Venous thromboembolism and its prevention in critical care

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Authors’ objectives
To determine the prevalence of deep venous thrombosis (DVT), the efficacy of thromboprophylaxis, and the rates of thromboprophylaxis use in critically ill patients.

Searching
MEDLINE and EMBASE were searched from 1966 to January 2002 for publications in the English language. The search terms were stated. The bibliographies of identified studies and the authors’ personal files were also searched.

Study selection
Study designs of evaluations included in the review
Studies assessing the prevalence of DVT had to be prospective, whereas those assessing the prevention of DVT had to be randomised controlled trials (RCTs). Patient audits that assessed compliance were also included.

Specific interventions included in the review
Studies of the prevention of DVT were eligible for inclusion. The included preventive studies compared heparin 5,000 U subcutaneously (sc) every 12 hours or nadroparin (about 70 anti-factor XA U/kg sc once daily) with placebo.

Participants included in the review
The inclusion criteria for preventive studies were not explicitly defined in terms of the participants. Studies assessing prevalence had to use patients who did not receive thromboprophylaxis. The included preventive studies were of critically ill medical, respiratory or surgical patients in intensive care units (ICUs).

Outcomes assessed in the review
Studies assessing the prevention of DVT had to use routine screening with objective diagnostic tests. Studies assessing the prevalence of DVT had to use routine screening with an objective diagnostic test for DVT, or investigate symptomatic patients with objective diagnostic strategies for DVT and pulmonary embolism (PE). Studies that assessed central venous catheter-related upper extremity venous thrombosis or small vessel thromboembolism in adults with respiratory distress syndrome or multisystem dysfunction were excluded.

The review assessed the prevalence of venous thromboembolism (VTE) at autopsy, the incidence of DVT and PE without thromboprophylaxis, DVT rates for thromboprophylaxis compared with placebo, and compliance with thromboprophylaxis. Studies assessing rates of DVT used fibrinogen leg scans, Doppler ultrasound or contrast venography. In studies of thromboprophylaxis, DVT was diagnosed using fibrinogen leg scan for 4 to 10 days, duplex ultrasonography on admission and every 3 days, or venography before 21 days.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the reviewers performed the selection.

Assessment of study quality
Study quality was assessed on the basis of study design, consecutive patient enrolment, blinding of interventions, blinding of outcome assessment and completeness of follow-up. The authors do not state how the papers were assessed for quality, or how many of the reviewers performed the quality assessment.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data
The information tabulated for studies of DVT prevalence included ICU setting, DVT screening test, quality criteria, noninvasive test confirmed by venography, follow-up for negative tests, sample size and DVT rate. The information on studies of VTE prevalence included ICU setting, numbers of ICU admissions and autopsies, deaths, and the numbers of PEs and fatal PEs. The data extracted from thromboprophylaxis studies were method of diagnosis, details of the intervention and control, and the percentage with DVT per intervention. The data extracted from studies of thromboprophylaxis use were ICU setting, the number of admissions and percentage use.

Methods of synthesis
How were the studies combined?
A narrative synthesis was undertaken.

How were differences between studies investigated?
Differences between the studies were discussed in the text of the review with respect to methodological problems.

Results of the review
Four prospective studies assessed DVT rates. Six studies assessed PE rates at autopsy. Three RCTs assessed thromboprophylaxis. Eleven patient audits assessed compliance.

VTE prevalence (6 studies; 436 autopsies).
The rates of PE at autopsy ranged from 7 to 27% (mean: 13%). PE was considered to cause or contribute to death in 0 to 12% (mean: 3%). In most cases (70%) the diagnosis of PE was not suspected before death.

DVT in patients not given thromboprophylaxis (3 RCTs and one prospective cohort; around 558 patients).
The rates of DVT ranged from 13 to 31%. In two studies the method used to select the patients was not adequately described, there was insufficient information on the patients' characteristics, positive fibrinogen leg scans were not confirmed by venography and negative scans were not followed up. One RCT was only published in abstract form and little information was given on the methods used. The only RCT (85 patients mechanically ventilated for chronic pulmonary disease) using contrast venography to diagnose DVT found rates of 28% and 8% for DVT and proximal DVT, respectively, with placebo.

Thromboprophylaxis (3 RCTs including one only reported in abstract form; 1,079 patients).
The RCTs found that low-dose heparin and low molecular weight heparin significantly reduced asymptomatic DVT in ICU patients compared with placebo. The DVT rates were 13% with low-dose heparin versus 29% with placebo (P<0.05) in one RCT (119 patients) and 11% with heparin versus 31% with placebo (P=0.001) in a second RCT (791 patients). The DVT rates were 15% with nadroparin versus 28% with placebo (P=0.45) in the third RCT (169 patients). One RCT found no significant difference in bleeding rates (6% with nadroparin versus 3% with placebo). The other two RCTs did not report bleeding rates.

Compliance with thromboprophylaxis (11 patient audits published since 1994, including 7 published only as abstract; 3,093 patients).
The rates of thromboprophylaxis use ranged from 33 to 100%. Only one study assessed compliance with appropriate prophylaxis.

Authors' conclusions
Only limited data were available on the epidemiology and prevention of VTE in critically ill patients.
CRD commentary
The review question was clear in terms of the study design, intervention and outcomes. The search was limited to English language publications listed in two databases, which may have resulted in the omission of other relevant studies. In addition, no attempt was made to locate unpublished studies, thus raising the possibility of publication bias. The methods used to select the studies, assess quality and extract the data were not described. Hence, the adequacy of the methods used cannot be judged. Quality was assessed using defined criteria and the results of the assessment were presented. Relevant information on the included studies was tabulated. A narrative synthesis was appropriate given the small number of studies. Methodological limitations of the studies were discussed in the synthesis.

The evidence presented appears to support the authors’ conclusions, although their recommendations were not based on the evidence in the review.

Implications of the review for practice and research
Practice: The authors state that all ICU patients should be assessed for their risk of VTE and that thromboprophylaxis should be used in most patients. They recommend that the agent should be selected on the basis of each patient's risk of thrombosis and bleeding, but that, generally, low-dose heparin or low molecular weight heparin should be used. Other recommendations are that: patients at high risk of bleeding should have mechanical prophylaxis until the risk of bleeding diminishes; prophylaxis should not be interrupted by procedures or surgery; when patients are transferred from the ICU, prophylaxis should be included in the transfer orders; and compliance should be encouraged and monitored.

Research: The authors state that further research is required to identify risk factors for VTE, and to determine the optimal thromboprophylaxis regimen and improve compliance.

Epidemiological areas requiring research include the prevalence of VTE on admission to ICU; ICU-acquired VTE; risk factors for VTE; accuracy of noninvasive and invasive diagnostic tests; ICU and hospital mortality and morbidity; and costs related to VTE. Areas of thromboprophylaxis requiring research include: comparison of mechanical and anticoagulant prophylaxis; comparison of low-dose heparin and low molecular weight heparin; safety of anticoagulant prophylaxis; effect of renal dysfunction on anti-XA levels and bleeding; effect of new antithrombotic agents like fondaparinux; effect of antithrombotic drugs on sepsis and organ dysfunction; and the effect of different strategies to improve compliance.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.