

Management of deep venous thrombosis in the emergency department

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SUMMARY

Task

The Centre for Clinical Effectiveness was asked to review research literature, focusing primarily on clinical guidelines, relevant to diagnosis and treatment of deep venous thrombosis in emergency department settings.

Conclusions and recommendations

The most comprehensive, authoritative and current evidence-based guidelines concerning deep venous thrombosis identified by the literature review are those published by the American College of Chest Physicians earlier this year (ACCP 2001). These guidelines are the most extensive of those identified by a considerable margin, incorporated a hand-search of the research literature in addition to a search of electronic databases, and provide decision-making rules in addition to general advice. Although they are not specific to emergency department settings many of their recommendations are directly relevant, especially those related to treatment.

Diagnosis is less well covered in ACCP 2001 but receives attention in other guidelines identified by the review (see, in particular, ICSI 1999 and EAST 1998).

The clinical guidelines that deal more directly with trauma and spinal injury (EAST 1998 and PVA 1997) are potentially more specific to emergency department practice but are less current and adopt a less rigorous approach to evidence evaluation. The AHRQ health technology assessment (AHRQ 2000) concerning prevention of venous thromboembolism after injury is relevant, current, and contains rigorous meta-analytic over-views of the available evidence in the area but is perhaps less clinically accessible than the other reports (see *Appendix 3*).

Feasibility

None of the identified reports provides an “off the shelf” solution for clinical practice guidelines suitable for diagnosis and treatment of deep venous thrombosis in the emergency department. The two most impressive documents (ACCP 2001, AHRQ 2000) will both require careful adaptation to extract the most relevant material. Nevertheless, sufficient evidence exists to provide an extensive framework for this task.

METHODOLOGY

Search Strategy

The Centre for Clinical Effectiveness defines the ‘best available evidence’ as that research we can identify that is least susceptible to bias. We determine this according to predefined NHMRC criteria (see *Appendix 3*).

First we search for systematic reviews, evidence-based clinical practice guidelines, or health technology assessments, and randomized controlled trials. If we identify sound, relevant material of this type, the search stops. Otherwise, our search strategy broadens to include studies that are more prone to bias, less generalizable, or have other methodologic difficulties. We include case-control and longitudinal cohort studies in our critical appraisal reports. While we cite observational and case series studies, and narrative reviews and consensus statements, in our reports we do not critically appraise them. Such studies can produce accurate results but they are generally too prone to bias to allow determination of their validity beyond their immediate setting.

Resources Searched

We searched the following databases and Internet websites:

- Cochrane Library CD-ROM
- Medline (OVID)
- CINAHL (OVID)
- SumSearch
- National Guidelines Clearinghouse
- NHS Centre for Reviews and Dissemination (NHS CRD)

Refinements, Searching & Reporting Constraints

We only included articles published since 1997, and applied the following inclusion and exclusion criteria:

Inclusion Criteria

- Focus on adult patients with deep venous thrombosis in the emergency department;
- Published primary studies;
- Published clinical practice guidelines (whether generated through evidence-based methods or through consensus)

Exclusion Criteria

- Study examined less than five patients
- Study was published in a language other than English
- Study presented data included in another published report

RESULTS:

Clinical Practice Guidelines

The search identified five relevant guidelines meeting the entry criteria (PVA 1997, EAST 1998, UMHS 1998, ICSI 1999, ACCP 2001). The guidelines are compared in Table 1, below. Brief summaries are included in Appendix 1.

Table 1. Comparison of guidelines.

Characteristic	ACCP 2001	ICSI 1999	EAST 1998	UMHS 1998	PVA 1997
Developers	American College of Chest Physicians	Institute for Clinical Systems Improvement	Eastern Association for the Surgery of Trauma	University of Michigan Health System	Paralyzed Veterans of America, Consortium for Spinal Cord Medicine
Category	Treatment, management, prevention	Diagnosis, treatment	Management, therapeutic effectiveness	Management	Management, prevention
Intended Users	Physicians	Physicians, nurses, physician assistants, allied health care practitioners	Physicians, nurses, physician assistants, allied health care practitioners	Physicians, nurses, pharmacists	Physicians, nurses
Target Population	Adult and paediatric candidates for antithrombotic therapy	Adult non pregnant patients, 18+ yrs, with lower extremity DVT, inpatients	Trauma patients aged 14 and older	Adults with suspected acute lower extremity DVT,	Individuals with spinal cord injury

		and outpatients.		pulmonary embolus, or both	
Endorsers	Not stated	Not stated	Eastern Association for the Surgery of Trauma	Not stated	American Spinal Injury Association, American Association of Spinal Cord Injury Nurses, American Academy of Physical Medicine and Rehabilitation, Department of Veterans Affairs, American Paraplegia Society
Outcomes Considered	Measures of antithrombotic efficacy in preventing TE, including quality-adjusted life expectancy including: rate of adverse events; rate of complications; mortality; survival; quality of life; short- and long-term morbidities; short- and long-term costs	Diagnosis: Positive predictive value, sensitivity, specificity of ultrasound in diagnosing DVT; positive and negative predictive values of Wells criteria for pretest probability of DVT. Treatment: Recurrent venous thromboembolism; major bleeding; death	Efficacy of treatment to prevent venous thromboembolism. Complications of prophylactic and treatment options. Diagnostic accuracy of ultrasound, impedance plethysmography, and venography to detect DVT.	Duration of clinical symptoms, length of hospital stay, recurrence rate of thrombosis, incidence of pulmonary embolism, mortality and complication rates	Morbidity and mortality due to complications of venous thromboembolism, complications of anticoagulant therapy
Methods to Collect Evidence	Searches of electronic databases; hand-searches of published literature	Searches of electronic databases	Searches of electronic databases	Searches of electronic databases	Searches of electronic databases
Methods to Analyse Evidence	Systematic review with evidence tables; decision analysis	Systematic review with evidence tables	Systematic review with evidence tables	Systematic review	Systematic review
Length	330 pages	53 pages	96 pages	10 pages	25 pages

Health Technology Assessments

The Agency for Healthcare Research and Quality (AHRQ 2000) completed a report in 2000 addressing prevention of DVT after injury. A summary is presented in Appendix 2.

Citations for Clinical Practice Guidelines and Health Technology Assessments

ACCP (2001). The sixth (2000) ACCP guidelines for antithrombotic therapy for prevention and treatment of thrombosis. *Chest* **119**

AHRQ (2000). *Prevention of venous thromboembolism after injury*. Agency of Healthcare Research and Quality, Rockville, MD, USA.

EAST (1998). Practice management guidelines for the management of venous thromboembolism in trauma patients In *EAST practice management guidelines for trauma*. Eastern Associate for the Surgery of Trauma, Allentown, PA, USA.

ICSI (1999). *Venous thromboembolism*. Institute for Clinical Systems Improvement, Bloomington, MN, USA.

PVA (1997). Prevention of thromboembolism in spinal cord injury. *J Spinal Cord Med* **20**: 259-283.

UMHS (1998). *Venous thromboembolism*. University of Michigan Health System, Ann Arbor, MI, USA.

Published Primary Literature

Eighteen articles were identified as meeting the entry criteria. Citations and abstracts are listed in Appendix 3. Given the availability of relevant clinical guidelines and a health technology assessment we did not perform further critical appraisal of the published primary literature.

APPENDIX 1 Clinical practice guidelines identified through the literature search

Introduction

The following summaries draw heavily on those provided by the National Guidelines Clearinghouse <www.guidelines.org>. They are intended to illustrate only the main recommendations of each set of guidelines. Readers are advised to consult the full documents for detailed findings.

Brief Summary 1

TITLE: Sixth ACCP consensus conference on antithrombotic therapy.

TABLE 1 CITATION: ACCP 2001

SOURCE(S): Chest 2001;119(1 Suppl)

RELEASE DATE: 2001

SUMMARY RECOMMENDATIONS:

The report provides comprehensive guidelines to general issues concerning antithrombotic therapy in a wide range of clinical situations.

The grade indicating the strength of each recommendation captures the strength of the methodology of supporting studies (A-C) and the trade-off between benefits and risks (1 or 2) (see *Definitions*, below).

Prevention of DVT and PE

Ischaemic stroke

Measures to reduce the risk of deep vein thrombosis (DVT) and pulmonary embolism (PE) are required in ischaemic stroke patients. It is strongly recommended that acute stroke patients with restricted mobility receive prophylactic treatment with low-dose subcutaneous (SC) heparin, LMWH, or heparinoids (*grade A1*). If anticoagulant therapy is contraindicated, use of intermittent pneumatic compression (IPC) devices is recommended (*grade C1*).

General prevention of venous thromboembolism post-surgery

It is recommended that aspirin is not used prophylactically in general surgery patients, because the measures below are more efficacious. Prophylactic measures must be based on the patient's specific clinical risk factors.

Low-risk general surgery patients

Early ambulation (*grade C1*)

Moderate-risk general surgery patients

Low-dose unfractionated heparin, low-molecular-weight heparin, intermittent pneumatic compression or elastic stockings (*grade A1*)

Higher-risk general surgery patients

Low-dose unfractionated heparin, or higher-dosage low-molecular-weight heparin (*grade A1*)

Higher-risk general surgery patients prone to wound complications, e.g. haematomas and infection

Intermittent pneumatic compression is an alternative recommended therapy (*grade A1*)

Very high-risk general surgery patients with multiple risk factors

Low-dose unfractionated heparin or low-molecular-weight heparin, combined with intermittent pneumatic compression (*grade B1*)

Selected very high-risk general surgery patients

Perioperative warfarin (goal INR 2.5; range, 2.0 to 3.0) (*grade A2*)

*Patients undergoing total hip replacement surgery*¹

Low-molecular-weight heparin, started 12 to 24 h after surgery or warfarin, started before or immediately after surgery (goal INR 2.5; range, 2.0 to 3.0); or adjusted-dose heparin, started preoperatively; possible adjuvant use of elastic stockings or intermittent pneumatic compression (*Low-dose unfractionated heparin, aspirin, dextran, and intermittent pneumatic compression reduce the overall incidence of venous thromboembolism but are less effective.*) (*grade A1*)

*Patients undergoing total knee replacement surgery*¹

Low-molecular-weight heparin, warfarin or intermittent pneumatic compression (*grade A1*)

Patients undergoing hip fracture surgery

Low-molecular-weight heparin or warfarin (goal INR 2.5; range, 2.0 to 3.0) started preoperatively or immediately after surgery (*grade A2*).

High-risk patients undergoing orthopedic surgery

Inferior vena cava filter placement, only if other forms of anticoagulant-based prophylaxis are not feasible, because of active bleeding; this should rarely be necessary (*grade C2*).

Patients undergoing intracranial neurosurgery

Intermittent pneumatic compression with or without elastic stockings. Low-molecular-weight heparin or low-dose unfractionated heparin may be acceptable alternatives (*grade A1*); consider intermittent pneumatic compression or EC, with low-molecular-weight heparin or low-dose unfractionated heparin for high-risk patients (*grade B1*).

