood chemistry, and endoscopic findings relevant to ERCP were collected and compared with those in 2018 and 2019 (pre-COVID-19 era), which were labeled as control groups. In this study, the emergency ERCP group was defined as ERCP cases in which patients visited the ER and underwent ERCP within 24 h and did not include cases that were referred from the other departments due to bile leak, incidental bile duct stone, or sudden obstructive jaundice. Patients who underwent total gastrectomy were excluded. This study was approved by the Institutional Review Board of Yeungnam University Hospital (IRB No. 2020-12-042). Written informed consent was waived owing to the retrospective nature of this study.

Endoscopic procedures

All patients were sedated by administering midazolam (3-5 mg) and pethidine (25-50 mg) at the start of the procedure, and then propofol (10-100 mg) was administered intravenously by nurses during the procedure, with the endoscopists' permission. All endoscopic procedures were performed using side-viewing endoscopes (TJF-240, Olympus Optical Corporation, Tokyo, Japan). When the side-viewing endoscope was not suitable, particularly for patients who underwent subtotal gastrectomy, such as Billroth II, it was changed to a forward-viewing endoscope. The use of either side-viewing or forward-viewing endoscopes in patients with surgically altered anatomy was determined by the endoscopist's preference.

COVID-19 quarantine and protective equipment

Since the COVID-19 outbreak, all ER-visiting patients were subjected to the comprehensive COVID-19 quarantine process. They were directly guided through the walk-in screening tent at the ER entrance upon arrival, where the body temperature was checked, and patients were intensively questioned regarding any clinical presentation of respiratory symptoms and any chance of contact with patients with COVID-19. All ER patients underwent reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 by swabbing the nose and throat. All emergency ERCPs were suspended until the RT-PCR results were identified, which took at least 6 h in our hospital. If the RT-PCR-based SARS-CoV-2 test was confirmed as positive, ERCP was delayed until the seroconversion of RT-PCR, except in urgent cases. If the RT-PCR test was negative, the patient was taken to the endoscopy center on the second floor, and ERCP was performed as usual. However, when the RT-PCR was pending, in urgent cases, the patient was fully covered with a negative pressure tent and taken to the endoscopy center through a designated pathway. Throughout the ERCP procedures, all doctors and nurses wore personal protective equipment (PPE), including an N95 mask, waterproof gown, goggles, surgical gloves, waterproof shoe covers, and facial shields [14,15]. Before the COVID-19 outbreak, to the best of my knowledge, there were no universal guidelines regarding the regulation of PPE and the sequential process of ERCP. In the pre-pandemic era, we usually used a disposable surgical gown, surgical mask, goggles, and disposable gloves during the ERCP procedure. The fluoroscopic units, endoscopic units, and patient's bed were exhaustively cleaned and disinfected, and the ERCP room was ventilated for 30 min before and after the procedures.

Statistical analyses

The numbers, indications, and endoscopic findings of ERCP from February 18 to March 28, in 2018, 2019, and 2020 were compared and analyzed. Fisher's exact test and one-way analysis of variance were used to compare categorical and continuous variables, respectively. Variables are described as means \pm SD (ranges) and numbers (%). A *P* value less than 0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA).

RESULTS

From February 18 to March 28, 269 ERCP procedures were performed. Of these, 113 (42.0%) cases were considered an emergency, and the others ($n = 156$, 58.0%) were elective. The number of ERCP procedures performed in 2018 ($n = 74$) and 2019 ($n = 136$) decreased by 20.2% and 56.6%, respectively, compared with that of the same period in 2020 ($n = 59$), which showed a statistically significant difference ($P < 0.01$) (Figure 1).

Excluding 156 elective ERCPs, 113 emergency ERCPs were further analyzed to investigate clinical outcomes. Of the 113 cases, the observed numbers in 2018 ($n = 42$) and 2019 ($n = 55$) dramatically dropped by 61.9% and 70.9%, respectively, compared with that in 2020 ($n = 16$) (Figure 1). The mean ages were 73.0 ± 13.7 years (range, 33-91 years) and 72.1 ± 14.0 years (range, 41-99 years) in 2018 and 2019, respectively. In comparison, the mean age of 66.3 ± 13.4 years (range, 48-95 years) in 2020 was lower than that of the control groups, without statistical difference. In terms of sex distribution, there were 26 (61.9%) female individuals in 2018; however, the male individuals ($n = 12$, 75.0%) were predominant in 2020, with a statistical difference ($P < 0.05$) (Table 1).

