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## Published In/Presented At

Walter, A. & Ottinger, J. (2020, December). *Evaluation of Enoxaparin Hybrid Dosing for VTE Prophylaxis in COVID-19 Positive Patients*. Poster presented at: ASHP Midyear Clinical Meeting and Exhibition, Virtual.

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# Evaluation of Enoxaparin Hybrid Dosing for VTE Prophylaxis in COVID-19 Positive Patients

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## Background

- Patients positive for COVID-19 have been observed to be at a higher risk for venous thromboembolism (VTE) due to theorized endothelial damage secondary to the infection.
- Factoring in prolonged hospital stays and other high-risk patient comorbidities with endothelial damage from hypoxic respiratory failure puts these patients at an enhanced probability of a hypercoagulable state. This confluence of events potentially leading to thromboembolic events.
- At the Lehigh Valley Health Network, enoxaparin 0.5 mg/kg q12h was utilized as part of an anticoagulation protocol. It was approved for use in select COVID-19 positive patients as VTE prophylaxis in the absence of bleeding contraindications, confirmed/known VTE, or continuous renal replacement therapy (CRRT).
- The observations from this study will help healthcare professionals treating patients with COVID-19 better understand the range of clinical outcomes that were associated with intermediate dosing anticoagulation with enoxaparin in this population.

## Purpose

The purpose of this medication use evaluation is to assess the observed outcomes associated with the utilization of enoxaparin hybrid dosing in select COVID-19 positive patients for VTE prophylaxis.

## Methods

### STUDY DESIGN

- This was a retrospective chart review that was performed at Lehigh Valley Hospital–Cedar Crest (LVH–Cedar Crest) in Allentown, Pa., assessing the clinical impacts of a protocol directed hybrid dose of enoxaparin in select COVID-19 positive patients treated from April 1, 2020 to June 30, 2020.
- Selected data was collected from patients who received enoxaparin 0.5 mg/kg subcutaneous q12h for VTE prophylaxis
  - Patients included in the analysis:
    - Patients with a documented positive COVID-19 test during treatment
    - At least one dose of (enoxaparin 0.5 mg/kg subcutaneous q12h) was administered during admission
  - Patients excluded from the design:
    - < 18 years old
    - Treated in the outpatient setting
- Counts and percentages were calculated using Microsoft Excel™

### PRIMARY ENDPOINT

- Identify the incidence of new onset of thrombosis or bleeding in COVID-19 patients within 24 hours after receiving a hybrid dose of enoxaparin 0.5 mg/kg q12h for VTE prophylaxis at LVH–Cedar Crest between April 1, 2020 to June 30, 2020.

### SECONDARY ENDPOINTS

- Identify COVID-19 patients who initially received enoxaparin 0.5 mg/kg q12h for VTE prophylaxis but then required a dose adjustment due to changes in eGFR, a new onset of thrombosis, or bleeding at LVH–Cedar Crest between April 1, 2020 to June 30, 2020.
- Calculate the percentage of COVID-19 patients who experienced a major bleeding event vs non-major bleeding event who received enoxaparin 0.5 mg/kg q12h for VTE prophylaxis within 24 hours of the event at LVH–Cedar Crest between April 1, 2020 to June 30, 2020.

## Results

A total of 96 patients were included in this analysis.

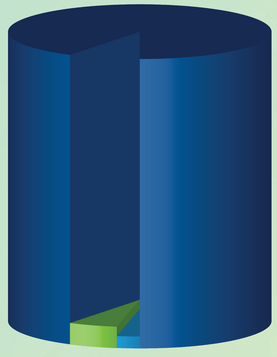
**TABLE 1: PATIENT DEMOGRAPHICS**

| | |
|---|---|
| **Mean Age (years)** | 63.7 |
| **Gender – Males, n (%)** | 38 (39.6%) |
| **ICU patients, n (%)** | 68 (70.8%) |
| **Mean weight (kg)** | 84.4 |
| >120 kg, n (%) | 6 (6.25%) |
| 90-120 kg, n (%) | 30 (31.3%) |
| 60-90 kg, n (%) | 53 (55.2%) |
| <60 kg, n (%) | 7 (7.3%) |

