A. PRACTICE MANAGEMENT GUIDELINES FOR THE MANAGEMENT OF VENOUS THROMBOEMBOLISM IN TRAUMA PATIENTS

EAST Practice Parameter Workgroup for DVT Prophylaxis

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Risk Factors For Venous Thromboembolism After Injury

I. Statement of the Problem

A number of factors have been reported to increase the risk for 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 concept becomes even more important, as the benefit from the different methods of prophylaxis is still unclear when compared to no prophylaxis. Because the literature is inconsistent, a systematic review is needed to produce the best available evidence.

II. Process

Three literature databases were searched (MEDLINE, EMBASE, and Cochrane Controlled Trials Register) for articles reporting on risk factors of VTE. All articles were reviewed by two independent reviewers and a third reviewer in cases of disagreement. The review was done against predetermined screening criteria, and the articles were given a 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 ration [OR] and their 95% confidence intervals [CI]) were estimated by the DerSimonian and Laird random-effects model. Shrinkage graphs were produced to display the effect size of each study and compare it with the overall model estimate. The heterogeneity among studies was tested by the Q-statistic and P value for the chi-square test of heterogeneity. A level of significance at $P < 0.05$ was used for all comparisons.

In order to include a risk factor for meta-analysis, three or more studies should have 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 standard deviation, the risk factor was simply “age”, a continuous variable.

III. Recommendations

A. Level I

Patients with spinal cord injuries or spinal fractures are at high risk for venous thromboembolism following trauma

B. Level II

1. Older age is an increased factor for venous thromboembolism but it is not clear at which exact age the risk increases substantially.

2. Increasing ISS and blood transfusion do appear to be associated with a high risk of venous thromboembolism in single institution studies, however, on meta-analysis these factors did not prove of major significance.

3. Likewise traditional risk factors such as long bone fractures, pelvic fractures or head injuries in many studies may constitutes a high risk patient population in single institution studies but on meta-analysis it did not prove of major significance.

IV. Scientific Foundation

Risk factors as dichotomous variables

The following variables were reported in 3 or more studies and for this reason included in the meta-analysis: gender,[1-4] head injury,[3,5-11] long-bone fracture,[3-8,11-16] pelvic fracture,[3,5,6,8,11,12,14,16] spinal fracture,[3, 5-7, 9-12,14,16] and spinal cord injury.[5,11,12,14,16] 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 analysis of this variable. The only risk factors found to place the patient at higher risk for development of DVT were spinal fractures (OR: 2.260, 95% CI: 1.415, 3.610) and even more spinal-cord injury (OR: 3.017, 95% CI: 1.794, 5.381). There was no significant heterogeneity among studies reporting on the different risk factors.

Risk factors as continuous variables

Three continuous variables, i.e. age,[4-6,11,14,17] injury severity score (ISS),[3,6,8,11,14,17] and units of blood transfused,[3,8,17] were reported in more than 3 studies and for this reason included in the meta-analysis. Compared to patients without deep venous thrombosis (DVT), patients with DVT were significantly older by 8.133 $\pm$ 1.504 (95% CI: 5.115, 11.141) years and had a significantly higher ISS by 1.430 $\pm$ 0.747 (95% CI: 0.000, 2.924). This statistical difference in ISS was marginal, as shown by the lower limit of the 95% CI, and has minimal clinical significance. The difference in the amount of blood transfused between patients with and without DVT was not statistically significant (1.882 $\pm$ 2.815, 95% CI: -3.637, 7.401). There was no heterogeneity among these studies.

V. Summary

The existing evidence supports the presence of two risk factors of post-traumatic VTE: spinal fractures and spinal cord injuries. Older age is an additional risk factor but it is not clear at which exact age the risk increases substantially. There is inadequate literature evidence to support that other frequently reported risk factors, such as long-bone fractures, pelvic fractures or head injuries, really increase the risk for VTE. There is a need for additional research in this area.

VI. Future Investigation

VII. References

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15. 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;335:701-7.

16. Knudson MM, Morabito D, Paiement GD, et al. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. J Trauma 1996;41:446-59.

17. 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;61:749-55.

Evidence Table. Studies reporting on risk factors of venous thromboembolism in trauma patients.

VTE: venous thromboembolism, DVT: deep venous thrombosis, PE: pulmonary embolism, LDH: low-dose heparin, LMWH: low-molecular weight heparin, SCD: sequential compression device, OR: operating room, PEEP: positive end-expiratory pressure, GCS: Glasgow Coma Scale, ISS: injury severity score, RTS: revised trauma score

