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Collateral Effect of Coronavirus Disease 2019 Pandemic on Hospitalizations and Clinical Outcomes in Gastrointestinal and Liver Diseases: A Territory-wide Observational Study in Hong Kong

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As of July 22, 2020 there were more than 14.9 million cases and 616,000 deaths due to coronavirus disease 2019 (COVID-19) worldwide.[1] Medical resources were shifted to management of infected patients, and declines in hospitalizations for acute coronary syndrome and stroke were observed.[2,3] The world is now being exposed to a third wave of the pandemic, and the disruption to endoscopy service is considerable, leading to potential delays in the diagnosis of cancers and management of gastrointestinal (GI) bleeding.[4,5] We evaluated the collateral effects of COVID-19 on hospitalizations and clinical outcomes in patients with GI and liver diseases.

Methods

A territory-wide, retrospective cohort study was performed involving patient-based hospital admissions in Hong Kong from January 1, 2019 to May 31, 2020. Major digestive diseases including luminal GI cancers, pancreatic-hepatobiliary cancers, benign pancreaticobiliary disorders, diseases of the liver, noninfective enteritis and colitis, and nonvariceal and variceal upper GI bleeding (UGIB) according to their respective International Classification of Diseases, 10th revision, codes were included. Hospital admissions through the emergency department or those with a length of stay of more than 1 day were included. We defined "season-adjusted pre-COVID19 period" from the fourth week of January 2019 to the fourth week of May 2019 and the "COVID-19 period" from the fourth week of January 2020 to the fourth week of May 2020, during which admission data were captured.[6]

The primary endpoint was the total number of hospital admissions, related to the principal or top 5 diagnoses of major diseases. Secondary endpoints included in-hospital mortality within the same episode of hospitalization, admission to an intensive care unit, and need of operation or endoscopy (elective or emergency). See a more detailed explanation of study design in the Supplementary Methods.

Results

During the study period, 195,867 hospital admissions related to major digestive diseases were recorded in Hong Kong. The final analysis included 125,049 hospital admissions fulfilling inclusion and exclusion criteria.

Hospitalization and Disease Spectrum

After the first local case of COVID-19 emerged in January 2020, there was a significant decline in hospital admissions. This observation was consistent in the following weeks, until a gradual return to baseline in late March, corresponding to a relatively flat epidemic curve.[6] There was another drop in April after a sudden surge of patients were diagnosed with COVID-19. An interrupted time series analysis was performed for the daily number of hospital admissions. The change in intercept was −178.27 (95% confidence interval, −263.70 to −92.85; $P < .001$), indicating an abrupt decline, whereas the slope was +2.27 (95% confidence interval, +0.86 to +3.68; $P = .002$), which reflected a trend of slow return to baseline (Figure 1).

Considering seasonal variation, the season-adjusted pre-COVID19 period and COVID-19 period were compared. An overall 17% reduction in median number of daily hospital admissions was observed ($P < .001$). It decreased by 19.7% ($P = .005$) for luminal GI cancers, 7.8% ($P = .136$) for pancreatic-hepatobiliary cancers, 8.8% ($P = .002$) for benign pancreaticobiliary disorders, 16.4% ($P < .001$) for liver

Abbreviations used in this paper: **COVID-19, coronavirus disease 2019; GI, gastrointestinal; UGIB, upper gastrointestinal bleeding.**