**TABLE 2: AVERAGE MAXIMUM AND MINIMUM LAB VALUES WHILE RECEIVING ENOXAPARIN HYBRID DOSE**

| | Average Maximum Values | Average Minimum Values |
|---|---|---|
| Hemoglobin (g/dL) | 12.0 | 10.0 |
| Platelets (thou/cmm) | 373 | 226 |
| eGFR (mL/min/1.73 m2) | 89.8 | 66.7 |
| D-dimer (µ/mL) | 4.05 | 2.01 |

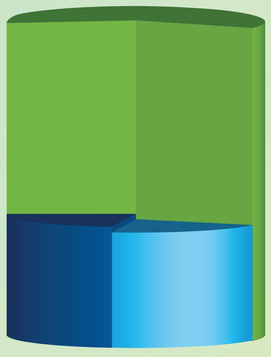
**FIGURE 1**



- Thrombotic Event (n = 3) **3.2%**
- Any Bleeding Event (n = 6) **6.25%**
- No Thrombotic or Bleeding Event (n = 87) **90.6%**

Onset of Thrombosis or Bleeding events in the enoxaparin hybrid dose COVID-19 population

**FIGURE 2**



- Changes in eGFR (n = 8) **57.1%**
- New Onset Thrombosis (n = 3) **21.4%**
- Any Bleeding Event (n = 3) **21.4%**

Therapeutic Adjustments observed in the enoxaparin hybrid dose COVID-19 population due to changes in eGFR, a New Onset of Thrombosis, or Bleeding

**FIGURE 3**

- Major Bleeding Events (n = 1) **16.6%**
- Non-Major Clinically Relevant Bleeding Events (n = 5) **83.3%**

Major Bleeding and Non-Major Bleeding Events observed in the enoxaparin hybrid dose COVID-19 population

## Conclusion

- The most common demographics in this study were older adults (mean = 64 years old), women (n = 58), and patients located within an ICU setting (n = 68).
- The most common reason recorded for adjustments made to therapy was a sudden change in eGFR (8 of 14) that prompted the use a different dose or an alternative anticoagulant.
- Out of the total number of bleeding events that occurred after receiving enoxaparin hybrid dosing, 1 was considered a major bleed while 5 were considered clinically-relevant non-major bleeds.
  - This major bleeding event contributed to a drop in hemoglobin >2 g/dL but did not lead to a fatal outcome.
    - Risk factors for bleeding in patients on VTE prophylaxis present in this patient included older age (79 years old), female, hypertension, and renal insufficiency.
- Only two of the five non-major clinically relevant bleeding events prompted a dose adjustment.
  - Events that lead to increased level of care or documentation include recurrent epistasis, tracheal, mucosal, arterial line, and GI bleeding.
  - Risk factors for bleeding in patients on VTE prophylaxis present in these patients include three female patients, three patients of older age, four with hypertension, and three with renal insufficiency.
- A total of three thrombotic events occurred that prompted a dosage increase to full anticoagulation from enoxaparin (1 mg/kg q12h subcutaneous) due to two occlusive thrombi and one superficial vein thrombosis.
  - Risk factors for thrombosis in patients on VTE prophylaxis in these patients include three patients >40 years old, three patients on bed rest ≥5 days, and 2 obese patients.
- The results of this MUE provide us with a better understanding of bleeding and thrombotic event incidence rates in COVID-19 patients receiving a hybrid dose of enoxaparin not typically used in other patient populations.
  - Although a small patient population was analyzed in this study, this information will contribute to current literature in regards on how to manage patients with this novel coronavirus.
  - The bleeding and thrombosis rates found in this MUE are comparable to what was found in a larger trial conducted in the United States in a similar patient population.

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### DISCLOSURES

The authors have nothing to disclose concerning possible financial or personal relationships with commercial entities.

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