Other clinical situations where prophylactic treatment is required

Patients with acute spinal cord injury

Low-molecular-weight heparin (*grade B1*); although elastic stockings and intermittent pneumatic compression appear ineffective when used alone, they may have benefit when used with low-molecular-weight heparin (*grade C1*), or if anticoagulants are contraindicated; during rehabilitation, consider continuation of

¹ Optimal duration of prophylaxis is uncertain; 7 to 10 days is recommended with low-molecular-weight heparin or warfarin; 29 to 35 days with low-molecular-weight heparin may offer additional protection

low-molecular-weight heparin or conversion to full-dose oral anticoagulation (*grade C2*).

Trauma patients with an identifiable risk factor for thromboembolism

Low-molecular-weight heparin, as soon as considered safe (*grade A1*); consider initial prophylaxis with intermittent pneumatic compression if administration of low-molecular-weight heparin will be delayed or is contraindicated (*grade C1*); in high-risk patients with suboptimal prophylaxis, consider screening with duplex ultrasonography or filter placement in the inferior vena cava (*grade C2*)

Patients with myocardial infarction

Low-dose unfractionated heparin or full-dose anticoagulation (*grade A1*); intermittent pneumatic compression and possibly elastic stockings may be useful when heparin is contraindicated (*grade C1*).

Patients with ischemic stroke and lower-extremity paralysis

Low-dose unfractionated heparin or low-molecular-weight heparin (*grade A1*); intermittent pneumatic compression with elastic stockings is also probably effective (*grade B1*).

General medical patients with clinical risk factors for venous thromboembolism, particularly those with congestive heart failure or chest infections

Low-dose unfractionated heparin or low-molecular-weight heparin (*grade A1*).

Patients with long-term indwelling central vein catheters

Warfarin (1 mg/d), or low-molecular-weight heparin, qd, to prevent axillary-subclavian venous thrombosis (*grade A1*).

Patients having spinal puncture or epidural catheters placed for regional anesthesia or analgesia

Low-molecular-weight heparin should be used with caution (*grade C1*).

Classification of level of risk (based on published data)

Risk Level	THROMBOEMBOLISM EVENT, %			
	Calf Vein Thrombosis	Proximal Vein Thrombosis	Clinical PE	Fatal PE
Low (Uncomplicated minor surgery in patients < 40 yr with no clinical risk factors)	2	0.4	0.2	0.002
Moderate (Any surgery in patients 40 to 60 yr with no additional risk factors; major surgery in patients < 40 yr with no additional risk factors; minor surgery in patients with risk factors)	10 to 20	2 to 4	1 to 2	0.1 to 0.4
High (Major surgery in patients > 60 yr without additional risk factors, or	20 to 40	4 to 8	2 to 4	0.4 to 1.0

40 to 60 yr with additional risk factors; patients with MI; medical patients with risk factors)				
Highest (Major surgery in patients > 40 yr with prior venous thromboembolism, malignant disease, or hypercoagulable state; patients with elective major lower extremity orthopedic surgery, hip fracture, stroke, multiple trauma, or spinal cord injury)	40 to 80	10 to 20	4 to 10	1 to 5

TREATMENT OF VENOUS THROMBOEMBOLIC DISEASE

Guidelines for Anticoagulation: Unfractionated Heparin

General

Patients with deep venous thrombosis (DVT) or pulmonary embolism (PE) should be treated with unfractionated IV heparin or adjusted-dose SC heparin. The heparin dosage should prolong the APTT to a range that corresponds to a plasma heparin level of 0.2 to 0.4 U/mL by protamine sulfate, or 0.3 to 0.6 U/mL by an amidolytic anti-Xa assay (*grade A1*).

For SC treatment with unfractionated heparin, give 250 U/kg q 12h to obtain an APTT within therapeutic range at 6 to 8 h.

Suspected venous thromboembolism (VTE)

Obtain baseline APTT, PT, CBC.

Check for contraindication to heparin therapy.

Give heparin 5,000 U IV; order imaging study.

Confirmed VTE

Rebolus with heparin 80 U/kg IV, and start maintenance infusion at 18 U/kg/h

Check APTT at 6 h, to maintain a range corresponding to a therapeutic heparin level.

Check platelet count daily.

Start warfarin therapy on day 1 at 5 mg; adjust subsequent daily dose according to the INR.

Stop heparin after 4 to 5 days of combined therapy, when INR is >2.0; range, 2.0 to 3.0.

Anticoagulate with warfarin for at least 3 mo (goal INR 2.5; range, 2.0 to 3.0)

Guidelines for Low-Molecular-Weight Heparin (LMWH)

LMWH can be substituted for unfractionated heparin in patients with DVT and in stable patients with PE. Treatment with heparin or LMWH should continue for at

least 5 days, overlapped with oral anticoagulation for at least 4 to 5 days (*grade A1*).

Suspected VTE

Obtain baseline APTT, PT, CBC.

Check for contraindication to heparin therapy.

Give unfractionated heparin 5,000 U IV.

Order imaging study

Confirmed VTE

Give LMWH (enoxaparin), 1 mg/kg SC q12h.

Start warfarin therapy on day 1 at 5 mg; adjust subsequent daily dose according to the INR.

Consider checking platelet count between days 3 and 5.

Stop LMWH after at least 4 to 5 days of combined therapy, when INR is >2.0 on 2 consecutive days.

Anticoagulate with warfarin for at least 3 mo (goal INR 2.5; range, 2.0 to 3.0).

Body Weight-Based Dosing of IV Heparin

Initial dosing: loading 80 IU/kg; maintenance infusion ¹: 18 IU/kg/h (APTT in 6 hr).

APTT, s ¹	Dose change, U/kg/h	Additional Action	Next APTT, hrs
<35 (<1.2 x mean normal)	+4	Rebolus with 80 IU/kg	6
35 to 45 (1.2 to 1.5 x mean normal)	+2	Rebolus with 40 IU/kg	6
46 to 70 ² (1.5 to 2.3 x mean normal)	0	0	6 ³
71 to 90 (2.3 to 3.0 x mean normal)	-2	0	6
>90 (>3 x mean normal)	-3	Stop infusion 1 h	6

Notes:

¹ The therapeutic range in seconds should correspond to a plasma heparin level of 0.2 to 0.4 IU/mL by protamine sulfate or 0.3 to 0.6 IU/mL by amidolytic assay. When APTT is checked at 6 h or longer, steady-state kinetics can be assumed.

² Heparin, 25,000 IU in 250 µL D5W. Infuse at rate dictated by body weight

through an infusion apparatus calibrated for low flow rates.

³During the first 24 h, repeat APTT every 6 h. Thereafter, monitor APTT once every morning unless it is outside the therapeutic range.

Oral anticoagulation should continue for at least 3 months (goal INR 2.5; range, 2.0 to 3.0). When oral anticoagulation is contraindicated or inconvenient, LMWH or unfractionated adjusted-dose heparin, to prolong the APTT to a time corresponding to a therapeutic plasma heparin level for most of the dosing interval, should be given (*grade A1*).

Duration of Treatment in Venous Thromboembolic Disease

Recommended length of treatment varies, subject to modification according to patient's age, comorbidity factors, likelihood of recurrence.

Most patients

Heparin or LMWH and warfarin can be started together; heparin or LMWH can be discontinued on day 5 or 6, if the INR has been therapeutic range for 2 consecutive days, continue warfarin for 3 to 6 months (*grade A1*).

Massive PE or severe iliofemoral thrombosis

Consider a longer period of heparin therapy (*grade A1*).

Reversible or time-limited risk factors (i.e., transient immobilization, trauma, surgical procedure, estrogen use) and a first event

Treat 3 to 6 months (*not graded*).

Heterozygous activated protein C (APC) resistance and a first event

Treat 3 to 6 months (*not graded*).

First episode of idiopathic deep vein thrombosis (DVT)

Treat at least 6 months (*grade A2*).

Recurrent venous thrombosis, or first event with a continuing risk factor (cancer, inhibitor deficiency states, antiphospholipid antibody syndrome)

Treat indefinitely (*grade C2*).

APC resistance (Factor V Leiden)

Probably treat indefinitely, if patients have recurrent disease, are homozygous for the gene, or have multiple thrombophilic conditions (**grade C2**).

Patients with symptomatic isolated calf vein thrombosis

Treat with anticoagulants for at least 3 months; if anticoagulation cannot be given, perform serial noninvasive studies of the lower extremity to assess for proximal extension of thrombus over the next 7 to 14 days (*not graded*).

Use of thrombolytic agents in the treatment of venous thromboembolism is highly individualized. In general, the best candidates are patients with hemodynamically unstable PE or massive iliofemoral thrombosis.

Filter placement in the inferior vena cava (IVC) is recommended for patients with:

- proximal vein thrombosis or PE, when anticoagulant therapy is contraindicated, or a complication of such therapy has developed
- thromboembolism recurring despite adequate anticoagulation
- chronic recurrent embolism and pulmonary hypertension
- concurrent surgical pulmonary embolectomy or pulmonary endarterectomy procedures

Oral Anticoagulants

Use of the INR in reporting prothrombin time (PT) has resulted in better control of oral anticoagulant therapy. Based on randomized trials and observational studies, a goal of 2.5 (range, 2.0 to 3.0) is recommended for most patients.

Recommended therapeutic range for oral anticoagulant therapy

INR GOAL 2.5; RANGE, 2.0 TO 3.0

Prophylaxis of venous thrombosis (high-risk surgery)

Treatment of venous thrombosis

Mechanical prosthetic valves (high risk)

Certain patients with thrombosis and the antiphospholipid syndrome

AMI (to prevent recurrent AMI)

INR GOAL 2.5; RANGE, 2.0 TO 3.0

Bileaflet mechanical valve in aortic position, normal sinus rhythm

Managing Patients with High INR Values (All recommendations are grade C2)

INR > therapeutic range but < 5.0, no clinically significant bleeding, rapid reversal not indicated for reasons other than surgical intervention

Lower the dose or omit the next dose; resume warfarin therapy at a lower dose when the INR approaches desired range

If the INR is only minimally above therapeutic range, dose reduction may not be necessary

INR > 5.0 but < 9.0, no clinically significant bleeding

Patients with no additional risk factors for bleeding: omit the next dose or two of warfarin, monitor INR more frequently, and resume warfarin therapy at a lower dose when the INR is in therapeutic range

Patients at increased risk of bleeding: omit the next dose of warfarin, and give vitamin K1 (1.0 to 2.5 mg orally)

Patients requiring more rapid reversal before urgent surgery or dental extraction: vitamin K1 (2 to 4 mg orally); if the INR remains high at 24 h: an additional dose of 1 to 2 mg

INR > 9.0, no clinically significant bleeding

Vitamin K1 (3 to 5 mg orally); closely monitor the INR; if the INR is not substantially reduced by 24 to 48 h, the vitamin K1 dose can be repeated

Serious bleeding, or major warfarin overdose (eg, INR > 20.0 requiring very rapid reversal of anticoagulant effect

Vitamin K1 (10 mg by slow IV infusion), with fresh plasma transfusion or prothrombin complex concentrate, depending upon urgency; vitamin K1 injections may be needed q12h.

Life-threatening bleeding or serious warfarin overdose

Prothrombin complex concentrate, with vitamin K1 (10 mg by slow IV infusion); repeat if necessary, depending upon the INR.