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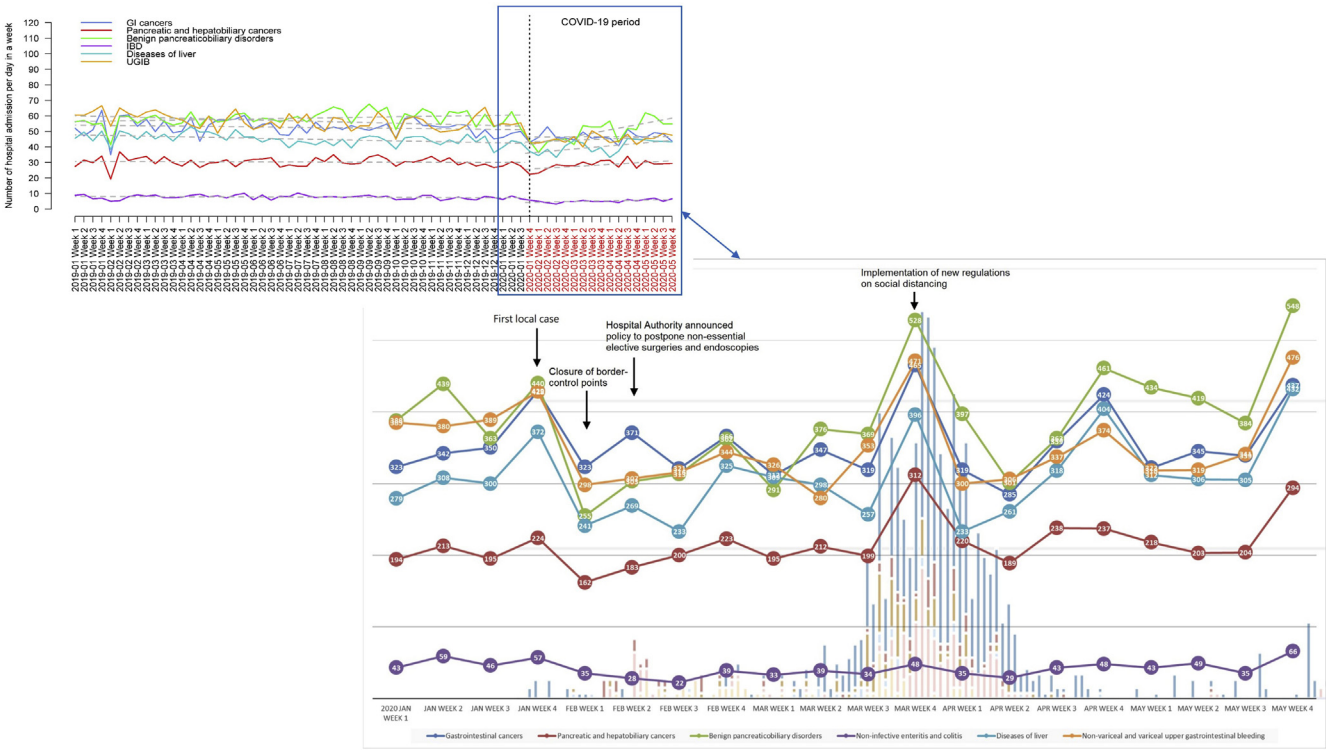

Figure 1. Interrupted time series analysis on the average number of hospital admission per day in a week before and during the COVID-19 outbreak in Hong Kong and weekly number of hospital admissions for digestive diseases in 2020. (Background: epidemic curve of COVID-19 in Hong Kong corresponding to time.)

diseases, 37.5% ($P < .001$) for inflammatory bowel disease, and 23.9% ($P < .001$) for UGIB (Supplementary Table 1).

Mortality and Intensive Care Unit Admissions

Despite the reduction in hospital admissions, we did not observe significant differences in the in-hospital mortality rate (11.2% vs 11.7%, $P = .063$) or the intensive care unit admission rate (5.3% vs 5.1%, $P = .218$) (Supplementary Table 2).

Surgery and Endoscopy

The total number of surgeries decreased from 5844 to 4704. The magnitude was, however, similar between 2 periods, with 75.5% and 74.8% of major or ultr-major surgeries, respectively.

A significantly higher percentage of patients underwent emergency operations during hospitalizations in the COVID-19 period (6.7% vs 8.0%, $P < .001$). The percentage of elective surgery was significantly lower (10.8% vs 8.7%, $P < .001$). Notably, no significant difference was observed in luminal GI cancers (elective, 19.5% vs 19.0%, respectively [$P = .457$]; emergency, 7.1% vs 7.8% [$P = .124$]) or pancreatic-hepatobiliary cancers (elective, 10.3% vs 9.4%, respectively [$P = .208$]; emergency, 2.0% vs 2.5% [$P = .176$]) (Supplementary Table 2).

