VTE prophylaxis in critical care patients
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Risks

Careful study of VTE in critical care patients has lagged behind many other patient groups because of the marked heterogeneity among critically ill patients with respect to their thrombosis and bleeding risks as well as in their lengths of stay and survival, and because routine screening is either more difficult to perform or may be less reliable in these patients.

Deep-vein thrombosis (DVT) and pulmonary embolism (PE) contribute significantly to morbidity and mortality associated with critical illness. Among patients who died while in the ICU, PE has been reported in 7 to 27% (mean, 13%) of postmortem examinations, and PE was thought to have caused or contributed to death in 0 to 12% (mean, 3%). A clinical suspicion of PE was present in only 30% of these patients before death.

The vast majority of patients admitted to a critical care unit have a major risk factor for VTE, and most have multiple risk factors. Many of these thrombosis risk factors precede the ICU admission, while others develop during the course of ICU stay. Factors that have been reported to predict an increased risk of ICU-related VTE include the following: increased age, previous VTE, malignancy, major trauma, prolonged pre-ICU hospital stay, mechanical ventilation, use of paralytic drugs, APACHE (acute physiology and chronic health evaluation) score, need for emergency surgical procedures, insertion of a femoral venous catheter, and failure to use thromboprophylaxis. However, adequately powered studies using multiple logistic regression analysis to determine the independent predictors for thrombosis in critically ill patients have not yet been conducted, to our knowledge.

After admission to the ICU, only four prospective studies used routine screening with an objective diagnostic test to assess the incidence of DVT in critically ill patients who were not administered thromboprophylaxis. One was a prospective cohort study, and three were randomized trials; one study has been presented in abstract form only. Among these four prospective studies, the DVT rates varied between 13% and 31% in critically ill patients who did not receive prophylaxis. The most reliable event rate is provided by Fraisse et al, who used contrast venography to detect thrombosis. Although the clinical consequences of asymptomatic DVT detected by routine screening are uncertain, a recent study showed that patients 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 cardiorespiratory reserve.

Despite the paucity of critical care-specific data about thromboembolism, the risks of VTE in other patient groups, including surgical, trauma/spinal cord injury, and medical patients, are well established and are relevant to those in critical care units. Objectively confirmed DVT rates were found to be in the range of 10 to 80% for patients admitted to ICUs or following trauma, neurosurgery, or spinal cord injury in a recent systematic review.

Unsuspected DVT may already be present on admission to critical care units. When Doppler ultrasonography was performed in 729 patients at entry to the critical care unit in four case series, DVT was detected in 6.4%.
Thromboprophylaxis studies in critical care

Only three randomized thromboprophylaxis trials have been conducted in critical care patients that used routine screening with an objective diagnostic test for DVT.

The trial reported by Cade 20 years ago randomized 119 general ICU patients to treatment with either placebo or low-dose heparin (LDH), 5,000 U subcutaneously q12h. Serial fibrinogen leg scanning detected DVT in 29% and 13% of the placebo and LDH groups, respectively (relative risk reduction with LDH, 55%; p < 0.05). Rates of proximal DVT and bleeding were not reported.

In the second prophylaxis trial, LDH was compared to placebo in patients admitted to a medical ICU. Serial Doppler ultrasonography detected DVT in 31% of the 390 control patients and 11% of the 401 patients who were administered LDH (relative risk reduction with LDH, 65%; p = 0.001). PE was found in 5% and 2% of placebo-treated and heparin-treated patients, respectively. Proximal DVT and bleeding rates were not reported.

In the most recent randomized trial, 223 patients who were receiving mechanical ventilation for an exacerbation of COPD were assigned placebo or the low-molecular-weight heparin, nadroparin, until they were weaned from mechanical ventilation or for 21 days, whichever occurred sooner. After a mean prophylaxis duration of 12 days, contrast venography detected DVT in 28% of placebo-treated patients and in 15% of those receiving nadroparin (relative risk reduction with nadroparin, 45%; p = 0.045). Major bleeding occurred in 3% and 6% of the placebo and nadroparin groups, respectively (p = not significant).