Continuing warfarin therapy indicated after:

Heparin, until the effects of vitamin K1 have been reversed, and patient is responsive to warfarin

DEFINITIONS

Grades of Recommendations:

A: Methods strong, results consistent - RCTs, no heterogeneity

1: Effect clear - clear that benefits do (or do not) outweigh risks

A: Methods strong, results consistent - RCTs, no heterogeneity

2: Effect equivocal - uncertainty whether benefits outweigh risks

B: Methods strong, results inconsistent - RCTs, heterogeneity present

1: Effect clear - clear that benefits do (or do not) outweigh risks

B: Methods strong, results inconsistent - RCTs, heterogeneity present

2: Effect equivocal - uncertainty whether benefits outweigh risks

C: Methods weak - observational studies

1: Effect clear - clear that benefits do (or do not) outweigh risks

C: Methods weak - observational studies

2: Effect equivocal - uncertainty whether benefits outweigh risks

CLINICAL ALGORITHM(S):

None provided

DEVELOPER(S):

American College of Chest Physicians - Medical Specialty Society

COMMITTEE:

ACCP Consensus Panel of Antithrombotic Therapy

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ENDORSER(S):

Not stated

GUIDELINE STATUS:

This is the current release of the guideline.

An update is in progress at this time and is scheduled for publication in October 2000.

GUIDELINE AVAILABILITY:

Electronic copies: Not available at this time.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook, IL 60062-2348. Available to order from the [American College of Chest Physicians Web site.](#)

COMPANION DOCUMENTS:

The following is available:

Fifth ACCP Consensus Conference on Antithrombotic Therapy (1998): summary recommendations. Northbrook, IL: ACCP, 1998. (Quick reference guide for clinicians).

Electronic copies: Available from the [American College of Chest Physicians Web site.](#)

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

PATIENT RESOURCES:

None available

Brief Summary 2

TITLE: Deep vein thrombosis.

TABLE 1 CITATION: ICSI 1999

SOURCE(S): Bloomington, MN: Institute for Clinical Systems Improvement; 1999 Jun. 53 p. [109 references]

ADAPTATION: Not applicable: Guideline was not adapted from another source.

RELEASE DATE: 1998 Jun (revised 1999 May)

SUMMARY RECOMMENDATIONS:

The recommendations for the management of deep vein thrombosis are presented in the form of an algorithm with 20 components, accompanied by detailed annotations.

See *Definitions*, below, for details of the classes of evidence (A-D, M, R, X) and conclusion grades (I-IV) used in this guideline.

Diagnosis (Conclusion Grade: I)

1. *Clinical suspicion of deep vein thrombosis (DVT)*

Determine the pretest probability of DVT based on the Wells criteria (see Appendix A in the original guideline document)

2. *Ultrasound*

Ultrasound should be the initial test done to confirm the diagnosis of DVT.

If DVT is strongly suspected and the ultrasound is negative, consider venography or repeat ultrasound in 3-7 days.

The combined use of clinical pretest probability and compression ultrasound is effective in confirming or excluding the diagnosis of DVT in the majority of cases. If clinical suspicion of DVT is high, and ultrasound is negative, consider further testing such as repeat ultrasound for suspected thrombosis or venography for suspected proximal thrombosis.

Complicated DVT/Co-morbidities

Patients with complicated DVT or certain co-morbidities may require therapy that is different than patients with uncomplicated DVT. This includes patients with suspected pulmonary embolism, contraindications to anticoagulation, known history of heparin induced thrombocytopenia (HIT), extensive iliofemoral thrombosis/phlegmasia, pregnancy, familial bleeding and clotting disorders, and severe renal dysfunction (creatinine clearance < 30 ml/mn).

Treatment

1. *Heparin (Conclusion Grade: I)*

The guideline work group feels that low molecular weight heparin (LMWH) is the preferred treatment for DVT when available. It is as safe and as effective as continuous unfractionated heparin. Suitable patients can be safely treated with LMWH in an outpatient setting. (Dosage recommendations are provided in the guideline document).

2. Warfarin

Warfarin therapy should be started at the same time as initiation of heparin unless thrombophilia is suspected, or the patient is pregnant.

The patient's medical history, medications and diet should be reviewed to be sure that they do not influence the patient's sensitivity to warfarin.

The work group strongly recommends the reporting of prothrombin time (PT) ratio as international normalized ratio (INR) with the use of a sensitive thromboplastin.

Heparin should be continued for at least 5 days after the initiation of warfarin therapy and until INR is above 2.0 for two consecutive days.

INR should be checked daily until in the therapeutic range for two days, then two or three times weekly for two weeks, then less often depending on the stability of INR results.

A therapeutic range of anticoagulation to keep the INR between 2.0-3.0 is recommended for patients with DVT. (Dosage recommendations are provided in the guideline document.)

3. Follow-up considerations (Conclusion Grade: II)

DURATION

Duration of anticoagulation varies. Recent studies suggest longer therapy imparts greater protection from recurrence.

- Transient risk (e.g. surgery, immobilization, estrogen use, trauma) 3-6 months
- Idiopathic or medical > 6 months
- Recurrent disease or continued risk factors: 12 months to lifetime.

ANTICOAGULATION MANAGEMENT

In the first several weeks of anticoagulation, INRs need to be checked at least weekly. After stabilization, the interval between INR checks can be increased from weekly to biweekly, up to but not beyond 4 weeks.

LONG-TERM COMPLICATIONS

- *Compression stockings.* Knee high 30-40 mmHg custom fitted, graded compression stockings help alleviate symptoms of edema and pain in patients who have postphlebotic syndrome. One report showed that graded compression stockings reduced the incidence of postphlebotic syndrome by 50%.
- *Malignancy.* In patients with known cancer, risk of DVT is increased. In patients who have idiopathic DVT there may be a cancer present at the time of presentation.
- *Thrombophilia.* Certain patients should be tested for thrombophilia. This testing should be done 2 weeks after discontinuation of anticoagulation. The work group recommends consideration be given to discussion with a thrombophilia expert.

- *Activity level.* There is no evidence that restricting activity is of benefit nor is there evidence to determine the activity level.

Assess appropriateness for outpatient treatment

Medical criteria for safe outpatient therapy include:

1. Uncomplicated DVT
2. Good cardiorespiratory reserve
3. No excessive bleeding risks
4. Creatinine clearance > 30 ml/mn

Other considerations include:

1. Patients need to be taught how to administer the drug and how to recognize complications
2. Daily INRs will be needed to guide the institution of warfarin therapy and the dose of warfarin will need to be adjusted to the INR.
3. Patients will need resources to answer questions and deal with problems.

Because of the need for an organized support system and time of day considerations for home care agencies many patients may need hospitalization during the first 24 hours to start therapy promptly.

Patient Education

- Instruction on appropriate techniques for self-injection or injection of the patient by a caregiver should be carried out by hospital, clinic or home health nurses.
- The patient should be instructed on the use and follow-up needed for warfarin therapy. This includes instructions on medication interactions with warfarin and communication issues with regard to INR PT testing and symptoms

DEFINITIONS

Evidence Grading System: Classes of Research Reports:

A. Primary Reports of New Data Collection:

Class A:

- Randomized, controlled trial

Class B:

- Prospective cohort study;
- Case-control study nested within a prospective cohort study

Class C:

- Non-randomized trial with concurrent or historical controls;
- Case-control study (except as above);
- Retrospective cohort study;
- Study of sensitivity and specificity of a diagnostic test;
- Population-based descriptive study

Class D:

- Cross-sectional study;

- Case series;
- Case reports;

B. Reports that Synthesize or Reflect upon Collections of Primary Reports

Class M:

- Meta-analysis;
- Decision analysis;
- Cost-benefit analysis;
- Cost-effectiveness study

Class R:

- Review article;
- Consensus statement;
- Consensus report

Class X:

- Medical opinion

Conclusion Grades:

Grade I: The evidence consists of results from studies of strong design for answering the question addressed. The results are both clinically important and consistent with minor exceptions at most. The results are free of serious doubts about generalizability, bias, and flaws in research design. Studies with negative results have sufficiently large samples to have adequate statistical power.

Grade II: The evidence consists of results from studies of strong design for answering the question addressed, but there is uncertainty attached to the conclusion because of inconsistencies among the results from different studies or because of doubts about generalizability, bias, research design flaws, or adequacy of sample size. Alternatively, the evidence consists solely of results from weaker designs for the question addressed, but the results have been confirmed in separate studies and are consistent with minor exceptions at most.

Grade III: The evidence consists of results from a limited number of studies of weak design for answering the question addressed. Evidence from studies of strong design is either unavailable because no studies of strong design have been done or because the studies that have been done are inconclusive due to lack of generalizability, bias, design flaws, or inadequate sample sizes.

Grade IV: The support for the conclusion consists solely of the statements of informed medical commentators based on their clinical experience, unsubstantiated by the results of any research studies.

CLINICAL ALGORITHM(S):

A detailed and annotated clinical algorithm is provided for the management of deep vein thrombosis.

DEVELOPER(S):

Institute for Clinical Systems Improvement (ICSI) - Private Nonprofit Organization

COMMITTEE:

Guideline Oversight Group (GOG)

GROUP COMPOSITION:

Work Group Members: Bruce Burnett, MD (Guideline Leader) (HealthSystem Minnesota) (Internal Medicine); Elizabeth Brackett, MD (HealthPartners) (Family Practice); Jeff Larsen, MD (River Falls) (Internal Medicine); Denise Dupras, MD (Mayo Clinic) (Internal Medicine); Vic Kelmenson, MD (HealthPartners) (Pulmonology); Mark Melin, MD (HealthSystem Minnesota) (Vascular Surgery); Peter Marshall, PharmD (HealthPartners) (Pharmacy); Laurie Ritz, RN (HealthSystem Minnesota) (Nursing); Jane Rodriguez (HealthPartners) (Health Education); Diane Davies (Pfizer) (Buyers Health Care Action Group); Jane Gendron (ICSI) (Measurement Advisor); Jane Erickson, RN (ICSI) (Facilitator).

ENDORSER(S):

Not stated

GUIDELINE STATUS:

This guideline has been updated by the guideline developer. NGC is in the process of reviewing the updated guideline and will post an updated NGC Summary to the site soon.

GUIDELINE AVAILABILITY:

Electronic copies: Available from the [Institute for Clinical Systems Improvement \(ICSI\) Web site](#).

Print copies: Available from ICSI, 8009 34th Avenue South, Suite 1200, Bloomington, MN 55425; telephone, (952) 814-7060; fax, (952) 858-9675; Web site: www.icsi.org; e-mail: icsi.info@icsi.org.

COMPANION DOCUMENTS:

None available

PATIENT RESOURCES:

Not stated

Brief Summary 3

TITLE: Practice management guidelines for the management of venous thromboembolism in trauma patients.

TABLE 1 CITATION: EAST 1998

SOURCE(S): EAST practice management guidelines for trauma. Allentown (PA): Eastern Association for the Surgery of Trauma; 1998 Jan 23. 66-162 [12 references]

ADAPTATION: Not applicable: Guideline was not adapted from another source.