Abdominal pain ($n = 86$, 76.1%) was the most common indication for emergency ERCP, followed by jaundice ($n = 14$, 12.4%) and fever ($n = 13$, 11.5%); however, no statistical difference was observed. The algorithm for all the ERCP procedures is shown in Figure 2. The distribution of endoscopic intervention was similar among the three groups (2018, 2019, and 2020). Endoscopic retrograde biliary drainage (ERBD) ($n = 42$, 37.2%) was the most commonly performed technique, followed by bile duct stone removal ($n = 41$, 36.3%), endoscopic sphincterotomy (EST) ($n = 22$, 19.5%) and endoscopic nasobiliary drainage (ENBD) ($n = 4$, 3.5%), showing no statistical difference. Of the 16 cases in 2020, stone removal was performed in five, ERBD in five, EST in five, and ENBD in one. Endoscopic diagnosis of the 113 cases demonstrated that bile duct stone removal was performed in 56 cases (49.6%), followed by probable spontaneous passage of stones ($n = 22$, 19.5%), pancreatobiliary malignancy ($n = 17$, 15.0%), and acute cholangitis due to stent occlusion ($n = 9$, 8.0%). Regardless of the time of the ERCP procedure, a similar pattern of endoscopic diagnosis was observed ($P > 0.05$). In terms of blood chemistry, such as hemoglobin, total bilirubin, alanine transaminase, aspartate transaminase, alkaline phosphatase, and gamma-glutamyl transpeptidase levels, no statistical difference was observed before and during the COVID-19 outbreak (Table 1).

Only one patient was RT-PCR negative before the ERCP procedure, and then ERCP was implemented with caution under the full PPE; however, he was later confirmed as SARS-CoV-2 positive after repeat RT-PCR test during the study period. Fortunately, no case of ERCP procedure-related SARS-CoV-2 infection in HCPs or to other patients was reported in our endoscopic center.

DISCUSSION

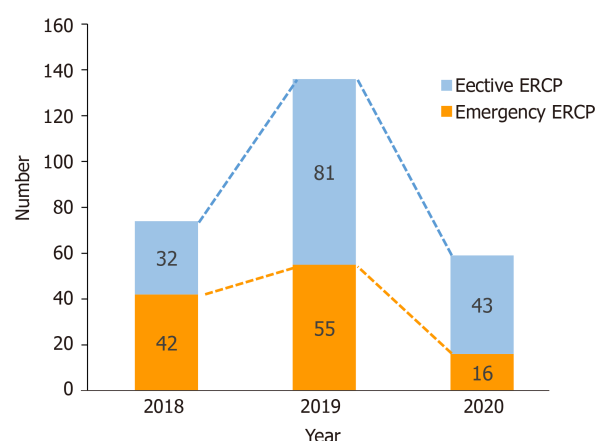
ERCP is a time-consuming and complicated; however, it is an essential technique for pancreatobiliary disease and is a common emergency procedure for common bile duct (CBD) stone removal or biliary decompression[12]. Delayed treatment may lead to the deterioration of cholangitis, organ failure, and septic conditions. With the rapid increase in COVID-19 cases in February 2020 in Daegu, the hardest-hit but later fully recovered city of South Korea, there were changes in the endoscopy section of a tertiary referral hospital. Since the first confirmed case of SARS-CoV-2 on February 18, 2020, SARS-CoV-2-positive cases were rapidly increased within the city. Due to the lack of experience and the highly contagious nature of the virus, all measures to stop the viral spread in and outside the hospital were prioritized. Initially, once the RT-PCR assay for SARS-CoV-2 was confirmed to be positive at the ER, the task force committee of the metropolitan city instructed the shutdown of the ER for 24 h as a preemptive measure, which was later modified. There are a few articles regarding the frameshift of endoscopic procedures, such as the reduction of the number of endoscopies following the lockdown order from the government[9,16,17]. However, little is known about the clinical impact of COVID-19 on ERCP procedures, despite the fact that many pancreatobiliary patients require urgent ERCP in the setting of COVID-19 pandemic.