Three additional, nonrandomized studies demonstrate high rates of DVT (12 to 33%) in ICU patients who received prophylaxis. Despite the use of thromboprophylaxis with LDH or intermittent pneumatic compression in 61% of 100 medical ICU patients, thrombosis was detected by twice-weekly Doppler ultrasound imaging in 33% of patients; of these, 28% were leg thrombi and the remaining 5% were upper-extremity thrombi related to central venous catheters. In a second study, 102 medical-surgical ICU patients underwent Doppler ultrasonography of the legs 4 to 7 days after ICU admission. Despite the use of thromboprophylaxis with LDH or intermittent pneumatic compression devices in 92% of these patients, 12% were reported to have DVT. Ibrahim et al screened 110 medical ICU patients with weekly duplex ultrasonography of the upper and lower extremities. Despite the use of LDH or sequential compression devices in all of the patients, 24% acquired DVT (19% in the leg veins and 5% in an upper extremity).
Prevention of VTE in Critical Care

In view of the high risk of thrombosis in critically ill patients, it is essential for critical care units to develop a policy for thromboprophylaxis. The three published trials of prophylaxis conducted in critical care patients suggest that both LDH and low-molecular-weight heparin are efficacious in reducing asymptomatic DVT. Extensive evidence from clinical trials in other patient groups, including the areas of acute medical illnesses, general surgery, neurosurgery, orthopedics, and trauma, provide important insights into effective and safe thromboprophylaxis methods that are likely to be relevant to critical care patients.

The following principles summarize our views about thromboprophylaxis in critical care patients:

1. An essential component of the assessment of all ICU admissions should be a review of thromboembolic risks and a consideration of thromboprophylaxis.

2. With few exceptions, some form of thromboprophylaxis should be used in all ICU patients, and should be commenced as soon as possible.

3. Decisions regarding the initiation of prophylaxis and selection of the specific method of prophylaxis should be individualized and based on each patient’s risks for bleeding and thrombosis. In general, anticoagulant-based prophylaxis with LDH or low-molecular-weight heparin is recommended because there is a substantially greater body of literature demonstrating its efficacy compared to mechanical prophylaxis and since the latter is often associated with poor compliance. LDH is appropriate for patients at low-to-moderate thrombosis risk, while low-molecular-weight heparin is recommended for high-risk patients since it is more efficacious in other high-risk groups such as those with major trauma or following orthopedic procedures. However, for patients at high risk for bleeding, mechanical prophylaxis with either graduated anti-embolic compression stockings alone or stockings combined with intermittent pneumatic compression devices is recommended until the bleeding risk decreases. Combined pharmacologic and mechanical methods of prophylaxis may provide greater protection than either alone, although this approach has never been tested rigorously in the ICU setting. Sequential prophylaxis, with the use of mechanical devices during an initial high bleeding risk phase followed by anticoagulant prophylaxis should be considered in relevant critical care patients.

4. Prophylaxis should be reviewed daily and changed, if necessary, taking into consideration each patient’s overall clinical status on that particular day.

5. Prophylaxis should generally not be interrupted for procedures or surgery unless there is a particularly high bleeding risk. The insertion or removal of epidural catheters should coincide with the nadir of the anticoagulant effect.

6. Routine screening of patients 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).

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<tr>
<th>Thrombosis Risk</th>
<th>Bleeding Risk</th>
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<tr>
<td>Moderate</td>
<td>Low: Low Dose Heparin 5000 U SC Twice a Day</td>
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<tr>
<td>High (Major trauma, spinal cord injury, major hip or knee surgery, major surgery for cancer)</td>
<td>LMWH 4000 – 6000 Anti-Xa once daily</td>
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Prophylaxis recommendations in critically ill patients
7. At the time of discharge from the critical care unit, further thromboprophylaxis recommendations should be included in the transfer orders.

8. Each critical care unit should have a written prophylaxis policy that is updated periodically as new evidence emerges.

9. Compliance with the prophylaxis policy should be enhanced with regular interactive education, the active involvement of a pharmacist on daily ICU rounds, preprinted orders, reminders, and computer decision support systems if possible.

10. Adherence to the thrombo-prophylaxis policy should be assessed using audits and, if sub-optimal, local quality improvement efforts should be undertaken.
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