

Practice Management Guidelines for the Prevention of Venous Thromboembolism in Trauma Patients: The EAST Practice Management Guidelines Work Group

Frederick B. Rogers, MD, Mark D. Cipolle, MD, PhD, George Velmahos, MD, PhD, Grace Rozycki, MD, and Fred A. Luchette, MD

J Trauma. 2002;53:142–164.

The Eastern Association for the Surgery of Trauma (EAST) has taken a leadership role in the development of evidenced-based practice guidelines for trauma.¹ These original guidelines were developed by interested trauma surgeons in 1997 for the EAST Web site (www.east.org), where a brief summary of four guidelines was published. A revised, complete, and significantly edited practice management guidelines for the prevention of venous thromboembolism in trauma patients is presented herein.

The step-by-step process of practice management guideline development, as outlined by the Agency for Health Care Policy and Research (AHCPR), has been used as the methodology for the development of these guidelines.² Briefly, the first step in guideline development is a classification of scientific evidence. A Class I study is a prospective, randomized controlled trial. A Class II study is a clinical study with prospectively collected data or large retrospective analyses with reliable data. A Class III study is retrospective data, expert opinion, or a case report. Once the evidence is classified, it can be used to make recommendations. A Level I recommendation is convincingly justifiable on the basis of the scientific information alone. Usually, such a recommendation is made on the basis of a preponderance of Class I data, but some strong Class II data can be used. A Level II rec-

ommendation means the recommendation is reasonably justifiable, usually on the basis of a preponderance of Class II data. If there are not enough Class I data to support a Level I recommendation, they may be used to support a Level II recommendation. A Level III recommendation is generally only supported by Class III data.

These practice guidelines address eight different areas of practice management as they relate to the prevention and diagnosis of venous thromboembolism in trauma patients. There are few Level I recommendations because there is a paucity of Class I data in the area of trauma literature. We believe it is important to highlight areas where future investigation may bring about definitive Level I recommendations.

RISK FACTORS FOR VENOUS THROMBOEMBOLISM AFTER INJURY

I. Statement of the Problem

A number of factors have been reported to increase the risk of venous thromboembolism (VTE) after injury. Because VTE prophylaxis is associated with complications, it is essential to identify subgroups of trauma patients in whom the benefit of VTE prophylaxis will outweigh the risk of its administration. This is important because the benefits from the different methods of prophylaxis are still unclear when compared with no prophylaxis. Because the literature is inconsistent, a systematic review is needed to produce the best available evidence. Below, we describe the results of a meta-analysis of the existing literature. The reader needs to remember the limitations of meta-analysis. In addition, the fact that a risk factor was not identified as significant in meta-analysis does not mean that this factor must be ignored. Absence of proof does not equal proof of absence. It only means that enough evidence does not exist and that further studies of high quality are needed.

II. Process

Three literature databases were searched (MEDLINE, EMBASE, and Cochrane Controlled Trials Register) for articles reporting risk factors of VTE. All articles were reviewed by two independent reviewers and a third reviewer in cases of disagreement. The review was prepared against predetermined screening criteria, and the articles were given a

Submitted for publication September 1, 2001.

Accepted for publication March 15, 2002.

Copyright © 2002 by Lippincott Williams & Wilkins, Inc.

From the University of Vermont, Department of Surgery, Fletcher Allen Health Care (F.B.R.), Burlington, Vermont, Department of Surgery, Lehigh Valley Hospital (M.D.C.), Allentown, Pennsylvania, Department of Surgery, Division of Trauma and Critical Care, University of Southern California (G.V.), Los Angeles, California, Department of Surgery, Emory University School of Medicine, Atlanta, Georgia, and Department of Surgery, Division of Trauma, Critical Care, and Burns, Loyola University Medical Center (F.A.L.), Maywood, Illinois.

Any reference in this guideline to a specific commercial product, process, or service by trade name, trademark, or manufacturer does not constitute or imply an endorsement, recommendation, or any favoritism by the authors or EAST. The views and opinions of the authors do not necessarily state or reflect those of EAST and shall not be used for advertising or product endorsement purposes.

Address for reprints: Frederick B. Rogers, MD, University of Vermont Department of Surgery, Fletcher Allen Health Care, 111 Colchester Avenue, Burlington, VT 05401; email: frederick.rogers@vtmednet.org.

numerical quality score. From an initial broad research that identified 4,093 relevant titles, 73 articles met all the inclusion criteria and were finally accepted for meta-analysis.

Pooled effect sizes (odds ratio [OR] and their 95% confidence intervals [CIs]) were estimated by the DerSimonian and Laird random-effects model. Shrinkage graphs were produced to display the effect size of each study and to compare with the overall model estimate. The heterogeneity among studies was tested by the Q statistic and p value for the χ^2 test of heterogeneity. A level of significance at $p < 0.05$ was used for all comparisons.

To include a risk factor for meta-analysis, three or more studies reported on the risk factor. Risk factors identified only in one or two studies were not included. The risk factors identified were treated as either dichotomous or continuous variables as appropriate. For instance, if three or more studies provided data on the incidence of VTE in patients who were older or younger than 55 years old, then the risk factor was “age > 55,” a dichotomous variable. On the other hand, if three or more studies provided data on the age of patients with or without VTE by using only a mean and SD, the risk factor was simply “age,” a continuous variable (Table 1).

III. Recommendations

A. Level I: Patients with spinal cord injuries or spinal fractures are at high-risk for venous thromboembolism after trauma.^{2–12}

B. Level II:

1. Older age is an increased factor for venous thromboembolism, but it is not clear at what exact age the risk increases substantially.^{4,5,9,11,13,14}

2. Increasing Injury Severity Score (ISS) and blood transfusion appear to increase the risk of venous thromboembolism, but this association is still unclear.^{3,5,8,9,14,15}

3. Traditional risk factors such as long bone fractures,^{3–6,9–13,15–17} pelvic fractures,^{3–5,9–12,15,18} or head injuries,^{3–9,15} although significantly associated with a high risk of venous thromboembolisms in single-institution studies, were not found to be powerful risk factors on meta-analysis.

IV. Scientific Foundation

Risk factors As Dichotomous Variables

The following variables were reported in three or more studies and were included in the meta-analysis: gender,^{3,13,18,19} head injury,^{3–9,15} long bone fracture,^{3–6,9–13,16,17,19} pelvic fracture,^{3–5,9–12,15} spinal fracture,^{3–12} and spinal cord injury.^{4,9–12} A number of studies included age as a risk factor, but the different cut-off points used in each study (age > 30, 40, 50, 55, etc.) did not allow an analysis of this variable. The only risk factors found to place the patient at higher risk for development of deep venous thrombosis (DVT) were spinal fractures (OR, 2.260; 95% CI, 1.415–3.610) and, even greater, spinal cord injury (OR, 3.017; 95% CI, 1.794–5.381). No significant heterogeneity was reported among studies on the different risk

factors. Although long bone fractures were not found to bear statistical significance on meta-analysis, at least one high-quality study¹⁷ with a valid regression model and an adequate sample size found long bone fractures to be a significant risk factor for venous thromboembolism.

Risk Factors As Continuous Variables

Three continuous variables (i.e., age,^{5,9,11,13,14} ISS,^{3,5,9,11,14,15} and units of blood transfused^{3,14,15}) were reported in more than three studies and were included in the meta-analysis. Compared with patients without DVT, patients with DVT were significantly older (8.133 ± 1.504 [95% CI, 5.115–11.141]) years and had a significantly higher ISS (1.430 ± 0.747 [95% CI, 0.000–2.924]). The statistical difference in ISS was marginal, as shown by the lower limit of the 95% CI, and had minimal clinical significance. The difference of blood transfused between patients with and without DVT was not statistically significant (1.882 ± 2.815 ; 95% CI, -3.637 – 7.401), and no heterogeneity was reported among these studies.

V. Summary

The existing evidence supports the presence of two risk factors of posttraumatic VTE: spinal fractures and spinal cord injuries. Older age was an additional risk factor, but it was not clear at what exact age the risk increases substantially. Inadequate literature evidence exists to support that other frequently reported risk factors, such as long bone fractures, pelvic fractures, or head injuries, really increase the risk for VTE. However, a need exists for additional research in this area. In particular, adequate sized prospective studies should reevaluate the role of long bone fracture, pelvic fractures, head injuries, as well as specific age, blood transfusion, and ISS thresholds.

V. Future Investigation

Adequately sized studies should reevaluate the role of long bone fracture, pelvic fractures, and head injuries, as well as age, blood transfusion, and ISS thresholds and their association with the development of VTE after trauma. Large databases could be used to quantify risk using logistic regression profiles and could be the basis of specific prevention strategies.

THE USE OF LOW-DOSE HEPARIN FOR DVT/PE PROPHYLAXIS

I. Statement of the Problem

The fact that DVT and pulmonary embolism (PE) occur after trauma is incontrovertible. The optimal mode of prophylaxis has yet to be determined. Low-dose heparin (LDH), given in doses of 5,000 units subcutaneously two or three times daily, represents one pharmacologic treatment modality for prophylaxis against DVT/PE.

In contrast, LDH has not been shown to be particularly effective in preventing VTE in trauma patients. Three recent

Table 1 Studies Reporting on Risk Factors of Venous Thromboembolism in Trauma Patients

| First Author | Year | Reference Title | Class | Conclusion |
|----------------|------|--|-------|---|
| Knudson MM | 1994 | Prevention of venous thromboembolism in trauma patients <i>J Trauma</i> . 37:480-487 | I | 15 patients developed DVT (5.8%). Risk factors for DVT were age > 30 yr, immobilization > 3 days, pelvic and lower extremity fractures. |
| Kudsk KA | 1989 | Silent deep venous thrombosis in immobilized multiple trauma patients. <i>Am J Surg</i> . 158:515-519 | II | 39 multiple trauma patients received no prophylaxis, and had venography 7-12 days after the injury. 24 developed DVT (61.5%) and 12 proximal DVT (31%). Risk factor for DVT was age. |
| Velmahos GC | 1998 | Inability of an aggressive policy of thromboprophylaxis to prevent deep venous thrombosis (DVT) in critically injured patients: are current methods of DVT prophylaxis insufficient? <i>J Am Coll Surg</i> . 187:529-533 | II | 200 critically injured patients received VTE prophylaxis (LDH and/or PCD), and had weekly Duplex scan. 26 developed proximal DVT (13%), 4 PE (2%). Risk factors for DVT were severe chest injuries, extremity fractures, and high levels of PEEP during mechanical support. |
| Spain DA | 1997 | Venous thromboembolism in the high-risk trauma patient: do risks justify aggressive screening and prophylaxis? <i>J Trauma</i> . 42:463-469 | III | 280 high-risk trauma patients received prophylaxis, and were compared to 2,249 low-risk patients. 12 high-risk (5%) and 3 low-risk (0.1%) developed DVT. PE found only in 4 high-risk. Only patients with venous injuries were at higher risk for VTE. |
| Dennis J | 1993 | Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high-risk groups. <i>J Trauma</i> . 35:132-139 | II | 395 trauma patients, 281 randomized to VTE prophylaxis and 113 to no prophylaxis, and screened by regular duplex. 18 (4.5%) developed DVT (8 with prophylaxis and 10 without) and 2 PE. Risk factor for VTE was spinal trauma. |
| Meyer CS | 1995 | Surveillance venous scans for deep venous thrombosis in multiple trauma patients. <i>Ann Vasc Surg</i> . 9:109-114 | III | 183 multiple trauma patients had VTE prophylaxis and irregular Duplex screening. 22 (12%) developed DVT. Risk factors for DVT were spinal injuries and symptoms of DVT. |
| Piotrowski JJ | 1996 | Is deep vein thrombosis surveillance warranted in high-risk patients? <i>Am J Surg</i> . 172:210-213 | II | 343 high-risk trauma patients had VTE prophylaxis and were screened by duplex. 20 developed DVT (5.8%) and 3 PE (1%). Independent risk factors for DVT were age and GCS score. |
| Napolitano LM | 1995 | Asymptomatic deep venous thrombosis in the trauma patient: is an aggressive screening protocol justified? <i>J Trauma</i> . 39:651-659 | III | 458 trauma patients had VTE prophylaxis and regular Duplex scan. 45 (10%) developed DVT and 1 PE. Independent risk factors of DVT were age, ISS, RTS, length of stay, and spinal injury. |
| Geerts WH | 1994 | A prospective study of venous thromboembolism after major trauma. <i>N Engl J Med</i> . 331:1601-1606 | II | 349 major trauma patients with venographic assessment 14-21 days after admission. 201 (57.6%) developed DVT and 63 (18%) proximal DVT. Independent risk factors of DVT were age, blood transfusion, surgery, fracture of femur of tibia, and spinal cord injury. |
| Knudson MM | 1996 | Use of low molecular weight heparin in preventing thromboembolism in trauma patients. <i>J Trauma</i> . 41:446-459 | I | 487 trauma patients stratified to receive LMWH or PCD, and had regular duplex. DVT was found only in 2.4% patients. Risk factors for DVT were immobilization > 3 days, age > 30 yr, and lower extremity or pelvic fractures. |
| Abelseth G | 1996 | Incidence of deep vein thrombosis in patients with fractures of the lower extremity distal to the hip. <i>J Orthop Trauma</i> . 10:230-235 | II | 102 patients with lower extremity fractures, receiving no prophylaxis, had venography after operative fixation. 253 major trauma patients randomized to PCD, LDH, or no prophylaxis and followed by regular duplex. 29 developed DVT (28%) and 2 PE. Risk factors for DVT were age > 60, OR time > 105 min, and time from injury to operation > 27 h. |
| Upchurch GR Jr | 1995 | Efficacy of subcutaneous heparin in prevention of venous thromboembolic events in trauma patients. <i>Am Surg</i> . 61:749-755 | III | 66 trauma patients received VTE prophylaxis and irregular duplex scan. 13 (19.6%) developed DVT and 3 (4.5%) PE. Risk factors for VTE were older age and head, spinal cord, pelvic, and lower extremity trauma. |
| Knudson MM | 1992 | Thromboembolism following multiple trauma. <i>J Trauma</i> . 32:2-11 | II | 113 multiple trauma patients randomized to PCD or LHD, and screened by regular Duplex scan. 12 (10.6%) developed VTE (5 DVT, 4 PE, 3 both), 9 in the PCD group and 3 in the LDH. Risk factors for VTE were age, immobilization, number of transfusions, and clotting abnormalities. |
| Hill SL | 1994 | Deep venous thrombosis in the trauma patient. <i>Am Surg</i> . 60:405-408 | II | 100 trauma patients. 50 received LDH and 50 did not nonrandomly, and had regular duplex screening. 15 developed DVT, 14 of them without prophylaxis. Risk factors were lower extremity injuries and a higher ISS. |
| Geerts WH | 1996 | A comparison of low-dose heparin with low-molecular weight heparin as prophylaxis against venous thromboembolism after major trauma. <i>N Engl J Med</i> . 335:701-770 | I | 265 major trauma patients randomized to LDH or LMWH, and had venography 10-14 days after admission. 60 (44%) LDH and 40 (31%) LMWH patients developed DVT. Proximal DVT in 15% and 6%, respectively. The incidence of DVT was higher in patients with leg fractures. |
| Waring W | 1991 | Acute spinal cord injury and the incidence of clinically occurring thromboembolic disease. <i>Paraplegia</i> . 29:8-16 | III | DVT developed in 14.5% and PE in 4.6%. Age was the only significant factor for PE. 1,419 spinal cord injury patients included and followed for development of VTE. Stratification according to age, gender, level, and type of injury. |
| Spannagel U | 1993 | Low molecular weight heparin for the prevention of thromboembolism in outpatients immobilized by plaster cast. <i>Semin Thromb Hemost</i> . 19 (suppl 1): 131-141 | I | DVT developed in 27 (10.6%), 21 from the no-prophylaxis group and 6 from LMWH. Risk factors for DVT were age > 30 yr, obesity, varicose veins, and fractures. 306 patients included, 257 analyzed; 127 randomized to receive no prophylaxis and 126 to LMWH. |

VTE, venous thromboembolism; DVT, deep venous thrombosis; PE, pulmonary embolism; LDH, low-dose heparin; LMWH, low-molecular-weight heparin; PCD, pneumatic compression device; OR, operating room; PEEP, positive end-expiratory pressure; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; RTS, Revised Trauma Score.