The total number of endoscopies decreased from 11,604 to 9477, but the number of emergency endoscopies increased from 4675 to 5136. The percentages of patients receiving emergency endoscopies during the COVID-19 period increased from 14.0% to 18.2% ($P < .001$), particularly for UGIB (30.0% vs 38.9%, $P < .001$), benign pancreaticobiliary disorders (17.5% vs 24.4%, $P < .001$), luminal GI cancers (6.6% vs 9.4%, $P < .001$), and pancreatic-hepatobiliary cancers (7.0% vs 9.7%, $P < .001$) (Supplementary Table 2).

Discussion

This territory-wide, population-based study involving more than 195,000 patient-based hospital admissions over 17 months provided real-life data on collateral effects of the COVID-19 pandemic in digestive diseases. We found a significant reduction of 17% in hospitalizations for digestive diseases, which echoes previous studies showing a decline in hospitalizations for common cardiovascular and GI emergencies.[2,3,5] However, no significant difference was demonstrated in clinical outcomes such as mortality and intensive care unit admission rates. One possible explanation could be the relatively flat local epidemic curve, allowing the health care system to cope with the burden. This effort is important to allow management of non–COVID-19 patients. We could also argue that certain hospitalizations are unnecessary. A more selective admission policy may be possible. Clinical models identifying low-risk patients who can be safely discharged from the emergency department for outpatient management should be developed.

During the early phase of the pandemic, Hong Kong adopted a policy to postpone nonessential elective services. Only emergency surgeries or endoscopies were performed for life-threatening or time-sensitive cancer-related indications. This practice was in line with international guidelines.[7,8] Consistently, we demonstrated an overall reduction in elective surgeries except for cancers. We also observed more patients undergoing emergency endoscopies. This finding could be related to the abrupt reduction of elective services. It may also represent sicker patients with UGIB and biliary sepsis who require more urgent life-saving interventions.

In conclusion, hospitalizations related to digestive diseases decreased drastically during the pandemic in Hong Kong, without excessive mortality observed. More patients underwent emergency surgeries and endoscopies during hospitalization. Our findings only reflect immediate outcomes and may not be generalizable to other countries with different pandemic situations. Future studies are warranted to review the long-term effects of COVID-19 and how to minimize collateral, noninfectious adverse health care outcomes from the pandemic.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2020.07.042.

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Conflicts of interest
The authors disclose no conflicts.

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Supplementary Methods

Study Design and Data Source

We performed a territory-wide, retrospective cohort study involving patients admitted to all public hospitals in Hong Kong from January 1, 2019 to May 31, 2020. Clinical parameters were retrieved through the Clinical Data Analysis and Reporting System (CDARS) of the Hospital Authority, Hong Kong. CDARS is an electronic health care database that records patient demographics, death, diagnoses, procedures, investigation results, and drug prescriptions from all public hospitals in Hong Kong, which represents approximately 90% of the entire 7.4-million population in Hong Kong. All patients are deidentified in CDARS to ensure confidentiality. A number of territory-wide studies were conducted by CDARS previously with the validity of data verified.

Clinical parameters, including demographic data, details of hospitalization (including admission date, emergency department attendance, length of stay, episode death, admission to the intensive care unit, emergency hospital readmission within 28 days), principal and relevant diagnoses, relevant procedures and endoscopies, laboratory tests, blood product use, and concomitant drugs, were retrieved and analyzed. The study was approved by the Joint Chinese University of Hong Kong–New Territories East Cluster Clinical Research Ethics Committee (CREC reference no. 2020.276).

Subjects

We searched the records of all patients who were admitted to public hospitals under the Hospital Authority in Hong Kong during the study period, with the principal or top 5 diagnosis codes of the index hospital admission included based on the International Classification of Diseases, 10th Revision, Clinical Modification.

