Hageman K. Updates in Hospital Medicine. *Brown Hospital Medicine*. 2023;2(2).
doi:10.56305/001c.73881

Updates in Hospital Medicine

Updates in Hospital Medicine

Kevin Hageman, DO[1,2]

[1] Department of Medicine, Section of Hospital Medicine, Vanderbilt University School of Medicine, Nashville, TN, USA, [2] Department of Veterans Affairs, Tennessee Valley Healthcare System, Nashville, TN, USA

Keywords: aspirin, enoxaparin, deep vein thrombosis, fracture, prophylaxis, cellulitis, necrotizing fasciitis, hemorrhagic bullae

https://doi.org/10.56305/001c.73881

Vol. 2, Issue 2, 2023

UPDATE 1

ASPIRIN FOR OPERATIVE ORTHOPEDIC DVT PROPHYLAXIS

Low-molecular-weight-heparin (LMWH) is often thought of as the "gold-standard" for post-operative deep-vein thrombosis (DVT) prophylaxis by hospitalists. Aspirin (ASA) use for DVT prophylaxis has been supported in the orthopedic literature for years, but without direct comparison to LMWH in the setting of fracture.[1–3]

A total of 12, 211 patients were randomized in this multicenter, non-inferiority trial comparing ASA (n=6101) to LMWH (n=6110).[4] All patients were ⩾ 18 years of age and were diagnosed with a fracture of an extremity (hip to mid-foot or shoulder to wrist) that was treated operatively, or with a pelvic or acetabular fracture. The mean age was approximately 45 years, 62% were male, 63% were white, and 2.5% of patients had cancer (for comparison, 0.9% of patients had cancer in the National Trauma Data Bank cohort). Sixty seven percent of fractures were lower extremity, 21% were both lower and upper extremity, and 45% of patients were recommended to be non-weight bearing at discharge. Patients were excluded if they had received ⩾ three doses of DVT prophylaxis prior to enrollment, were already on therapeutic anticoagulation or > 81mg ASA daily, if they presented > 48 hours after the fracture, had a VTE within the past 6 months, or a creatinine clearance < 30 mL/min.

The patients were randomized to either LMWH 30mg twice daily or ASA 81mg twice daily. The primary outcome was death from any cause at 90 days. The secondary outcomes were nonfatal pulmonary embolism (PE), DVT, and bleeding. The mean number of inpatient doses of a trial medication was 8.6±10.8 in the aspirin group and 9.1±10.5 in the LMWH group. At discharge, 91% of the patients were prescribed thromboprophylaxis: 93.6% in the ASA group and 88.8% in the LWMH group. Protocol-adherence at discharge was 94.4% in the ASA group and 86.6% in the LMWH group. The decision to continue prophylaxis at discharge was based on clinician discretion, with a median duration of 21 days prescribed.

At 90 days, death occurred in 0.78% of patients in the ASA group and 0.73% of patients in the LMWH group (96.2% confidence interval [CI], −0.27 to 0.38). Aspirin was noninferior to LMWH (P<0.001) but not superior (P=0.63) in preventing death from any cause. In the intention-to-treat analysis, 151 (2.51%) patients in the ASA group developed a DVT (87 distal) versus 103 (1.71%, 52 of which were distal) in the LMWH group (95% CI [0.28 to 1.31]). A similar correlation was seen in the per-protocol population. Nonfatal pulmonary embolism occurred in 90 patients (90-day probability, 1.49%) in the ASA group and in 90 patients (90-day probability, 1.49%) in the LMWH group. Serious bleeding occurred with similar frequency between the groups.

Take-away: Aspirin 81mg twice daily can be considered as an alternative to traditional LMWH DVT prophylaxis in the setting of an operative fracture. The clinician should account for the potential increased incidence of DVT with an ASA-based regimen, while recognizing that this oral regimen may promote adherence.

UPDATE 2

CLINICAL MARKERS TO DIFFERENTIATE CELLULITIS FROM NECROTIZING FASCIITIS

Cellulitis and necrotizing fasciitis (NF) have historically been challenging to differentiate, especially early in the course of the illness. The Laboratory Risk Indicator for NF (LRINEC) score traditionally has been used to help identify NF, however, it performs suboptimally with highly variable sensitivity and specificity.[5,6]

Researchers at a single tertiary hospital in Taiwan conducted a prospective study, ultimately identifying 159 patients with cellulitis and 145 patients with NF.[7] They aimed to identify microbiologic etiologies and clinical features that would differentiate NF from cellulitis upon presentation to the emergency department (ED).

