Arkansas Trauma System Evidence-Based Guidelines for Diagnosis and Prevention of Venous Thromboembolism (VTE)

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Introduction-

Venous thromboembolism (VTE) has two main manifestations: Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE). The first document in this series dealt with prophylaxis of VTE.

The incidence of thrombosis in the venous system, particularly the lower extremities and pelvic veins has long been a problem and issue in care of the acutely traumatized patient. There have been many articles written about both the incidence as well as the steps to be taken to reduce the incidence of both venous thromboembolism (VTE), pulmonary embolism (PE), as well as the more severe forms of venous clotting, such as phlegmasia cerula dolens and cerula alba.

Our review will focus on both modern literature's view of incidence, various high-risk patients, as well as steps that can be taken to reduce the risk of major complications due to VTE. [1]

A second EBG will then focus on therapy of patients with confirmed DVT and PE.

Complicating the whole matter are two major problems: 1) ignoring invasive radiologic tests, such as venography, our non-invasive tests (ultrasound and hematologic tests) have some areas of weakness that cloud the picture as to who does- and does not- have DVT. This weakness then leads to sometimes widely varying statistics on the incidence of VTE, opinions as to who is most at risk, and to generalization of prophylactic treatment regimens; and 2) is the obvious fact that most, if not all, trauma patients have some element of hemorrhage, either on presentation or as an aftermath of trauma. Thus, carefree anticoagulation is not an option, but instead much be used in a judicious and patient-centered manner.

Rather than get caught in the revolving door of competing and contradictory statistics on incidence and prevalence of VTE in trauma patients, we will simply conclude that there is no disagreement that patient with trauma, or patients undergoing elective surgery (elective

trauma) all have an increased risk of venous clotting, and some will go onto life-threatening pulmonary embolism. Thus, all agree that trauma and elective surgery patients should all be considered for VTE prophylaxis, with the understanding the wide variability of factors that go into that medical decision-making. We will therefore focus on who, when, what, and how VTE prophylaxis should be administered.

Current Evidence-Based Guidelines for Estimating Risk of VTE and PE – Scoring Systems

There are several established risk scoring tools for VTE, but none of them have been developed specifically for the trauma patient. Therefore, while these are very helpful, good clinical judgment is also essential to decide how much risk each patient has for VTE. The Western Trauma Association recently published an excellent review [2] of this topic and recommend the simplified Greenfield scoring system. Published by Meisozo [3]

Table 3. Multiple logistic regression model for VTE prediction using Greenfield's risk factors.

Risk factor	Odds ratio	95% Confidence interval	*P* value
Four or more transfusions in first 24 h	2.60	1.64-4.13	<0.0001
Operation >2 h	1.80	1.14-2.85	0.012
GCS <8 for >4 h	2.13	1.28-3.54	0.003
Pelvic fracture	2.26	1.44-3.57	<0.0001
Age 40-59 y	1.70	1.10-2.63	0.017

Meizoso JP, Karcutskie CA 4th, Ray JJ, Ruiz X, Ginzburg E, Namias N, Schulman CI, Proctor KG. A simplified stratification system for venous thromboembolism risk in severely injured trauma patients. J Surg Res. 2017;207:138–144.

They also recommended the Trauma Embolic Scoring System (TESS) [4] shown in Table 3 and 4 from the original article.

TABLE 3. Significant Prediction Factors for VTE in Multivariate Model (n = 16,383)

Predictor	Coefficient	OR	*p*	95% CI	TESS Score
Age, y					
18–29	Referent	1.00			0
30–64	0.480556	1.62	0.039	1.03–2.55	1
≥65	0.827127	2.29	0.001	1.44–3.64	2
ISS					
1–9	Referent	1.00			0
10–16	1.42017	4.14	<0.001	2.32–7.38	3
17–25	1.62973	5.10	<0.001	2.79–9.33	3
>25	2.18105	8.86	<0.001	4.91–15.97	5
Preexisting obesity					
No preexisting obesity	Referent	1.00			0
Preexisting obesity	0.557299	1.75	0.041	1.02–2.98	1
Ventilation days					
No ventilation days	Referent	1.00			0
Ventilation days	1.88068	6.56	<0.001	4.33–9.94	4
Lower-extremity fracture					
No lower-extremity fracture	Referent	1.00			0
Lower-extremity fracture	0.925682	2.52	<0.001	1.72–3.70	2
Constant	−7.06655				

Hosmer-Lemeshow $p = 0.101$.
Area under the ROC curve, 0.89.

Surg. 2012;73(2):511–515.Rogers FB, Shackford SR, Horst MA, Miller JA, Wu D, Bradburn E, Rogers A, Krasne M. Determining venous thromboembolic risk assessment for patients with trauma: the Trauma Embolic Scoring System. J Trauma Acute Care

In the TESS scoring system, low risk is defined as a score of <3 is no risk, and no prophylaxis is needed, while a score of 3 to 6 is considered to be low risk, and mechanical prophylaxis is recommended, with pharmacologic prophylaxis recommended for scores of 7 and above, due to the patient being in the high risk category.