The major digestive diseases included in this study were luminal GI cancers (C15 cancer of esophagus, C16 cancer of stomach, C17 cancer of small intestine, C18 cancer of colon, C19 cancer of rectosigmoid junction, C20 cancer of rectum, C21 cancer of anus and anal canal), pancreatic and hepatobiliary cancers (C22 cancer of liver/intrahepatic ducts, C23 cancer of gallbladder, C24 cancer of biliary tract, other/not otherwise specified, C25 cancer of pancreas), benign pancreaticobiliary disorders (K80 gallstones, K81 cholecystitis, K82 other diseases of gallbladder, K83 other diseases of biliary tract, K85 acute pancreatitis, K86 other diseases of pancreas, K87 gallbladder/biliary/pancreatic disorder, other diseases), diseases of the liver (K70 alcoholic liver disease, K71 toxic liver disease, K72 hepatic failure, K73 chronic hepatitis, K74 fibrosis and cirrhosis of liver, K75 other inflammatory liver diseases, K76 other diseases of liver, K77 liver disorders in other diseases), noninfective enteritis and colitis (K50 Crohn's disease, K51 ulcerative colitis, K52 other noninfective gastroesophageal/colitis), and nonvariceal and variceal UGIB (K25 gastric ulcer, K26 duodenal ulcer, K27 peptic ulcer, site unspecified, K28 gastrojejunal ulcer, K92.0 hematemesis, K92.1 melena, K92.2 GI bleeding, unspecified, I85 esophageal varices, I86.4 gastric varices, I98.2 esophageal varices in other diseases, I98.3 esophageal varices with bleeding in diseases). These were the common and potentially life-threatening diseases, including different spectrum of benign (cholangitis, pancreatitis, GI bleeding, inflammatory bowel disease, liver failure, and cirrhosis) and malignant conditions (luminal, pancreaticobiliary and hepatic cancers), which represented most hospitalizations in daily clinical practice.

We further excluded patient-based hospital admissions without emergency department attendance and a length of hospital stay $\geq$ 1 day, because these entries largely represented day ward admissions related to blood product transfusion, parental drug/chemotherapy administration, or simple diagnostic procedures. As a result, we included patients admitted to hospitals during January 1, 2019 to May 31, 2020 either with emergency department attendance or with length of stay $>$ 1 day related to the above principal or top 5 diagnoses of major GI diseases for subsequent analysis.

Endpoints

The primary endpoint was total number of index hospital admissions during the study period, related to the principal or top 5 diagnoses of major digestive diseases mentioned above. The secondary endpoints included in-hospital mortality within the same episode of hospitalization, admission to the intensive care unit, and need of operation or endoscopy (elective or emergency).

Time of Events and Recruitment Periods

In Hong Kong, there were 2020 confirmed cases of COVID-19 and 14 deaths as of July 22, 2020. The first local case was diagnosed on January 22, 2020 (ie, January 2020 week 4). On January 24, the "emergency response level" of the preparedness and response plan against infectious disease outbreak was activated, followed by closure of border-control points. In early February 2020, the Hospital Authority announced the policy to postpone nonessential elective surgeries and endoscopies. Emergency services and essential surgeries for cancer treatment were maintained. In this study, we defined the pre–COVID-19 period to be January 2019 week 1 to January 2020 week 3 and the COVID-19 period to be January 2020 week 4 to May 2020 week 4.

Statistical Analysis

Data were analyzed using IBM Corporation SPSS version 25.0 (IBM SPSS, Inc, Chicago, IL) and R software (version 4.0.0; R Foundation for Statistical Computing, Vienna, Austria). Continuous variables are expressed in mean $\pm$ standard deviation or median (interquartile range) as appropriate, whereas categorical variables are presented as frequency (percentage).