Table 2 Lose-Dose Heparin

| First Author | Year | Reference Title | Class | Conclusion |
|----------------|------|---|-------|---|
| Shackford SR | 1990 | Venous thromboembolism in patients with major trauma. <i>Am J Surg.</i> 159:365–369 | III | 177 high-risk patients received LDH, PCD, LDH and PCD, or no prophylaxis. Nonrandomized, uncontrolled study. VTE rate: LDH, 6%; PCD, 6%; PCD and LDH, 9%; no prophylaxis, 4%. No difference in VTE rates between groups. |
| Dennis JW | 1993 | Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high-risk groups. <i>J Trauma.</i> 35:132–139 | III | Prospective, nonrandomized study of 395 patients with ISS > 9 received LDH, PCD, or no prophylaxis. VTE rate: LDH, 3.2%; PCD, 2.7%; no prophylaxis, 8.8%. Subgroup analysis revealed no significant difference in VTE rates between LDH and no prophylaxis. Some randomization problems with study. |
| Ruiz AJ | 1991 | Heparin, deep venous thrombosis, and trauma patients. <i>Am J Surg.</i> 162:159–162 | III | Nonrandomized study in which 100 consecutive patients received LDH or no prophylaxis. VTE rate: LDH, 28%; no prophylaxis, 2%. LDH patients were more severely injured and at bed rest for a longer period. |
| Knudson MM | 1994 | Prevention of venous thromboembolism in trauma patients. <i>J Trauma.</i> 37:480–487 | I | Randomized, prospective study of 251 patients receiving LDH, PCD or no prophylaxis. No significant benefit or VTE with prophylaxis. No significant benefit on VTE with prophylaxis except in the subgroup of neurotrauma patients in whom PCD seemed to offer protection. |
| Upchurch GR Jr | 1995 | Efficacy of subcutaneous heparin in prevention of venous thromboembolic events in trauma patients. <i>Am Surg.</i> 61:749–755 | III | Meta-analysis on the use of LDH in 1,102 trauma patients revealed no significant benefit on VTE rate: LDH, 10%; no prophylaxis, 7% ($p = 0.771$). |
| Napolitano LM | 1995 | Asymptomatic deep venous thrombosis in the trauma patient: is an aggressive screening protocol justified? <i>J Trauma.</i> 39:651–659 | III | 437 screened for DVT, nonrandomized. VTE rate: LDH, 8.6%; PCD, 11.6%; LDH and PCD, 8.0%; no prophylaxis, 11.9%. No difference in VTE rates between groups. |
| Velamahas GC | 2000 | Prevention of venous thromboembolism after injury: an evidence-based report—part I: analysis of risk factors and evaluation of the role of vena cava filters. <i>J Trauma.</i> 49:132–139 | I | Meta-analysis; 4 randomized control studies of LDH vs. no prophylaxis; no difference in DVT rate (OR, 0.965; 95% CI, 0.353–2.636). |
| Geerts WH | 1996 | A comparison of low-dose heparin and low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. <i>N Engl J Med.</i> 335:701–707 | I | Randomized, double-blind, prospective trial in 334 trauma patients of LDH vs. LMWH. LMWH significantly decreased DVT rate (31% vs. 44% for LDH, $p = 0.014$). |
| Velamahas GC | 1998 | Inability of an aggressive policy of thromboprophylaxis to prevent deep venous thrombosis (DVT) in critically injured patients: are current methods of DVT prophylaxis insufficient? <i>J Am Coll Surg.</i> 187:529–533 | II | 200 critically injured patients received VT prophylaxis (LDH and/or PCD) with weekly duplex; 26 developed proximal DVT (13%), 4 PE (2%). Risk factors were severe chest injuries; extremity fractures, high PEEP levels during mechanical ventilation. |

prospective trials demonstrated that LDH was no better in preventing DVT than no prophylaxis at all in patients with an ISS > 9. Sample sizes in these studies were small, and hence a type II statistical error cannot be excluded. The results of LDH use in trauma, with regard to PE, are even more vague.

II. Process

A MEDLINE review from 1966 to the present revealed several hundred articles related to the use of LDH in medical and general surgical patients. Only the nine articles related to the use of LDH in trauma patients were used for the following recommendations (Table 2).

III. Recommendations

A. Level I: A Level I recommendation on this topic cannot be supported because of insufficient data.

B. Level II: Little evidence exist to support the benefit of LDH as a sole agent for prophylaxis in the trauma patient at high-risk for VTE.^{3,7,10,14,20–22}

C. Level III: For patients in whom bleeding could exacerbate 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 non-operatively), the safety of LDH has not been established, and an individual decision should be made when considering anticoagulant prophylaxis.

IV. Scientific Foundation

Heparin is a naturally occurring polysaccharide varying in molecular weight from 2,000 to 40,000. LDH augments the activity of antithrombin III, a potent, naturally occurring inhibitor of activated factor X (Xa) and thrombin, which produces interruption of both the intrinsic and extrinsic pathways. Low-dose heparin causes only minimal or no change in conventional clotting tests, such as the partial thromboplastin time.

Studies on the use of LDH in trauma patients are inconclusive. In addition, many of these studies are single-institution studies with small sample sizes and lack randomization. These studies are summarized in Table 2.^{7,20,21} Studies with larger sample sizes and randomization will be discussed herein.^{3,5,10,14,17,22}

Knudson et al.³ reported on 251 patients in a cohort study who received LDH, a pneumatic compression device (PCD), or no prophylaxis. These authors failed to show any effectiveness with prophylaxis in most trauma patients, except in the subgroup of patients with neurotrauma in which PCD was more effective in preventing DVT than control. Upchurch et al.¹⁴ compared 66 intensive care unit (ICU)-dependent trauma patients who received either LDH or no VTE prophylaxis. No significance difference was seen in VTE rates between the two groups. In this same study, the authors performed a meta-analysis of the current literature concerning the use of LDH in 1,102 trauma patients. This meta-analysis demonstrated no benefit of LDH as prophylaxis compared with no prophylaxis (10% vs. 7%; $p = 0.771$). Geerts et al.¹⁷ randomized 344 trauma patients to receive low-molecular-weight heparin (LMWH) or LDH and found significantly fewer DVTs with LMWH than with LDH (31% vs. 44%, $p = 0.014$ for all DVT; and 15% vs. 6%, $p = 0.012$ for proximal DVT). This study had no control group. However, when compared with the predicted DVT rate if the study patients had not received prophylaxis, the risk reduction for LDH was only 19% for DVT and only 12% for proximal DVT, whereas the comparative risk reductions for LMWH were 43% and 65%, respectively. Napolitano et al.¹⁰ used a serial ultrasound screening protocol for DVT in 437 patients who were given four types of prophylaxis (LDH, PCD, LDH and PCD, and no prophylaxis) according to their attending surgeon's preference. No significant difference was seen in DVT rates between groups (8.6%, 11.6%, 8.0%, and 11.9%, respectively).

Velmahos et al.⁵ looked at the use of LDH and PCD or PCD alone in 200 critically injured patients who were then followed with biweekly Doppler examinations to detect proximal lower extremity DVT. The incidence of DVT was 13% overall, and no difference was seen between the two groups. The majority (58%) of DVT developed in the first 2 weeks. In a meta-analysis conducted under the auspices of the Agency for Healthcare Research and Quality, Velmahos and colleagues²² looked at all randomized controlled and nonrandomized studies on the use of LDH in trauma patients. The four randomized controlled studies on the use of LDH in trauma patients showed no difference in the incidence of DVT between those receiving LDH versus no prophylaxis (OR, 0.965; 95% CI, 0.360–2.965; vs. OR, 1.33; 95% CI, 0.360–2.965).

V. Summary

In summary, to date, LDH has very little proven efficacy in the prevention of VTE after trauma. 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.

VI. Future Investigation

Enough accumulated data do not exist to support the use of LDH in a trial in high-risk trauma patients. Future studies

should focus on the potential benefit of more efficacious agents such as low-molecular-weight heparin.

THE ROLE OF ARTERIOVENOUS FOOT PUMPS IN THE PROPHYLAXIS OF DVT/PE IN THE TRAUMA PATIENT

I. Statement of the Problem

In 1983, Gardner and Fox²³ discovered a venous pump on the sole of the foot that consists of a plexus of veins that fills by gravity and empties on weightbearing, thus increasing femoral blood flow without muscular assistance. A mechanical device, the arteriovenous (A-V) foot pump, has been developed to mimic this effect of weightbearing. The major advantage of this system is that it only requires access to the foot, which enables its use in patients with Jones dressings, casts, or externally fixed limbs that previously were unsuitable for a PCD. One study has shown that the pulsatile action of the A-V foot pump increased venous blood flow velocity in the popliteal vein by 250%.²⁴

II. Process

With the recent clinical introduction of the A-V foot pump, there is a paucity of relevant literature related to this subject. A MEDLINE review dating back to 1980 revealed 12 articles on A-V foot pumps, with 8 articles specifically related to the use of A-V foot pumps in the trauma patient. These eight studies were the basis for the recommendations below (Table 3).

III. Recommendations

A. Level I: A Level I recommendation for this topic cannot be supported because of insufficient data.

B. Level II: A Level II recommendation for this topic cannot be supported because of insufficient data.

C. Level III: A-V foot pumps may be used as a substitute for pneumatic compression devices in those high-risk trauma patients who cannot wear PCDs because of external fixators or casts and cannot be anticoagulated because of their injuries. It should be noted that in trauma patients, A-V foot pumps have not been shown to be as efficacious as PCDs and are associated with some significant complications.^{12,25,26}

IV. Scientific Foundation

Most of the studies involving the use of A-V foot pumps are found in the orthopedic literature, and many of these series involve small numbers of patients. Although little has been documented on the effects of A-V footpumps on DVT in trauma patients, other beneficial effects have been observed. In 71 patients who had operations or casts for traumatic lower extremity injuries, Gardner and Fox²⁷ showed a significant decrease in pain, swelling, and measurement of compartment pressures in the affected extremities with the use of the A-V foot pumps. In the discussion to this article, the authors hypothesized that the increased blood flow seen with the pumps was because of hyperemia mediated by endothelial-derived relaxing factor (now

Table 3 A-V Foot Pumps

| First Author | Year | Reference Title | Class | Conclusion |
|--------------|------|--|-------|---|
| Gardner AMN | 1983 | The venous pump of the human foot: preliminary report. <i>Bristol Med Chir J.</i> 98:109-112 | III | First description of the physiologic pumping mechanism on the sole of the foot. |
| Laverick MD | 1990 | A comparison of the effects of electrical calf muscle stimulation and the venous foot pump on venous blood flow in the lower leg. <i>Phlebography.</i> 5:285-290 | III | This study demonstrated that A-V foot pump increases venous blood flow in popliteal vein by 250%. |
| Knudson MM | 1996 | The use of low molecular weight heparin in preventing thromboembolism in trauma patients. <i>J Trauma.</i> 41:446-459 | II | A-V foot pumps used as one limb of prospective study on DVT prophylaxis. Foot pumps had a higher DVT rate (not significant) than LMWH or PCD and complications with their use. |
| Spain DA | 1998 | Comparison of sequential compression devices and foot pumps for prophylaxis of deep venous thrombosis in high-risk trauma patients. <i>Am Surg.</i> 64:522-526 | III | Nonrandomized study of 184 high-risk patients, incidence of DVT was similar between groups (7% PCD, 3% A-V foot pumps) as was number of PEs (2 AV foot pumps, 1 PCD). |
| Anglen JO | 1998 | A randomized comparison of sequential-gradient calf compression with intermittent plantar compression for prevention of venous thrombosis in orthopedic trauma patients: preliminary results. <i>Am J Orthop.</i> 33:53-57 | II | Prospective, randomized controlled study of high-risk patients followed with serial duplex. DVT rates: 0% PCD; 4% A-V foot pump. |
| Gardner AM | 1990 | Reduction of post-traumatic swelling and compartment pressure by impulse compression of the foot. <i>J Bone Joint Surg Br.</i> 72:810-815 | III | Multicenter trial showed decrease in pain and compartment pressures with the use of A-V foot pumps. Hypothesized that this was because of release of endothelial-derived relaxing factor in microcirculation. |
| Morgan RH | 1991 | Arterial flow enhanced by impulse compression. <i>Vasc Surg.</i> 25:8-15 | III | 22 patients with peripheral vascular disease had relief of ischemic rest pain with use of A-V foot pump. |
| Abu-Own A | 1993 | Effects of intermittent pneumatic compression of the foot on the microcirculatory function in arterial disease. <i>Eur J Vasc Surg.</i> 7:488-492 | III | A-V foot pumps increased transcutaneous oxygen and laser Doppler fluxmetry in patients with severe claudication. |
| Anglen JO | 1998 | Foot pump prophylaxis for deep venous thrombosis: the rate of effective usage in trauma patients. <i>Am J Orthop.</i> 580-582 | III | Trauma population found that A-V foot pumps were applied properly and functioning only 59% of the time. |
| Comerota AJ | 1992 | Why does prophylaxis with external pneumatic compression for deep vein thrombosis fail? <i>Am J Surg.</i> 164:265-268 | III | A-V foot pumps increased transcutaneous oxygen and laser Doppler fluxmetry in patients with severe claudication. |

thought to be nitric oxide) that was liberated by the endothelium secondary to sudden pressure changes, which could have been caused by the A-V pumps. This endothelial-derived relaxing factor release could encourage the opening of critically closed capillaries, enabling reabsorption of fluid, hence the decrease in compartment pressures. In addition, reports have been documented of A-V foot pumps improving arterial blood flow with the relief of ischemic rest pain.^{28,29} In addition to preventing VTE, all of these proposed foot pump mechanisms of action may be potentially beneficial in healing extremity injuries.

In a recent prospective randomized study by Knudson et al.,¹² A-V foot pumps were one arm of a number of prophylactic measures (LMWH and PCDs were the other arms) used to prevent DVT in high-risk trauma patients. Of 372 patients enrolled in the study, the DVT rate was 5.7% for the A-V foot pumps, 2.5% for the PCDs, and 0.8% for the low-molecular-weight heparin as determined on follow-up serial duplex ultrasound. Of note, in 8 of 53 patients who wore foot pumps, severe skin changes, including blistering and wound problems, occurred. This required three patients to be removed early from the study.

Spain et al.²⁵ compared the use of A-V foot pumps to PCDs in 184 consecutively injured patients. In this nonrandomized study, patients who could not receive a PCD because of lower extremity injuries were placed in A-V foot pumps. Overall, no significant difference was seen in DVT rates between the two groups, with PCDs at 7% and A-V foot pumps at 3%. The authors of this study concluded that A-V foot pumps were a reasonable alternative to PCDs when lower extremity fractures preclude the use of PCDs. Anglen et al.²⁶ performed a randomized prospective trial comparing A-V foot pumps with PCDs in high-risk orthopedic patients and followed them with serial ultrasound. In 124 patients, the overall incidence of DVT was 4% in those with A-V foot pumps and 0% in those with PCDs. Unfortunately, meaningful analysis of such a study was confounded by the heterogeneity of the two groups and the fact that a sizable number of patients received either aspirin or warfarin postoperatively. In another study by Anglen et al.³⁰ in a trauma population of ICU and ward patients, the A-V foot pumps were found to be applied properly and functioning correctly only 59% of the

time, a problem similar to that reported by Comerota et al.³¹ for PCDs.

