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LETTER TO THE EDITOR

Anticoagulation does not increase risk of mortality or ICU admission in hospitalized COVID-19 patients with gastrointestinal bleeding: Results from a New York health system

KEYWORDS
COVID-19;
Gastrointestinal bleeding;
Anticoagulation

Introduction

The novel coronavirus disease 2019 (COVID-19) has spread rapidly around the globe, leading to numerous hospitalizations and deaths worldwide. Although initially described as a respiratory disease, subsequent studies have demonstrated its impact on other organ systems including the gastrointestinal tract [1]. Gastrointestinal bleeding (GIB) has been reported in 4—13.7% of patients [2].

Furthermore, COVID-19 has been found to promote a prothrombotic state, resulting in guidelines recommending anticoagulation (AC) for these patients to reduce the risk of thromboembolic events, including pulmonary embolism, myocardial infarction or cerebrovascular accident [3,4]. These findings and practices led to the implementation of a system-wide AC protocol within our hospital system. AC is a well-established risk for GIB [5].

This study aims to assess the impact of AC for COVID-19 on GIB by comparing patient characteristics and outcomes before and after the implementation of a system-wide AC protocol in a health care system at the pandemic epicenter.

Methods

All patients with a positive SARS-CoV2 test admitted to the Mount Sinai Health System between February 29th and May 15th, 2020 and International Classification of Diseases (ICD-10) code for anemia or GIB were reviewed. Patients were excluded if they did not have overt GIB (hematemesis, melena or hematochezia). Charts were reviewed for demographic information, length of stay (LOS), ICU admission, laboratory test results, medications, COVID-19 severity and GIB management. April 10, 2020 was identified as the date when a system-wide AC protocol was initiated, wherein COVID-19 patients who met certain clinical criteria were recommended to start AC on admission and continue for two weeks after discharge. Patients were included in the pre and post AC cohorts by date of hospital discharge.

Results

There were 146 patients admitted with a positive SARS-CoV2 test and GIB during admission (Table 1). 38 (26.0%) were discharged prior to AC protocol initiation. Patient age, sex, race and body mass index (BMI) were not significantly different between the two groups. The mean BMI was 28.5 ± 6.9, and 63% were never smokers. The most common comorbidities were hypertension (62%), diabetes mellitus (35.6%), and chronic kidney disease (30.1%). There were no significant differences in comorbidities between the two groups. 22.6% of patients were on AC prior to admission. There were no differences between the two groups in terms of prehospitalization AC, antiplatelet, and NSAID use. 80 patients (54.8%) had GIB on admission whereas the remainder had delayed GIB during the course of their hospitalization. This was not different between the two time periods (63.2% pre AC vs. 51.8% post AC protocol, $p = 0.23$).

Next we evaluated outcomes of these patients during hospitalization. Almost half of patients had severe COVID-19, defined as high oxygen requirement, need for vasopressors, or end organ damage (42.1% pre AC and 54.6% post AC protocol, $p = 0.18$). After initiation of the AC protocol, significantly more patients were treated with AC (48.2% post AC vs 29.0% pre AC protocol, $p < 0.01$). More patients were treated with steroids as inpatients (18.4% pre AC vs. 38.9% post AC protocol, $p < 0.05$). There was no difference in ICU admission rates (44.7% pre AC vs 44.4% post AC, $p = 0.98$), ICU LOS (6.92 ± 10.8 days vs 7.30 ± 12.3 days, $p = 0.87$), or mortality (36.2% pre AC vs 35.2% post AC, $p = 0.85$). Hospital

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Table 1 Demographic and Clinical Characteristics and Outcomes of Patients Pre And Post Initiation of a System-Wide Anticoagulation Protocol.