Age, sex, comorbidity, infection site, results of bacteriological tests, condition of skin lesions, laboratory findings at the time of admission, vital signs upon presentation, the LRINEC score, and clinical outcomes were compared between the NF and cellulitis groups. The mean age, sex, fever, comorbidities, and platelet count did not differ between the groups. The NF mortality rate was 10.3% compared to cellulitis at 1.3%. Patients with NF were more likely to have Gram-negative infection (*Vibrio* and *Aeromonas* were the most common bacteria isolated) while those with cellulitis more commonly had Gram-positive infection (*Streptococcus* and *Staphylococcus* were the most common). Ninety-seven NF patients had hemorrhagic bullae (67%) compared to only seven cellulitis patients (4.4%). The mean white blood cell count (WBC) in NF was 14.4 cells/mm^3 versus 10.9 cells/mm^3 in patients with cellulitis. The mean C-reactive protein (CRP) in NF was 140mg/L versus 54mg/L in cellulitis. Eighty-two percent of patients with

confirmed NF had a LRINEC score of < 6. No patients in the cellulitis group had a systolic blood pressure < 90 at presentation.

Clinical and laboratory findings at admission that were significantly associated with NF are as follows:

- Hemorrhagic bullae (OR 43.8, 95% CI [19.1-100.9] P < 0.0001)
- Systolic blood pressure ⩽90 mm Hg (OR 87.8, 95% CI [5.3-1449.1) P = 0.0018)
- Band forms > 0% (OR 15.4, 95% CI [8.4-28.3] P < 0.0001)
- CRP >100mg/l (OR 5.4, 95% CI (3.2-8.9) P <0.0001)
- WBC count >11,000 cells/mm^3 (OR 2.2, 95% CI [1.4-3.5] P = 0.0007)

The researchers argue that patients with any two of these indicators at the time of presentation can be diagnosed early as NF to enable urgent surgical intervention.

Limitations to the study include its single center, coastal location where most patients were fishermen, farmers, or laborers with a high incidence of *Vibrio* and *Aeromonas* infections. Many patients were excluded due to the lack of microbiologic data. Additionally, a scoring system for the five variables was not created and there remains a lack of validity, sensitivity, and specificity for the noted clinical indicators.

Take-away: In patients presenting with a concern for cellulitis, the presence of hemorrhagic bullae, hypotension, and bandemia should prompt careful consideration of necrotizing fasciitis.

ACKNOWLEDGEMENTS

Kelly Sponsler, MD for review and suggestions

DISCLOSURES

None

CONFLICT OF INTEREST

The author declares they have no conflicts of interest

FUNDING

None

AUTHOR CONTRIBUTIONS

All authors have reviewed the final manuscript prior to submission. All the authors have contributed significantly to the manuscript, per the International Committee of Medical Journal Editors criteria of authorship.

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Submitted: March 07, 2023 EDT, Accepted: March 24, 2023 EDT

REFERENCES

1. Azboy I, Barrack R, Thomas AM, Haddad FS, Parvizi J. Aspirin and the prevention of venous thromboembolism following total joint arthroplasty: commonly asked questions. *Bone Joint J*. 2017;99-B(11):1420-1430. doi:10.1302/0301-620X.99B11.BJJ-2017-0337.R2

2. Chisari E, Tan TL, Shah R, et al. Aspirin Is an Effective Prophylaxis for Venous Thromboembolism in Ambulatory Patients with Femoral Neck Fracture Undergoing Hip Arthroplasty. *J Bone Joint Surg Am*. 2022;104(7):603-609. doi:10.2106/jbjs.21.00168

3. DeDea L. DVT prophylaxis with aspirin in orthopedic surgery patients. *JAAPA*. 2012;25(4):21. doi:10.1097/01720610-201204000-00002

4. Major Extremity Trauma Research Consortium (METRC). Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture. *N Engl J Med*. 2023;388(3):203-213. doi:10.1056/nejmoa2205973

5. Tarricone A, Mata KDL, Gee A, et al. A Systematic Review and Meta-Analysis of the Effectiveness of LRINEC Score for Predicting Upper and Lower Extremity Necrotizing Fasciitis. *J Foot Ankle Surg*. 2022;61(2):384-389. doi:10.1053/j.jfas.2021.09.015

6. Fernando SM, Tran A, Cheng W, et al. Necrotizing Soft Tissue Infection: Diagnostic Accuracy of Physical Examination, Imaging, and LRINEC Score. *Ann Surg*. 2019;269(1):58-65. doi:10.1097/sla.0000000000002774

7. Tsai YH, Chen HY, Huang TY, Chen JL, Hsiao CT, Huang KC. Bullous skin signs and laboratory surgical indicators can quickly and effectively differentiate necrotizing fasciitis from cellulitis. *Int J Infect Dis*. 2022;128:41-50. doi:10.1016/j.ijid.2022.12.012