V. Summary

Only one clinical series in trauma patients compares A-V foot pumps with other standard techniques of DVT prophylaxis. The results from this series were not definitive in terms of benefits of A-V foot pumps preventing DVT. However, a use of A-V foot pumps may exist in the high-risk trauma patient who has a contraindication to heparin because of injuries or who cannot have PCDs placed on lower extremities secondary to external fixators or large bulky dressings.

VI. Future Investigations

Prospective randomized studies are needed comparing A-V foot pumps to standard prophylactic measures in trauma patients at high risk for the development of DVT.

THE USE OF PNEUMATIC COMPRESSION DEVICES IN THE PREVENTION OF DVT/PE

I. Statement of the Problem

The role of intermittent PCDs for prophylaxis against DVT has been studied and increasingly used in general surgery patients,³² orthopedic patients,^{33,34} and trauma patients.^{4,5,7,22,35,36}

Attacking the long-recognized risk factor of stasis, PCDs have been shown to increase mean and peak femoral venous blood velocities in the lower extremity.³⁷ In addition, PCDs have been shown to have a direct effect on the fibrinolytic pathway that acts to shorten the euglobulin lysis time, increases levels of coagulation cascade inhibitor molecules, and affects the balance of plasminogen activation.^{38,39} In a number of prospective randomized studies, PCDs have been shown to reduce the incidence of both DVT and PE.^{7,36,40} Unanswered questions regarding the use of PCDs include the mechanism by which PCDs act, the efficacy of PCDs worn on the upper extremities or a single lower extremity compared with both lower extremities, the nature of risk involved in discontinuing PCDs periodically during use, and the duration of PCD use. Reports suggest that PCDs should be worn with thromboembolism-deterrent stockings (TEDS); however, this practice has not been widely used. Complications of PCDs have been noted in case reports and have been associated with improper positioning of the lower extremity during surgery, which should be avoided.

II. Process

A MEDLINE search from 1986 to the present produced a large number of articles on this topic. Those articles pertinent to trauma-related thromboembolism prevention were reviewed. Twenty-three of these trauma-related articles were evaluated to formulate the following guidelines (Table 4).

III. Recommendations

A. Level I: A Level I recommendation on this topic cannot be supported because of insufficient data.

B. Level II: A Level II recommendation on this topic cannot be supported because of insufficient data.

C. Level III: In a meta-analysis of pooled studies on the benefit of PCDs in trauma patients, no benefit of the use of PCDs over no prophylaxis was reported.²² In the subset of head-injured patients,^{3,41} PCDs may have some benefit in isolated studies.

IV. Scientific Foundation

The factors that are felt to form the basis of the pathophysiology of venous thromboembolic disease are *stasis* (reduction of blood flow in the veins), *injury* (to the intimal surface of the vessel), and *hypercoagulability*. Scientific and clinical evaluations of PCDs strongly suggest that the nature of the effect on DVT prophylaxis derives from their ability to increase mean and peak femoral vein velocity and possibly affect the systemic coagulation and fibrinolytic mechanisms.

Keith et al.³⁷ measured peak venous velocity (PVV) at the common femoral vein using Doppler ultrasound in postoperative nontrauma patients and in healthy control subjects. In the control subjects, PVV was increased from a mean velocity of 23.8 cm/s at rest to 45.5 cm/s with knee-high PCDs and 53.2 cm/s with thigh-high PCDs. In postoperative patients, the PVV was similarly raised from a resting velocity of 21.8 cm/s to 55.1 cm/s. In both of these evaluations, the differences were statistically significant when compared with controls and were not further augmented by the concomitant use of TEDS. Spectral recording of blood flow velocity during inflation and deflation of the PCDs revealed a temporal association with inflation and increased PVV that suggested a mechanical effect derived from inflation of the PCDs.

Studies^{38,39} have evaluated in vivo fibrinolytic effects of PCDs. In a well-designed study, Jacobs et al.³⁹ showed that euglobulin lysis times were not reproducible as a marker for fibrinolytic activation. Their study focused on measured changes in tissue plasminogen activator (tPA), plasminogen activator inhibitor (PAI-1), and tPA-PAI-1 complex. They demonstrated a significant increase in tPA-PAI-1 (hence an obligatory decrease in PAI) in patients undergoing pneumatic compression and postulated a (complex and incompletely proven) role of PCDs in the systemic balance of plasminogen activation and inhibition. They found that fibrinolytic activity began to decay within minutes of discontinuing PCDs. This observation proved to have important clinical implications in that PCDs must be worn continuously to avoid rapid decay in fibrinolytic activity. A recent study documented patients in whom PCDs have been ordered, but who spent less than 50% of the time actually wearing the devices, which possibly decreased their effectiveness.³¹ Another important finding in the study by Jacobs et al. was that there appeared to be an

Table 4 Pneumatic Compression Devices

| First Author | Year | Reference Title | Class | Conclusion |
|--------------|------|--|-------|--|
| Caprini JA | 1994 | Prevention of venous thromboembolism in North America: Results of a survey among general surgeons. <i>J Vasc Surg.</i> 20:751-758 | III | Most recent ACS survey documents PCDs as the most frequently used prophylaxis (75% of respondents) with efficacy and safety cited as reasons. |
| Pidala MJ | 1992 | A prospective study on intermittent pneumatic compression in the prevention of deep vein thrombosis in patients undergoing total hip or total knee replacement. <i>Surg Gynecol Obstet.</i> 175:47-51 | III | Prospective, uncontrolled study of PCDs in elective joint replacement surgery. Overall DVT incidence 4% by IPG with duplex confirmation. Authors believed, but did not prove that PCDs contributed to the low DVT incidence. |
| Woolson ST | 1991 | Intermittent pneumatic compression to prevent proximal deep venous thrombosis during and after total hip replacement: a prospective, randomized study of compression alone, compression and aspirin, and compression and low-dose warfarin. <i>J Bone Joint Surg Am.</i> 3:507-512 | II | The addition of aspirin or Coumadin to PCDs does not improve DVT or PE prophylaxis in elective hip replacement surgery. |
| Knudson MM | 1992 | Thromboembolism following multiple trauma. <i>J Trauma.</i> 32:2-11 | II | Prospective comparison of 113 trauma patients prophylaxed with PCDs (76) or LDH (37). Thromboembolic complications occurred in 12% and 8%, respectively. |
| Dennis JW | 1993 | Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high-risk groups. <i>J Trauma.</i> 35:132-139 | III | PCDs were comparable to the effect of LDH in significantly lowering DVT incidence compared with controls with no prophylaxis. Some randomization problems. |
| Gersin K | 1994 | The efficacy of sequential compression devices in multiple trauma patients with severe head injury. <i>J Trauma.</i> 37:205-208 | III | Of 32 severe head-injured patients, 14 received PCD and 18 received no prophylaxis because of lower extremity fracture. 2 DVTs, 2 PEs resulted in the no-prophylaxis group, and 4 PEs and no DVTs in the PCD group. Small numbers and no description of randomization limit the value of this study. |
| Fisher CG | 1995 | Effectiveness of pneumatic leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients: a prospective, randomized study of compression alone versus no prophylaxis. <i>J Orthop Trauma.</i> 9:1-7 | II | 304 ortho-trauma patient showed venous thromboembolic event in 4% prophylaxed vs. 11% control, with subgroup differences among hip vs. pelvic fracture patients. Mechanical prophylaxis effective only in hip fracture group. |
| Velmahos GC | 1998 | Inability of an aggressive policy of thromboprophylaxis to prevent deep venous thrombosis (DVT) in critically injured patients: are current methods of DVT prophylaxis insufficient? <i>J Am Coll Surg.</i> 187:529-533 | III | DVT rate the same for (13%) for critically injured patients prophylaxed with either SCH, LDH, or a combination of above. |
| Velmahos GC | 2000 | Prevention of venous thromboembolism after injury: an evidence-based report—part I: analysis of risk factors and evaluation of the role of vena cava filters. <i>J Trauma.</i> 49:132-139 | I | Meta-analysis of PCD vs. no prophylaxis revealed PCD offered no benefit over no prophylaxis in both pooled randomized control studies (OR, 0.769; 95% CI, 0.265-2.236) and in nonrandomized studies (OR, 0.527; 95% CI, 0.190-1.46). |
| Keith SL | 1992 | Do graduated compression stockings and pneumatic boots have an additive effect on the peak velocity of venous blood flow? <i>Arch Surg.</i> 127:727-730 | II | Good study demonstrates PCD effect of increased peak venous velocity in femoral vein not augmented by addition of graduated compression stockings. |
| Inada K | 1988 | Effects of intermittent leg compression for prevention of postoperative deep venous thrombosis with special reference to fibrinolytic activity. <i>Am J Surg.</i> 155:602-605 | II | Prospective, nonrandomized study from Japan. Overall DVT incidence of 6.25% attributed to shortening of the euglobulin lysis time during first 48 h postoperatively and activating fibrinolysis. |
| Jacobs DG | 1996 | Hemodynamic and fibrinolytic consequences of intermittent pneumatic compression: Preliminary results. <i>J Trauma.</i> 40:710-717 | II | A well-designed and well-described study of the effect of PCDs on the plasma levels of various compounds involved in the regulation of fibrinolysis. The discussion in the article describes these components well. |
| Knudson MM | 1994 | Prevention of venous thromboembolism in trauma patients. <i>J Trauma.</i> 37:480-487 | II | PCDs significantly reduced DVT complications vs. control in neutrotrauma group only. |
| Lachmann EA | 1992 | Complications associated with intermittent pneumatic compression. <i>Arch Phys Med Rehabil.</i> 73:482-485 | III | Case report (×2) of PCD complications, both with PCDs worn during surgery. Peroneal nerve compression in setting of weight loss and compartment syndrome with legs in the lithotomy position. |

incremental decrease in fibrinolytic activity when blood was sampled in sites remote from the area of PCD placement. This difference in local and systemic effects has important implications on the ability of PCDs worn on the arms to prevent DVT in the legs.

A paucity of studies exists specifically regarding the use of PCDs in trauma patients with multiple injuries. In a prospective study by Knudson et al.,¹⁵ 113 trauma patients received either PCDs and TEDS or LDH. This study showed a

12% rate of VTE in the PCD group versus 8% in the LDH group, which was not significantly different. This study did not demonstrate that either method of attempted prevention (LDH or PCD) was better than no prophylaxis. Dennis et al.⁷ conducted a prospective, nonrandomized study of 395 trauma patients admitted with an ISS > 9 who received either PCDs, LDH, or no prophylaxis, and who underwent serial ultrasound screening for DVT at 48 hours, 5 days, and 10 days after admission. They demonstrated a VTE rate of 8.8% in the

no-prophylaxis group, 2.7% in the PCD group, and 3.2% in the LDH group. No statistically significant difference was noted in VTE rates in the prophylaxis groups, but a significant difference was seen in those who received prophylaxis versus no prophylaxis ($p < 0.02$). Head- and spinal cord-injured patients, two very-high-risk groups, seemed to benefit greatly from prophylaxis. Overall, risk reduction of VTE with prophylaxis was from 16.7% to 1.4% in head-injured patients and 27.3% to 10.3% in spinal cord-injured patients. However, problems occurred during the course of this study in that 67 patients (37%) originally assigned to receive no prophylaxis were switched to receive some sort of prophylaxis at the discretion of the attending surgeon. This may have confounded the DVT rates for each prophylactic modality assignment. In a prospective trial, Knudson et al.³ compared PCD, LDH, and no prophylaxis. Neither LDH nor PCD appeared to offer any protection to trauma patients with multiple injuries, except in the specific subgroup of patients with neurotrauma in which PCD was more effective in preventing DVT than control ($p = 0.057$). In contrast to the study by Knudson et al., Gersin et al.,³⁵ in a nonrandomized prospective study, looked at the incidence of VTE in a group of 32 severely head-injured patients with Glasgow Coma Scale (GCS) scores < 8 . Fourteen patients received PCDs and 18 did not because of concomitant lower extremity fractures. Within the group receiving PCDs, four (28%) developed PE and none developed DVT. In the group not receiving prophylaxis, two developed PE and two developed DVT. Although the study population was small, the findings in this study questioned the efficacy of PCD even in severe head-injured patients. In a group of 304 orthopedic trauma patients with hip and pelvic fractures, PCDs were found to reduce thromboembolic events significantly over those who had no prophylaxis (11% vs. 4%; $p = 0.02$). In subgroup analysis, PCDs were only effective in the hip fracture group, not in those with pelvic fractures.

Compression devices appear to be well-tolerated, with minimal side effects. Isolated cases of pressure necrosis from a too tightly fitted PCD have been reported.⁴² Also, peroneal palsy and compartment syndromes have been reported with PCDs.⁴³ A potential complication of PCDs is elevated intracranial pressure (ICP) in patients with severe head injury. This was addressed by Davidson et al.⁴¹ in 24 severely brain-injured patients (mean GCS score of 6) who had ICP and cerebral perfusion pressure (CPP) calculated after 0, 10, 20, and 30 minutes of intermittent pneumatic leg compression. The authors found no significant increase in ICP or CPP with the use of PCDs at any time points, and concluded that PCDs can be used safely in stable head-injured patients.

In an evidenced-based meta-analysis sponsored by the Agency of Healthcare Research and Quality on the incidence of DVT after trauma, Velmahos et al.²² found that PCDs offered no benefit over no prophylaxis in both pooled randomized control studies (OR, 0.769; 95% CI, 0.265–2.236) and in pooled nonrandomized controlled studies (OR, 0.527;

95% CI, 0.190–1.460). In another study, Velmahos et al.⁵ compared PCD, LDH, and a combination of PCD and LDH in a prospective study of 200 critically injured patients followed by weekly Doppler ultrasound to detect proximal DVT. In all three groups, the proximal DVT rate was 13%, leading the authors to question whether any of the three prophylactic regimens were sufficient in the high-risk patient.

V. Summary

Clinical studies demonstrating the effectiveness of PCDs in trauma patients are few. Although the exact mechanism of action of PCDs is unknown, their effect is believed to be based on a combination of factors addressing stasis (which is well accepted) and the fibrinolytic system (which is less clear). Until these mechanisms are better studied and understood, answers to specific questions regarding the appropriate use of PCDs are forthcoming.

VI. Future Investigation

More studies need to be performed specifically relating to the use of PCDs in trauma patients at risk for VTE. Questions regarding the efficacy of using the device on one lower extremity versus two, and whether an arm versus a leg provides equal protection, all need to be addressed. A number of commercial vendors supply compression devices. Whether all compression devices provide equal protection or whether one vendor's brand is superior needs to be determined. PCD effects on the fibrinolytic system need to be better elucidated and the contribution (if any) of the changes of PCDs on the fibrinolytic system in the prevention of VTE needs to be further delineated. Finally, the role of multimodality therapy (mechanical and pharmacologic) to provide any additional protection from VTE needs to be ascertained.

THE ROLE OF LOW-MOLECULAR-WEIGHT HEPARIN IN VENOUS THROMBOEMBOLISM PROPHYLAXIS IN TRAUMA PATIENTS

I. Statement of the Problem

The use of LMWH has gained popularity in medical and general surgical patients for reducing the risk of VTE in the past 20 years. LMWH may be better suited than LDH as a prophylaxis against VTE in the trauma patient (which is reviewed in the section The Use of Low-Dose Heparin for DVT/PE Prophylaxis, above). LDH has been shown not to be efficacious. Concerns are ongoing with regard to the potential for LMWH to exacerbate bleeding in the trauma patient with multiple injuries.