RELEASE DATE: 1998.

SUMMARY RECOMMENDATIONS

This guideline covers the management of thromboembolism in trauma patients. It grades its recommendations according to defined levels that reflect both the quality of scientific evidence and the views of the authors (see *Definitions*, below).

The use of low-dose heparin (LDH) for deep vein thrombosis (DVT) and pulmonary embolus (PE)

The overall effectiveness of LDH for the prophylaxis of VTE in trauma patients remains unclear. Most studies show no effect of LDH on VTE. Most studies on the use of LDH in trauma patients suffer from severe methodologic errors, poor study design, and small sample size, suggesting the possibility of a type II statistical error.

Level I

LDH has little, if any, benefit as a sole agent for prophylaxis in the trauma patient at high risk for VTE.

Level II

For patients in whom bleeding could exacerbate their injuries (such as those with intracranial hemorrhage, incomplete spinal cord injuries, intraocular injuries, severe pelvic or lower extremity injuries with traumatic hemorrhage, and intra-abdominal solid organ injuries being managed nonoperatively), the safety of LDH has not been established, and an individual decision should be made when considering anticoagulant prophylaxis.

Level III

There may be a role for the use of LDH in combination with sequential compression devices (SCDs) in trauma patients at high risk for VTE, although there is little data in trauma patients to support such a combination.

The use of sequential compression devices (SCDs) in the prevention of DVT/PE

The use of SCDs worn on the lower extremity in patients at high risk for DVT and to reduce the rate of DVT is widely accepted, however, clinical studies demonstrating their effectiveness in trauma patients are few. While the exact mechanism of action of SCDs is not known, their effect is felt to be based on a combination of factors addressing stasis and hypercoagulability. Until these mechanisms are better studied and understood, answers to specific questions regarding the appropriate use of SCDs are forthcoming.

Level I

There are insufficient data to support Level I recommendations on this topic.

Level II

Trauma patients at high risk for DVT, such as head-injured patients or those with spinal cord injury and ortho-trauma patients such as pelvis or hip fracture patients, should receive SCDs for prophylaxis against DVT.

Level III

For patients in whom the lower extremity is inaccessible to place SCDs at the calf level, foot pumps may act as an effective alternative to lower the rate of DVT formation.

Patients who have surgery in lithotomy position or have evidence of significant weight loss should have precautions taken in positioning to prevent the occasional complications of peroneal nerve compression.

Prophylactic use of low molecular weight heparin (LMWH) for venous thromboembolism (VTE) in trauma patients:

There is a wealth of Class I data supporting the use of LMWH as VTE prophylaxis in orthopedic surgery. This literature is derived primarily from total hip and knee replacement patients. Overall, LMWH appears to be equivalent or superior to unfractionated heparin for prophylaxis in general surgery patients. There is now Class I data inferring that LMWH is superior to unfractionated heparin for prophylaxis in moderate to high risk trauma patients. However, selection of VTE prophylaxis in trauma patients can be a challenging balance between VTE risk and bleeding risk. Most data in many different types of patients confirm improved efficacy of LMWH with the same or even less bleeding risk compared to prophylaxis with unfractionated heparin. LMWH should be the standard form of VTE prophylaxis in trauma patients with complex pelvic and lower extremity injuries as well as spinal cord injuries. Class I data would imply that LMWH should be strongly considered for use in all high risk trauma patients when their bleeding risk is acceptable.

Level I

There are insufficient data to make Level I recommendations for general use of LMWH as VTE prophylaxis in trauma patients.

Level II

Low molecular weight heparin (LMWH) should be used for VTE prophylaxis in trauma patients with the following injury patterns:

- pelvic fractures requiring operative fixation or prolonged bed rest (>5 days);
- complex lower extremity fractures (defined as open fractures or multiple fractures in one extremity) requiring operative fixation or prolonged bed rest (> 5 days); and
- spinal cord injury with complete or incomplete motor paralysis.

Level III

Trauma patients with an ISS >9, who can receive anticoagulants, should receive LMWH as their primary mode of VTE prophylaxis.

The use of LMWH or oral anticoagulants for several weeks post-injury should be considered in patients who remain at high risk for VTE [i.e. elderly pelvic fracture

patients, spinal cord injury patients, patients who remain at prolonged bed rest (> 5 days), and patients who require prolonged hospitalization or rehabilitation].

Prophylactic use of arteriovenous (A-V) foot pumps for DVT/PE in trauma patients

Small clinical series in elective orthopaedic patients support the use of A-V foot pumps to prevent DVT. Only one clinical series in trauma patients compare A-V foot pumps to other standard techniques of DVT prophylaxis. The results from this series are not definitive in terms of the benefits of A-V foot pumps in preventing DVT. However, there is a theoretical advantage for the use of A-V foot pumps in high risk trauma patients who have a contraindication to heparin because of their injuries and who cannot have SCDs placed on lower extremities secondary to external fixators or large bulky dressings.

Level I

There are insufficient data to suggest Level I recommendations for this topic.

Level II

There are insufficient data to suggest Level II recommendations for this topic.

Level III

A-V foot pumps may be used as a substitute for SCDs in those high risk trauma patients who cannot wear SCDs due to external fixators or casts.

Prophylactic and therapeutic use of vena cava for PE:

There is virtually no Class I literature to support insertion of a vena cava filter in a trauma patient without an established DVT or PE. There is starting to accumulate a fair amount of Class II and III data which may support its use in "high-risk" trauma patients without a documented occurrence of a DVT or PE. At this time, we recommend consideration of IVC filter insertion in patients without a documented DVT or PE who meet high-risk criteria and cannot be anticoagulated.

Level I

There is a large body of evidence not reviewed in this section to support insertion of a vena cava filter for "traditional" indications in trauma patients. These indications include:

- Recurrent PE despite full anticoagulation;
- Proximal DVT and contraindications to full anticoagulation;
- Proximal DVT and major bleeding while on full anticoagulation;
- Progression of iliofemoral clot despite anticoagulation (rare).

Level II

"Extended" indications for prophylactic vena cava filter placement in a patient with established DVT or PE include:

- Large free-floating thrombus in the iliac vein or IVC;
- Following massive PE in which recurrent emboli may prove fatal;
- During/after surgical embolectomy.

Level III

Insertion of a "prophylactic" vena caval filter should be considered in patients without a DVT/PE if they:

- Cannot receive anticoagulation because of increased bleeding risk, and
- Have one or more of the following injury patterns:
 - Severe closed head injury (GCS < 8);
 - Incomplete spinal cord injury with para or quadriplegia;
 - Complex pelvic fractures with associated long-bone fractures;
 - Multiple long-bone fractures.

Anticoagulation in the treatment of established DVT/PE in trauma patients

Anticoagulation is a well-established treatment for DVT/PE. Current evidence suggests that a three to six-month period provides adequate treatment for a first time DVT/PE in a patient without a clotting abnormality. Those in whom the risk of recurrent VTE extends beyond six months may have anticoagulation extended indefinitely. In addition, those patients whose injuries preclude the use of anticoagulants because bleeding would exacerbate their injuries, should have consideration given to placement of a vena cava filter. Recent evidence also supports initial treatment of VTE with low molecular weight heparin as an outpatient.

Level I

For a documented DVT or PE in a patient with a contraindication to and/or complication of anticoagulation, vena caval interruption with a mechanical device is warranted.

Level II

- For a documented first episode of DVT/PE and no contraindication to receiving anticoagulation, at least six months duration of anticoagulation therapy is warranted.
- Patients with congenital deficiency of antithrombin III, protein C or protein S, or who, due to the nature of their injuries (such as those with spinal cord injury and permanent neurologic deficit), are at permanent high risk for DVT/PE or recurrent VTE, should receive anticoagulant therapy indefinitely. An alternative to anticoagulant therapy in these patients is vena caval interruption with a mechanical device.

Level III

Low molecular weight heparin administered subcutaneously at home may be substituted for unfractionated intravenous heparin in the hospital as the initial anticoagulant treatment for established DVT.

The treatment of asymptomatic calf DVT is controversial, and according to the literature, the rates of proximal extension of calf DVT vary from 0 to 30%. Patients with symptomatic calf DVT seem to be at higher risk of extension and should be treated for 3 to 6 months with anticoagulation. Asymptomatic calf DVT are particularly prevalent in trauma and joint replacement patients (20-40%), even with prophylaxis. The current evidence (Hyers et al.) indicates that patients with asymptomatic calf DVT should either undergo 3 months of anticoagulation or be followed with serial duplex ultrasound for 10 to 14 days to identify proximal extension of the thrombus

Ultrasonography for the diagnosis of DVT in trauma patients:

Numerous studies in the non-trauma literature attest to the overall accuracy of both Doppler and duplex ultrasound in the detection of DVT in the symptomatic patient. The overall accuracy of screening ultrasound in the asymptomatic patient is less clear. Many reports on the use of screening ultrasound, (either Doppler or

duplex), lack corroboration of accuracy with contrast venography. Of concern is that many of these studies report on PEs in the presence of negative screening ultrasound exams, leading one to speculate on the ability of duplex to detect clinically significant DVT.

Level I

Duplex ultrasound may be used to assess **symptomatic** trauma patients with suspected DVT without confirmatory venography.

Level II

There are insufficient data to suggest Level II recommendations for this topic.

Level III

- Hand-held Doppler ultrasound may be used to assess **symptomatic** trauma patients with suspected DVT. Confirmatory venography may be needed in patients who screen positive for DVT with Doppler ultrasound.
- Serial duplex ultrasound imaging of high-risk asymptomatic trauma patients to screen for DVT may be cost-effective and decrease the incidence of PE. However, the use of ultrasound in screening asymptomatic patients is burdened by a low sensitivity when compared to venography.

Plethysmography (IPG) for the diagnosis of DVT in trauma patients

Most studies demonstrate that IPG has a high sensitivity and specificity in the detection of proximal DVT in symptomatic patients. Its low sensitivity in detecting DVT in asymptomatic patients precludes its use as a surveillance technique in trauma patients at high risk for DVT. There are few specific studies that specifically address the role of IPG in the trauma patient.

Level I

There are insufficient data to suggest a standard for this topic.

Level II

There are insufficient data to suggest a guideline for this topic.

Level III

- IPG testing may be used in **symptomatic** patients to diagnose DVT. In those patients in whom the clinical suspicion for DVT is high, and who test negative for DVT on IPG, confirmatory ultrasound or venogram is recommended.
- The reported low sensitivity of IPG makes it unsuitable for screening of **asymptomatic** high risk trauma patients.

Venography for the diagnosis of DVT in trauma:

Although venography traditionally has been the diagnostic modality for DVT by which all other diagnostic modalities have been compared, logistical problems and complications associated with the procedure make it less appealing than other non-invasive diagnostic measures. Nevertheless, it still has a role in confirming DVT in trauma patients when diagnostic studies are equivocal, or possibly, as an outcome measure in clinical trials of thromboprophylaxis efficacy.

Level I

There are insufficient data to support a Level I recommendation on this topic.

