Venous Thromboembolism In Intensive Care Unit

R.J. Tamanna

1Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, (BSMMU), Shahbag, Dhaka.

Address for Communication
Dr. Rownak Jahan Tamanna, Department of Cardiology, Bangabandhu Sheikh Mujib Medical University, (BSMMU), Shahbag, Dhaka.
E-mail: rownakj@ yahoo.co.uk

Abstract
Venous thromboembolism (VTE) represents a spectrum of disease which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), a common complication in critically ill patients. VTE is difficult to diagnose, expensive to treat and occasionally lethal despite therapy. Therefore preventive measures are paramount. DVT and PE contribute significantly to morbidity and mortality associated with critical illness. But VTE remains an underestimated problem in ICU patients, despite the findings of many randomized controlled trials performed in the fields of DVT prophylaxis during the past few decades. This article reviews the risk of VTE in critical care patients, thromboprophylaxis and suggests strategies to reduce the burden of thrombo-embolic disease in critical care unit.

Key words: Venous thromboembolism, Intensive Care Unit.

Introduction
Venous Thromboembolism Deserves Attention Venous Thromboembolism is highly prevalent in critically ill patients. who deserves our attention. Objectively confirmed DVT rates varies from 13 to 31%. Among patients who died while in ICU, PE has been reported in 7 to 27% (mean 13%) of postmortem examination and PE was thought to have caused or contributed to death in 0 to 12% 6-12. DVT is considered to be the most important causative factor for PE. Approximately 90% of pulmonary emboli are thought to originate in lower extremity deep venous system. The overall incidence of DVT in ICU population ranges from 0 to 33%.

VTE in the Critical Care Unit: Risks:
a) Thromboembolic risk factors that may be acquired during ICU stay include:
- Immobilization, sepsis, mechanical ventilation, vasopressor use, haemodialysis, pharmacological paralysis, central venous line, insertion of femoral venous catheter, surgical procedures & failure to use thromboprophylaxis.

b) Thromboembolic Risk factors that predate the ICU admission includes:
- Advanced age, serious medical illnesses, prolonged pre-ICU hospital stay, previous VTE, recent surgery, sepsis, malignancy, burn, major trauma, cardiac and respiratory failure, AMI, immobilization & paralysis.

Although the clinical consequences of asymptomatic DVT detected by routine screening are uncertain, a recent study showed that patient documented to have DVT by Doppler ultrasound had a significantly greater frequency of subsequent PE during their hospitalization (11.5% vs 0%, p=0.01). Furthermore even small PE may be poorly tolerated by critically ill patients, many of whom have reduced cardio-respiratory reserve.22,23

Risk categories shown in Table 1

<table>
<thead>
<tr>
<th>Category</th>
<th>Low risk</th>
<th>Moderate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor surgery</td>
<td>(&lt; 30 min)</td>
<td>Major surgery</td>
<td>Major surgery</td>
</tr>
<tr>
<td>Major surgery</td>
<td>(&gt; 30 min with age less than 40)</td>
<td>Minor surgery</td>
<td>+hx of DVT or PE</td>
</tr>
<tr>
<td>Medical illness</td>
<td>(except MI, stroke)</td>
<td>Major trauma or burns</td>
<td>Acute MI or stroke</td>
</tr>
<tr>
<td>Wells and colleagues have developed a rapid seven question bedside assessment that is useful.24-27 (Table 2).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
- They designated a score of 4 or lower as pulmonary embolism unlikely.
- Wells Criteria: stratifies probability: High prob >6.0; Moderate prob 2.0-6.0; Low prob <2.0
Wells Clinical Bedside Scoring System for Suspected Pulmonary Embolism  Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical sign and symptoms of DVT (minimum leg swelling and pain with palpation of deep veins)</td>
<td>3</td>
</tr>
<tr>
<td>An alternative is less likely than PE</td>
<td>3</td>
</tr>
<tr>
<td>Heart rate greater than 100</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization or surgery in the previous 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT/PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>1</td>
</tr>
<tr>
<td>Malignancy (on treatment in last 6 month or palliative)</td>
<td></td>
</tr>
</tbody>
</table>

Most Common Symptoms and Signs among the 2454 Patients in the International Cooperative Pulmonary Embolism registry (ICOPER) (Table 3) 31