II. Process

A MEDLINE search and review of the literature revealed hundreds of articles examining the use of LMWH in VTE prophylaxis in general surgery. Trauma studies that appeared in the literature were reviewed (Table 5).

Table 5 Low-Molecular-Weight Heparin

| First Author | Year | Reference Title | Class | Conclusion |
|---------------|------|--|------------------|---|
| Green D | 1990 | Prevention of thromboembolism after spinal cord injury using low-molecular-weight heparin. <i>Ann Intern Med.</i> 113:571–574 | I | Compared Logiparin 3,500 units daily for 8 wk (n = 20) vs. SH 5,000 units tid q8h for 8 wk (n = 21) in spinal cord injury patients. DVT and bleeding rates were 0/20 in Logiparin group and 7/21 in SH group. LMWH is safe and effective for VTE prevention in selected patients with spinal cord injury and complete motor paralysis, and is superior to SH. |
| Geerts WH | 1996 | A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. <i>N Engl J Med.</i> 335:701–707 | I | Landmark study of trauma patients with ISS ≥ 9 who could receive anticoagulants. 173 had low-dose heparin and 171 had enoxaparin 30 mg bid. DVT rate: 31% enoxaparin vs. 44% heparin group ($p = 0.014$). Proximal DVT rate lowered 15% to 6% ($p = 0.012$) in enoxaparin group compared with heparin group. 5 bleeding cases in enoxaparin group and 1 in heparin group ($p = 0.12$). LMWH was more effective than low-dose heparin to prevent VTE after major trauma. |
| Knudson MM | 1996 | Use of low molecular weight heparin in preventing thromboembolism in trauma patients. <i>J Trauma.</i> 41:446–459 | II | Prospective trial in trauma patients with AIS ≥ 3 , major head injury, spine, pelvic or lower extremity fractures, acute venous injury, or age > 50 years assigned to heparin vs. no heparin, depending on injury. Heparin patients were randomized to receive LMWH (enoxaparin 30 mg bid) or mechanical compression with PCDs or AVIs. Enoxaparin was safe and effective for preventing DVT in high-risk trauma patients. When heparin is contraindicated, mechanical compression is warranted. |
| Greenfield LJ | 1997 | Posttrauma thromboembolism prophylaxis. <i>J Trauma.</i> 42:100–103 | II (pilot study) | Small pilot study of 53 patients compared enoxaparin vs. SH vs. PCDs in high-risk trauma patients with ISS > 9 and in patients considered to be at high-risk for DVT. Overall DVT rate was 43%. Enoxaparin group had half the DVTs of either SH or PCD groups, though not statistically significant because of sample size. |
| Velmahos GC | 2000 | Prevention of venous thromboembolism after injury: an evidence-based report—part I: analysis of risk factor and evaluation of the role of vena cava filters. <i>J Trauma.</i> 49:132–139 | I | SH vs. LMWH meta-analysis (for PE) revealed 3 studies (2 RCT and 1 non-RCT); showed no difference in PE (OR, 3.01; 95% CI, 0.585–15.485). However, CIs were wide and a significant difference could not be excluded. |

SH, subcutaneous heparin; AIS, Abbreviated Injury Scale; RCT, randomized controlled trial.

III. Recommendations

A. Level I: A Level I recommendation on this topic cannot be supported because of insufficient data.

B. Level II: LMWH can be used for VTE prophylaxis in trauma patients with the following injury patterns:

1. Pelvic fractures requiring operative fixation or prolonged bed rest (> 5 days).^{12,17,44}

2. Complex lower extremity fractures (defined as open fractures or multiple fractures in one extremity) requiring operative fixation or prolonged bed rest (> 5 days).^{12,17,44,45}

3. Spinal cord injury with complete or incomplete motor paralysis.^{12,17,44,46} The use of LMWH is predicated on the fact that these patients do not have other injuries that put them at high risk for bleeding.

C. Level III:

1. Trauma patients with an ISS > 9, who can receive anticoagulants, should receive LMWH as their primary mode of VTE prophylaxis.^{12,17}

2. LMWH has not been sufficiently studied in the head-injured patient with intracranial bleeding to justify its use at this time.¹⁷

3. LMWH should not be used when epidural catheters are placed or removed.⁴⁷

IV. Scientific Foundation

The use of LMWH for VTE prophylaxis and treatment has gained popularity in the past 20 years. Three LMWHs are Food and Drug Administration (FDA) approved for VTE prophylaxis or other uses in the United States. Enoxaparin has been approved for use in orthopedic joint replacement surgery and dalteparin has been approved for use in general surgery. Tinzaparin (Innohep, Leo Pharmaceutical Products Ltd., Ballerup, Denmark) has been approved to treat symptomatic DVT with or without PE. Class I data now exist for the use of enoxaparin in trauma patients, but no FDA indication for the use of LMWH in trauma patients has been approved.

LMWHs vary in mass from 2,000 to 9,000 daltons and contain the unique pentasaccharide that is required for specific binding to antithrombin III (ATIII), but in a lower proportion than that contained in the parent unfractionated heparin (UH). LMWHs have proportionally more anti-factor Xa activity compared with anti-factor II activity because they are less able to bind thrombin and ATIII simultaneously to accelerate the inactivation of thrombin by ATIII. However, LMWHs retain their ability to catalyze the inhibition of factor Xa by ATIII. In general, LMWHs have anti-factor Xa/anti-factor II ratios between 4:1 and 2:1. LMWHs have bioavailability superior to that of unfractionated heparin and produce less bleeding for equivalent antithrombotic doses, probably the result of the different effects on platelet function and vascular permeability.⁴⁸ However, the relationship between in vitro and in vivo studies has to be carefully examined when looking at LMWHs. Although in vitro anti-factor IIa activity is less than that of UH, the superior bioavailability of LMWHs results in their anti-IIa activity being proportionally greater in vivo.⁴⁸ Overall, LMWHs are clearly superior to placebo for VTE prophylaxis in general surgery, orthopedic surgery, and medical patients with small to minimal bleeding risk.

To give a Level I recommendation for the use of enoxaparin in trauma patients, more studies are needed. However, two studies report good efficacy when enoxaparin was given in moderate- to high-risk trauma patients.^{12,17} In a prospective trial of trauma patients who were considered high-risk for DVT, Knudson et al.¹² randomized 487 consecutive high-risk trauma patients to receive LMWH, PCD, or A-V foot pumps as prophylaxis against DVT. These patients were followed up by serial ultrasounds. The DVT rate was 0.87% for LMWH,

2.5% in the PCD group, and 5.7% in the A-V foot pump group (not statistically significant between groups). Geerts et al.¹⁷ randomized 265 patients to receive LDH or LMWH and followed up with serial venograms. The DVT rate was 44% for LDH and 31% for LMWH ($p = 0.014$). Quite a disparity existed between the two studies with regard to the incidence of DVT. The study by Geerts et al. used venography as the diagnostic modality, whereas Knudson used serial ultrasound. It is well known that venograms will pick up more DVTs than ultrasound (the clinical significance of an isolated, small calf DVT is open to conjecture). Another issue these studies did not address was bleeding complications. In both studies, bleeding complications were greater with LMWH; in the study by Geerts et al., major bleeding was 0.6% for LDH and 2.9% for LMWH ($p = 0.12$). In an editorial response to the study by Geerts et al., Osler and Rogers⁴⁹ noted that the study was possibly not significantly powered to detect a difference in major bleeding complications despite being able to detect a difference in DVT rates.

One study clearly showed Logiparin (Novo/Nordisk Pharmaceuticals, Inc., Princeton, NJ) 3,500 units every 8 hours is superior to LDH 5,000 units every 8 hours in spinal cord-injured patients. Event rates (DVT and bleeding) were 0 of 20 in the Logiparin group and 7 of 21 in LDH group.⁴⁶

In a meta-analysis on the prevention of venous thromboembolism after injury, Velmahos et al.²² showed no difference in PE rates when LMWH was compared with LDH (OR, 3.010; 9% CI, 0.585–15.485). However, the confidence intervals were wide and the authors concluded that a significant difference could not be excluded.

V. Summary

Class I data that now exist infer that LMWH is superior to LDH 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. Data in many different types of patients confirm improved efficacy of LMWH with the same or less bleeding risk compared with LDH prophylaxis. The Class I data would imply that LMWH should be strongly considered for use in all high-risk trauma patients (except those with head injuries) when their bleeding risk is acceptable.

VI. Future Investigation

Many unresolved issues remain concerning VTE prophylaxis of trauma patients that need to be studied in a multi-center fashion. Further studies on the efficacy of LMWH, not only on DVT but also on PE, need to be implemented in a multi-institutional format. The risk of major bleeding needs to be addressed in high-risk trauma patients. This is especially true in the head-injured patients when LMWHs are safe. Finally, new synthetic pentasaccharides that specifically activate factor Xa^{50,51} have been shown in elective orthopedic surgery to be even more efficacious against DVT than

LMWH.⁵¹ What role these synthetic pentasaccharides would have as a prophylaxis against VTE needs to be established.

THE ROLE OF THE VENA CAVA FILTER IN THE PROPHYLAXIS OF PE

I. Statement of the Problem

Vena caval interruption is a form of PE prophylaxis that is being used more frequently in trauma patients. Many trauma patients have ongoing bleeding or recent brain, spinal cord, or ocular injury that will not tolerate even minor amounts of bleeding. These patients cannot have pharmacologic prophylaxis with heparin or heparin-like derivatives. Furthermore, patients with multiple injuries often have extremity injuries, which preclude the use of PCDs. The decision to place a “prophylactic” vena cava filter (VCF) in a trauma patient requires a fundamental understanding of the risk/benefit ratio. In this review, the risk/benefit ratio is explored in the high-risk trauma patient.

II. Process

A MEDLINE search from 1980 to 2001 was performed in which “vena cava filter” was cross-referenced with “trauma.” Four articles specifically addressed complications and long-term follow up and are included in this review (Table 6).

III. Recommendations

A. Level I: A Level I recommendation on this topic cannot be supported because of insufficient data.

B. Level II: A Level II recommendation on this topic cannot be supported because of insufficient data.

C. Level III: Insertion of a “prophylactic” VCF should be considered in very-high-risk trauma patients:

1. Who cannot receive anticoagulation because of increased bleeding risk, and
2. Have an injury patterns rendering them immobilized for a prolonged period of time, including the following:^{52–69}
 - a. Severe closed head injury (GCS score < 8).
 - b. Incomplete spinal cord injury with paraplegia or quadriplegia.
 - c. Complex pelvic fractures with associated long bone fractures.
 - d. Multiple long bone fractures.

Patients at high risk for bleeding complications for 5 to 10 days after injury would include those with intracranial hemorrhage, ocular injury with associated hemorrhage, solid intra-abdominal organ injury (i.e., liver, spleen, kidney), and/or pelvic or retroperitoneal hematoma requiring transfusion. Other risk factors for bleeding include cirrhosis; active peptic ulcer disease; end-stage renal disease; and coagulopathy caused by injury, medication, or congenital/hereditary. In addition, it appears that age is a significant risk factor for VTE, but it is unclear at what age risk of VTE significantly increases. The need to place a prophylactic VCF may be increased in an older patient with one of the above-mentioned injuries.⁷⁰

IV. Scientific Foundation

The placement of a VCF in a trauma patient who does not have an established DVT or PE is certainly controversial; however, there is no question that VCFs are efficacious. They prevent the occurrence of PE from lower extremity DVT with a success rate of about 98%.⁷¹ The real issue is defining who should receive these filters, and whether they are without significant complications and are cost-effective.

Several studies have reported on the use of VCFs for prophylactic indications. Golueke et al.⁷² reported on 21 filters placed prophylactically before total joint replacement. All patients received LDH, aspirin and, when possible, graduated compression stockings. No filter-related complications or episodes of PE occurred in this group. Likewise, in 1992, Webb et al.⁵² reported their results of using a prophylactic filter in 24 of 52 patients undergoing acetabular fracture repair with sufficient risk factors. No insertion complications were reported. Four patients had leg edema, one with phlegmasia, and no PEs. In the 27 patients who did not receive a filter, 2 PEs were noted, one of which was fatal. Rohrer et al.⁷³ reported on the use of VCFs for “extended” indications in 66 patients (many of whom were trauma patients). Only one PE was fatal in this group, and 22 patients had no documented DVT before filter insertion. The recurrent non-fatal PE rate was 3% and symptomatic occlusion of the inferior vena cava (IVC) occurred 4.5% of the time in this study. Major limitations of this study include the retrospective design, the inability to distinguish outcomes in the 21 patients with VCF used as prophylaxis from the 45 others, and unspecified follow-up duration. Jarrell et al.⁵³ reported a favorable experience with 21 Greenfield filters that were placed in spinal cord-injured patients with documented DVT or PE. Only one PE death occurred in this group, and two instances of IVC thrombus were noted, both of which were well tolerated.

Several reports now exist in the literature on the use of prophylactic vena caval filters in trauma patients.^{53–62,64–69,74–78} Six of these studies^{55,56,63,64,69} demonstrated a significant reduction in the incidence of PE in their trauma population compared with historical controls. Minimal insertion and short-term complications were reported, with 1-year patency rates ranging from 82% to 96%,^{56,58} and 2-year patency rates at 96%⁵⁶ in prophylactic filters inserted in trauma patients. Moreover, a higher DVT rate was not seen in prophylactic filter patients compared with nonfilter patients.^{55,79} A recent follow-up study with a minimum of 5 years in 199 patients showed that the filters were well tolerated. Patients went on to live active lives, with a minimal migration or cava thromboses.⁶⁶ Likewise, Greenfield et al.⁶⁷ reported on 249 prophylactic VCFs for trauma and noted an incidence of PE in 1.5%, a caval occlusion rate of 3.5%, and good outcome with regard to the mechanical stability of the filter. The authors concluded that the prophylactic VCF placement was associated with a low incidence of adverse outcomes and