Level II

- Ascending venography should be used as a confirmatory study in those trauma patients who have an equivocal IPG or ultrasound for DVT.
- Ascending venography should not be used to screen asymptomatic trauma patients at high risk for DVT. There may be a role for ascending venography in research studies on the incidence of DVT in trauma patients.

DEFINITIONS

The correlation between the evidence and the recommendations is as follows:

Level 1: This recommendation is convincingly justifiable based on the available scientific information alone. It is usually based on Class I data, however, strong Class II evidence may form the basis for a level 1 recommendation, especially if the issue does not lend itself to testing in a randomized format. Conversely, weak or contradictory Class I data may not be able to support a level 1 recommendation.

Level 2: This recommendation is reasonably justifiable by available scientific evidence and strongly supported by expert critical care opinion. It is usually supported by Class II data or a preponderance of Class III evidence.

Level 3: This recommendation is supported by available data but adequate scientific evidence is lacking. It is generally supported by Class III data. This type of recommendation is useful for educational purposes and in guiding future studies.

Class I evidence: Prospective randomized controlled trials (PRCTs) - the gold standard of clinical trials. Some may be poorly designed, have inadequate numbers, or suffer from other methodological inadequacies, and thus may not be clinically significant.

Class II evidence: Clinical studies in which the data were collected prospectively, and retrospective analyses which were based on clearly reliable data. These types of studies include observational studies, cohort studies, prevalence studies and case control studies.

Class III evidence: Most studies based on retrospectively collected data. Evidence used in this class includes clinical series, databases or registries, case reviews, case reports, and expert opinion.

Technology assessment: The assessment of technology, such as ICP monitoring devices, does not lend itself to classification in the above-mentioned format. Thus, for technology assessment, the devices were evaluated in terms of their accuracy, reliability, therapeutic potential, and cost-effectiveness.

CLINICAL ALGORITHM(S):

None applicable

DEVELOPER(S):

Eastern Association for the Surgery of Trauma (EAST) - Professional Association

COMMITTEE:

EAST Practice Parameter Workgroup for DVT Prophylaxis

GROUP COMPOSITION:

Names of Workgroup Members: Frederick B. Rogers, MD, FACS; Mark D. Cipolle, MD, PhD; James Cushman, MD; Paul Kearney, MD; Grace Rozycki, MD; and William H. Geerts, MD.

ENDORSER(S):

Eastern Association for the Surgery of Trauma (EAST) - Professional Association

GUIDELINE STATUS:

This is the current release of this guideline.

According to the guideline developer, an update is in progress.

GUIDELINE AVAILABILITY:

Electronic copies: Available from the [Eastern Association for the Surgery of Trauma Web site](#).

Print copies: Available from the EAST Guidelines, c/o Judith Schultz, Trauma Program Development Office, Lehigh Valley Hospital, Cedar Crest and I-78, PO Box 689, Allentown, PA 18105. Fax: (610) 402-1611.

COMPANION DOCUMENTS:

The following is available:

Practice Management Guidelines for Trauma: East Ad Hoc Committee on Guideline Development (Unabridged: Revised 1998 Mar 20).

Electronic copies: Available from the [Eastern Association for the Surgery of Trauma Web site](#).

An excerpt is also available:

J Trauma 1998 Jun;44(6):941-56; discussion 956-7.

PATIENT RESOURCES:

Not stated

Brief Summary 4

TITLE: Venous thromboembolism (VTE).

TABLE 1 CITATION: UMHS 1998

SOURCE(S): Ann Arbor (MI): University of Michigan Health System; 1998. 10 [6 references]

ADAPTATION: Not applicable: Guideline was not adapted from another source.

RELEASE DATE: 1998 Jun

SUMMARY RECOMMENDATIONS:

This guideline provides a general, practical, overview of clinical issues related to venous thromboembolism. The evidence supporting the recommendations is graded according to a hierarchy of evidence developed by the authors (see *Definitions*, below).

Initiate treatment immediately.

Patients without contraindications to heparin should begin full-dose heparinization at once [*evidence: A**]. If PE is clinically likely, initiation should not await testing; if only DVT is suspected and testing will be prompt, initiation may await testing. Therapeutic levels should be achieved as quickly as possible. Warfarin should be initiated on day 1 of treatment, after heparin loading is complete.

Diagnosis of venous thromboembolism

Clinical findings uncertain.

Symptoms and signs are not adequately sensitive or specific for diagnosis or exclusion of DVT.

Lower extremity DVT

Venous duplex imaging is the standard for diagnosis.

Pulmonary embolism

Lab tests are inadequate. ECG and laboratory (including blood gas determination) are not adequately sensitive or specific to diagnose or exclude PE.

Diagnosis requires a combination of clinical likelihood estimation plus ventilation-perfusion (V/Q) scanning.

Pulmonary angiography is indicated when the clinical likelihood estimate yields a reasonable likelihood of PE but V/Q results are neither high probability nor normal and lower extremity Doppler studies are negative, and when the risk of complications of treatment is high.

Treatment

Heparin

Low molecular weight heparin (LMWH) preferred for DVT. LMWH is preferred over unfractionated heparin (UFH) for treatment of DVT for both safety and cost reasons [*evidence: A**]. **PE should be treated with full-dose IV UFH** at this time.

Outpatient use of LMWH.

LMWH is appropriate for selected patients to use at home after initial brief hospital admission and stabilization. It may be appropriate for use without admission, but patient selection criteria for such use are not yet defined.

Unfractionated heparin.

If UFH is used, it should be initiated and dosed in a structured manner, in order to achieve therapeutic levels quickly and without excessive adjustment of dosing [evidence: A*].

Minimum time period.

Heparin must be continued for at least five days in order to minimize the risk of extension of thrombosis or occurrence or recurrence of embolism [evidence: B*].

Warfarin.

Patients should begin warfarin on day one of heparin therapy after heparin loading is complete, and INRs must be in the 2-3 range before discontinuation of heparin [evidence: A, B*].

If heparin contraindicated.

Patients who are not candidates for heparin anticoagulation due to risk of major bleeding or to drug sensitivity should have an inferior vena cava filter placed to prevent pulmonary embolization [evidence: B*].

If warfarin contraindicated.

Patients who can receive heparin but cannot take warfarin (e.g. during pregnancy) may be anticoagulated for several months with full-dose subcutaneous heparin [evidence: A*], preferably LMWH.

DEFINITIONS

Levels of evidence for the most significant recommendations:

- A. Randomized controlled trials
- B. Controlled trials, no randomization
- C. Observational trials
- D. Opinion of expert panel

CLINICAL ALGORITHM(S):

An algorithm is provided for the diagnosis of pulmonary embolism.

DEVELOPER(S):

University of Michigan Health System (UMHS) - Academic Institution

COMMITTEE:

Venous Thromboembolism Guideline Team

GROUP COMPOSITION:

Team Leader: Lee Green, MD, MPH.

Team Members: William Fay, MD; Van Harrison, PhD; Mary Kleaveland, MD; Richard Wahl, MD; Thomas Wakefield, MD; John Weg, MD; David Williams, MD.

UMHS Guidelines Oversight Team: Connie Standiford, MD; Lee Green, MD, MPH; Van Harrison, PhD; Christopher Wise, PhD.

ENDORSER(S):

Not stated

GUIDELINE STATUS:

This is the current release of the guideline. An update is not in progress at this time.

GUIDELINE AVAILABILITY:

Electronic copies: Available for download (in Portable Document Format [PDF]) from the [University of Michigan Health System Web site](#).

COMPANION DOCUMENTS:

None available

PATIENT RESOURCES:

Not stated

Brief Summary 5

TITLE: Prevention of thromboembolism in spinal cord injury.

TABLE 1 CITATION: PVA 1997

SOURCE(S): J Spinal Cord Med 1997 Jul;20(3): 259-83 [60 references]

ADAPTATION: Not applicable: Guideline was not adapted from another source.

RELEASE DATE: 1997 Feb

SUMMARY RECOMMENDATIONS:

This report provides guidelines for the specific clinical situation of prevention of thromboembolism in spinal cord injury. Evidence was graded according to a specific evidence hierarchy and the level of expert consensus was also rated (see *Definitions*, below)

Mechanical Methods of Prophylaxis

Whenever possible, compression hose or pneumatic devices should be applied to the legs of all patients for the first 2 weeks following injury. External pneumatic compression devices may be knee or thigh length with single or sequential chamber compression. Combining them with other antithrombotic agents may enhance the effectiveness of these devices. (*Scientific evidence-level I; expert opinion-strong consensus*).

During every nursing shift, compression modalities should be inspected for proper placement and the underlying skin examined for evidence of abrasions, ecchymoses, or injury. In patients whose thromboprophylaxis has been delayed for more than 72 hours after injury, tests to exclude the presence of leg thrombi should be performed prior to applying compression devices. (*Scientific evidence-NA; expert opinion-strong consensus*).

Vena cava filter placement is indicated in SCI patients who have failed anticoagulant prophylaxis or who have a contraindication to anticoagulation, such as active or potential bleeding sites not amenable to local control (e.g. the central nervous system, gastrointestinal tract, or lungs). Filters should also be considered in patients with complete motor paralysis due to lesions in the high cervical cord (C2, C3), with poor cardiopulmonary reserve, or with thrombus in the inferior vena cava despite anticoagulant prophylaxis. However, filter placement is not a substitute for thromboprophylaxis, which should be commenced as soon as feasible. (*Scientific evidence-level IV; expert opinion-moderate consensus*).

Anticoagulant prophylaxis

Anticoagulant prophylaxis with either low molecular weight heparin (LMWH) or adjusted dose unfractionated heparin should be initiated within 72 hours after SCI, provided there is no active bleeding, evidence of head injury, or coagulopathy. (*Scientific evidence-one level II study; expert opinion-strong consensus*).

Anticoagulants should be continued for 8 weeks in patients with uncomplicated complete motor injury and for 12 weeks or until discharge from rehabilitation for those with complete motor injury and other risk factors (e.g. lower limb fractures, a history of thrombosis, cancer, heart failure, obesity, or age over 70). This recommendation also applies to those with inferior vena cava filters, because such persons remain at risk for deep vein thrombosis. (*Scientific evidence-level IV studies; expert opinion-strong consensus*).

Prophylaxis based on patient stratification for risk

Patients with complete motor and/or incomplete nonfunctional motor involvement should be on prophylactic measures for venous thromboembolism as early as possible. (*Scientific evidence-level I; expert opinion-strong consensus*).

Spinal cord injured patients with functional motor movements or with no significant motor/neurological deficits should be on prophylactic measures as early as possible. (*Scientific evidence-level I; expert opinion-strong consensus*).

The duration of the prophylaxis for thromboembolism should be individualized, depending on the need, medical condition, functional status, support services, and risk of the patient. (*Scientific evidence-level II; expert opinion-strong consensus*).

Reinstitution of prophylactic measures should be considered in chronic SCI patients if they are immobilized with bed rest for a prolonged period of time, are readmitted for medical illnesses or altered medical conditions, or undergo surgical procedures. (*Scientific evidence-level I; expert opinion-strong consensus*).