Endoscopy can cause human-to-human viral transmission by producing massive aerosol droplets throughout the procedure, particularly during therapeutic interventions such as ERCP[12,18]. The ERCP providers should be aware that manipulation

Table 1 Comparison of the basic characteristics of emergency endoscopic retrograde cholangiopancreatography from February 18 to March 28 during 2020, before and during the Coronavirus Disease 2019 outbreak (*n* = 113)

Variable	Year			P value
	2018 (<i>n</i> = 42)	2019 (<i>n</i> = 55)	2020 (<i>n</i> = 16)	
Sex (M/F)	16/26 (38.1/61.9)	28/27 (50.9/49.1)	12/4 (75.0/25.0)	0.041
Age (yr)	73.0 ± 13.7 (33-91)	72.1 ± 14.0 (41-99)	66.3 ± 13.4 (48-95)	0.244
Hemoglobin (g/dL)	11.7 ± 1.8	13.7 ± 11.6	12.0 ± 2.8	0.487
Total bilirubin (mg/dL)	4.2 ± 4.4	5.7 ± 5.1	5.5 ± 7.4	0.388
AST (IU/L)	356.6 ± 543.4	290.8 ± 385.6	274.6 ± 336.8	0.722
ALT (IU/L)	253.9 ± 327.3	306.4 ± 406.7	234.7 ± 239.9	0.693
ALP (IU/L)	311.5 ± 286.5	378.2 ± 361.9	275.6 ± 196.0	0.408
GGT (IU/L)	328.9 ± 286.2	478.7 ± 476.6	464.1 ± 422.2	0.186

Values are presented as means ± SD (ranges) or numbers (%). ALT: Alanine transaminase; AST: Aspartate transaminase; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transpeptidase.

**Figure 1 Comparison of all endoscopic retrograde cholangiopancreatography performed from February 18 to March 28, before and during the COVID-19 outbreak (*n* = 269) (*P* < 0.005).** ERCP: endoscopic retrograde cholangiopancreatography.

of the scope can increase the risk of exposure to the virus-contaminated body fluids [16]. The presumed mechanism is as follows: First, the large-bore working channel can splash the body fluid during suction or irrigation. A tight suction cap can minimize fluid leakage through the working channel. Facial shields and PPEs are indispensable for preventing exposure to body fluids [12]. Second, repeated exchange of accessories through the endoscope can increase the risk of infection. The frequent exchange of therapeutic accessories (*e.g.*, baskets, papillotome, retrieval balloon, dilating balloon catheter, and others) increases the possibility of exposure to viral secretions. Minimal accessory manipulation can reduce the contact with the contaminated fluid. In case of difficulties, two sessions of procedures are recommended to shorten each procedural time, thereby lowering the risk of viral contamination. Lastly, endoscopy can form aerosols by inducing sneeze, coughing, or belching with or without sedation. Owing to the features of side-view images, blind insertion of the duodenoscope is highly likely to irritate the oropharyngeal mucosa, causing profuse salivary secretion. In the clinical setting, endotracheal intubation under general anesthesia can lower the aerosol-forming process during the procedure; however, all ERCP procedures in South Korea are carried out under midazolam-/propofol-based sedation, and not under general anesthesia [19,20]. Given that ERCP can be a nidus of nosocomial viral propagation, it is strongly recommended that ERCP providers wear PPE for safety during the COVID-19 outbreak [8,21,22].

European countries and the United States experienced a drastic reduction in the number of endoscopies and a change in the pattern of endoscopies after the lockdown