<table>
<thead>
<tr>
<th>Symptoms and Signs</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnoea</td>
<td>82</td>
</tr>
<tr>
<td>Respiratory rate &gt;20 per min</td>
<td>60</td>
</tr>
<tr>
<td>Heart rate &gt;100 bpm</td>
<td>40</td>
</tr>
<tr>
<td>Chest pain</td>
<td>49</td>
</tr>
<tr>
<td>Cough</td>
<td>20</td>
</tr>
<tr>
<td>Syncope</td>
<td>14</td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>07</td>
</tr>
</tbody>
</table>

The Geneva Point Score to Assess Pulmonary Embolism Prognosis (Table 4) 31

<table>
<thead>
<tr>
<th>Variable</th>
<th>Point score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>+2</td>
</tr>
<tr>
<td>Hypotension</td>
<td>+2</td>
</tr>
<tr>
<td>Prior DVT</td>
<td>+1</td>
</tr>
<tr>
<td>Heart failure</td>
<td>+1</td>
</tr>
<tr>
<td>Hypoaxaemia</td>
<td>+1</td>
</tr>
<tr>
<td>DVT on ultrasound</td>
<td>+1</td>
</tr>
</tbody>
</table>

VTE In ICU A Difficult Diagnosis

- VTE in ICU patients has unusual characteristics that makes its clinical diagnosis difficult.
- Because of body wall oedema or surgical dressings - signs and symptoms of DVT are often masked making a clinical diagnosis problematic.
- Physical examination is rarely helpful because DVT is generally asymptomatic.
- Moreover diagnosis is not always easy to confirm.
- DVT may not be suspected in ICU patient until the patient manifest symptoms of PE.
- Even when a pulmonary embolism leads to death, diagnosis is often difficult to confirm in a patient who has already been treated and ventilated for a pulmonary condition.
- The insensitivity of Doppler ultrasound and major difficulty in performing venography in ICU patient generally lead to blind anticoagulant prophylaxis.
- Neither D dimer levels nor tests of hypercoagulability (activated protein C resistance ratio, prothrombin 20210A gene mutation, levels of protein C, protein S, or antithrombin, antcardiolipin antibody titre and lupus anticoagulant) had any predictive value for DVT in critically ill patients.

Prevention of VTE in Critical Care

Mechanical Thromboprophylaxis in Critically Ill patients
- Classified as either static and dynamic.
- Consists of graduated compression stockings and pneumatic compression devices. 28
- Should systematically be used alone or in combination with pharmacological prophylaxis in ICU patients.

Potential benefits--
- Useful as an interim alternative measureuntill pharmacological prophylaxis can be safely introduced 28.
Venous Thromboembolism In Intensive Care Unit

- Act in a synergistic manner and provide additional protective benefit when combined with mainstay pharmacological prophylaxis.

Pharmacological prophylaxis options include: BRAUN WALD
- Unfractionated Heparin
- LMWH
- Fondaparinux
- Warfarin
- Aspirin confers a slight benefit.
- The oral direct thrombin inhibitor Ximelagarten appears promising when compared with enoxaparin or warfarin.

Inferior Vena Cavafilter (IVCF)

**IVC filter prevents PE not DVT.**

Indications
- Major haemorrhage that precludes anticoagulation.
- Recurrent pulmonary embolism despite well documented anticoagulation.

General approach to thromboprophylaxis in high risk patient

Routine thromboprophylaxis should be provided to critical patients based on an individual assessment of their bleeding and thrombosis risk.

**Major trauma, spinal cord injury, critical care unit admission High risk of bleeding**

Active bleeding, frank intracranial bleeding
Primary haemostasis not yet established
Yes
Mechanical thromboprophylaxis
IPC, GCS or IPC and GCS
Observe daily for bleeding risk
No
Pharmacological prophylaxis
Moderate TE risk: LMWH or LDH
High TE risk: LMWH or LMWH & Mechanical
High Risk of bleeding resolves
Yes
Pharmacological prophylaxis
Continue mechanical thromboprophylaxis
Consider screening with DUS day 4-7
Start pharmacological prophylaxis ASAP
Reassess daily for bleeding and thrombosis risk
After 1-2 weeks
If VTE risk continues, patient haemodynamically stable, consider warfarin (INR 2-3) for longer term prophylaxis in acute care and rehabilitation

Management strategy for acute PE based on risk stratification

**Acute pulmonary embolism**

**Risk stratification**

Clinical evaluation
Anatomical aspect of PE
Troponin, pro BNP, BNP
Right ventricular function

High risk
- Thrombolysis or embolectomy plus anticoagulation

Low risk
- Anticoagulation alone

**Thrombolytics**: tPA 100 mg as a continuous infusion over 2 hrs within 2 wks of onset of symptoms and sign.

**LMWH**: Enoxaparin treatment. 1 mg/kg SC bid, 1 mg/kg qd for CrCl <30.

Heparin: Bolus of 5000 to 10000 units of intravenous UFH, followed by a continuous intravenous infusion using nomogram based on weight. Most patients require at least 30,000 units/hrs.

