Timing and Type of Venous Thromboembolic Chemoprophylaxis is Associated with Acute Traumatic Brain Injury Outcomes

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Background

Venous thromboembolic (VTE) prophylaxis in acute traumatic brain injury (TBI) is a controversial topic with wide practice variations across the United States. This study examines the association of type and timing of VTE chemoprophylaxis with inpatient mortality and VTE events.

Methods

Following IRB approval, a multicenter retrospective cohort study of 87 trauma centers within a large hospital system in the United States was conducted.

- Included patients:
  - 23,548 with isolated TBI
  - Subset of 7,977 with moderate to severe TBI with head abbreviated injury scores ≥ 3.

- Excluded patients with:
  - History of VTE events
  - History of outpatient anticoagulation use other than low molecular weight heparin (LMWH) and unfractionated heparin (UFH)
  - Patients who died within 24 hours of admission were excluded.

- Primary outcomes:
  - inpatient mortality
  - VTE events, (pulmonary embolism and deep vein thrombosis)

- Four patient groups:
  - No chemoprophylaxis (control)
  - LMWH only
  - UFH only
  - Both LMWH and UFH

- Multivariable regression accounted for confounders.

- Outcomes were stratified by:
  - timing of administration
  - body mass index
  - TBI type

Results

<table>
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<tr>
<th>Isolated TBI</th>
<th>Without LMWH or UFH (N=18,208)</th>
<th>LMWH (N=2,808)</th>
<th>UFH (N=2,184)</th>
<th>Combination LMWH/UFH (N=348)</th>
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</table>
| VTE (PVD/T)
| 0.5% | 2.6% | 3.9% | 26.85 (11.60, 61.07) |
| Adjusted Odds Ratio* | 7.22 (3.70, 14.08) | 10.63 (5.65, 20.01) | 26.85 (11.60, 61.07) |
| Mortality | 4.2% | 2.6% | 8.6% | 7.8% |
| Adjusted Odds Ratio* | 0.24 (0.14, 0.42) | 1.09 (0.77, 1.54) | 0.42 (0.18, 0.99) |

<table>
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<th>HAIS ≥3 (Moderate to Severe TBI)</th>
<th>Without LMWH or UFH (N=6,382)</th>
<th>LMWH (N=700)</th>
<th>UFH (N=767)</th>
<th>Combination LMWH/UFH (N=128)</th>
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| VTE (PVD/T)
| 0.3% | 2.9% | 4.2% | 9.4% |
| Adjusted Odds Ratio* | 8.36 (4.01, 17.44) | 11.03 (5.54, 21.98) | 19.86 (7.83, 50.38) |
| Mortality | 6.2% | 4.1% | 10.6% | 8.6% |
| Adjusted Odds Ratio* | 0.25 (0.14, 0.44) | 0.99 (0.68, 1.42) | 0.41 (0.17, 1.00) |

• Most isolated TBI patients (77%) did not receive VTE chemoprophylaxis and had the least VTE events, even after multivariable risk adjustment and exclusion of patients with interrupted VTE chemoprophylaxis.

• LMWH VTE chemoprophylaxis had the lowest mortality for both all-isolated and moderate-to-severe isolated TBI populations at aOR 0.24 (95% CI 0.14 – 0.43) and aOR 0.25 (95% CI 0.14 – 0.44) respectively.

• Clinically significant progression of TBI requiring surgical intervention was lowest among the LMWH group (0.1%), p-value 0.001.

• After stratifying by timing of VTE chemoprophylaxis, only patients with subdural hematoma and LMWH between 6-24 hours (N= 62), as well as patients with ≥ 35 BMI and LMWH between 6-24 hours (N=65) or > 24-48 hours (N=54), had no VTE events.

Conclusion

• While timing of VTE chemoprophylaxis may have prevented VTE in certain subgroups of isolated TBI patients, this study did not find that VTE chemoprophylaxis prevented VTE for the majority of isolated TBI patients.

• For isolated TBI patients, regardless of severity, LMWH was associated with reduced mortality, consistent with early evidence of its neuroprotective effects.

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