

Trends in upper gastrointestinal bleeding during the COVID-19 pandemic

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The COVID-19 pandemic has significantly impacted the entire world, including the United States and specifically its healthcare system. Based on recommendations from all major Gastrointestinal Societies [1], we postponed all non-urgent procedures at our institution with effect from March 16th, 2020. After postponing non-emergent procedures, we aimed to evaluate the trends of upper gastrointestinal (GI) bleeding and esophagogastroduodenoscopy (EGD) performed during the COVID-19 pandemic. We conducted a retrospective review of all patients undergoing EGDs at our institution during the study period (March 16 to April 15, 2020). In addition, we collected similar data from the preceding 2 months (January 1 to February 29, 2020) and the same time period from the preceding year (March 16 to April 15, 2019) for comparison, to account for any seasonal variation.

Prior to COVID-19, we performed an average of 398 ± 38.3 EGDs per month, of which 23.5% (93.67 ± 13.58) were performed on an inpatient basis. With an overall reduction in inpatient procedures of about 49.82%, the proportion of patients undergoing inpatient EGD for GI bleeding was comparatively higher (78.7% vs. 65.1%; $P=0.0925$), as well as the

proportion of EGDs for GI bleeding performed in the intensive care unit (ICU) (51.4% vs. 33.3%; $P=0.0415$) (Table 1). There was no change in the proportion of patients with GI bleeding requiring endoscopic intervention during this time period (32.4% vs. 32.2%; $P=1$). Despite a shift in the proportion of patients, there was no trend noted in the absolute number of inpatients with hemodynamically unstable GI bleeding, EGDs performed in the ICU or the number of inpatients undergoing EGD for variceal bleeding (Table 1).

When preparing for the COVID-19 pandemic, we expected the same baseline prevalence of emergent conditions, including acute exacerbations of chronic disease, acute infections, GI emergencies, cerebrovascular and coronary events, with the addition of the patients presenting with COVID-19. This was however refuted by studies on other acute emergencies such as myocardial infarction [2,3].

However, we found no change in the absolute number of patients with hemodynamically unstable GI bleeding, the number of EGDs performed in the ICU or the number of EGDs performed for variceal bleeding. This may in part be attributed to the more vivid presentation of overt GI bleeding, making it hard to ignore. There was, however, a significant reduction in the number of EGDs done on an inpatient basis, indicating fewer overall inpatient admissions and more stringent triage criteria for endoscopy during this COVID-19 study period. The increased proportions can be explained by a reduction in the number of non-urgent procedures.

It is imperative for gastroenterologists to be aware that GI symptoms were noted to be among the repertoire of COVID-19, especially in patients with severe disease and in the later stages of the pandemic. Further data suggest that GI bleeding was present in about 4-13.7% patients with COVID-19 [4]. Based on our data, and given that our region still has not reached

Table 1 EGD volume and indications during the study period compared to prior months

Characteristics	1/1/2020-1/31/2020	2/1/2020-2/29/2020	3/16/2020-4/15/2020	3/16/2019-4/15/2019
Total EGD volume	424	354	140	416
Inpatient	108	81	47	92
Outpatient	316	273	93	324
Characteristics of inpatient EGDs				
Age	54.6 \pm 17.6	53.7 \pm 15	53.8 \pm 15.8	57.8 \pm 14.8
Sex (female %)	42.6	42	44.7	41.3
Indications				
Non-bleeding	33	27	10	38
Bleeding	75	54	37	54
HD unstable	17	14	11	28
Variceal	13	11	9	7
Non-variceal	62	43	28	47
Location				
Endoscopy unit	83	68	28	69
ICU, reason for ICU admission	25	13	19	23
GI bleed	18	8	13	18
Variceal GIB	6	3	6	2
Non-GIB-related admission	7	5	6	5
Endoscopic therapy for GIB	20	16	12	23

EGD, esophagogastroduodenoscopy; HD, hemodynamically; ICU, intensive care unit; GI, gastrointestinal; GIB, gastrointestinal bleeding

its expected peak of COVID-19, we expect to see an increase in the number of patients with hemodynamically unstable bleeding with the surge of COVID-19.

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Meta-analysis associates proton pump inhibitor use with higher pneumonia risk in cirrhotic patients: mining for “diamonds” in the coal

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In a recently published meta-analysis, the authors reported a significantly higher pneumonia risk among cirrhotic patients exposed to proton pump inhibitors (PPIs) [1]. A second read,

however, raises concerns *calling* for cautious interpretation of the results.

Defining a clinically well-focused and scientifically relevant question, together with the application of strict inclusion/exclusion criteria, is of paramount importance when pursuing high-quality meta-analyses [2]. In this case, the authors evaluated observational studies of different designs, definitions and populations; none of those studies was initially conducted to explore the primary outcome of the meta-analysis. Trying to mathematically harmonize data from irrelevant studies increases the risk of heterogeneity and introduces bias. Moreover, one would expect an adjustment for major cofounders, such as the severity of the underlying liver disease, the dose and duration of PPI administration, and the presence or not of significant comorbidities. However, such an adjustment would be the interest of a meta-regression analysis that is difficult to perform when putting together observational studies. In our opinion, performing a systematic review without a meta-analysis would be more reasonable, since the retrieved data did not fulfill the necessary criteria to calculate a summarized measure effect [3]. Besides, heterogeneity is an issue that must always be anticipated before conducting any analysis. Numerical estimation of heterogeneity may be statistically possible but remains imperfect, since it depends on several parameters [4]. Even if statistical tests fail to demonstrate significant heterogeneity, the quality of the findings may still be undermined, and the authors should *a priori* present a rigorous sensitivity analysis to investigate it [3].

Significant publication bias was also evident in this study. Publication bias is one of the most powerful sources of bias, appearing when a considerable amount of data has been missed or overlooked [5]. Performing a broad and expert-assisted search across many databases (including also the so-called “gray zone”) is considered mandatory to prevent the omission of references and minimize its possibility. Arguably, the consequences of publication bias have been studied in relation to meta-analyses of randomized controlled trials, while its effect when observational studies are included is less clear [6]. Still, it could be even more important, because the incidence of adverse events may be estimated erroneously, leading to imprecise associations between clinical variables [7]. Instead of simply listing this as a study limitation, the authors should have tried to deal with it effectively, given that this may impact the effect sizes.

Lastly, the authors report as statistically significant the finding that PPI use is associated with greater pneumonia risk (risk ratio 1.36, 95% confidence interval 1.00-1.85). However, as witnessed both by the result itself (P=0.05) and by the corresponding forest plot, where the diamond shape touches the line of no effect, this is incorrect. There is a trend towards a link between PPI use and pneumonia development, but it fails to reach significance. This gives a totally different perspective, raising at the same time concerns about the *results'* credibility, magnitude and precision. Whenever a mathematical combination of extracted data is sufficiently justified, implementation of sound statistical methodology, according to established guidance [3], is imperative.