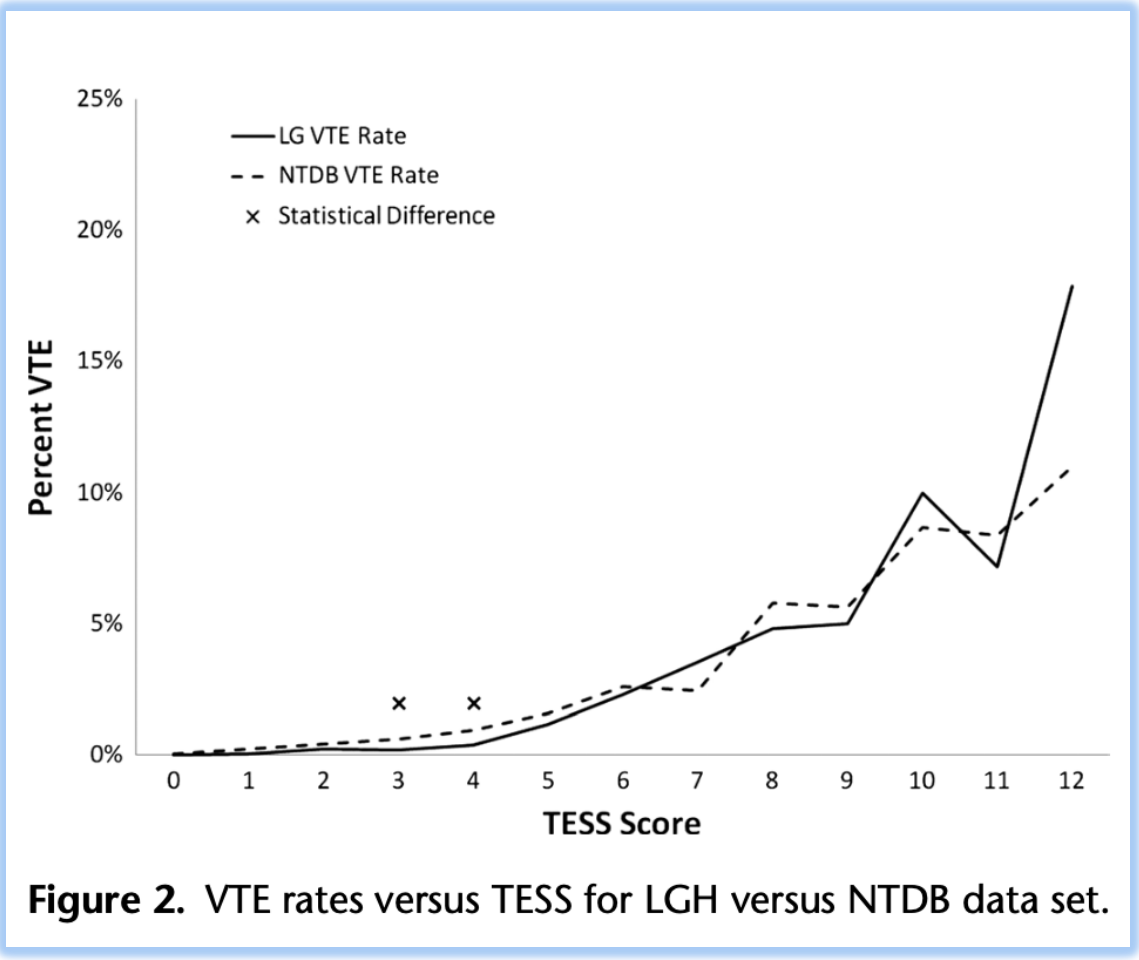

Figure 2. VTE rates versus TESS for LGH versus NTDB data set.

Surg. 2012;73(2):511–515.Rogers FB, Shackford SR, Horst MA, Miller JA, Wu D, Bradburn E, Rogers A, Krasne M. Determining venous thromboembolic risk assessment for patients with trauma: the Trauma Embolic Scoring System. J Trauma Acute Care

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Current Evidence-Based Guidelines for Estimating Risk of VTE and PE – General Considerations

It is now generally agreed that while aggressive surveillance programs for VTE will indeed find more patients with VTE, the benefit does not outweigh the cost, especially if most patients will be treated with pharmacologic and mechanical prophylaxis in any event. [5] [6] It is sometimes hard to stop and calculate scores, especially in the heat of battle, and thus there are some general guidelines and consensus recommendations as to which patients fall into low, medium, and high risk categories:

Low risk (no prophylaxis generally needed)

Ambulatory trauma patients with minor injuries and short hospital stays may not require pharmacologic prophylaxis, as a general rule. Thus, if the patient is in the hospital for a day or less, and is ambulatory to the bathroom, then they would fall into this category. Since they are ambulatory with only a short period of immobility, mechanical VTE prophylaxis may also be unnecessary or unwieldy for the patient to use. [7]

Moderate to Higher Risk (pharmacologic prophylaxis needed)

It is the combination of trauma and other risk factors that really drives the need for pharmacologic prophylaxis, and in many cases, combined with mechanical prophylaxis. Here are the recognized risk factors for VTE that when combined rapidly raise the risk of VTE and its complications: [1] [8] All of these risk factors paint the picture of a patient with multiple trauma requiring multiple methods of supportive care, combined with extended immobility.