**Intra venous unfractionated heparin "Raschke Nomogram"**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial heparin bolus</td>
<td>80 unit/kg bolus, then 18u/kg/hr</td>
</tr>
<tr>
<td>PTT&lt;35, (&lt;1.2X control)</td>
<td>80 unit/kg bolus, then increase by 4 unit/kg/hr</td>
</tr>
<tr>
<td>PTT 35-45 sec, (1.2-1.5X control)</td>
<td>40 unit/kg bolus, then increase by 2 unit/kg/hr</td>
</tr>
<tr>
<td>PTT 46-70sec (1.5-2.3X control)</td>
<td>No change</td>
</tr>
<tr>
<td>PTT 71-90 sec, 2.3-3X3 control</td>
<td>Decrease infusion rate by 2unit/kg/hr.</td>
</tr>
<tr>
<td>PTT &gt;90 sec (&gt;3Xcontrol)</td>
<td>Hold infusion for 1 hr then decrease infusion rate by 3 unit/kg/hr</td>
</tr>
</tbody>
</table>

**Outpatient anticoagulation:**

Warfarin: Initiated in hospital and transitioned to outpatient maintenance (3-4 days): Goal INR 2-3.

Length of therapy: DOTAVK study
- 3 month for DVT with PE
- 6 months or longer for high risk of recurrence
- 6 weeks for isolated DVT

**Optimal Duration And Intensity Of Anticoagulation**
- Therefore 6 months of full-intensity anticoagulation (INR 2-3) followed by indefinite-duration low intensity (INR 1.5-2) anticoagulation is recommended for all suitable patients with idiopathic PE or DVT.

**Complication and management**
- Haemorrhage
Heparin protamine sulphate (1mg/100 units of heparin slowly, 50 mg over 10 to 30 min).

WARFARIN SODIUM
Fresh frozen plasma, Human recombinant factor VIIa concentrate, Vit K parenterally
Cryoprecipitate
- Heparin induced thrombocytopenia

On Need of A Policy for Thromboprophylaxis
Following principles summarize our views about thromboprophylaxis in critical care patients.
✓ An essential component of the assessment of all ICU admissions should be a review of thromboembolic risks and consideration of thromboprophylaxis.
✓ With few exceptions, some form of thromboprophylaxis should be used in all ICU patients and should be commenced as soon as possible.
✓ Decisions regarding the initiation of prophylaxis and selection of specific method of prophylaxis should be individualized and based on each patient's risk for bleeding and thrombosis.
✓ In general anticoagulant based prophylaxis with LDH or LMWH is recommended.
LDH is appropriate for patient at low to moderate thrombosis risks, while LMWH is recommended for high-risk patients.
✓ Sequential prophylaxis, with the use of mechanical devices during initial high bleeding risks phase followed by anticoagulant prophylaxis should be considered in relevant critical care patients.
✓ Prophylaxis should be reviewed daily and changed if necessary, taking into consideration each patient's overall clinical status on that particular day.
✓ Prophylaxis should generally not be interrupted for procedures or surgery unless there is a particularly high bleeding risk.
✓ Routine screening of patient for asymptomatic DVT is not recommended since this strategy is neither effective, nor cost effective.
✓ However for selected high-risk patients who have not received adequate prophylaxis either before or during ICU admission, a single proximal Doppler ultrasound examination will identify patients who require a therapeutic intervention (ultrasound positive), or prophylaxis (ultrasound negative).
✓ At the time of discharge from critical care unit, further thromboprophylaxis recommendation should be included in transfer order.
✓ Each critical care unit should have a written prophylaxis policy that is updated periodically as new evidence emerges.

Conclusion
Venous thromboembolism is a common, potentially lethal complication of hospitalization for major trauma, SCI and other critical illnesses. Despite the availability of evidence-based prophylaxis recommendations for these groups, the use of this important patient safety interventions is frequently sub-optimal. Effective strategies to ensure that high-risk patient receive appropriate thromboprophylaxis include the creation of local written prophylaxis policy, and the use of preprinted orders or computer decision support system with mandatory fields addressing prophylaxis.

References