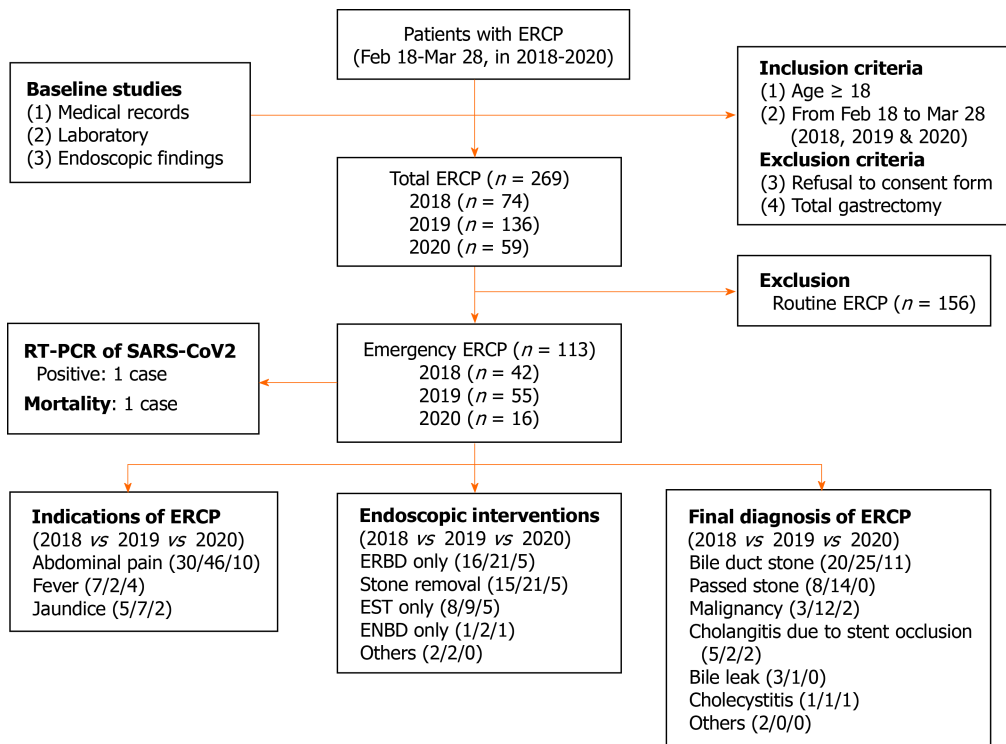


Figure 2 Flowchart of all patients who underwent endoscopic retrograde cholangiopancreatography from February 18 to March 28, before and during the COVID-19 outbreak. The values are presented as numbers. ERCP: endoscopic retrograde cholangiopancreatography; RT-PCR of SARS-CoV-2: reverse-transcription polymerase chain reaction of severe acute respiratory syndrome coronavirus-2; ERBD: endoscopic retrograde biliary drainage; EST: endoscopic sphincterotomy; ENBD: endoscopic nasobiliary drainage.

order[9,16]. We experienced a 20%-50% decrease in the number of ERCPs during the COVID-19 outbreak, compared with that in the equivalent period in 2018 and 2019, consistent with the report in Ireland[23]. How can we explain this decrease in the number of elective ERCP procedures? A few explanations can be provided for this phenomenon[17]. First, the main indications for elective ERCP were asymptomatic bile duct stones, interval ERBD change, ERBD removal, follow-up ERCP for remnant stones with inserted ERBD, or incidental jaundice due to potential pancreatobiliary malignancy. Most cases were canceled or postponed until the resolution of the viral upsurge, except malignancy-associated jaundice[12]. Given that East Asia, including South Korea, has a high prevalence of intra- or extrahepatic biliary cancer and, since the incidence of pancreatic cancer is steadily rising recently, the deferral of endoscopic intervention may cause a delay in the diagnosis or progression of the disease[16]. Unfortunately, follow-up data were not available in this study, and some might have been treated at other hospitals. Second, consultation ERCP cases from other departments, such as bile leaks, incidental CBD stones, postoperative bile duct stricture, or incidental obstructive jaundice, decreased. In addition, cancellation or postponement of major pancreatobiliary surgery, following the strict infection control policy of the hospital, might have contributed to the decrease in elective ERCP cases.

Meanwhile, emergency ERCPs dropped remarkably by more than 60% during the COVID-19 era, compared with that in the pre-COVID-19 era. A previous study demonstrated that the number of ERCPs fell by 36% in 2020, compared with that in 2019, which is similar to our study[23]. Unlike upper endoscopy and colonoscopy, pancreatobiliary disorders such as bile duct obstruction or associated cholangitis usually require urgent treatment. The decrease in the number of ERCP procedures performed during the COVID-19 outbreak was largely attributed to a reduction in emergency ERCP. The most common cause of ER visits was abdominal pain in all consecutive years. Interestingly, the number of abdominal pain episodes during the COVID-19 period dramatically decreased by approximately 70% compared with that in the pre-COVID-19 period, without statistical difference. There are several hypotheses for a notable reduction in the number of emergency ERCP procedures. First, a reduced referral from a medium-volume or primary care facility led to a decline in ER visitors[23]. These patients might have been managed by either a percutaneous approach or a conservative approach, without a referral. Second,

extremely elderly or physically weak patients were advised to stay at home and to minimize ER visits to a tertiary hospital, if possible, due to their vulnerability to infection. A previous study reported a fatality rate of up to 62% [23]. Based on our data, the mean age in 2020 was, to some extent, lower than that of the non-COVID-19 period, without statistical difference. This might be due to the elderly's refusal to visit the ER until obvious cholangitic symptoms developed. As mentioned in a previous study, the fear of leaving home and lockdown might have shunned the visit to the ER [23]. Third, a ban on social gatherings might have lowered alcohol-induced pancreatitis by abstinence of alcohol intake. Additionally, a lower chance of binge eating under home quarantine might have diminished gallstone-related complications such as acute cholecystitis, Mirizzi syndrome, secondly CBD stone, acute cholangitis, or biliary pancreatitis.