	Total		Feb 29 - April 9[a]		April 10 - May 15		
	n	%	n	%	n	%	p value
Total	146		38	26.0	108	74.0	
Age (mean, SD)	67.4	15.2	63.6	17.8	68.8	14.0	0.06
Sex							0.91
Male	78	53.4	20	52.6	58	53.7	
Race							
White	37	25.3	11	29.0	26	24.1	0.55
Black	25	17.1	3	7.9	22	20.4	0.08
Other	84	57.5	24	63.2	60	55.6	0.41
BMI (mean, SD)	28.5	6.9	29.1	5.9	28.3	7.2	0.17
Smoking Status							0.42
Never	92	63.0	26	68.4	66	61.1	
Initial GI symptoms							
Nausea	41	28.1	16	42.1	25	23.2	**0.03**
Vomiting	31	21.2	14	36.8	17	15.7	**<0.01**
Diarrhea	44	30.1	11	29.0	33	30.6	0.85
GIB on admission	80	54.8	24	63.2	56	51.9	0.23
COVID-19 status	146	100	38	100.0	108	100.0	0.18
Mild/Moderate	71	48.6	22	57.9	49	45.4	
Severe/Severe with EOD	75	51.4	16	42.1	59	54.6	
Inpatient Medications							
Pre GIB inpatient AC	63	43.2	11	29.0	52	48.2	**<0.05**
Pre GIB inpatient steroids	49	33.6	7	18.4	42	38.9	**<0.05**
Pre GIB inpatient PPI	93	63.7	27	71.1	66	61.1	0.27
Hydroxychloroquine	86	58.9	22	57.9	64	59.3	0.88
Azithromycin	85	58.2	18	47.4	67	62.0	0.11
Outcomes							
ARDS	28	19.2	3	7.9	25	23.2	**<0.05**
Acute VTE	3	2.1	0	0.0	3	2.8	0.30
AKI	64	43.8	12	31.6	52	48.2	0.07
GIB hospital day number (mean)	7.34	13.7	7.55	13.8	7.26	13.7	0.91
Hospital LOS (mean)	12.7	12.0	6.79	6.3	18.1	16.4	**<0.01**
ICU admission	65	44.5	17	44.7	48	44.4	0.98
ICU LOS (mean)	7.2	11.9	6.92	10.8	7.30	12.3	0.87
Expired	52	35.6	14	36.8	38	35.2	0.85
Treatment							
Endoscopy	17	11.6	4	10.5	13	12.0	0.80
Interventional Radiology	3	2.1	1	2.6	2	1.9	0.77
Surgery	1	0.6	0	0.0	1	0.9	0.40
Medical treatment only	125	85.6	33	86.8	92	85.2	0.80
Transfusions	101	69.2	25	65.8	76	70.4	0.60
Number of PRBC (mean)	2.86	3.5	3.03	4.0	2.81	3.3	0.74
Reversal Agent	17	11.6	3	7.9	14	13.0	0.40

SD: Standard deviation.
Reversal agent refers to medication used to reverse anticoagulation administered or lab abnormalities with regards to coagulation. EOD: end organ damage. ARDS: acute respiratory distress syndrome. GIB: gastrointestinal bleeding. AC: anticoagulation. PPI: proton pump inhibitor. Hgb: hemoglobin. Hct: hematocrit. CRP: C-reactive protein. VTE: venous thromboembolism. LOS: length of stay. ICU: intensive care unit. PRBC: packed red blood cells.
[a] Anticoagulation protocol implemented April 10th.

LOS was longer in the post AC protocol group (18.1 ± 16.4 days vs 6.79 ± 6.3 days, $p < 0.01$).

Seventeen patients underwent 26 endoscopic exams and one video capsule endoscopy (Supplemental Table 1). Among these patients, only 6 (4.1%) required endoscopic intervention with hemostatic clips or argon plasma coagulation. Two were on anticoagulation at time of endoscopy.

To further evaluate differences between the two groups, we performed Cox proportional hazard ratios (HR) to evaluate the risk of death after controlling for other factors. Discharge after the AC protocol was initiated was protec-

tive against mortality (HR 0.36, 95% confidence interval 0.15—0.86, Supplemental Table 2). Age was associated with increased risk of death (HR 2.37, 95% CI 1.38—5.17).

Discussion

To our knowledge, this is the first study comparing outcomes of COVID-19 patients and GIB before and after the initiation of a system-wide AC protocol. Initiation of this protocol was not associated with increased mortality or ICU admission among hospitalized patients with GIB. However, hospital LOS was longer for those in the post AC protocol group. Although endoscopy is usually standard of care for hospitalized patients with GIB, it was frequently deferred in endoscopy suites internationally [6,7]. Most patients were treated medically with PPI therapy. Among the small number of patients (n = 17) who did undergo endoscopy, few required therapeutic intervention.

The mortality rate in our cohort was high (35.6%). On multivariable analysis controlling for other factors, age was the only independent risk factor associated with mortality, consistent with other studies of COVID-19 hospitalized patients [8]. Interestingly, discharge after initiation of the AC protocol was protective against mortality in our study, consistent with previous studies [9]. This finding may be limited by unobserved confounding factors, including improved knowledge in caring for COVID-19 patients later in the pandemic.

Our study has multiple strengths. We report the clinical characteristics of a diverse patient population in a large NYC health system. The initiation of a system-wide AC protocol in the midst of the NYC COVID-19 pandemic allows us to directly compare two otherwise similar cohorts. Another strength of our study is that we only included patients with overt GIB.

Limitations include that this was a retrospective, single hospital system study, where practices were evolving. Elective endoscopies were cancelled and staff were redeployed to care for COVID patients. The patient population for this study was identified using ICD-10 codes, which is limited by physician coding and risks underselection of patients. However, all charts were manually reviewed for accuracy. Finally, due to the short time period we did not evaluate outcomes after discharge.

Our study suggests that initiation of treatment dose AC to minimize COVID-19 related thromboembolic complications does not result in increased mortality for patients with GIB despite limited access to endoscopy. However, the benefits of initiating AC and risk of subsequent bleeding should be carefully evaluated on an individualized basis.

Conflicts of interest

NK: Consultant for Apollo Endosurgery, Boston Scientific, GLG consulting, Gyrus ACMI Inc, Olympus.

The remaining authors had no personal or financial conflicts to declare.

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CRediT authorship contribution statement

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.clinre.2020.101602.

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