Failure of prophylaxis

In symptomatic patients, ultrasound of the lower extremities and/or ventilation/perfusion lung scanning should be performed. If clinical suspicion is strong but the tests are negative or indeterminate, venography of the legs and/or pulmonary angiography should be obtained. (*Scientific evidence-level I; expert opinion-strong consensus*).

Exercise, passive movement, and early mobilization

Early mobilization and passive exercise should be initiated as soon as the patient is medically and surgically stable. These activities should be coordinated with other preventative modalities. With documented DVT, mobilization and exercise of the lower extremities should be withheld 48 to 72 hours until appropriate medical therapy is implemented. (*Scientific evidence-NA; expert opinion-strong consensus*).

Educational priorities for health care professionals

Health care professionals should be aware of the signs and symptoms of DVT and should perform physical assessment to detect this complication. Appropriate prophylactic measures, including application of mechanical devices and administration of anticoagulant agents, should be implemented. Patients, family members, and significant others should be educated in the recognition and prevention of DVT. (*Scientific evidence-NA; expert opinion-strong consensus*).

DEFINITIONS

Hierarchy of scientific evidence:

- I. Large randomized trials with clear-cut results
- II. Small randomized trials with uncertain results
- III. Nonrandomized trials with concurrent or contemporaneous controls
- IV. Nonrandomized trials with historical controls
- V. Case series with no control

CLINICAL ALGORITHM(S):

None provided

DEVELOPER(S):

Paralyzed Veterans of America (PVA) - Private Nonprofit Organization
Consortium for Spinal Cord Medicine (CSCM) - Private Nonprofit Organization

COMMITTEE:

Guideline Development Panel

GROUP COMPOSITION:

The panel was composed of three specialists in internal medicine, two in physical medicine and rehabilitation, and one specialist each in nursing, physical therapy, pharmacology and radiology, and a methodologist.

Names of Panel Members: David Green, MD, PhD (Chair); Andrea K. Biddle, PhD, MPH (Methodologist); Victoria Fahey, RN, MSN; Geoffrey A. Gardiner, Jr., MD; Russell Hull, MD; Michael Y. Lee, MD; Geno J. Merli, MD; Kurt Mossberg, PT, PhD; Graham Pineo, MD; Kristjan Ragnarsson, MD (Steering Committee Liaison); David Rosenbloom, Dpharm; Kit N. Simpson, PhD (Methodologist); Jonathan R. Strayer, MD

ENDORSER(S):

American Spinal Injury Association (ASIA) - Disease Specific Society
American Association of Spinal Cord Injury Nurses (AASCIN) - Professional Association
American Academy of Physical Medicine and Rehabilitation - Medical Specialty Society
Department of Veterans Affairs - Federal Government Agency [U.S.]
American Paraplegia Society - Disease Specific Society

GUIDELINE STATUS:

This is the current release of the guideline.

GUIDELINE AVAILABILITY:

Electronic copies: Available from the [Paralyzed Veterans of America Web site](#).
Print copies: Single copies available from the Consortium for Spinal Cord Medicine, Clinical Practice Guidelines, 801 18th Street, NW, Washington, DC 20006.

COMPANION DOCUMENTS:

None available

PATIENT RESOURCES:

None available

APPENDIX 2 Health technology assessment identified through the literature search

Prevention of Venous Thromboembolism After Injury

The following summary of a health technology assessment performed by the Agency for Healthcare Research and Quality (AHRQ) comes from online material available at their website (see below).

Overview

Venous thromboembolism (VT) is a major national health problem, claiming 50,000 lives and resulting in 300,000 to 600,000 hospitalizations annually in the United States. VT presents in two forms:

- Deep venous thrombosis (DVT).
- Pulmonary embolism (PE).

Injured patients are at high risk for VT because of changes in coagulation and thrombolysis mechanisms that are induced by trauma.

Methods for preventing VT include, among others:

- Sequential compression devices (SCDs).
- Low-dose heparin (LDH).
- Low-molecular-weight heparin (LMWH).
- Vena caval filters (VCFs).
- Combinations of these.

All of these methods are associated with contraindications and morbidity. Therefore, selecting the appropriate method for the appropriate trauma patient is important. The difficulty of selecting the appropriate prophylaxis is in part a result of the inconclusiveness of the relevant trauma literature. This allows wide variability among physician practices and prevents consistency in quality of care.

With this report, we evaluate and meta-analyze the existing data in the literature to produce scientific answers in controversial areas related to this topic. We also identify research gaps in areas in which the scientific evidence is absent or minimal. Also, we hope to assist interested organizations in producing relevant guidelines and directing future research.

Reporting the Evidence

A panel of 17 technical experts, consisting of national authorities in the field and representing the academic, private, and managed care sectors, was formed to assist in the design and execution of the project. Important questions on the topic were distributed to the experts, who ranked them in order of importance. After two conference calls, several refined key questions were developed:

- What is the best method of prevention of VT after injury?
- Which groups of trauma patients are at high risk of developing VT?
- What is the best method of screening for VT in trauma patients?
- What is the role of VCF in preventing PE after injury?

The panel decided to use data restricted to trauma patients only and avoid extrapolation of conclusions from nontrauma patients to the trauma population. Defining "the trauma patient" was difficult. The panel decided to exclude elderly patients with injuries following low-energy trauma (e.g., hip fractures after ground-level falls) from consideration. We subsequently developed causal pathways for each key question. We believed that it was important to report on the rates of DVT and PE from combined literature data because these rates varied widely among studies.

We summarized the existing evidence on all trauma patients included in the available literature as well as that on individual trauma patient groups (i.e., orthopedic trauma, neurosurgical trauma, minor trauma) when data were available. We evaluated the quality of studies included in our analysis using previously published methods of determining quality scores. We entered all data in a computerized database specifically designed for this project.

Methodology

We searched three literature databases:

- MEDLINE (1966-January 31, 1999).
- EMBASE (1980-January 31, 1999).
- The Cochrane Controlled Trials Register (1980-January 1999).

After a broad initial search, we performed multiple literature searches tailored to each question. Finally, we identified a total of 4,093 titles, which were screened according to specific inclusion and exclusion criteria by three independent medical reviewers. The third reviewer assisted in case of disagreements.

After screening, 2,437 titles were accepted for abstract review. The three reviewers screened all abstracts against specific criteria; 227 of these were accepted for complete review. Of 225 articles retrieved, 73 were accepted for meta-analysis.

We designed forms to extract relevant data on study design and quality, methods used, risk factors, and outcomes. Two reviewers extracted data, which were cross-examined by the third. Discrepancies were resolved in meetings among all three reviewers. A random-effects model was used for all pooled results.

We first evaluated the reported incidence of DVT and PE in trauma patients. We extracted these rates from all studies as well as from studies grouped together by study design (randomized, nonrandomized comparative cohorts, single cohort), method of VT diagnosis (routine screening or based on clinical suspicion), use of VT prophylaxis (yes or no), and type of trauma patients (i.e., all trauma, orthopedic trauma, neurosurgical trauma, minor trauma).

We addressed the question of the best method of VT prophylaxis in three ways:

- We examined the incidence of DVT and PE after combining groups of patients from different randomized trials who received LDH or LMWH or mechanical prophylaxis (MP) or no prophylaxis.
- We performed a meta-analysis of randomized controlled trials (RCTs) evaluating the same methods of prophylaxis.
- We performed a meta-analysis of RCTs and non-RCTs, evaluating the same methods of prophylaxis.

This last meta-analysis, although methodologically weak, was performed because the number of RCTs available for the first meta-analysis was limited.

We addressed the question of risk factors for developing VT by performing a meta-analysis on studies (RCT and non-RCT) that used risk factors as either dichotomous variables (e.g., age greater or less than 55) or continuous variables (e.g., age, without specifying a particular age cutoff point). We evaluated six dichotomous risk factors (gender, head injury, long-bone fracture, pelvic fracture, spinal fracture, and spinal-cord injury) and

three continuous risk factors (age, Injury Severity Score [ISS], and units of blood transfused).

We were unable to address the question about methods of screening for VT using the current literature data. Only three studies addressed this issue in trauma patients, and each compared different methods of screening. The data could not be combined for analysis.

We addressed the question about VCF by combining studies that included patients treated with VCF and patients without VCF and estimating the rates of PE in the two groups. None of these studies was an RCT. Other outcome parameters relevant to VCF placement, such as related complications, long-term outcome, or appropriate population to be treated with this modality, could not be extracted from the limited data available.

We also performed supplemental analyses on the two most frequent complications related to prophylactic heparin administration—bleeding and thrombocytopenia—as well as on the incidence of fatal PE and the length of hospital stay in patients who develop VT. Finally, we developed a cost-effectiveness model.

Findings

The main findings from this evidence report include the following:

- The reported incidence of DVT and PE varies widely among different studies depending on study design, type of trauma patients included, and methods of screening and prophylaxis. The pooled rates of DVT and PE across all studies are 11.8 percent (95 percent confidence interval [CI]: 0.104, 0.131) and 1.5 percent (95 percent CI: 0.011, 0.018), respectively.
- Only a few RCTs address methods of VT prophylaxis in trauma patients. Most of these studies use different methods. Combining the limited data from studies using the same methods produces small sample sizes.
- LDH is not statistically superior to no prophylaxis in preventing VT after injury (odds ratio [OR]: 0.965, 95 percent CI: 0.353, 2.636). This conclusion is based on a meta-analysis of four RCTs with a total of 219 patients.
- MP is not statistically superior to no prophylaxis in preventing VT after injury (OR: 0.769, 95 percent CI: 0.265, 2.236). This conclusion is based on a meta-analysis of three RCTs with a total of 234 patients.
- The addition of non-RCTs to the meta-analyses of studies examining DVT rates in trauma patients receiving LDH vs. no prophylaxis or MP vs. no prophylaxis does not change these conclusions.
- Comparison of LMWH vs. LDH shows no statistically significant difference between the two methods in preventing PE (OR: 3.010, 95 percent CI: 0.585, 15.485). This conclusion is based on a meta-analysis of three studies reporting on the incidence of PE (two RCTs and one non-RCT, total number of patients: 355). Although the difference in PE rates is not statistically significant, the limits of the 95 percent CI for this result are very wide.
- Three RCTs (one of them with the highest possible quality score) showed separately statistical superiority of LMWH against LDH or SCD in preventing DVT. The reported DVT rates vary widely among these studies (38 percent, 7 percent, and 2 percent). Because the method of prophylaxis used to compare against LMWH was not the same, a meta-analysis was not done.
- Comparison of LDH vs. MP after meta-analysis of seven studies (four RCTs and three non-RCTs, total number of patients: 620) shows no statistically significant difference between the two methods in preventing DVT (OR: 1.161, 95 percent CI: 0.495, 2.723).