Ventilator days >3

≥4 units of blood transfusions in the first 24 hours

>2 hour operation

Age ≥40 years, especially when combined with morbid obesity

Venous injury in Pelvis, Abdomen, or Lower Extremity

Lower extremity fracture with abbreviated injury score (AIS) ≥3

Pelvic fracture

Major operative procedure

Head injury with AIS ≥3 & or Glasgow Coma Score <8 for >4 hours

When should we delay initiation of pharmacologic prophylaxis?

There are times and conditions where the risk of excessive bleeding due to anticoagulants exceeds the risk of VTE and the benefit of pharmacologic VTE prophylaxis.

Active bleeding and hemodynamic instability are felt to be contraindications to anticoagulants. However, most bleeding stops within 24-36 hours and then the patient needs to be re-evaluated in regard to the risk of renewed bleeding versus the risk of VTE. Patients with lower grades of solid organ injury can safely undergo VTE prophylaxis, although individual factors and surgical judgment come into play for the more severe (Grade IV and V) solid organ injuries as to when to start pharmacologic VTE prophylaxis. [1]

Injury to the brain and spine are also conditions that call for careful evaluation and judgment due to the danger of increased bleeding in a confined space. As a general rule, once intracerebral bleeding has stabilized on repeat CT scan (24-48 hours is now the standard time for consideration of initiation of VTE prophylaxis), it is felt to be safe to begin VTE prophylaxis. [9],[10] Spinal trauma patients, once stable or post-operative, are still at some of the highest risks for VTE, and it is likewise felt to be safe to begin pharmacologic VTE prophylaxis at that stage of care. [1, 11 12]

In any event, in almost all cases mechanical thromboprophylaxis can and should be started immediately on most all trauma patients. (As noted above, for minor trauma with early ambulation, mechanical prophylaxis may not be practical). Mechanical prophylaxis has been shown to be both safe and additive to pharmacologic VTE prophylaxis, so that if pharmacologic VTE prophylaxis is delayed, there is at least some protection for the patient in the interim. [13], [14]

Selecting the right agent for pharmacologic thromboprophylaxis

There are typically three agents to choose from for both thromboprophylaxis and anticoagulation in trauma patients, each based upon the heparin molecule and each becoming progressively shorter in molecular length. Each has its own strengths and weaknesses, but you should be familiar with how to use and also when to avoid using each. Unfiltered Heparin (UFH) is the classic drug in use for many years and has the advantage of being reversible with Protamine. Thus, it may have the best utility in those patients with a higher risk of bleeding in which reversal may be necessary. UFH does have the side-effect of Heparin Induced

Thrombocytopenia (HIT) in some patients, and platelet counts should be monitored on a regular basis while it is being used. UFH is preferred in those with severe renal insufficiency (eg, creatinine clearance <20 to 30 mL/min). Low Molecular Weight Heparin (LMW) is now the most commonly used drug for VTE prophylaxis for trauma patients due to multiple randomized, controlled studies showing a benefit compared with UFH in reducing risk of VTE in trauma patients. [1, 9] However, there are two more recent solid analyses showing no significant differences between the two drugs when used in the right dosing and timing patterns. [15], [16], Thus, it is still not a clear picture that one is better than the other. Fondaparinux is typically used for VTE prophylaxis in patients with known or suspected HIT. Usage with insertion and removal of epidural catheters is contraindicated, and timing of resumption and catheter manipulation is critical. [1]

Dosage of UFH, LMW, and Fondaparinux for VTE prophylaxis

While there is still an area of uncertainty regarding which agent to use, there is even more lack of clarity on the appropriate dosage and frequency of administration to best use. This is due to whether the outcome measured is adequate anti-Xa levels versus the measured reduction in VTE incidence. [17] The summary quote from this large review of articles is something to note:

> **"Weight-based and high fixed-dose chemoprophylaxis regimens achieved target anti-Xa concentrations more frequently than standard fixed-dose regimens but were not associated with a reduction in VTE. Additionally, high fixed-dose approaches are associated with increased bleeding complications."**

Thus, rather than recommending a dosage for these drugs, we encourage the reader to review this extensive review and the recent AAST Consensus Statement [1] and decide for themselves and their trauma center.

Prophylactic IVC filters

Inferior vena cava filters (IVCF) are typically used when the patient is at a high risk of VTE and subsequent PE but cannot be anticoagulated. Over the past 40 years, use of IVCF has gone through several stages of: investigational use, to large applications of badly injured patients, to decreasing usage in the last few years. While clearly beneficial for patients with PE, especially in those who cannot be anticoagulated, many recent studies have failed to show significant differences in mortality for high-risk patients with and without prophylactic IVCF placement. IVCFs should be removed as soon as protection is no longer needed or when the patient can safely have chemoprophylaxis or therapeutic anticoagulation, to avoid long-term complications related to their presence. [1, 18, 19]

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