Table 6 Vena Cava Filters

| First Author | Year | Reference Title | Class | Conclusion |
|--------------|------|--|-------|---|
| Webb LX | 1992 | Greenfield filter prophylaxis of pulmonary embolism in patients undergoing surgery for acetabular fracture. <i>J Orthop Trauma</i> . 6:139-145 | II | Outlined predisposing factors for VTE. In patients undergoing acetabular fracture repair with 2 or more risk factors, prophylactic filter was placed (24/51). No insertion complications and no PEs. 4 patients had leg edema and 1 had phlegmasia. 27 patients did not receive preoperative filter; 2 PEs in this group, 1 fatal. All patients had SQ heparin and aspirin. |
| Jarrell BE | 1983 | A new method of management using the Kim-Ray Greenfield filter for deep venous thrombosis and pulmonary embolism in spinal cord injury. <i>Surg Gynecol Obstet</i> . 157:316-320 | III | 21 SCI patients with filter placed for "traditional" indications. 1 death secondary to PE in filter patients secondary to misplacement in right iliac vein. 2 thrombosed IVCs. Overall DVT rate in SCI population 62%. Emphasis on knowing exact location of DVT, anatomy of IVC, that filter must protect from all sources of emboli in lower extremity, and that there is a risk of thrombosis through large collateral vessels. |
| Cipolle M | 1995 | Prophylactic vena caval filters reduce pulmonary embolism in trauma patients [abstract]. <i>Crit Care Med</i> . 23:A93. | III | Review of 43 high-risk trauma patients who had VCFs placed, 16 for traditional indications and 27 for prophylaxis. 0 PEs in prophylactic group and 5 PEs in traditional indications group. Overall PE rate was 11.6%. |
| Rodriguez JL | 1996 | Early placement of prophylactic vena cava filters in injured patients at high-risk for pulmonary embolism. <i>J Trauma</i> . 40:797-804 | II | 40 VCFs placed in consecutive patients with 3 or more risk factors compared to 80 matched historic controls. 1 PE in VCF group, 14 PEs in non-VCF group. PE-related mortality and overall mortality was the same in each group, as was the incidence of DVT, 15% in VCF group and 19% in no-VCF group. |
| Rogers FB | 1995 | Routine prophylactic vena cava filter insertion in severely injured trauma patients decreases the incidence of pulmonary embolism. <i>J Am Coll Surg</i> . 180:641-647 | II | Continued follow-up from <i>J Trauma</i> 1993. 63 prophylactic VCFs placed in high-risk patients as previously outlined. DVT rate: 30%, 1 PE (fatal). No insertion complications, 3.5% insertion-related thromboses. 30-day patency, 100% (n = 36); 1 year, 96% (n = 34); 2 year, 96% (n = 16). |
| Rosenthal D | 1994 | Use of the Greenfield filter in patients with major trauma. <i>Cardiovasc Surg</i> . 2:52-55 | II | Control group 1984-88, 94 patients with 22 PEs (23%) and 5% fatal PE rate. 1988-92, after adoption of protocol to place prophylactic filters, 67 patients with only 1 PE and no fatal PEs. Minimal insertion morbidity. No long-term follow-up reported. |
| Wilson JT | 1994 | Prophylactic vena cava filter insertion in patients with traumatic spinal cord injury: preliminary results. <i>Neurosurgery</i> . 35:234-239 | II | Retrospective analysis of 111 SCI patients showed 7 PEs (6.3%) accounting for 31% of trauma PEs. 6 PEs occurred after patient discharge, mean time 78 days (9-5,993). 15 prophylactic filters placed in SCI patients. No insertion problems or PEs. 30-day patency rate, 100% (n = 14); 1-year, 82% (n = 9). |
| Winchell RJ | 1994 | Risk factors associated with pulmonary embolism despite routine prophylaxis: implications for improved protection. <i>J Trauma</i> . 37:600-606 | III | 8-year retrospective registry review at Level I trauma center (9,721 patients). Overall PE rate, 37%. 29 prophylactic VCFs placed with no PEs or short-term complications. Average time to PE in this group was 14.5 days. High-risk categories: head + spinal cord injury (4.5%); head + long bone fracture (8.8%); severe pelvis + long bone fracture (12%); multiple long bone fractures (10%). Patients with estimated risk of PE, despite prophylaxis of > 2-5%, are reasonable candidates for prophylactic VCF placement, especially if conventional measures cannot be used. |
| Zolfaghari D | 1995 | Expanded use of inferior vena cava filters in the trauma population. <i>Surg Annu</i> . 27:99-105 | III | Retrospective analysis of 45 filters placed in 3,005 patients. 38/45 had extended indications for filter placement as they were placed for no DVT or in patients with DVT or PE but no contraindication to anticoagulation. No PEs after filter placement, and there was 1 death secondary to closed head injury. |
| Rogers FB | 1993 | Prophylactic vena cava filter insertion in severely injured trauma patients: indications and preliminary results. <i>J Trauma</i> . 35:637-642 | II | Prospective criteria for prophylactic filter insertion after retrospective review of trauma registry. Prophylactic filters placed in patients who could not receive anticoagulation and grouped: (1) age > 55 with long bone fracture; (2) severe closed head injury and coma; (3) multiple long bone fractures and pelvic fractures; (4) spinal cord injury. 34 patients had prophylactic filters placed. No PEs, 17.6% DVT rate. 30-day patency, 100%; 1-year patency, 89% (n = 17). |
| Patton JH Jr | 1996 | Prophylactic Greenfield filter: acute complications and long-term follow-up. <i>J Trauma</i> . 41:231-237 | II | Follow-up of prophylactic filters placed between 1991 and 1994. 69 filters with 9% insertion rate. 15 patients died. 30 patients were located and 19 returned for follow-up evaluation (35%). Average follow-up was 770 days (246-1,255). No caval thrombosis. 14 patients had chronic DVT. 11/14 had chronic venous insufficiency. No long-term caval thromboses. Not clear, however, whether filter caused chronic venous insufficiency because there was no nonfilter group. |

Table 6 Continued

| First Author | Year | Reference Title | Class | Conclusion |
|---------------------------|------|--|-------|---|
| Leach TA | 1994 | Surgical prophylaxis for pulmonary embolism. <i>Am Surg.</i> 16:292–295 | II | 205 VCFs placed for indications that were outlined prospectively, although many were inserted for “traditional” indications. No PEs in these filters, patients, and minimal insertion complications. |
| Khansarinia S | 1995 | Prophylactic Greenfield filter placement in selected high-risk trauma patients. <i>J Vasc Surg.</i> 22:235–236 | I | 108 filters placed in high-risk trauma patients over a 2-year period with injury-matched controls who did not receive a filter. PEs in filter group vs. 13 PEs in control group, 9 of which were fatal. The differences were significant for both PE ($p < 0.009$) and PE-related death ($p < 0.03$). |
| Gosin JS | 1997 | Efficacy of prophylactic vena cava filters in high-risk trauma patients. <i>Ann Vasc Surg.</i> 11:100–105 | II | 99 prophylactic filters placed in high-risk trauma population over 2-year period. This decreased PEs in trauma population to 1.6% from 4.8% in historical controls ($p < 0.045$ Fisher’s exact). |
| Sekharan J | 2001 | Long term follow up prophylactic Greenfield filters in multisystem trauma patients. <i>J Trauma.</i> 51:1087–1091 | III | 5-year follow-up study of 199 patients showed that filters are well-tolerated in trauma patients, with minimal migration on caval thrombosis. |
| Greenfield LJ | 2000 | Prophylactic vena cava filters in trauma: the rest of the story. <i>J Vasc Surg.</i> 32:490–495 | II | 249 patients had prophylactic filters and prospectively followed. Caval occlusion rate was 3.5% and new PE was 1.5%. Authors concluded that prophylactic VCF was associated with low adverse outcome rate while protecting from fatal PE. |
| Van Natta TL | 1998 | Elective bedside surgery in critically injured patients is safe and cost effective. <i>Ann Surg.</i> 227:618–624 | III | 71 ICU filters placed at bedside in the ICU in trauma patients under ultrasound guidance. No complications associated with IVC filter placement. Decreased cost and OR use. |
| Langan EM 3 rd | 1999 | Prophylactic inferior vena cava filters in trauma patients at high-risk: follow-up examination and risk/benefit assessment. <i>J Vasc Surg.</i> 30:484–488 | III | 160 prophylactic filters inserted: 75 (45%) returned for follow-up, a mean of 19.4 mo (range, 7–60 mo) after insertion. 93% patency of vena cava on follow-up ultrasound; 13.3% had DVT with one nonfatal PE. Filter insertion complications occurred in 3 (1.6%) patients including one groin hematoma, one A-V fistula, and one misplacement in common iliac vein. |
| Velmahos GC | 2000 | Prevention of venous thromboembolism after trauma: an evidence-based report—part II: analysis of risk factors and evaluation of the role of vena cava filters. <i>J Trauma.</i> 49:140–144 | I | Meta-analysis of literature on prophylactic vena cava filters. Patients with prophylactic vena cava filters had a lower incidence of PE (0.2%) compared with those without filters (1.5%) vs. historical controls (5.8%). |
| Greenfield LJ | 1988 | Twelve-year clinical experience with the Greenfield vena cava filter. <i>Surgery.</i> 104:706–712 | III | Long-term follow-up of 469 patients with mean follow-up of 43 months (0.3–138) from 1974–1986. 81 filters placed for “extended” indications (17%), 40 trauma patients included in follow-up. 96% IVC patency, 98% filter patency rate, 4% misplacement rate, 3% recurrent PE rate. |
| Golueke PJ | 1988 | Interruption of the vena cava by means of the Greenfield filter: expanding the indications. <i>Surgery.</i> 103:111–117 | III | 16 filters inserted prophylactically before joint replacement surgery in patients with history of VTE. 72 filters inserted for “traditional” indications. Mean follow-up, 16.4 mo (range 1–60 mo) in 65 patients. Complications: 3% recurrent PE, 9% leg edema, 7.5% caval occlusion 92.5% patency. No PEs in prophylactic group that received antiplatelet and pneumatic compression therapy. Indications should be extended for VCFs to help reduce preventable deaths secondary to PE. |
| Rohrer MJ | 1989 | Extended indications for placement of inferior vena cava filters. <i>J Vasc Surg.</i> 10:44–50 | III | 264 filters placed in all types of patients. 66 placed prophylactically. “Extended” indications: (1) no documented DVT but high risk; (2) small PE would be fatal because of poor cardiopulmonary reserve; (3) large iliofemoral thrombus; (4) procedure in conjunction with venous thrombectomy; (5) thrombus above previously placed IVC filter. No deaths in either group. Prophylactic group had minimal morbidity. 3 PEs (4.5%) despite filter, 1 mortality, and 4.5% occlusion. Recommend liberalizing indications for insertion of Greenfield filter since they had an insertion mortality rate of 0% and fatal PE rate of 1.5% in high-risk prophylactic group. |
| Ferris EJ | 1993 | Percutaneous inferior vena cava filters: follow-up of seven designs in 320 patients. <i>Radiology.</i> 188:851–856 | III | 324 filters placed over 7 yr. No placement-related mortality or morbidity. Average follow-up, 404 days (1–2,392). 19% caval thrombosis; 9% delayed penetration through IVC wall; 6% migration more than 1 cm, 2% fracture strut. Insertion site DVT was 2%. Long-term radiologic follow-up recommended for IVC filters. |
| Nunn CR | 1997 | Cost-effective method for bedside insertion of vena cava filters in trauma patients. <i>J Trauma.</i> 45:752–758 | III | Ultrasound-guided IVC filter insertion in 55 trauma patients. 49 successful; 6 failed. |
| Headrick JR | 1997 | The role of ultrasonography and inferior vena cava filter placement in high-risk trauma patients. <i>Am Surg.</i> 63:1–8 | II | 228 high-risk patients were followed with serial ultrasound. 39 (17%) developed DVT with 29 undergoing immediate IVC filter placement. Decreased incidence of PE compared with historical controls. |
| McMurtry AL | 1999 | Increase use of prophylactic vena cava filters in trauma patients failed to decrease overall incidence of pulmonary embolism. <i>J Am Coll Surg.</i> 189:314–320 | III | Review of 299 patients with prophylactic filters over an 8-yr period, yielded no demonstrable decrease in PE incidence compared with historical controls. |

Table 6 Continued

| First Author | Year | Reference Title | Class | Conclusion |
|---------------|------|--|-------|--|
| Ashley DW | 2001 | Accurate deployment of vena cava filters: comparison of intravascular ultrasound and contrast venography. <i>J Trauma</i> . 50:975-981 | III | 21 patients had VCF placed via intravascular ultrasound in the OR, followed by contrast venography. In four cases, contrast venography missed "best location" by 3 mm or more. Contrast venography overestimated vena cava diameter on average (24.4 ± 3.3 mm venography vs. 20.6 ± 3.1 mm intravascular ultrasound; $p < 0.0001$). |
| Greenfield LJ | 1996 | Posttrauma thromboembolism prophylaxis. 8th Annual American Venous Forum | I | Pilot study for large, multicenter trial. 53 patients randomized to receive PCD, LMWH, or unfractionated heparin and 1/2 randomized to receive VCF. Inclusion criteria were ISS > 9 and VTE risk factor score developed by investigators. 26 patients got VCF. No complications of filter placement or evidence of vena caval occlusion. No PEs in either group. 12 DVTs in nonfilter patients and 11 DVTs in filter patients. |
| Tola JC | 1999 | Bedside placement of inferior vena cava filters in the intensive care unit. <i>Am Surg</i> . 65:833-837 | III | 25 patients underwent prophylactic IVC filters in the ICU with digital C-arm with no postoperative or intraoperative complications. Average saving of \$1,844 when filters were placed in ICU vs. OR. |
| Lorch H | 2000 | Current practice of temporary vena cava filter insertion: a multicenter registry. <i>J Vasc Interv Radiol</i> . 11:83-88 | III | 188 patients (Antheor filter, 54%; Guenther filter, 26%; Prolyser filter, 18%). 4 patients died of PE. 16% filter thrombosis; filter dislodgement, 4.8%. |
| Neuerburg JM | 1997 | Results of a multicenter study of the retrievable tulip vena cava filter: early clinical experience. <i>Cardiovasc Intervent Radiol</i> . 20:10-16 | III | 83 patients implanted with retrievable Tulip filter; 3 filter insertion problems, 1 fatal recurrent PE; 2 nonfatal PEs; 8 caval occlusions. |

SCI, spinal cord injury; SQ, subcutaneous.

provided protection from fatal PE. However, none of these studies were Class I studies.

In contrast to the above-mentioned studies, McMurty et al.,⁷⁷ in a retrospective review of 299 patients who had prophylactic filters placed over an 8-year period, failed to demonstrate an overall decrease in their trauma population compared with historical controls. This is the only study to date that failed to report a benefit of prophylactic VCFs in high-risk trauma patients. This study only looked at the incidence of PE in their overall trauma population and could have missed a significant decrease of PE in their high-risk population if subset analysis was performed.

The data presented herein would indicate that the risk/benefit ratio is favorable in the high-risk trauma patients. The problem is defining the high-risk patient. In the first section of this review (Risk Factors for Venous Thromboembolism after Trauma), we defined the high-risk patient for DVT, but not necessarily for PE (arguably a more serious complication of VTE). One trauma study⁶¹ identified four injury patterns that accounted for 92% of PEs: spinal cord injury with paraplegia or quadriplegia; severe closed head injury with a GCS score ≤ 8 for $>$ than 48 hours; age > 55 years with isolated long bone fractures; and complex pelvic fractures associated with long bone fractures. This single-institution study may seem at conflict with what was presented in the first section of this review, which showed that on meta-analysis, head injury was not a high-risk factor. It must be noted, however, the meta-analysis dealt only with DVT. Furthermore, this study found those patients who had a GCS score > 8 for greater than 48 hours at greater risk for PE, whereas the meta-analysis did not make such a distinction. This may explain the apparent conflict in head injury as a risk factor after injury. Another retrospective review including 9,721

patients⁵⁹ showed that the high-risk categories include head injury plus spinal cord injury, head injury plus long bone fracture, severe pelvic fracture plus long bone fracture, and multiple long bone fractures. These authors estimate that if they had used a prophylactic filter in these 2% of patients, a very dramatic reduction in PE would have been seen. They suggested that patients with an estimated risk of PE of 2% to 5%, despite prophylaxis, are reasonable candidates for prophylactic VCF placement, especially if conventional prophylactic measures cannot be used. Many years of experience with the Greenfield filter indicate that it has a patency rate of about 96%, a recurrent PE rate of 3% to 5%, and a caval penetration rate of about 2%.⁷⁹ These complication rates were reasonable, but multiplied over the lifetime of a young patient, these rates could become important. One study indicated a significant amount of chronic venous insufficiency in long-term follow-up of prophylactic filter patients.⁶² However, with no nonfilter group to compare with, whether the filter was the cause of this chronic venous insufficiency in this very-high-risk group is not clear.

The more recent literature on this subject of VCFs discusses the bedside placement of filters^{68,75,80} and the use of ultrasound as an imaging modality in the placement of filters.^{68,75,78} These studies showed that filters could be placed safely at the bedside, resulting in a decrease in operating room use and cost. Ashley et al.⁷⁸ compared intravascular ultrasonography to contrast venography in 21 trauma patients who had prophylactic VCF placement. The authors noted that contrast venography overestimated the size of the vena cava in all cases (average vena cava diameter was 26.4 ± 3.3 mm by venography vs. 20.6 ± 3.1 mm by intravascular ultrasound). The use of contrast venography presents a significant concern when one notes that a vena cava of greater

than 28 mm is a contraindication to the placement of a Greenfield VCF.

More recently, interest and experience have been increasing for the many types of retrievable filters. Much of this early work has been performed in Europe.^{81,82} The use of retrievable filters is particularly appealing to trauma surgeons whose patients are at high risk for PE for a relatively short period. Technical problems with the retrievable filters have prevented their widespread application at the present time. Nevertheless, they may have potential in the future. A recent survey of 620 trauma surgeons across the United States revealed that the potential removability of filters would significantly increase ($p < 0.01$) prophylactic filter placement from 29% to 53%.

V. Summary

No Class I studies exist to support insertion of a VCF in a trauma patient without an established DVT or PE. A fair amount of Class II and III data that may support VCF use has been accumulated 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.

VI. Future Investigation

Important unresolved issues with regard to filter use in trauma patients include the following:

- Do VCFs significantly reduce the incidence of clinically important PE in patients who receive "optimal" prophylaxis?
- If so, can a group of patients be identified who have a high failure rate with "optimal" prophylaxis?
- What are the short-term and long-term complications of VCF insertion used as primary prophylaxis in trauma patients?
- Is VCF insertion cost-effective?
- Do temporary VCFs have a role in trauma patients whose risk of PE may be high for only a short time?

THE ROLE OF ULTRASOUND IN DIAGNOSTIC IMAGING FOR DVT IN TRAUMA

I. Statement of the Problem

Early identification of DVT in trauma patients would allow treatment to be initiated and decrease the frequency of complications. Ultrasound scanning has the advantage as a diagnostic tool to detect DVT because it is noninvasive, requires no contrast medium, can be performed at the bedside, and is able to detect nonocclusive thrombus. Two types of ultrasound scanning will be discussed. Doppler ultrasound involves a hand-held probe placed over the skin of the vein being studied. Duplex ultrasonography uses real-time B-mode sonography that produces a two-dimensional image using high-frequency sound waves and Doppler ultrasound. The addition of color flow to duplex provides additional

advantages. It may help with identification of the deep venous system, especially the veins below the knee. Partially occluding thrombi may be noted as a defect in the lumen's color, and completely occlusive thrombi as the absence of color from the vein. It is important for the reader to distinguish between these two technologies for accuracy of ultrasound to detect DVT. Furthermore, in the critical review of ultrasound technology in detecting DVT, a dichotomy exists in the sensitivity of ultrasound in symptomatic versus asymptomatic patients.

II. Process

A MEDLINE search from 1966 to the present revealed several thousand articles related to the diagnosis of DVT using ultrasound. Several of the more seminal articles and review articles related to the ultrasound diagnosis of DVT in the nontrauma patient are included to provide a perspective on the current state of the technology. Sixteen articles related to the ultrasound diagnosis of DVT in the trauma patient are discussed in this review (Table 7).

III. Recommendations

A. Level I: Duplex ultrasound may be used to diagnose *symptomatic* trauma patients with suspected DVT without confirmatory venography.^{83,84}

B. Level II: A Level II recommendations cannot be supported on this topic because of insufficient data.

C. Level III: Serial duplex ultrasound imaging of high-risk asymptomatic trauma patients to screen for DVT may be cost-effective and may decrease the incidence of PE.^{15,85-90} However, the use of ultrasound in screening asymptomatic patients is burdened by a low sensitivity when compared with venography.^{7,91,92}

IV. Scientific Foundation

A. Ultrasound Diagnosis of DVT in the Nontrauma Patient

1. Doppler Ultrasound. The use of a Doppler flowmeter for the diagnosis of DVT has some appeal because of its relatively low cost and the additional benefit of being able to be performed at the bedside or on an outpatient basis. The accuracy is very much dependent on the experience of the user.⁸³ Wheeler and Anderson⁸⁴ compiled a meta-analysis of 23 studies examining the accuracy of Doppler ultrasound compared with venography. Overall, in symptomatic patients, Doppler ultrasound had a sensitivity of 85% (722 of 847) and a specificity of 88% (1,415 of 1,615) to detect proximal DVT.

2. Duplex Ultrasound. Duplex ultrasound using both real-time B-mode scanning and Doppler ultrasound allows for noninvasive visualization of the veins of the leg. In most patients, it is easy to visualize the common femoral, proximal superficial femoral, and popliteal veins. It can be difficult to visualize the superficial femoral vein in Hunter's canal and also to detect calf DVTs. An acute DVT is identified by the presence of a dilated vein, lack of compressibility, and ab-

Table 7 Ultrasound

| First Author | Year | Reference Title | Class | Conclusion |
|---------------|------|---|-------|--|
| Burns GA | 1993 | Prospective ultrasound evaluation of venous thrombosis in high-risk trauma patients. <i>J Trauma</i> . 35:405–408 | III | 58 high-risk trauma patients underwent total body biweekly Doppler U/S. There was a 21% incidence of DVT, all occult. 23% of patients had incomplete U/S exams. |
| Napolitano LM | 1995 | Asymptomatic deep venous thrombosis in the trauma patient: is an aggressive screening protocol justified? <i>J Trauma</i> . 39:651–659 | III | Retrospective review of serial U/S performed on trauma patients admitted to ICU. 10% DVT rate multiple logistic regression revealed ISS, length of stay, Trauma Score, and spinal cord injury as risk factors. |
| Meythaler JM | 1996 | Cost-effectiveness of routine screening for proximal deep venous thrombosis in acquired brain injury patients admitted to rehabilitation. <i>Arch Phys Med Rehabil</i> . 77:1–5 | II | 8.5% of head-injured patients admitted to rehabilitation have DVT on screening duplex U/S. Cost analysis revealed routine screening for DVT in this patient population was more cost-effective than screening for either breast cancer or colorectal cancer. |
| White RH | 1990 | Deep-vein thrombosis after fracture of the pelvis: assessment with serial duplex-ultrasound screening. <i>J Bone Joint Surg Am</i> . 72:495–500 | III | 60 pelvic fractures screened with duplex U/S. 15% DVT rate; 1 PE noted in patient who became positive on duplex that day. |
| Meredith JW | 1993 | Femoral catheters and deep venous thrombosis: a prospective evaluation of venous duplex sonography. <i>J Trauma</i> . 35:187–191 | III | Serial B-mode duplex U/S showed a 14% incidence of ileofemoral DVT on the side of 8 French femoral venous catheter. |
| Knudson MM | 1992 | Thromboembolism following multiple trauma. <i>J Trauma</i> . 32:2–11 | II | Prospective U/S evaluation in 113 patients identifying risk factors for DVT (age, No. of days immobilized, No. of transfusions, abnormal admission clotting studies). |
| Brasel KJ | 1997 | Cost effective prevention of pulmonary embolus in high-risk trauma patients. <i>J Trauma</i> . 42:456–463. | II | Cost-effectiveness study of biweekly ultrasound vs. prophylactic VCF in high-risk trauma patients using decision-tree analysis. Ultrasound cheaper if length of stay < 2 wk, but VCF more cost-effective if length of stay > 2 wk. |
| Agnelli G | 1995 | Diagnosis of deep vein thrombosis in asymptomatic high-risk patients. <i>Haemostasis</i> . 25:40–48 | I | Review of both U/S and IPG studies which were classified as Level I or Level II by author. Both U/S and IPG proved low sensitivity in detecting asymptomatic DVT in meta-analysis. |
| Dennis JW | 1993 | Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high-risk groups. <i>J Trauma</i> . 35:132–139 | III | 281 high-risk trauma patients screened with duplex or Doppler U/S revealed 4.6% incidence of DVT and 6% incidence of PE. Of those patients with PE (all fatal), none had DVT by U/S. |
| Wells PS | 1995 | Accuracy of ultrasound for the diagnosis of deep venous thrombosis in asymptomatic patients after orthopedic surgery: a meta-analysis. <i>Ann Intern Med</i> . 122:47–54 | I | Meta-analysis comparing contrast venography to ultrasound in 2,000 orthopedic patients, ultrasound found only to have a sensitivity of 62% in detecting proximal asymptomatic DVT. |
| Chu DA | 1985 | Deep venous thrombosis: diagnosis in spinal cord injured patients. <i>Arch Phys Med Rehabil</i> . 66:365–368 | III | Systematic clinical exam for DVT was successful in diagnosing 2 DVTs out of 21 patients. Both were confirmed with Doppler U/S. |
| Knudson MM | 1994 | Prevention of venous thromboembolism in trauma patients. <i>J Trauma</i> . 37:480–487 | I | 25 trauma patients randomized to PCD, LCH, or no prophylaxis were followed with serial duplex. DVT rates were not significant between groups except in isolated neurotrauma where PCDs were more effective than control in preventing DVT ($p = 0.057$). |
| Satiani B | 1997 | Screening for major deep venous thrombosis in seriously injured patients: a prospective study. <i>Ann Vasc Surg</i> . 11:626–629. | III | Cost of routine screening (\$18,586 per DVT identified) did not justify its use in patients receiving routine prophylaxis. |

U/S, ultrasound.

sence of Doppler flow sounds. Again, the technical quality of the study is very much user-dependent. In patients who present with symptoms of DVT, ultrasound has a high sensitivity and specificity. Comerota's collective review of 25 studies in which duplex was used to diagnose proximal DVT in symptomatic patients had a sensitivity of 96% (1,132 of 1,178) and a specificity of 96% (1,384 of 1,450).³¹ In the 10 series in which duplex was used to diagnose calf DVT in symptomatic patients, it had a sensitivity of 80% (122 of 153).

In asymptomatic high-risk patients, duplex ultrasound does not appear as accurate as a screening technique for

DVT; however, the reports are quite variable in success rates. Most of these studies have been performed in orthopedic patients undergoing elective surgery. Agnelli et al.⁹¹ attempted to shed some light on the diagnostic accuracy of duplex ultrasonography in patients with asymptomatic DVT by performing an overview on the studies, taking into account their study methodology. A study was classified as Level I if consecutive patients were admitted, bilateral venography was performed, and ultrasonography was performed and judged before venography. Studies not fulfilling these criteria were considered Level II. Overall, there were four Level I studies and eight Level II studies (Table 8).

Table 8 Sensitivity and Specificity of Duplex Ultrasound in Asymptomatic Patients to Screen for DVT According to Experimental Design

| | Sensitivity ^a (%) | Specificity ^a (%) |
|-------------------------|------------------------------|------------------------------|
| Level I (4 studies) | 61 (51–73) | 97 (95–99) |
| Level II (8 studies) | 92 (83–93) | 98 (94–100) |

^a 95% confidence intervals in parentheses. Adapted from Agnelli et al.⁹ with permission. The differences in sensitivity and specificity between Level I and Level II studies were statistically significant ($p < 0.001$).

B. Ultrasound Diagnosis of DVT in the Trauma Patient

Several studies exist on the use of ultrasound to screen for DVT in asymptomatic patients at high risk for DVT. Unfortunately, most of these studies had significant methodologic flaws, and few if any used a confirmatory venogram to check the accuracy of their techniques. Of additional concern was the fact that several of these series reported on a number of PEs that occurred in the absence of documented DVT, leading to speculation on the possibility that ultrasound screening missed a clinically significant DVT. One must be reminded, however, that other sources of PE, such as the upper extremity and heart,⁹³ would not be picked up by ultrasound of the lower extremity. Prandoni and Bernardi⁹³ noted that upper extremity DVT accounts for 1% to 4% of all DVTs and that PEs can occur in up to 36% of these cases. Nevertheless, these ultrasound studies do offer a glimpse of the incidence of the occult DVTs that occur in high-risk trauma patients, and they provide additional data as to their location and origins as well as the role that prophylaxis plays in decreasing the incidence of DVT.

Burns et al.⁸⁵ performed a comprehensive color Doppler ultrasound examination twice weekly of all major venous structures in 57 patients classified as high risk during an 8-month period. Both upper and lower extremities were examined as well as the internal jugular, subclavian, and axillary veins; the inferior vena cava; and the common iliac, internal, and external veins. Twelve high-risk trauma patients (21%) were identified as having occult DVT. A complete ultrasound examination was unable to be attained in 23% of patients. No confirmatory study was performed in those who tested positive on ultrasound. Of note, there were two PEs in this high-risk patient group (confirmed by pulmonary angiography), and both patients at the time had screened negative for DVT. Napolitano et al.⁸⁶ retrospectively reviewed the results of biweekly duplex screening in 458 trauma patients admitted to their ICU over a 5-year period. The incidence of DVT was 10%, and all were asymptomatic. Multiple logistic regression revealed age, length of stay, spinal cord injury, ISS, and TRISS scores as being significant risk factors for the development of DVT. No confirmatory study was used in those patients who tested positive for DVT, and a PE occurred in this population. In a commentary that accompanied

the article, Knudson pointed out several methodologic flaws with the study. The issues were the timing of the scans obtained, the retrospective nature of the study, and the use of only ICU patients in the screening protocol, which introduces a bias eliminating other high-risk patients such as those with pelvic or lower extremity fractures that may not need ICU admission.

Meythaler et al.⁸⁷ performed a cost analysis of routine screening for proximal DVT using color-Doppler ultrasound in 116 head-injured patients being admitted to a rehabilitation unit over a 21-month period. Fourteen (8.5%) patients were found to have DVT on initial screening. No confirmatory studies were performed and all were asymptomatic. The authors conducted a complicated cost-benefit analysis of ultrasound screening for DVT in this population and found that the cost per year of life saved was \$2,977.65 (\$129,527.83/43.5 years). This compared favorably to the \$8,280 per year of life saved for biennial mammograms for women aged 50 to 59 years and the \$35,054 per year of life saved for annual fecal occult blood tests beginning at age 65. As is indicative of such an analysis, a number of underlying assumptions exist that may not reflect reality; nevertheless, it does lend perspective on the cost issues relative to other screening programs.

In a study of 60 patients with major fractures of the pelvis, White et al.⁸⁸ performed serial duplex sonography to determine the incidence of DVT. In this study, confirmatory contrast venography was used in those who tested positive for DVT on ultrasound. Eight (15%) patients developed DVT, of which six were proximal and two were distal (calf). All were asymptomatic for DVT. One PE presented in this population in a patient who subsequently tested positive for a proximal DVT. One weakness of the study was that the screening ultrasound was first performed 7 days after admission. The authors stated that they checked the accuracy of duplex ultrasound as a screening test in 32 high-risk orthopedic patients (including those with lower extremity and pelvic fractures) by comparing it to ascending venography. Eleven patients had positive duplex sonograms, and all had positive venograms. One patient had a negative duplex but a positive venogram. Overall, the predictive value of a positive duplex sonogram in this study population was 100% (11 of 11) and that of a negative duplex sonogram was 95% (21 of 22).

Chu et al.⁹⁴ looked at the 21 spinal cord-injured patients admitted to a rehabilitation unit over an 11-month period who were screened with Doppler ultrasound and impedance plethysmography on alternate weeks. Only two patients developed DVT during an 8-week period, and both were detected clinically before diagnostic testing. It should be noted that this study somewhat contradicts other studies of DVT in spinal cord-injured patients in which the incidence of DVT approached 100%.^{95,96} In addition, the authors of this study used Doppler ultrasound with an unknown sensitivity and specificity as a screening procedure in the asymptomatic patient.

Table 9 Venography

| First Author | Year | Reference Title | Class | Conclusions |
|---------------|------|--|-------|--|
| Wheeler HB | 1995 | Diagnostic methods for deep vein thrombosis. <i>Haemostatis</i> . 25:6–26 | III | Excellent review of current state of the art on the diagnostic modalities to detect DVT. Good discussion of limitations of venography. |
| Sandler DA | 1984 | Diagnosis of deep-vein thrombosis: comparison of clinical evaluation, ultrasound, plethysmography and venoscan with x-ray venogram. <i>Lancet</i> . 2:716–719 | III | 50 patients with suspected DVT underwent numerous diagnostic studies. Least accurate was IPG and most accurate was venogram, but this was only 90%. |
| Burke B | 1995 | The diagnostic approaches to deep venous thrombosis. <i>Clin Chest Med</i> . 16:253–268 | II | Review of diagnostic modalities for DVT. Venogram considered “gold standard” to which other modalities are compared. |
| Geerts WH | 1994 | A prospective study of venous thromboembolism after major trauma. <i>N Engl J Med</i> . 331:1601–1606 | II | Major incidence study of DVT after trauma in patients who received no prophylaxis. Diagnosis of DVT was made by contrast venography. |
| Kudsk KA | 1989 | Silent deep vein thrombosis in immobilized multiple trauma patients. <i>Am J Surg</i> . 158:515–519 | III | Incidence study of DVT using venogram as diagnostic modality. 63% of immobilized patients for 10 days or longer developed DVT. |
| Freeark RJ | 1967 | Posttraumatic venous thrombosis. <i>Arch Surg</i> . 95:567–575 | II | Early study using venogram in 124 trauma patients in hospital 3 weeks or longer. 35% incidence of DVT in this population. |
| Montgomery KD | 1995 | Magnetic resonance venography to evaluate the deep venous system of the pelvic in patients who have an acetabular fracture. <i>J Bone Joint Surg Am</i> . 77:1639–1649 | III | 45 patients with acetabular fracture; MRV detected 24 asymptomatic DVTs, 7 in internal iliac vein, an area not seen on ultrasound or venography. |
| Rabinov K | 1972 | Roentgen diagnosis of venous thrombosis in the leg. <i>Arch Surg</i> . 104:134–144 | III | This study refined and standardized the technique of venography in the detection of DVT. |
| Bettman MA | 1987 | Contrast venography of the leg: diagnostic efficacy, tolerance, and complication rates with ionic and nonionic contrast material. <i>Radiology</i> . 165:113–116 | II | Multi-institutional study comparing ionic and nonionic contrast material for venography. Demonstrated 9% postvenography DVT by ¹²⁵ I-fibrinogen scanning. |
| Kakkar VV | 1970 | Deep vein thrombosis of the leg: is there a “high-risk” group? <i>Am J Surg</i> . 120:527–530 | III | Radioactive fibrinogen study that demonstrated a significant number of calf emboli extends proximally. |
| Brathwaite CE | 1973 | Complications of anticoagulation for pulmonary embolism in low risk trauma patients. <i>Chest</i> . 104:718–720 | III | Study demonstrated anticoagulation had a high bleeding complication rate (36%) even in low-risk trauma patients. |

Meredith et al.⁸⁹ looked at the incidence of DVT with femoral vein catheterization using 8.5 French Swan-Ganz introducer catheters. Patients were followed with serial duplex ultrasonography. Not surprisingly, these large-bore catheters were associated with a 14% iliofemoral DVT rate on the side of the catheter. All were clinically occult.

In a study examining modes of prophylaxis in 281 high-risk trauma patients, Dennis et al.⁷ scanned for DVT at admission and every 5 days thereafter with a duplex scanner or Doppler ultrasound. Approximately 25% were scanned using duplex and 75% using Doppler. The authors did not indicate the reason for different modes. No confirmatory study was performed in patients who tested positive on ultrasound, and in 20% of examinations the study was incomplete. There were 18 cases of DVT (4.6%) and 4 cases of PE (1%) in the absence of DVT, three of which were fatal. Of concern in all three fatal PEs, none had shown evidence of DVT on routine surveillance with ultrasound before their deaths. In a similar prospective study examining prophylaxis of DVT in trauma patients, Knudson et al.¹⁵ used serial duplex ultrasound to detect thigh vein thrombus. In a few cases, the authors used venography to confirm a positive duplex result that was 100% accurate. Overall, approximately a 10%

DVT rate was reported, but again there were four cases of PE in the absence of detectable DVT, leading to speculation on the sensitivity of duplex to detect clinically significant DVT. In a larger study, again examining modes of DVT prophylaxis in trauma patients, Knudson et al.³ used weekly serial duplex ultrasound as the diagnostic modality to detect DVT. Of 251 patients in this randomized prospective study, 15 (6%) developed DVT as detected by duplex. Only 20% had clinical symptoms of DVT, and the rest were occult. Again, two patients developed PE, one of which was fatal, after repeated negative ultrasound examinations.

Brasel et al.⁹⁰ examined the cost-effectiveness of biweekly ultrasound screening versus placement of prophylactic VCFs on reducing PE in high-risk trauma patients using a decision-tree type of analysis. The authors found that ultrasound was more cost-effective than VCF, with a cost per PE prevented of \$46,300 versus \$97,000. However, ultrasound screening became more expensive than VCF when the anticipated length of stay was greater than or equal to 2 weeks. Again, a number of assumptions exist that underlie such a decision-tree analysis that may not reflect clinical reality. In contrast, Satiani et al.⁹⁷ concluded that the cost (\$18,586 per DVT identified) of routine

screening did not justify its use in patients receiving routine prophylaxis.

V. Summary

Numerous studies in the nontrauma 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 examinations, leading one to speculate on the ability of duplex to detect clinically significant DVT.

VI. Future Investigation

To serially screen all trauma patients for DVT is not cost-effective; therefore, the high-risk trauma patient who is prone to develop DVT likewise needs to be identified. The emphasis in future research ought to be placed on (1) identifying the source of DVT in patients with negative duplex but who develop PE, (2) cost-effectiveness of ultrasound screening in high-risk patients, (3) determining the clinical significance of asymptomatic calf DVT, and (4) the role of serial duplex in calf DVT progression and in patients with equivocal ultrasound examinations.

THE ROLE OF VENOGRAPHY IN THE DIAGNOSIS OF DVT IN TRAUMA PATIENTS

I. Statement of the Problem

All invasive or noninvasive diagnostic modalities for DVT are compared with venography, often referred to as the “gold standard” for the diagnosis of DVT in trauma patients. The problem with venography is that it is not feasible as a screening study because it is time-consuming, invasive, and has inherent risks and complications associated with its use. As such, it is rarely used clinically and is used more as a research modality.

II. Process

A MEDLINE search from 1966 to the present identified 3,520 articles related to venography in the diagnosis of DVT. Only eight articles were specifically related to the use of venography to diagnose DVT in the trauma patient. These articles, as well as some seminal review articles, were reviewed (Table 9).

III. Recommendations

A. Level I: A Level I recommendation on this topic cannot be supported because of insufficient data.

B. Level II:

1. Ascending venography should be used as a confirmatory study in those trauma patients who have an equivocal IPG or Doppler ultrasound examination for DVT.^{82,98,99}

2. Ascending venography should not be used to screen asymptomatic trauma patients at high risk for DVT. A role

for ascending venography may exist in research studies on the incidence of DVT in trauma patients.^{4,11,100}

C. Level III:

1. Magnetic resonance venography may have a role in diagnosing acute DVT in the trauma patient, especially with clots in the calf and pelvis (areas where venography and ultrasound are less reliable).¹⁰¹

IV. Scientific Foundation

Ascending contrast venography as a diagnostic modality has been around since the 1920s but was considered unreliable or even dangerous until Rabinov and Paulin¹⁰² standardized the technique in 1972. When this proper technique is used by a skilled radiologist, the entire lower extremity venous system should be visualized in a normal patient. Rabinov and Paulin¹⁰² described the four cardinal signs of DVT: (1) constant filling defects, (2) abrupt termination of the dye column, (3) nonfilling of the entire deep venous system or portions thereof, and (4) diversion of flow. Despite improvements in technique, several logistical problems remain for venography. A venogram requires patient transport to the radiology suite, which is often difficult for critically ill trauma patients. Venography requires a cooperative patient who can be examined in a semierect position on a tilting fluoroscopy table. Venous access is not always possible, especially in those with massive leg swelling. Usually 150 to 300 mL of contrast material is required for adequate visualization of the deep venous system. With the use of non-ionic contrast agents, the risk of allergic reactions and nephrotoxicity is very uncommon. Although the possibility of contrast-induced DVT exists,¹⁰³ the risks of this complication are unknown but are likely to be low. Injection of the contrast media may result in local discomfort and, if significant extravasation of contrast occurs, skin necrosis may result. Despite its common label as the gold standard in DVT diagnostic imaging, up to 30% of venograms will fail to visualize some segment of the venous system.⁸² Because of problems visualizing the entire venous system, a review of consecutive series of venograms by independent radiologists has resulted in only a 90% accuracy for venography.⁹⁸ As a result, most radiologists now believe that accurate, noninvasive imaging procedures such as duplex ultrasound are the imaging procedure of choice for suspected DVT above the knee. However, the accuracy of venography in the calf appears to exceed noninvasive tests in most centers.⁹⁹ Accordingly, it can be considered the gold standard for the diagnosis of calf DVT.

The most notable study in which venography was used as a screening technique in high-risk trauma patients was that of Geerts et al.¹¹ In this study, all patients admitted with an ISS > 9 were assessed with contrast venography for evidence of DVT. No patient received any DVT prophylaxis. In 349 patients, DVT was found in 201 (58%) and proximal DVT was found in 63 (18%). Multivariate analysis identified five independent risk factors for DVT: increasing age, blood transfusion, surgery, fracture of the femur or tibia, and spinal cord injury. Most of these thrombi were asymptomatic. The authors did not articulate

on the nature of the thrombi, such as how many were nonocclusive or were small and confined to single venous segments below the knee. A criticism of venography is that it may detect small isolated thrombi such as those on valve cusps that are clinically insignificant.⁸² It can be difficult to predict which ones will emerge as one of the 5% to 30%¹⁰⁴ that go on to propagate an extensive, proximal (dangerous) thrombus. A decision to treat these patients is important, as anticoagulant treatment can be associated with substantial morbidity in the trauma patient. Brathwaite et al.,¹⁰⁵ in a cohort of 70 trauma patients treated with full anticoagulation, found a 36% complication rate requiring termination of anticoagulation.

Magnetic resonance venography (MRV) has been used to diagnose proximal and acute pelvic vein DVT preoperatively in patients undergoing complex pelvic or acetabular fixation. Montgomery et al.¹⁰¹ used MRV in 45 consecutive patients with displaced acetabular fracture and diagnosed 24 asymptomatic DVTs, 7 of which were in the internal iliac vein, an area that could not have been seen with contrast venography or ultrasound. Nevertheless, it is an expensive examination that requires transport to the magnetic resonance suite and a dedicated radiologist with an interest in this technique. Many of these patients have recently placed external fixators or implants that prohibit the use of MRV in these patients. No study to date has compared that accuracy of MRV to any other diagnostic modality in trauma patients.

V. Summary

Although venography traditionally has been the diagnostic modality for DVT with which all other diagnostic modalities have been compared, logistical problems and complications associated with the procedure make it less appealing than other noninvasive 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.

VI. Future Investigation

Future studies may want to look at the role MRV has as a screening modality in diagnosing DVT in trauma patients.

ACKNOWLEDGMENT

We thank Jody Ciano for her help in the preparation of this article.

REFERENCES

- Pasquale M, Fabian TC, and the EAST Ad Hoc Committee on Guidelines Development. Practice management guidelines for trauma from the Eastern Association for the Surgery of Trauma. *J Trauma*. 1998;44:941–957.
- Interim Manual for Clinical Practice Guideline Development*. Rockville, MD: Agency for Health Care Policy and Research; May 1991.
- Knudson MM, Lewis FR, Clinton A, et al. Prevention of venous thromboembolism in trauma patients. *J Trauma*. 1994;37:480–487.
- Kudsk KA, Fabian T, Baum S, et al. Silent deep venous thrombosis in immobilized multiple trauma patients. *Am J Surg*. 1989;158:515–519.
- Velmahos GC, Nigro J, Tatevossian R, et al. Inability of an aggressive policy of thromboprophylaxis to prevent deep venous thrombosis (DVT) in critically injured patients: are current methods of DVT prophylaxis insufficient? *J Am Coll Surg*. 1998;187:529–533.
- Spain DA, Richardson JD, Polk JR, et al. Venous thromboembolism in the high-risk trauma patient: do risks justify aggressive screening and prophylaxis? *J Trauma*. 1997;42:463–469.
- Dennis JW, Menawat S, Von Thron J, et al. Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high-risk groups. *J Trauma*. 1993;35:132–139.
- Meyer CS, Blebea J, Davis K Jr, Fowl R, Kempczinski RF. Surveillance venous scans for deep venous thrombosis in multiple trauma patients. *Ann Vasc Surg*. 1995;9:109–114.
- Piotrowski JJ, Alexander JJ, Brandt CP, et al. Is deep vein thrombosis surveillance warranted in high-risk patients? *Am J Surg*. 1996;172:210–213.
- Napolitano LM, Garlapati VS, Heard SO, et al. Asymptomatic deep venous thrombosis in the trauma patient: is an aggressive screening protocol justified? *J Trauma*. 1995;39:651–659.
- Geerts WH, Code KJ, Jay RM, et al. A prospective study of venous thromboembolism after major trauma. *N Engl J Med*. 1994; 331:1601–1606.
- Knudson MM, Morabito D, Paiement GD, et al. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. *J Trauma*. 1996;41:446–459.
- Abelseth G, Buckley RE, Pineo GE, et al. Incidence of deep vein thrombosis in patients with fractures of the lower extremity distal to the hip. *J Orthop Trauma*. 1996;10:230–235.
- Upchurch GR Jr, Demling RH, Davies J, et al. Efficacy of subcutaneous heparin in prevention of venous thromboembolic events in trauma patients. *Am Surg*. 1995;61:749–755.
- Knudson MM, Collins JA, Goodman SB, et al. Thromboembolism following multiple trauma. *J Trauma*. 1992;32:2–11.
- Hill SL, Berry RE, Ruiz AJ. Deep venous thrombosis in the trauma patient. *Am Surg*. 1994;60:405–408.
- Geerts WH, Jay RM, Code KI, et al. A comparison of low-dose heparin with low-molecular weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med*. 1996; 335:701–707.
- Waring WP, Karunas RS. Acute spinal cord injury and the incidence of clinically occurring thromboembolic disease. *Paraplegia*. 1991;29:8–16.
- Spannagel U, Kujath P. Low molecular weight heparin for the prevention of thromboembolism in outpatients immobilized by plaster cast. *Semin Thromb Hemost*. 1993;19(suppl 1):131–141.
- Shackford SR, Davis JW, Hollingsworth-Fridlund P, et al. Venous thromboembolism in patients with major trauma. *Am J Surg*. 1990; 159:365–369.
- Ruiz AJ, Hill SL, Berry RE. Heparin, deep venous thrombosis, and trauma patients. *Am J Surg*. 1991;162:159–162.
- Velmahos GC, Kern J, Chan L, et al. Prevention of venous thromboembolism after injury: an evidence-based report—part I: analysis of risk factors and evaluation of the role of vena cava filters. *J Trauma*. 2000;49:132–139.
- Gardner AMN, Fox RH. The venous pump of the human foot: preliminary report. *Bristol Med Chir J*. 1983;98:109–112.
- Laverick MD, McGivern RC, Crone MD, Mollan RAB. A comparison of the effects of electrical calf muscle stimulation and the venous foot pump on venous blood flow in the lower leg. *Phlebology*. 1990;5:285–290.

25. Spain DA, Bergamini, Hoffman JF, et al. Comparison of sequential compression devices and foot pumps for prophylaxis of deep venous thrombosis in high-risk trauma patients. *Am Surg.* 1998; 64:522–526.
26. Anglen JO, Bagby C, George R. A randomized comparison of sequential-gradient calf compression with intermittent plantar compression for prevention of venous thrombosis in orthopedic trauma patients: preliminary results. *Am J Orthop.* 1998;33:53–57.
27. Gardner AM, Fox RH, Lawrence C, et al. Reduction of post-traumatic swelling and compartment pressure by impulse compression of the foot. *J Bone Joint Surg Br.* 1990;72:810–815.
28. Morgan RH, Carolan G, Psaila JV, et al. Arterial flow enhancement by impulse compression. *Vasc Surg.* 1991;25:8–15.
29. Abu-Own A, Cheadle T, Scurr JH, et al. Effects of intermittent pneumatic compression of the foot on microcirculatory function in arterial disease. *Eur J Vasc Surg.* 1993;7:488–492.
30. Anglen JO, Goss K, Edwards J, Heckfeldt RE. Foot pump prophylaxis for deep venous thrombosis: the rate of effective usage in trauma patients. *Am J Orthop.* 1998;27:580–582.
31. Comerota AJ, Katz ML, White JV. Why does prophylaxis with external pneumatic compression for deep vein thrombosis fail? *Am J Surg.* 1992;164:265–268.
32. Caprini JA, Arcelus JI, Hoffman K, et al. Prevention of venous thromboembolism in North America: results of a survey among general surgeons. *J Vasc Surg.* 1994;20:751–758.
33. Pidala MJ, Donovan DL, Kepley RF. A prospective study on intermittent pneumatic compression in the prevention of deep vein thrombosis in patients undergoing total hip or total knee replacement. *Surg Gynecol Obstet.* 1992;175:47–51.
34. Woolson ST, Watt JM. Intermittent pneumatic compression to prevent proximal deep venous thrombosis during and after total hip replacement: a prospective, randomized study of compression alone, compression and aspirin, and compression and low-dose warfarin. *J Bone Joint Surg Am.* 1991;73:507–512.
35. Gersin K, Grindlinger GA, Lee V, et al. The efficacy of sequential compression devices in multiple trauma patients with severe head injury. *J Trauma.* 1994;37:205–208.
36. Fisher CG, Blachut PA, Salvian AJ, et al. Effectiveness of pneumatic leg compression devices for the prevention of thromboembolic disease in orthopaedic trauma patients: a prospective, randomized study of compression alone versus no prophylaxis. *J Orthop Trauma.* 1995;9:1–7.
37. Keith SL, McLaughlin DJ, Anderson FA Jr, et al. Do graduated compression stockings and pneumatic boots have an additive effect on the peak velocity of venous blood flow? *Arch Surg.* 1992; 127:727–730.
38. Inada K, Koike S, Shirai N, et al. Effects of intermittent pneumatic leg compression for prevention of postoperative deep venous thrombosis with special reference to fibrinolytic activity. *Am J Surg.* 1988;155:602–605.
39. Jacobs DG, Piotrowski JJ, Hoppensteadt DA, et al. Hemodynamic and fibrinolytic consequences of intermittent pneumatic compression: preliminary results. *J Trauma.* 1996;40:710–717.
40. Bradley JG, Krugener GH, Jager HJ. The effectiveness of intermittent plantar venous compression in prevention of deep venous thrombosis after total hip arthroplasty. *J Arthroplasty.* 1993; 8:57–61.
41. Davidson JE, Willms DC, Hoffman MS. Effect of intermittent pneumatic leg compression on intracranial pressure in brain-injured patients. *Crit Care Med.* 1993;21:224–227.
42. Parra RO, Farber R, Feigl A. Pressure necrosis from intermittent-pneumatic-compression stockings [letter]. *N Engl J Med.* 1989; 321:1615.
43. Lachmann EA, Rook JL, Tunkel R, et al. Complications associated with intermittent pneumatic compression. *Arch Phys Med Rehabil.* 1992;73:482–485.
44. Greenfield LJ, Proctor MC, Rodriguez JL, et al. Posttrauma thromboembolism prophylaxis. *J Trauma.* 1997;42:100–103.
45. Monreal M, Lafoz E, Navarro A, et al. A prospective double-blind trial of a low molecular weight heparin once daily compared with conventional low-dose heparin three times daily to prevent pulmonary embolism and venous thrombosis in patients with hip fracture. *J Trauma.* 1989;29:873–875.
46. Green D, Lee MY, Lim AC, et al. Prevention of thromboembolism after spinal cord injury using low-molecular-weight heparin. *Ann Intern Med.* 1990;113:571–574.
47. Litz RJ, Hubler M, Koch T, Albrecht DM. Spinal-epidural hematoma following epidural anesthesia in the presence of antiplatelet and heparin therapy. *Anesthesiology.* 2000;95:1031–1033.
48. Hirsh J, Warkentin TE, Shaughnessy SG, et al. Heparin and low molecular weight heparin: mechanism of action, pharmacokinetics, dosing, monitoring, safety. *Chest.* 2001;119:64S–94S.
49. Osler TM, Rogers FB. Prophylaxis against venous thromboembolism after major trauma. *N Engl J Med.* 1997; 336:586.
50. Turpie AGG, Gallus AS, Hoek JA. A synthetic pentasaccharide for the prevention of deep-vein thrombosis after total hip replacement. *N Engl J Med.* 2001;344:619–625.
51. Bauer KA, Eriksson BI, Lassen MR, et al. Fondaparinux compared with enoxaparin for the prevention of venous thromboembolism after elective major knee surgery. *N Engl J Med.* 2001;345:1305–1310.
52. Webb LX, Rush PT, Fuller SB, et al. Greenfield filter prophylaxis of pulmonary embolism in patients undergoing surgery for acetabular fracture. *J Orthop Trauma.* 1992;6:139–145.
53. Jarrell BE, Posuniak E, Roberts J, et al. A new method of management using the Kim-Ray Greenfield filter for deep venous thrombosis and pulmonary embolism in spinal cord injury. *Surg Gynecol Obstet.* 1983;157:316–320.
54. Cipolle M, Marcinczyk M, Pasquale M, et al. Prophylactic vena caval filters reduce pulmonary embolism in trauma patients [abstract]. *Crit Care Med.* 1995;23:A93.
55. Rodriguez JL, Lopez JM, Proctor MC, et al. Early placement of prophylactic vena caval filters in injured patients at high-risk for pulmonary embolism. *J Trauma.* 1996;40:797–804.
56. Rogers FB, Shackford SR, Ricci MA, et al. Routine prophylactic vena cava filter insertion in severely injured trauma patients decreases the incidence of pulmonary embolism. *J Am Coll Surg.* 1995;180:641–647.
57. Rosenthal D, McKinsey JF, Levy AM, et al. Use of the Greenfield filter in patients with major trauma. *Cardiovasc Surg.* 1994;2:52–55.
58. Wilson JT, Rogers FB, Wald SL, et al. Prophylactic vena cava filter insertion in patients with traumatic spinal cord injury: preliminary results. *Neurosurgery.* 1994;35:234–239.
59. Winchell RJ, Hoyt DB, Walsh JC, et al. Risk factors associated with pulmonary embolism despite routine prophylaxis: implications for improved protection. *J Trauma.* 1994;37:600–606.
60. Zolfaghari D, Johnson B, Weireter LJ, et al. Expanded use of inferior vena cava filters in the trauma population. *Surg Annu.* 1995;27:99–105.
61. Rogers FB, Shackford SR, Wilson J, et al. Prophylactic vena cava filter insertion in severely injured trauma patients: indications and preliminary results. *J Trauma.* 1993;35:637–642.
62. Patton JH Jr, Fabian TC, Croce MA, et al. Prophylactic Greenfield filter: acute complications and long-term follow up. *J Trauma.* 1996;41:231–237.

63. Leach TA, Pastena JA, Swan KG. Surgical prophylaxis for pulmonary embolism. *Am Surg.* 1994;60:292–295.
64. Khansarinia S, Dennis JW, Veldenz HC, Butcher JL, Hartland L. Prophylactic Greenfield filter placement in selected high-risk trauma patients. *J Vasc Surg.* 1995;22:235–236.
65. Gosin JS, Graham AM, Ciocca RG, Hammond JS. Efficacy of prophylactic vena cava filters in high-risk trauma patients. *Ann Vasc Surg.* 1997;11:100–105.
66. Sekharan J, Dennis JW, Miranda FE, et al. Long-term follow-up of prophylactic Greenfield filters in multisystem trauma patients. *J Trauma.* 2001;51:1087–1091.
67. Greenfield LJ, Proctor MC, Michaels AJ, Taheri PA. Prophylactic vena cava filters in trauma: the rest of the story. *J Vasc Surg.* 2000;32:490–495.
68. Van Natta TL, Morris JA Jr, Eddy VA, et al. Elective bedside surgery in critically injured patients is safe and cost effective. *Ann Surg.* 1998;227:618–624.
69. Langan EM III, Miller RS, Casey WJ, et al. Prophylactic inferior vena cava filters in trauma patients at high-risk: follow-up examination and risk/benefit assessment. *J Vasc Surg.* 1999;30:484–488.
70. Velmahos GC, Kern J, Chan L, et al. Prevention of venous thromboembolism after trauma: an evidence-based report—part II: analysis of risk factors and evaluation of the role of vena cava filters. *J Trauma.* 2000;49:140–144.
71. Greenfield LJ, Proctor MC. Recurrent thromboembolism in patients with vena cava filters. *J Vasc Surg.* 2001;33:510–514.
72. Golueke PJ, Garrett WV, Thompson JE, et al. Interruption of the vena cava by means of the Greenfield filter: expanding the indications. *Surgery.* 1988;103:111–117.
73. Rohrer MJ, Scheidler MG, Wheeler HB, et al. Extended indications for placement of inferior vena cava filter. *J Vasc Surg.* 1989;10:44–50.
74. Ferris EJ, McCowan TC, Carver DK, et al. Percutaneous inferior vena cava filters: follow-up of seven designs in 320 patients. *Radiology.* 1993;188:851–856.
75. Nunn CR, Neuzil D, Naslund T, et al. Cost-effective method for bedside insertion of vena cava filters in trauma patients. *J Trauma.* 1997;45:752–758.
76. Headrick JR, Barker DE, Pate LM, Horne K, Russell WL, Burns RP. The role of ultrasonography and inferior vena cava filter placement in high-risk trauma patients. *Am Surg.* 1997;63:1–8.
77. McMurtry AL, Owings JT, Anderson JT, Battistella FD, Gosselin R. Increase use of prophylactic vena cava filters in trauma patients failed to decrease overall incidence of pulmonary embolism. *J Am Coll Surg.* 1999;189:314–320.
78. Ashley DW, Gamblin TC, Burch ST, Solis MM. Accurate deployment of vena cava filters: comparison of intravascular ultrasound and contrast venography. *J Trauma.* 2001;50:975–981.
79. Greenfield LJ. Post trauma thromboembolism prophylaxis. Paper presented at: Eighth Annual Meeting of the American Venous Forum, February 1996; San Diego, CA.
80. Tola JC, Hotzman R, Lottenberg L. Bedside placement of inferior vena cava filters in the intensive care unit. *Am Surg.* 1999;65:833–837.
81. Lorch H, Welger D, Wagner V, et al. Current practice of temporary vena cava filter insertion: a multicenter registry. *J Vasc Intervent Radiol.* 2000;11:83–88.
82. Neuberger JM, Gunther RW, Vorwerk D, et al. Results of a multicenter study of the retrievable tulip vena cava filter: early clinical experience. *Cardiovasc Intervent Radiol.* 1997;20:10–16.
83. Wheeler HB, Anderson FA Jr. Diagnostic methods for deep vein thrombosis. *Haemostasis.* 1995;25:6–26.
84. Wheeler HB, Anderson FA Jr. Use of noninvasive tests as the basis for treatment of deep vein thrombosis. In: Bernstein EF, ed. *Vascular Diagnosis.* 4th ed. St. Louis: Mosby; 1993:1894–1912.
85. Burns GA, Cohn SM, Frumento RJ, et al. Prospective ultrasound evaluation of venous thrombosis in high-risk trauma patients. *J Trauma.* 1993;35:405–408.
86. Napolitano LM, Garlapati VS, Heard SO, et al. Asymptomatic deep venous thrombosis in the trauma patient: is an aggressive screening protocol justified? *J Trauma.* 1995;39:651–659.
87. Meythaler JM, DeVivo MJ, Hayne JB. Cost-effectiveness of routine screening for proximal deep venous thrombosis in acquired brain injury patients admitted to rehabilitation. *Arch Phys Med Rehabil.* 1996;77:1–5.
88. White RH, Goulet JA, Bray TJ, et al. Deep-vein thrombosis after fracture of the pelvis: assessment with serial duplex-ultrasound screening. *J Bone Joint Surg Am.* 1990;72:495–500.
89. Meredith JW, Young JS, O'Neil EA, et al. Femoral catheters and deep venous thrombosis: a prospective evaluation of venous duplex sonography. *J Trauma.* 1993;35:187–191.
90. Brasel KJ, Borgstrom DC, Weigelt JA. Cost effective prevention of pulmonary embolus in high-risk trauma patients. *J Trauma.* 1997;42:456–463.
91. Agnelli G, Radicchia S, Nenci GG. Diagnosis of deep vein thrombosis in asymptomatic high-risk patients. *Haemostasis.* 1995;25:40–48.
92. Wells PS, Lensing AW, Davidson BL, et al. Accuracy of ultrasound for the diagnosis of deep venous thrombosis in asymptomatic patients after orthopedic surgery: a meta-analysis. *Ann Intern Med.* 1995;122:47–54.
93. Prandoni P, Bernardi E. Upper extremity deep vein thrombosis. *Curr Opin Pulm Med.* 1999;5:222–226.
94. Chu DA, Ahn JH, Ragnarson KT, et al. Deep venous thrombosis: diagnosis in spinal cord injured patients. *Arch Phys Med Rehabil.* 1985;66:L365–L368.
95. Myllynen P, Kammonen M, Rokkanen P, et al. Deep venous thrombosis and pulmonary embolism in patients with acute spinal cord injury: a comparison with nonparalyzed patients immobilized due to spinal fractures. *J Trauma.* 1985;25:541–543.
96. Brach BB, Moser KM, Cedar L, et al. Venous thrombosis in acute spinal cord paralysis. *J Trauma.* 1977;17:289–292.
97. Satiani B, Falcone R, Shook L, Price J. Screening for major deep venous thrombosis in seriously injured patients: a prospective study. *Ann Vasc Surg.* 1997;11:626–629.
98. Sandler DA, Martin JF, Duncan JS, et al. Diagnosis of deep-vein thrombosis: comparison of clinical evaluation, ultrasound, plethysmography and venoscan with x-ray venogram. *Lancet.* 1984;2:716–719.
99. Burke B, Sostman HD, Carroll BA, Witty LA. The diagnostic approach to deep venous thrombosis. *Clin Chest Med.* 1995;16:253–268.
100. Freeark RJ, Boswick J, Fardin R. Posttraumatic venous thrombosis. *Arch Surg.* 1967;95:567–575.
101. Montgomery KD, Potter HG, Helfet DL. Magnetic resonance venography to evaluate the deep venous system of the pelvis in patients who have an acetabular fracture. *J Bone Joint Surg Am.* 1995;77:1639–1649.
102. Rabinov K, Paulin S. Roentgen diagnosis of venous thrombosis in the leg. *Arch Surg.* 1972;104:134–144.
103. Bettmann MA, Robbins A, Braun SD, et al. Contrast venography of the leg: diagnostic efficacy, tolerance, and complication rates with ionic and nonionic contrast media. *Radiology.* 1987;165:113–116.
104. Kakkar VV, Howe CT, Nicolaidis AN, et al. Deep vein thrombosis of the leg: is there a “high-risk” group? *Am J Surg.* 1970;120:527–530.
105. Brathwaite CE, Mure AJ, O'Malley K, et al. Complications of anticoagulation for pulmonary embolism in low risk trauma patients. *Chest.* 1993;104:718–720.