Evaluation of an Elevated VTE Thromboprophylaxis Guideline for Critically Ill patients Infected with COVID-19

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BACKGROUND

- Individuals infected with the Coronavirus-19 Disease (COVID-19) are associated increased inflammation and inducing a prothrombotic state.
- Historically, non-COVID-19 critically ill patients are at a greater risk for VTE due to ICU related risk factors. Thromboprophylaxis is commonly routinely deployed in this population utilizing chemical thromboprophylaxis such as unfractionated heparin or low molecular weight heparin.
- Parameters evaluated and used to assess for clinical benefit include coagulation markers and inflammatory markers, such as D-dimer, C-reactive protein (CRP), and ferritin. However, as stated by the NIH, there lacks direct evidence to show an association between risk stratifying patients with this method despite elevated D-dimer, CRP, and ferritin exhibiting an association with increased mortality.

OBJECTIVES

- Determine the effect of various anticoagulation dosing schemes for the prevention of VTEs in critically ill patients infected with SARS-CoV-2.

METHODS

- Study design: Single-center, retrospective chart review comparing pre- and post-guideline implementation
- Inclusion criteria: Individuals ≥ 18 years old with laboratory confirmed infection of SARS-CoV-2 virus and who received any anticoagulation during hospital stay.
- Exclusion criteria: Patients who are pregnant/breastfeeding, incarcerated, on an anticoagulant prior to admission, and/or diagnosed with a thromboembolism upon admission.
- Primary outcomes: Risk of thromboembolism between standard, treatment, and non-standard anticoagulation dosing regimens.
- Secondary outcomes: Risk of bleeding, 30-day readmission rates for thromboembolic or bleeding complications, rate of VTE prophylaxis prescribed upon discharge
- Definitions:

Standard Prophylaxis Dosing
  - BMI < 40 kg/m2: Enoxaparin 40 mg SQ once daily
  - BMI ≥ 40 kg/m2: Enoxaparin 40 mg SQ twice daily
  - Weight < 50 kg: Enoxaparin 30 mg SQ once daily
  - Heparin 5,000IU SQ every 8 hours

Treatment Dosing
  - Enoxaparin 1 mg/kg SQ every 12 hours
  - Enoxaparin 1.5 mg/kg SQ every 24 hours
  - Direct-acting anticoagulation, any for the prevention or treatment of current or history of thromboembolic disease

Non-standard/Intermediate Dosing
  - Enoxaparin 0.5 mg/kg SQ twice daily
  - Anticoagulation total daily dose greater than "standard prophylactic dosing" and less than "treatment dosing"

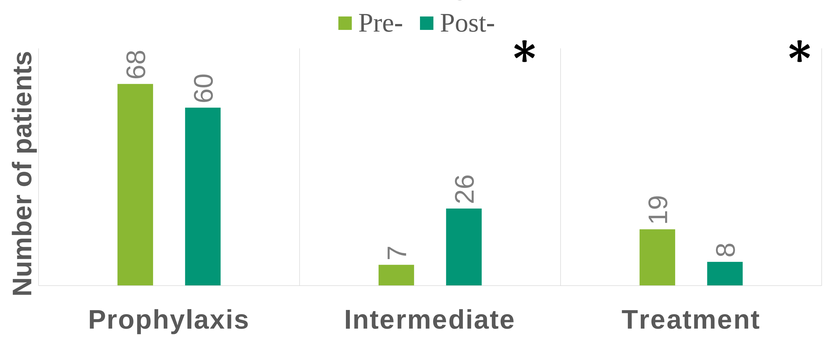
RESULTS

Table 1. Baseline Characteristics

Characteristics	Pre-implementation (N = 94)	Post-implementation (N = 93)
Age – yr	66 (55-75)	69 (59-69)
Male sex – no. (%)	62 (66.0)	62 (66.7)
White Hispanic – no. (%)	76 (80.9)	84 (90.32)
Weight – kg/m²	30.3 ± 5.9	30.0 ± 5.8
Weight Distribution – no. (%)		
BMI ≤ 30	49 (52.1)	47 (50.5)
BMI > 30-39.9	38 (40.4)	42 (45.2)
BMI ≥ 40	7 (7.5)	4 (4.3)
More than 3 Comorbidities	16 (17.0)	22 (23.7)
Concomitant antiplatelet – no. (%)	19 (20.2)	45 (48.4)
Hemoglobin, mg/dL	13.3 ± 1.8	13.4 ± 2.1
Platelet, count	212.3 ± 86.3	248.2 ± 103.7
INR*	1.1 (1.1-1.1)	1.1 (1.1-1.2)
Prothrombin time, ms	34.8 ± 20.5	31.1 ± 4.9
D-dimer, mcg/mL*	3.6 ± 10.3	2.8 ± 4.7
Ferritin, mcg/L	1468.2 ± 3337.4	

Bolded results indicate a statistically significant difference and baseline characteristic variable.
Nominal variables are expressed as frequency (%). Ordinal variables are expressed as sample median (IQR).
Continuous variables are shown as sample means ± the standard deviation.

Figure 1. Anticoagulation Orders by Dose Intensity



* Indicates statistically significant difference

Table 2. Sub-group Analysis

	Prophylaxis		Intermediate		Treatment	
Outcome – no. (%)	Pre- N = 68	Post- N = 60	Pre- N = 7	Post- N = 26	Pre- N = 19	Post- N = 8
Venous Thromboembolism	7 (10.3)	9 (15.0)	0 (0)	4 (15.4)	0 (0)	2 (25)
In-hospital mortality	23 (33.8)	20 (33.3)	2 (28.6)	9 (34.6)	11 (58.9)	2 (25)
Any bleeding	6 (8.8)	7 (11.7)	1 (14.3)	2 (7.7)	3 (15.8)	3 (37.5)

CONCLUSION

Implementation an institutional VTE prophylaxis guideline for patients infected with COVID-19 resulted in a statistically significant difference in the number of intermediate and treatment regimens. There was statistically significant difference in the number of VTEs or clinically significant bleeding found in the post implementation group.

LIMITATIONS

- Retrospective chart review
- Homogenous population, majority of patients are white-Hispanic adults, and a high proportion of patients are male
- Etiology of cardiac arrest for patients with the review is unknown.
- Relied heavily on accurate documentation of providers and accurate charting of medication history and administration.
- Patients had a very fluctuating course. E.g., escalating and deescalating level of care from step-down to critical care.
- Prescribing habits took a very temporal course, with treatment doses occurring earlier in the pandemic and intermediate dosing becoming more routine in the later half.

DISCUSSION

The data suggests there is not a statistically significant difference in the relative risk of venous thromboembolism before and after the implementation of the treatment guideline. Currently recommendations from leading bodies have not changed their stance on the use of treatment or intermediate intensity anticoagulation. Despite a non-statistically significant difference in the relative risk of venous thromboembolism there appears to be a clinically significant difference and is under investigation. The increase number of venous thromboembolism's Further, currently pending is the completion of the peer-review the multi-study report from REMAP-CAP, ACTIV-4 and ATTACC. We expect institutional recommendations will be adjusted to adhere to the findings of these trials in our COVID-19 population.

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DISCLOSURES

All authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation