Traumatic Brain Injury Patients and Deep Vein Thrombosis

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Terminology

- Deep Vein Thrombosis = Blood Clot
- Anticoagulation = Keeping Blood Thin
Virchow’s Triad - Factors leading to DVT

- Hypercoagulability
- Endothelial Injury - injury to lining of blood vessels
- Hemodynamic Changes (stasis, turbulence)
Deep Vein Thrombosis

• It is the formation of a blood clot in the deep veins oftentimes of the legs
• Can travel in vasculature to cause Pulmonary Emboli
Traumatic Brain Injury

• TBI Patients are often in:
  - Hypercoagulable State- s/p surgery and resulting blood loss
  - Stasis- less ambulatory
  - Endothelial Injury- polytrauma with LE injuries, cerebrovascular injuries
Less Ambulatory
Traumatic Brain Injury

• Patients often cannot be anticoagulated:
  - for fear of rebleeding after surgery
  - patients’ high fall risk
2010 Study by Ekeh MD

- Sequential Compression Devices were routinely used
- Anticoagulation was not used on brain injuries
- DVT Screenings performed at 7-10 days after admission and weekly thereafter
RESULTS

• 34.3% had DVT in patients with combined head and extracranial injuries
• 25.8% had DVT with only head injury
Preventing DVT

• 8.5%-18% incidence of DVT on admission to inpatient rehabilitation

• Therefore, in a patient that cannot be anticoagulated and at a high risk of developing DVT. What can be done?
Ultrasound to Detect DVT

• U/S regarded as most sensitive and specific noninvasive test for detection of lower extremity DVT
• Positive Predictive Value for Positive Scan is 97%-98% in both symptomatic and asymptomatic patients
• Downside of U/S: Expense? Yes and No
U/S

- Previous study shows that U/S is as cost effective as mammography recommendations for woman per year of life saved
- But as people are transferred more rapidly from Acute Care to Rehab, Could anything else work in a more cost-effective manner over an extended time period?
D-Dimer

• Monitor D-Dimer Levels on Admission and Weekly
What is D-Dimer?

- Obtained from Plasma
- Generated when the endogenous fibrinolytic system degrades fibrin such as when a venous thrombosis forms
- Fibrin is a protein involved in blood clotting
- Consists of 2 fibrin molecules
Generation of D-dimer from cross-linked fibrin

Fibrinogen

Thrombin cleavage

Fibrin

Fibrinopeptide A & B

Fibrin polymer

Factor XIIIa cross-linking

Crosslinked Fibrin

Plasmin cleavage

Fibrin Degradation Products

D-dimer
D-Dimer

- Acute Phase reactant like ESR or CRP
- Value increases when fibrinolytic system degrades Fibrin such as in trauma, surgery, myocardial infarct, liver disease, malignancy, pregnancy
- Sensitive test, not a specific test
- Two D-Dimer Tests: Latex Immunosorbent Agglutination (LIA) and Enzyme Linked Immunosorbent Assay (ELISA)
LIA vs ELISA

• LIA- Inexpensive and rapid to perform, numerous studies have shown that they lack the sensitivity to detect D-dimers in critical clinical situations
LIA vs ELISA

• ELISA-In spite of their high sensitivity and specificity, it is expensive, labor intensive, and time consuming to perform. Therefore, it has not been practical in most clinical situations, where rapidly available results are needed.
Another Study

• Assessed whether D-Dimer assays are predictive of DVT during the first 2 weeks after TBI at a predictive value of:
  LIA-0.5 mg/L  ELISA-500ug/L

• Over 8 weeks the second generation LIA Assay was correlated with the ELISA after an acute TBI
Methods

• Prospective Longitudinal Study TBI Model System Hospital (UAB)
• Subjects screened for DVT with U/S at week 2 after acute TBI
• Subjects screened for DVT with LIA and ELISA at weeks 2, 4, 6, 8 (+/- 3 days) after acute TBI whether patient was inpatient or outpatient.
• Time Interval: 3 year period
Participants

- 35 patients
- GCS mean score of 6.5 (range of 3-15)
- 33 had D-Dimers levels drawn at week 2.
- 21 subjects followed for 8 weeks after injury
- 25 men. 10 women.
- Average age 33 (range 17-66 y/o)
- Recruited in acute care at UAB
Inclusion Criteria

• At least 16 y/o of age
• No history of DVT
• Injuries were severe enough to require inpatient rehabilitation after 48 hours
• Informed Consent obtained
Results

• At 4, 6, 8 weeks D-Dimer Levels remained elevated, yet trended downward
Decreasing Values

Cell Line Chart
Error Bars: ±1 SE(s)

Fig 2. Change over time of the LIA measurement for D-dimer over 2 to 8 weeks. LIA is represented in milligrams per liter.
2009 Study by Chua and Kong

• 70%-80% of DVT are asymptomatic and found on autopsy
• Higher prevalence of Protein C and S deficiency in patients from Hong Kong and Taiwan
• Acute DVT in hospitalized patients is on the rise. 7.9 per 10,000 admissions in 1990 to 15.1 per 10,000 admissions in 2002.
2009 Study by Chua and Kong

- 56 Patients older than 15 years of age
- Admitted between November 2005-April 2007
- TBI diagnoses made by Admitting Neurosurgeon or ED based on history, admission GCS, and CT and/or MRI Scans
- Excluded if recurrent TBI or diagnosed with DVT or PE prior to transfer to rehabilitation
2009 Study by Chua and Kong

- D-Dimer obtained within 48 hours of Rehab Admission
- If D-Dimer elevated, U/S of weaker extremity was performed
- Bilateral Thigh length graduated-pressure compressive stockings for DVT prevention used during entire rehabilitation stay
2009 Study by Chua and Kong

- Average age 49.3
- Mean GCS- 9.9 (30%=13-15, 33%=9-12, 35%=3-8)
- Mean Post Traumatic Amnesia 51.3 days
- Mean Rehab Length of Stay 37.7 days
2009 Study by Chua and Kong

- 3 DVT’s found when D-Dimer elevated
- Women, Non-Chinese, Lower Limb and Pelvic fractures, Lower FIM Walking scores- all had an increase risk of DVT but these did not reach statistical significance
- Found to be falsely elevated in patients with tracheostomy and those with greater dependency
- Limitations: small study, D-Dimer drawn only once
Current Research I

• The previously studies helped to formulate the study I performed
• Previous studies showed that TBI patients are at an increased risk of developing DVT and that D-Dimers may correlate to the development of DVT
• Previous studies also indicated that D-Dimer levels generally decrease as time progresses from initial injury
Objective

• Study investigated if it is reasonable to use the D-Dimer as a surveillance tool when deciding to order diagnostic lower extremity ultrasound for the detection of DVT in the TBI patient population
• Also, if it is reasonable, is there a specific rate of change in D-Dimer levels to indicate obtaining ultrasound
Participants

• 113 individuals enrolled in the TBI Model System Database at UAB Spain Rehabilitation
• Moderate to severe TBI (PTA>24 hours or LOC >30 minutes or GCS in ED<13 or intracranial neuroimaging abnormalities)
• Admitted to system’s hospital emergency department within 72 hours of injury
• 19 years of age and older
• Received acute care and comprehensive inpatient rehabilitation within the model system hospital (UAB and Spain Rehabilitation Center)
Design

- Retrospective Chart Review
- Enrolled between 2012-2014
- Ultrasound of lower extremities were obtained prior to admission to Spain Rehab in patients not already receiving anticoagulation
- D-Dimer values collected on admission and weekly
- Ultrasound obtained if D-Dimer values increased by no specific percentage
Results

Total Participants
113

Participants with D-Dimer Value Increase
4

Participants with no change or decreased D-Dimer Value
109

Participants positive for DVT
1

Participants negative for DVT
3
Results

- D-Dimer values remained equal or decreased in 109 patients
- D-Dimer values increased in 4 patients
- 75% of the increased values were negative for DVT
- 25% of the increased values were positive for DVT
- 69 patients had ultrasound reports negative for DVT prior to admittance
- 12 patients were positive for DVT prior to admittance
- 32 patients did not have ultrasound prior to admittance
Discussion

- Results suggest obtaining consecutive values are of minimal value in determining when to obtain ultrasound
- No deaths occurred from the DVT/PE found
- Data only limited to TBI Model System patients
- Future studies could examine functional status, anticoagulation status, presence of DVT, patients with brain tumor resection as these patients are hypercoagulable
Discussion

• Returns to the question; Anticoagulate vs IVC Filter Placement vs Leg Compression Devices
• D-Dimer may be a marker of inflammatory processes involving neuronal cell death after TBI and not just marker of possible DVT
• Below Knee vs Proximal and ultrasound
Current Research II

- Prior studies did not differentiate between proximal and distal DVT (below and above the knee)
- Proximal DVT more likely to migrate to heart and lungs
- Distal DVT less likely to migrate to heart and lungs
- Therefore, the location of DVT helps to inform treatment
Objective

- Is it common for distal DVT to migrate to a proximal location?
- Are there any specific factors that might affect a migration of DVT from distal to proximal positions?
Participants

- 140 TBI patients hospitalized at JFK Johnson Rehab Institute Brain Trauma Unit in the years 2013, 2014, 2015
Design

- Exploratory Study
- Retrospective Chart Review
- Accounting of Medical Codes of Comorbidity and indexing them with presence and location of DVT
Results

- 15 with Distal DVT
- 4 with Proximal DVT
- 3 with both Distal and Proximal DVT (migration)
- Hemiplegia: 1 patient with migration
- Abnormality of Gait: 2 patients with migration
- Dysphagia: 2 patients with migration
- No Pulmonary Embolus: 3 patients with migration
- Male: 2 patients with migration
- Female: 1 patient with migration
Results

Motor FIM Score
Mean Admission for migration: 27
Mean Discharge for migration: 68
Mean Admission with no DVT: 27
Mean Discharge with no DVT: 54

Remember only 3 with migration vs 118 with no DVT.
Discussion

- Low Yield on patient’s with migration of distal to proximal to establish results of true significance
- Need larger enrollment numbers
- Excludes oncologic patients
- Future Study could include correlating D-Dimer Values to DVT that migrates
DVT Prophylaxis

After TBI timing is controversial

Studies:

Subcutaneous Heparin can be begun within 12 hours

LMWH (Lovenox) can be begun as soon as 36 hours after intracranial or spinal trauma.

Discuss with referral service
DVT Prophylaxis

ASA, low-dose Coumadin, and non-thigh high sequential compression devices (SCD) reduce risk, but not to an optimal level and therefore should not be used as primary prophylaxis.
DVT Prophylaxis

• IVC or SVC filters are not appropriate DVT prophylaxis for any patient.
• One-third of patients with DVT will develop post-Phlebitic Syndrome.
• DVT prophylaxis should continue until:
  • Patient is ambulating to/from restroom prn
  • Appropriate time has passed (SCI 8-12 weeks, hip/femur fx 4 weeks)
  • Coma: 12 weeks
References


Reference


THANK YOU

Brian Greenwald MD
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QUESTIONS?