- Spinal fractures and spinal-cord injury are risk factors for DVT. Other frequently reported risk factors, such as head injury, pelvic fractures, or long-bone fractures, were not shown in the meta-analysis to increase the risk for DVT. It is possible that the studies reporting on these factors included severely injured patients who were already at high risk regardless of the presence of the individual risk factor.
- Trauma patients who develop DVT are older and have more severe injuries than patients who do not develop DVT. However, a specific age or ISS threshold could not be extracted from the available data.
- The reported incidence of PE in patients who undergo VCF placement is 0.2 percent, which is lower than the incidence observed in concurrently managed patients without VCF (1.5 percent) and historical controls without VCF (5.8 percent). The observational design of these studies does not allow firm conclusions to be drawn.
- LDH or LMWH administration for VT prophylaxis produces a low and similar incidence of adverse events (on average, 3 percent for bleeding and 1 percent for thrombocytopenia). These low rates may occur because patients at high risk for bleeding were not given heparin.
- Fatal PE has been reported in one-third of trauma patients who develop PE, based on data from 16 studies that reported on both rates (PE, and fatal PE).
- The length of hospital stay in patients who develop DVT is significantly longer (by 15 days) than for patients without DVT. Although a cause-effect relationship between DVT and length of hospital stay cannot be established, DVT is associated with increased costs and use of health care resources.
- There are significant gaps in the literature regarding the prevention of VT after trauma.

Future Research

Future research should be directed to two areas:

- Identifying the appropriate groups of trauma patients in need of VT prophylaxis.
- Evaluating different methods of prophylaxis with regard to their safety and efficacy in trauma patients.

Although evaluating different methods of screening for DVT would be useful, we do not feel that this should be a priority for future research. Duplex ultrasonography is the most convenient, noninvasive, and inexpensive method of screening severely injured patients. Even if other methods of screening prove to be more sensitive, associated technical and logistical difficulties make them impractical.

To address these two areas, we propose a large multicenter trial. This trial should have a randomized controlled design, compare the most commonly used methods of prophylaxis (LDH, LMWH, SCD), identify DVT by routine screening, and evaluate multiple risk factors. A no-prophylaxis group should be included, following the results of this evidence report. Equally important future research should be directed towards evaluating the role of VCF in trauma patients. This question could be incorporated in our proposed multicenter trial or become the sole objective of a separate randomized trial. Both designs should have a predetermined protocol for diagnosing PE:

- An aggressive autopsy policy to identify the cause-effect relationship of PE to death.
- Careful, long-term followup to detect VCF-related complications.

Availability of Full Report

The full evidence report from which this summary was derived was prepared for the Agency for Healthcare Research and Quality by the [Southern California Evidence-based](#)

[Practice Center/RAND](#) under contract No. 290-97-0001. Print copies of this report are available free of charge from the AHRQ Publications Clearinghouse by calling 800-358-9295. Requestors should ask for Evidence Report/Technology Assessment No. 22, *Prevention of Venous Thromboembolism After Injury* (AHRQ Publication No. 00-E027). The Evidence Report is also available online at: <http://hstat.nlm.nih.gov/ftrs/dbaccess/vti> or can be downloaded as a zipped file at: <http://www.ahrq.gov/clinic/evrptfiles.htm>
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Prevention of Venous Thromboembolism After Injury. Summary, Evidence Report/Technology Assessment: Number 22, August 2000. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/clinic/vtsumm.htm>

APPENDIX 3

Published primary literature identified through the literature search

The CCE literature review identified the following reports from the primary literature but they have not been critically appraised. Their abstracts are copied here for information.

Anderson DR, Wells PS, Stiell I, MacLeod B, Simms M, Gray L, Robinson KS, Bormanis J, Mitchell M, Lewandowski B and Flowerdew G (2000). Management of patients with suspected deep vein thrombosis in the emergency department: combining use of a clinical diagnosis model with D-dimer testing. *Journal of Emergency Medicine* **19**: 225-230.

The management of patients presenting to hospital Emergency Departments with suspected deep vein thrombosis is problematic since urgent diagnostic imaging is at times unavailable. We evaluated the accuracy of a rapidly available D-dimer test and the potential of combining D-dimer testing with an explicit clinical model to improve the management of patients with suspected deep vein thrombosis. Two hundred and fourteen patients with suspected deep vein thrombosis presenting to the Emergency Departments of two tertiary care institutions were enrolled in this prospective cohort study. Patients were evaluated by an Emergency Physician who determined the pre-test probability for deep vein thrombosis to be either low, moderate, or high using an explicit clinical model. Patients were managed according to their pre-test probability category by specific algorithms that in all cases included venous ultrasound imaging within 24 h and a 90-day follow-up for the development of thromboembolic complications. Patients also underwent fingerstick SimpliRED(R) whole blood agglutination D-dimer testing; however, D-dimer results did not influence subsequent patient management. D-dimer had a sensitivity of 82.5% and a specificity of 84.9% for the diagnosis of deep vein thrombosis. The observed negative predictive value of D-dimer was 96.9% (95% CI, 93.0% to 99.1%) overall, and 100% (95% CI, 96.3% to 100%) in low probability patients, 94.1% (95% CI, 83.8% to 98.8%) in moderate probability patients, and 86.7% (95% CI, 59.4% to 98.3%) in high probability patients. SimpliRED(R) D-dimer has a high negative predictive value and may be useful in excluding the diagnosis in patients at low pre-test probability for deep vein thrombosis.

Armstrong PA, Peoples JB, Vitello WA and Lemmon GW (1998). Improved selection criteria for ordering stat venous ultrasounds from the emergency department. *American Journal of Surgery* **176**: 226-228.

BACKGROUND: The accuracy and convenience of venous ultrasound (VU) to exclude deep vein thrombosis (DVT) has led to indiscriminate use and low positive yield rates. **METHODS:** A total of 256 patients were referred from our emergency department (ED) for stat VU during a 2-year period (1995 to 1996). The VUs were interpreted as normal in 198 (77%). Positive findings were discovered in 58 (23%), with DVT accounting for 43 (17%). Retrospective multivariate analysis was used to identify predictive indicators. **RESULTS:** Unilateral leg swelling/edema identified 36 of 40 (90%) patients with DVT and 8 of 10 (80%) with other thrombotic disorders (saphenous and/or chronic venous thrombosis). A history of leg pain with prior DVT or recent trauma < or = 3 days' duration increased DVT duration to 98% (39 of 40). Using these criteria, a 47% charge reduction would have been recognized. **CONCLUSIONS:** Improving ED screening criteria can safely increase yield rate and reduce charges with minimal loss of VU sensitivity.

Baron RM and Goldhaber SZ (1999). Deep venous thrombosis: early discharge strategies and outpatient management. *Journal of Thrombosis & Thrombolysis* **7**: 113-122. Conventional management of acute deep venous thrombosis (DVT) consists of initiating

continuous infusion intravenous unfractionated heparin (UFH) for 5 days in the hospital as well as warfarin. Low-molecular-weight heparins (LMWHs) appear to confer similar protection against recurrent DVT compared with UFH but exhibit prolonged bioavailability; increased ease of dosing, and fewer side effects. The advent of LMWH has resulted in increased numbers of patients undergoing initial management of acute DVT with only several days of hospitalization. While 3-month follow-up studies with LMWH demonstrate similar efficacy and safety to UFH, longer term experience with these new agents is necessary to determine their optimal use and safety. We suggest a system for triage in the initial management of DVT patients for: (1) complete outpatient management with LMWH, or (2) short-term hospitalization for initiation of LMWH, or (3) 5-day hospitalization for treatment with UFH. A review of DVT management with LMWH and algorithms for each of these pathways are provided.

Blaivas M, Lambert MJ, Harwood RA, Wood JP and Konicki J (2000). Lower-extremity Doppler for deep venous thrombosis--can emergency physicians be accurate and fast? *Academic Emergency Medicine* **7**: 120-126.

Clinical diagnosis of lower-extremity (LE) deep venous thrombosis (DVT) requires confirmation by an imaging study before committing the patient to anticoagulation therapy. Studies have shown that demonstrating compressibility of leg veins under ultrasound is accurate for ruling out DVTs when performed by vascular specialists. Although LE Doppler has become the preferred test for diagnosing DVTs, it is not always available 24 hours per day. OBJECTIVES: To evaluate the accuracy and speed with which emergency physicians (EPs) could perform LE color duplex ultrasonography for the detection of DVT. METHODS: Patients presenting to an urban community emergency department (ED) between August 1, 1998, and March 3, 1999, were enrolled into this prospective study. The EPs, who underwent brief and standardized training, scanned patients at high risk for DVT with leg pain, swelling, or both. Physicians performed color duplex ultrasound examinations with compression at the common femoral and popliteal veins. The time until completion of the ED scan was recorded with a standardized method. The vascular laboratory performed a complete duplex ultrasound examination within eight hours. RESULTS: One hundred twelve patients were enrolled in the study, with 34 positive for DVT. The median examination time was 3 minutes 28 seconds (95% CI = 2 min 45 sec to 4 min 2 sec; IQR 3 min 9 sec). Times ranged from 1:02 to 18:20 minutes. The ED results had a high correlation with vascular laboratory studies, giving a kappa of 0.9 and a 98% agreement (95% CI = 95.4% to 100%). CONCLUSION: Emergency physicians can perform LE duplex ultrasound examinations accurately and quickly.

Brottman P, Propp D and Goldstein C (1997). The use of light reflection rheography to rule out deep venous thrombosis in emergency patients. *American Journal of Emergency Medicine* **15**: 215-216.

Daniel KR, Jackson RE and Kline JA (2000). Utility of lower extremity venous ultrasound scanning in the diagnosis and exclusion of pulmonary embolism in outpatients. *Annals of Emergency Medicine* **35**: 547-554.

STUDY OBJECTIVE: Emergency physicians frequently rely on normal findings from a lower extremity venous ultrasound examination as a method to decrease the probability of pulmonary embolism (PE) in outpatients with a nondiagnostic ventilation-perfusion lung scan (V/Q scan). The objective of this study was to evaluate the diagnostic utility of bilateral lower extremity venous ultrasound scanning in the diagnosis of PE in emergency department patients with a low-, moderate-, or indeterminate-probability (nondiagnostic) V/Q scan. METHODS: This prospective, 2-center, descriptive study was conducted at the EDs of 2 large teaching hospitals. From an initial cohort of 570 nonreferred outpatients, a convenience sample of 156 patients who had both a nondiagnostic V/Q scan and a lower extremity venous ultrasound scan performed was selected as the study population. The sensitivity and specificity for a single lower extremity venous ultrasound scan and the posttest probability of PE were determined for the study population. RESULTS: In the study population, the best-case sensitivity of the lower extremity venous ultrasound scan

for PE was 54% (95% confidence interval [CI] 37% to 71%) and the specificity was 98% (95% CI 94% to 100%). The likelihood ratio of a positive test result was 27. The likelihood ratio of a negative test result was 0.49, yielding a lowest possible posttest probability of PE of 12% (95% CI 6% to 17%). CONCLUSION: This study demonstrates that the combination of a nondiagnostic (low, moderate, or indeterminate) V/Q scan plus a single negative result from lower extremity venous ultrasound examination, even in a best-case scenario, does not exclude the diagnosis of PE.

Della Santina PJ and Jolly BT (1997). Vascular ultrasonography. *Emergency Medicine Clinics of North America* **15**: 849-876.

Although vascular ultrasonography has been established as an essential diagnostic tool in many clinical settings, its role in the emergency department patient population is uncertain. Preliminary reports of emergency physician--directed ultrasonography are promising. Further studies are needed to establish its reliability and suitability in the emergency department setting. [References: 121]

Drescher MJ and Smally AJ (1997). Thrombophlebitis and pseudothrombophlebitis in the ED. *American Journal of Emergency Medicine* **15**: 683-685.