The endoscopic diagnosis was mostly consistent with the causes of emergency endoscopy in this study. Of the 16 cases in 2020, the most commonly performed endoscopic therapies were stone removal and stent placement, which showed a pattern similar to that in previous years. With the introduction of a simple and schematic algorithm from the ER door to the endoscopic center, no case of SARS-CoV-2 infection in other patients or medical personnel was reported in our center [21]. There was one case of mortality in a patient with severe biliary pancreatitis, in which an emergency ERCP was performed because of the impacted CBD stone. Despite aggressive treatment, however, he died due to multi-organ failure.

Our study has a few limitations. First, this was a single-center observational study with a limited number of patients during a short period. Large and long-term studies are required to determine changes in endoscopic activities. Second, follow-up data of elective ERCPs were lacking. There is a possibility that bile duct malignancy, such as hilar malignancy, might have affected the survival of elderly patients. Third, patients who visited the ER and underwent ERCP were labeled as emergency ERCP patients regardless of the situation; therefore, there is a possibility that non-emergency patients might have been included in this group, such as jaundiced patients without cholangitis or asymptomatic CBD stones, particularly in 2018 and 2019.

CONCLUSION

In conclusion, ERCP is a well-established and indispensable technique in the field of pancreatobiliary emergencies. The novel viral outbreak resulted in a significant reduction in the number of ERCP procedures performed, particularly emergency ERCPs, from February 18 to March 28, 2020. In practice, the ERCP procedure can function as a potential vector for viral transmission, which can be a threat to both HCPs and other patients. All emergency ERCP procedures were performed successfully and safely without causing infection in our endoscopy center. Nevertheless, a long-term follow-up is warranted to observe the clinical outcomes of ERCP procedures after the cessation of the COVID-19 outbreak.

ARTICLE HIGHLIGHTS

Research background

The coronavirus disease 2019 (COVID-19) outbreak has markedly influenced endoscopic patterns. Endoscopic retrograde cholangiopancreatography (ERCP) is an essential technique for pancreatobiliary disease but increases the risk of exposure to virus-containing body fluid; however, the impact of COVID-19 on ERCP is unknown.

Research motivation

Unlike upper endoscopy and colonoscopy, pancreatobiliary disorders such as bile duct obstruction or associated cholangitis usually require urgent treatment. However, endoscopy can cause human-to-human viral transmission by producing massive aerosol droplets throughout the procedure, particularly during therapeutic interventions such as ERCP. Due to the lack of experience and the highly contagious features of COVID-19, all measures to stop the viral spread in and outside the hospital were prioritized.

Research objectives

This study aimed to compare and to analyze the change in the number of ERCP procedures, causes, and clinical outcomes of emergency ERCP between pre-COVID-19 and during the COVID-19 outbreak in Daegu city, the worst-hit area in South Korea.

Research methods

This retrospective cohort study included patients aged ≥ 18 years who underwent ERCP between February 18 and March 28, 2020, at a tertiary hospital. Baseline demographics, causes of an ER visit, blood chemistry, ERCP indications, and endoscopic details relevant to ERCP were collected and compared with those from the same period in 2018 and 2019 as control groups.

Research results

The number of ERCP procedures in 2018 and 2019 decreased by 20.2% and 56.6%, respectively, compared with that in 2020 ($P < 0.01$); among the 113 emergency ERCPs, the observed numbers in 2018 ($n = 42$) and 2019 ($n = 55$) dramatically dropped by 61.9% and 70.9%, respectively, compared with that in 2020 ($n = 16$). No case of ERCP-related infection has been reported in medical providers or other patients.

Research conclusions

The COVID-19 outbreak significantly reduced the number of ERCPs; however, no difference was observed in the indications and endoscopic interventions before and during the COVID-19 outbreak.

Research perspectives

All emergency ERCP procedures were performed safely without causing any viral infection in our endoscopy center. However, a long-term follow-up is warranted to observe the clinical outcomes of ERCP procedures after the cessation of the COVID-19 outbreak.

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