First Author	Year	Reference Title	Class	Conclusions
Waring W et al[1]	1991	Acute spinal cord injury and the incidence of clinically occurring thromboembolic disease. *Paraplegia;29:8-16*	III	DVT developed in 14.5% and PE in 4.6%. Age was the only significant factor for PE. 1419 spinal cord injury patients included and followed for development of VTE. Stratification according to age, gender, level and type of injury.
Spannagel U et al[2]	1993	Low molecular weight heparin for the prevention of thromboembolism in outpatients immobilized by plaster cast. *Semin Thromb Hemost 19 (suppl 1);131-41*	I	DVT developed in 27 (10.6%), 21 from the no prophylaxis group and 6 from LMWH. Risk factors for DVT were age>30 years, obesity, varicose veins, and fractures. 306 patients included, 257 analyzed; 127 randomized to receive no prophylaxis and 126 to LMWH.
Knudson MM et al[3]	1994	Prevention of venous thromboembolism in trauma patients. *J Trauma;37:480-7*	I	15 developed DVT (5.8%). Risk factors for DVT were age>30 years, immobilization>3 days, pelvic and lower extremity fractures.
Abelseth G et al[4]	1996	Incidence of deep vein thrombosis in patients with fractures of the lower extremity distal to the hip. *J Orthop Trauma;10:230-5*	II	102 patients with lower extremity fractures, receiving no prophylaxis, had venography after operative fixation. 253 major trauma patients randomized to SCD, 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 minutes, and time from injury to operation >27 hours.
Kudsk KA et al[5]	1989	Silent deep venous thrombosis in immobilized multiple trauma patients . *Am J Surg;158:515-9*	II	39 multiple trauma patients included, 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 et al[6]	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? *J Am Coll Surg;187:529-33*	II	200 critically injured patients included, received VTE prophylaxis (LDH and/or SCD), 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 et al[7]	1997	Venous thromboembolism in the high-risk trauma patient: do risks justify aggressive screening and prophylaxis? *J Trauma;42:463-9*	III	280 high-risk trauma patients included, received prophylaxis, and were compared to 2,249 low-risk patients. 12 high-risk developed DVT (5%) and 3 low-risk (0.1%). PE found only in 4 high-risk. Only patients with venous injuries were at higher risk for VTE.
Knudson MM et al[8]	1992	Thromboembolism following multiple trauma. *J Trauma;32:2-11*	II	113 multiple trauma patients included, randomized to SCD or LHD, and screened by regular Duplex scan. 12 (10.6%) developed VTE (5 DVT, 4 PE, 3 both), 9 in the SCD group and 3 in the LDH. Risk factors for VTE were age, immobilization, number of transfusions, and clotting abnormalities.

Dennis JW et al[9]	1993	Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high -risk groups. *J Trauma;35:132-9.*	II	395 trauma patients included, 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 withou t) and 2 PE. Risk factor for VTE was spinal trauma.
Meyer CS et al[10]	1995	Surveillance venous scans for deep venous thrombosis in multiple trauma patients. *Ann Vasc Surg;9:109-14*	III	183 multiple trauma patients included and had VTE prophylaxis and irre gular Duplex screening. 22 (12%) developed DVT. Risk factors for DVT were spinal injuries and symptoms of DVT.
Piotrowski JJ et al[11]	1996	Is deep vein thrombosis surveillance warranted in high-risk patients? *Am J Surg;172:210-3*	II	343 high-risk trauma patients included, 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.
Napolitano LM et al[12]	1995	Asymptomatic deep venous thrombosis in the trauma patient: is an a ggressive screening protocol justified? *J Trauma;39:651-9*	III	458 trauma patients included, 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 inju ry.
Hill SL et al[13]	1994	Deep venous thrombosis in the trauma patient. *Am Surg;60:405-8*	II	100 trauma patients included, 50 received LDH and 50 did not non-randomly, 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 et al[14]	1994	A prospective study of venous thromboembolism after major trauma. *N Engl J Med;331:1601-6*	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 or tibia, and spinal cord injury.
Geerts et al[15]	1996	A comparison of low-dose heparin with low-molecular weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med;335:701-7*	I	265 major trauma patients included, 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.
Knudson MM et al[16]	1996	Use of low molecular weight heparin in preventing thromboembolism in trauma patients. *J Trauma;41:446-59*	I	487 trauma patients included and stratified to receive LMWH or SCD, and had regular Duplex. DVT was found only in 2.4% patients. Risk factors for DVT were immobilization >3 days, age >30 years, and lower extremity or pelvic fractures.
Upchurch GR, Jr et al[17]	1995	Efficacy of subcutaneous heparin in prevention of venous thromboembolic events in trauma patients. *Am Surg;61:749-55*	III	66 trauma patients included, 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.

The Use of Low Dose Heparin (LDH) for DVT/PE Prophylaxis

I. Statement of the Problem

The fact that DVT and PE occur following trauma is incontrovertible. The optimal mode of prophylaxis has yet to be determined. Low dose heparin (LDH) given in doses of 5000 units subcutaneously two or three times daily represents one pharmacologic treatment modality used for prophylaxis against DVT/PE. A meta-analysis of 29 trials in over 8000 surgical patients demonstrated that LDH significantly decreased the incidence of DVT from 25.2%, in patients with no prophylaxis, to 8.7% in treated patients ($p< 0.001$). Similarly, PE was halved by LDH treatment (0.5% in treated patients compared to 1.2% in controls, $p<0.001$). In double-blind trials, the incidence of major hemorrhage was higher in treated patients (1.8%) than controls (0.8%) but this was not significant. Minor bleeding complications, such as wound hematomas, were more frequent in LDH treated patients (6.3%) compared to controls (4.1%, $p<0.001$).