Wilcoxon signed-rank test was used to compare the number of hospital admissions among hospitalized patients from January 2019 week 4 to May 2019 week 4 (season-adjusted pre–COVID-19 period) versus January 2020 week 4 to May 2020 week 4 (COVID-19 period). The Mann-Whitney test was used to compare the number of hospital admission, and the χ^2 test was used to compare mortality rate, intensive care unit use, and rate of elective and emergency operations. The possible correlation between the 2 time periods was not accounted for by Mann-Whitney and χ^2 tests in the comparison.

An interrupted time series analysis by piecewise linear regression was performed to examine the trend in hospitalization before and after the COVID-19 outbreak in Hong Kong. Autocorrelation of the residuals of the fitted models was checked by autocorrelation functions, partial autocorrelation functions, and Durbin-Watson tests. For detected autocorrelation, regression standard errors were adjusted for autocorrelation at the identified order using Newey-West covariance matrix estimators. All statistical tests were 2-sided. Statistical significance was taken as $P < .05$.

Supplementary Table 1. Hospital Admissions per Day in a Week in Pre–COVID-19 and COVID-19 Periods and Interrupted Time Series Analysis by Piecewise Linear Regression on Trend of Average Number of Hospital Admissions per Day in a Week Before and After COVID-19 Outbreak

	Entire Pre–COVID-19 Period[a]	Season-Adjusted Pre–COVID-19 Period[a]	COVID-19 Period[a]	Percentage of Change Between Season-Adjusted Pre–COVID-19 Period and COVID-19 Period[b]	*P* Value[b]	Change in Intercept After vs Before Outbreak[c,d]	*P* Value[d]	Slope in COVID-19 Period[c,e]	*P* Value[e]
GI cancers	53 (50–56)	57 (50–60)	46 (45–49)	–19.7	.005	–8.80 (–36.98 to 19.39)	.535	0.02 (–0.44 to 0.49)	.927
Pancreatic and hepatobiliary cancers	30 (28–32)	31 (28–33)	29 (27–31)	–7.8	.136	–22.32 (–39.42 to –5.23)	.011	0.34 (0.05–0.62)	.021
Benign pancreaticobiliary disorders	59 (55–62)	57 (55–60)	52 (44–55)	–8.8	.002	–70.85 (–97.99 to –43.72)	<.001	1.07 (0.63–1.52)	<.001
Diseases of the liver	45 (43–48)	49 (45–50)	41 (37–44)	–16.4	<.001	–38.18 (–57.95 to –18.41)	<.001	0.51 (0.18–0.83)	.003
Noninfective enteritis and colitis (inflammatory bowel disease)	8 (7–9)	8 (7–9)	5 (5–6)	–37.5	<.001	–9.39 (–16.43 to –2.34)	.010	0.11 (–0.01 to 0.22)	.071
Nonvariceal and variceal UGIB	57 (53–61)	59 (55–63)	45 (43–47)	–23.9	<.001	–28.73 (–54.03 to –3.44)	.027	0.23 (–0.19 to 0.64)	.286
All digestive diseases	252 (243–261)	261 (248–270)	216 (204–228)	–17.0	<.001	–178.27 (–263.70 to –92.85)	<.001	2.27 (0.86–3.68)	.002

NOTE. The entire pre–COVID-19 period was from January 2019 week 1 to January 2020 week 3. The season-adjusted pre–COVID-19 period was from January 2019 week 4 to May 2019 week 4. The COVID-19 period was from January 2020 week 4 to May 2020 week 4.

[a]Values are median (interquartile range).

[b]Median number of hospital admissions per day of a week in the same period of the year in pre–COVID-19 and COVID-19 periods were compared by the Wilcoxon signed-rank test.

[c]Values in parentheses are 95% confidence intervals.

[d]Change in intercept estimated the immediate change in number of hospital admissions per day in a week right after the COVID-19 outbreak (ie, January 2020 week 4).

[e]The slope estimated the trend of average number of hospital admissions per day in a week (ie, the increase, or decrease if negative trend) of the number of hospital admissions per day in a week during the study period.