The patient presenting to the emergency department (ED) with a painful swollen lower extremity is considered to have deep venous thrombosis (DVT) until this diagnosis can be ruled out. This clinical presentation, however, is far from specific and the differential diagnosis includes symptomatic Baker's cyst, also known as pseudothrombophlebitis syndrome (PTP). This article presents two cases of PTP and reviews the literature relevant to diagnosis of DVT and PTP. Ultrasonography is now the diagnostic test of choice for both DVT and PTP, being safe, accurate, noninvasive, and rapid, and should ideally be available for use in the ED. [References: 30]

Farrell S, Hayes T and Shaw M (2000). A negative SimpliRED D-dimer assay result does not exclude the diagnosis of deep vein thrombosis or pulmonary embolus in emergency department patients. *Annals of Emergency Medicine* **35**: 121-125.

STUDY OBJECTIVE: To determine whether a negative SimpliRED D-dimer assay result excludes the diagnosis of deep vein thrombosis (DVT) or pulmonary embolus (PE) in emergency department patients. METHODS: This prospective, institutional review board-approved, clinical trial enrolled consecutive adult ED patients with the suspected diagnosis of venous thromboembolism (VTE) (DVT or PE). Initial ED evaluation included the SimpliRED D-dimer assay (American Diagnostica Inc, Greenwich, CT). Physicians were blinded to assay results. The diagnosis of DVT was made with positive findings on lower-extremity ultrasonography. PE was confirmed by a high-probability ventilation/perfusion (V/Q) scan, a positive pulmonary angiogram, or a positive finding on lower-extremity ultrasonography. A presumptive diagnosis of VTE was made in patients who had VTE at follow-up or unexplained death during the study period. RESULTS: One hundred ninety-eight patients were enrolled during the study period. Twenty-five patients were excluded from data analysis; 9 had no diagnostic testing and 16 were lost to follow-up. Of the 173 patients analyzed, 57 (33%) had VTE-16 of 48 evaluated for DVT and 41 of 125 for suspected PE. The SimpliRED assay had a sensitivity of 65% and a negative predictive value of 81% for detection of VTE. In patients evaluated for DVT alone, the sensitivity was 56% and the negative predictive value was 77%. For patients with suspected PE, the sensitivity and negative predictive value were 68% and 83%, respectively. CONCLUSION: In contrast to earlier reports on the SimpliRED D-dimer assay, a negative result failed to exclude the diagnosis of VTE in our ED population.

Frazer BW and Snoey ER (1999). Diagnostic role of ED ultrasound in deep venous thrombosis and pulmonary embolism. *American Journal of Emergency Medicine* **17**: 271-278.

Proximal deep venous thrombosis (DVT), which may lead to pulmonary embolism (PE), is one of the serious and underrecognized causes of lower extremity pain and swelling. The diagnosis of DVT requires a confirmatory objective test because clinical signs and symptoms are unreliable. Assessment of thigh vein compressibility with real-time

ultrasound is an accurate test for DVT that may be performed rapidly at the bedside. Although unproven, we propose that wider use of this test in the emergency department by emergency physicians might increase the diagnosis of DVT, prevent PE, and reduce utilization of other more costly and invasive diagnostic tests. Evaluation of DVT by compression ultrasound may also be incorporated in the diagnostic workup of suspected PE. In the case of a nondiagnostic ventilation/perfusion scan, demonstration of proximal DVT by ultrasound represents a likely source of PE and an indication for anticoagulation, eliminating the need for pulmonary angiography. In the critically ill patient whose presentation is consistent with massive PE, one rapid approach to the diagnosis may be to combine transthoracic echocardiography with lower extremity ultrasound.

Harris M and Grange J (2000). Management of calf deep venous thrombosis. *Annals of Emergency Medicine* **35**: 629.

Jones S and Harrison M (2001). Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. SimpliRed and diagnosis of deep venous thrombosis. *Emergency Medicine Journal* **18**: 120-122.

Lane B and Harrison M (2000). Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. Low molecular weight heparin or unfractionated heparin in the treatment of patients with uncomplicated deep vein thrombosis. *Emergency Medicine Journal* **17**: 402-403.

Leong WA (1998). Outpatient deep vein thrombosis treatment models. *Pharmacotherapy* **18**: 170S-174S.

Approximately 9000 patients are admitted annually to Canadian hospitals with a primary diagnosis of deep vein thrombosis (DVT). Although this is a serious medical condition, potentially more than 40% of all patients with uncomplicated DVT, or 3600 Canadian patients/year, may be safely treated as outpatients with low-molecular-weight heparin. Outpatient treatment avoids costly hospitalization that is required for the standard 5-10 days of intravenous unfractionated heparin therapy. Although institutions vary widely in the available resources, five core models can assist with successful implementation of an outpatient DVT treatment program while providing optimum use of each site's resources and clinical expertise. These models are as follows: anticoagulation clinic (thromboembolic clinic-service), medical day care clinic, emergency department fast-track, one visit and self-injection, and physician-office follow-up. A program was implemented at Burnaby Hospital in May 1996 using the medical day care clinic model as a pilot. Formal evaluation of the program is still in progress but interim evaluation demonstrated overwhelming success.

Nawaz S, Chan P and Ireland S (1999). Suspected deep vein thrombosis: a management algorithm for the accident and emergency department. *Emergency Medicine Journal* **16**: 440-442.

Patton JH, Jr., Fabian TC, Croce MA, Minard G, Pritchard FE and Kudsk KA (1996). Prophylactic Greenfield filters: acute complications and long-term follow-up. *Journal of Trauma-Injury Infection & Critical Care* **41**: 231-236; discussion 236-237. The efficacy of prophylactic vena caval filters (VCF) in reducing morbidity and mortality from pulmonary embolism (PE) in high-risk trauma patients has been shown, but minimal follow-up data is currently available. VCFs were prophylactically placed in 110 patients between August 1991 and June 1995. There was an early VCF complication rate of 7%. Twenty-two patients died; the remaining 88 patients formed the basis for the follow-up study. Forty-five patients were located and interviewed by phone, and 30 of these patients (34%) returned for evaluation. The mean follow-up time was 18 months (range, 4-42 months). There was no incidence of caval thrombosis on follow-up. Eleven patients had physical findings, and duplex evidence consistent with postphlebotic syndrome. An additional three patients had evidence of old deep venous thrombosis (DVT) by duplex,

but no significant symptomatology. VCF are effective in preventing PE related deaths and have few major complications. The long-term morbidity associated with posttraumatic venous thrombosis is significant. This morbidity is related not to PE or VCF, but to the underlying DVT. Improved strategies against DVT are necessary.

Quirke TE, Ritola PC and Swan KG (1997). Inferior vena caval filter use in U.S. trauma centers: a practitioner survey. *Journal of Trauma-Injury Infection & Critical Care* **43**: 333-337.

Questionnaires were mailed to 620 U.S. "trauma surgeons" to determine a consensus regarding indications for inferior vena caval (IVC) filter placement; 210 (34%) responded. Eighty-seven percent of respondents practiced in Level I trauma centers; 78% were in urban areas and 75% reported more than 1,000 trauma admissions per year. One-half (52%) of those responding were "trauma directors" at their centers. Filter insertion was done by radiologists at 81% of centers, by trauma surgeons at 34%, by vascular surgeons at 33%, and by general surgeons at 13%. Each month, 60% of trauma centers inserted zero or one filter, whereas 27% inserted two to three filters. Complications per year were reported as one or fewer in 85% of trauma centers. Respondents agreed that "absolute indications" for inserting IVC filters were pulmonary embolism while anticoagulated (93%), deep venous thrombosis present and anticoagulation contraindicated (89%), and free-floating ileofemoral thrombus by venogram (54%) and by duplex imaging (45%). "Relative indications" for placement were deep venous thrombosis by duplex imaging (41%) or by venogram (38%), spinal cord injury (40%), pelvic fractures (39%), multiple lower-extremity fractures (29%), concurrent cancer (19%), prolonged bed rest (14%), and obesity (10%). The permanent nature of the filter affected its rate of application. For example, potential removability would significantly ($p < 0.01$) increase prophylactic placement from 29 to 53% in the patient with multiple lower-extremity fractures. Only 12% considered sepsis and 10% young age as contraindications to IVC filter insertion. Contraindications and complications were few, yet frequency of use was surprisingly low. Radiologists insert the filter more than twice as often as surgeons.

Vinson DR and Berman DA (2001). Outpatient treatment of deep venous thrombosis: a clinical care pathway managed by the emergency department. *Annals of Emergency Medicine* **37**: 251-258.

STUDY OBJECTIVE: We evaluate the effectiveness and safety of an outpatient clinical care pathway for the initial treatment of acute proximal lower-extremity deep venous thrombosis (DVT) with low molecular weight heparin (LMWH) managed by the emergency department of 2 affiliated community hospitals. **METHODS:** This observational, retrospectively defined, population-based study with 39(1/2) months of preintervention analysis and 32(1/2) months of postintervention analysis was conducted in 2 suburban EDs of a large group model health maintenance organization. Our outpatient DVT clinical care pathway used careful patient selection and multidisciplinary follow-up. Ninety-six patients before the intervention and 178 patients after the intervention met eligibility criteria for the pathway. Adverse events during the first 2 weeks of treatment included symptomatic pulmonary embolism (PE), progressive DVT, minor and major bleeding, and death. **RESULTS:** Demographic and baseline clinical characteristics of the 2 groups were similar. Five (5.2%) of 96 preintervention subjects (95% confidence interval [CI] 2.4 to 8.1) developed adverse events compared with 5 (2.8%) of 178 postintervention subjects (95% CI 1.5 to 4.1; difference between groups 2.4%; $P = .50$). In each group, 1 (1.0% versus 0.6%) subject developed a PE, 2 (2.1% versus 1.1%) developed progressive symptoms of progressive DVT, and 2 (2.1% versus 1.1%) developed minor bleeding. Major bleeding occurred in 1 (1.0%) preintervention subject and no postintervention subjects. No patient in either cohort died. **CONCLUSION:** Managed by the ED, an outpatient DVT clinical care pathway using careful patient selection and an integrated multidisciplinary approach can provide a similar degree of effectiveness and safety as customary inpatient therapy.

APPENDIX 4

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Levels of evidence used by the CCE search

As defined by "How to use the evidence: assessment and application of scientific evidence" (National Health & Medical Research Council, Canberra, 2000):

- | | |
|-----------|--|
| Level I | Evidence obtained from a systematic review (or meta-analysis) of all relevant randomised controlled trials. |
| Level II | Evidence obtained from at least one randomised controlled trial. |
| Level III | <ol style="list-style-type: none">1 Evidence obtained from pseudorandomised controlled trials (alternate allocation or some other method).2 Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies or interrupted time series with a control group.3 Evidence obtained from comparative studies with historical control, two or more single-arm studies or interrupted time series without a parallel control group. |
| Level IV | Evidence obtained from case series, either post-test or pretest/post-test. |