Supplementary Table 2. Rates of Mortality, ICU Admission, Elective and Emergency Surgery, and Elective and Emergency Endoscopy in Hospitalized Patients During Pre–COVID-19 and COVID-19 Periods

	Season-Adjusted Pre–COVID-19 Period (January 2019 Week 4 to May 2019 Week 4)						COVID-19 Period (January 2020 Week 4 to May 2020 Week 4)						*P* Value[a]					
			Surgery		Endoscopy				Surgery		Endoscopy				Surgery		Endoscopy	
	Mortality	ICU	Elective	Emergency	Elective	Emergency	Mortality	ICU	Elective	Emergency	Elective	Emergency	Mortality	ICU	Elective	Emergency	Elective	Emergency
GI cancers	15.6 (1110/7109)	5.0 (356/7109)	19.5 (1385/7109)	7.1 (504/7109)	13.7 (977/7109)	6.6 (468/7109)	16.5 (1006/6083)	5.1 (311/6083)	19.0 (1153/6083)	7.8 (475/6083)	10.3 (629/6083)	9.4 (569/6083)	.156	.815	.457	.124	<.001	<.001
Pancreatic and hepatobiliary cancers	19.2 (760/3957)	3.9 (155/3957)	10.3 (408/3957)	2.0 (78/3957)	10.1 (398/3957)	7.0 (278/3957)	19.2 (714/3713)	4.3 (160/3713)	9.4 (350/3713)	2.5 (91/3713)	8.0 (297/3713)	9.7 (362/3713)	1.000	.420	0208	.176	.002	<.001
Benign pancreaticobiliary disorders	5.7 (420/7409)	4.8 (358/7409)	13.8 (1026/7409)	9.3 (689/7409)	28.5 (2109/7409)	17.5 (1296/7409)	5.8 (381/6544)	5.0 (325/6544)	6.9 (454/6544)	11.5 (754/6544)	22.3 (1462/6544)	24.4 (1600/6544)	.725	.743	<.001	<.001	<.001	<.001
Diseases of the liver	11.3 (699/6195)	5.8 (362/6195)	5.9 (368/6195)	5.2 (325/6195)	7.6 (473/6195)	4.8 (297/6195)	11.5 (607/5271)	5.3 (278/5271)	4.1 (217/5271)	6.5 (344/5271)	7.0 (371/5271)	5.4 (284/5271)	.718	.200	<.001	.004	.237	.161
Noninfective enteritis and colitis (inflammatory bowel disease)	1.8 (19/1035)	1.8 (19/1035)	6.6 (68/1035)	1.9 (20/1035)	11.4 (118/1035)	3.1 (32/1035)	0.4 (3/683)	0.9 (6/683)	3.7 (25/683)	3.8 (26/683)	6.4 (44/683)	3.8 (26/683)	.021	.157	.012	.028	<.001	.505
Nonvariceal and variceal UGIB	9.7 (746/7678)	6.9 (528/7678)	4.7 (362/7678)	8.0 (611/7678)	37.2 (2854/7678)	30.0 (2304/7678)	10.1 (595/5894)	6.1 (358/5894)	4.2 (248/5894)	9.6 (567/5894)	26.1 (1538/5894)	38.9 (2295/5894)	.481	.066	.170	<.001	<.001	<.001
All digestive diseases	11.2 (3754/33,383)	5.3 (1778/33,383)	10.8 (3617/33,383)	6.7 (2227/33,383)	20.8 (6929/33,383)	14.0 (4675/33,383)	11.7 (3306/28,188)	5.1 (1438/28,188)	8.7 (2447/28,188)	8.0 (2257/28,188)	15.4 (4341/28,188)	18.2 (5136/28,188)	.063	.218	<.001	<.001	<.001	<.001

NOTE. Values are % (n/N). ICU, intensive care unit.

[a]The proportion of mortality, ICU admission, elective and emergency surgery, and elective and emergency endoscopy between the season-adjusted pre–COVID-19 period and the COVID-19 period were compared by the χ^2 test. The possible correlation between the 2 time periods was not accounted for in the comparison.