Unfractionated LDH has not been shown to be particularly effective in preventing VTE in trauma patients. Three recent prospective trials demonstrated that LDH was not better in preventing DVT than no prophylaxis in patients with an ISS of > 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 regards to PE, are even more vague. We are aware of only two studies employing a combined modality of LDH and mechanical prophylaxis.

Defining the trauma patient who is at high risk for VTE is subjective, and this definition has been variable in the literature. The following injury patterns appear to differentiate high risk patients for VTE: severe closed head injury (GCS < 8), pelvis plus long bone fractures, multiple long bone fractures, and spinal cord injury. A group of trauma surgeons have developed a risk factor assessment tool for VTE and preliminary evidence supports it as a valid indicator of the development of VTE (Greenfield, EAST 1998). The various risk factors are weighted (Table 1), patients with a score of < 3 may be considered low risk, 3-5 is moderate risk, and > 5 is high risk.

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 8 articles related to the use of LDH in trauma patients were utilized for the following recommendations.

III. Recommendations

A. Level I – There are insufficient data to support a standard on two subject.

B. Level II – There is little evidence to support a benefit of LDH as a sole agent for prophylaxis in the trauma patient at high risk for venous thromboembolism (VTE).

C. Level III

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

IV. Scientific Foundation

Heparin is a naturally occurring polysaccharide in varying molecular weight from 2,000-40,000. Low dose heparin 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 PTT.

A meta-analysis of 29 trials in over 8000 surgical patients demonstrated that LDH significantly decreased the incidence of DVT from 25.2%, in patients with no prophylaxis, to 8.7% in treated patients ($p< 0.001$). [1] Similarly, PE was halved by LDH treatment; the incidence was 0.5% in treated patients compared to 1.2% in controls ($p<0.001$).[1] In double-blind trials, the incidence of major hemorrhage was higher in treated patients (1.8%) than controls (0.8%) but this was not significant.[1] Minor bleeding complications, such as wound hematomas, were more frequent in LDH treated patients (6.3%) compared to controls (4.1%, $p<0.001$).[1]

Studies on the use of LDH in trauma patients are inconclusive. Shackford et al.[2] in a nonrandomized, uncontrolled trial of 177 high risk trauma patients compared no prophylaxis (n=25), LDH (n=18), LDH + SCD (n=53), and SCD only (n=81) according to physician preference. There was no significant difference in VTE rate in the groups receiving no prophylaxis (4%) vs. those who received prophylaxis (LDH 6%; LDH + SCD 9%; SCD 6%). In a relatively large, nonrandomized, unblinded prospective study of 395 trauma patients admitted with an ISS > 9 who received either LDH, SCD, or no prophylaxis, Dennis et al.[3] demonstrated a VTE rate of 3.2%, 2.7%, and 8.8%, respectively, with a hand-held Doppler flow probe. There was no statistically significant difference in VTE rate for the two types of prophylaxis, but there was a statistically significant difference in VTE in those who received prophylaxis vs. those who didn't ($p<0.02;X^2$). Specific analysis of those who received LDH vs. no prophylaxis revealed no significant difference in DVT rate. Ruiz et al.,[4] in 100 consecutive trauma patients admitted to their trauma center with an ISS > 10, looked at the incidence of VTE according to type of prophylaxis received. In the 50 patients who received LDH, there was a DVT rate of 28% vs. a DVT rate of only 2%, in the 50 patients who received no prophylaxis. Closer scrutiny of this nonrandomized study revealed that the patients who received LDH were more severely injured (mean ISS 31 vs. 22) and had a longer period of immobilization (17.9 vs. 8.0 days), which certainly could have contributed to the higher DVT rate seen in the LDH prophylaxis group. Knudson et al.[5] reported on 251 patients in a cohort study who received LDH, SCD, or no prophylaxis. They failed to show any effectiveness with prophylaxis in most trauma patients, except in the subgroup of patients with neurotrauma in which SCD was more effective than control in preventing DVT. Upchurch et al.[6] compared 66 ICU-dependent trauma patients who received either no VTE prophylaxis or LDH. The groups were well matched according to age, ISS, length of stay, and mortality. There was no significance in VTE rate between the two groups. In this same study, the authors performed a meta-analysis of the current literature concerning the use of LDH in trauma patients. Five studies met their entry criteria for inclusion in the meta-analysis which included 1,102 patients.[2,3,4,5] This meta-analysis demonstrated no benefit of LDH as prophylaxis compared to no prophylaxis (10% vs.7%; P=0.771). Geerts et al.[7] randomized 344 trauma patients to receive LMWH vs. 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 but, 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 while the comparative risk reductions for LMWH were 43% and 65%, respectively. Napolitano et al.[8] used a serial ultrasound screening protocol for DVT in 437 patients who were given four types of prophylaxis (LDH, VCB, LDH and VCB, no prophylaxis) according to their attending surgeon's preference. There was no significant difference in DVT rate between groups (8.6%, 11.6%, 8.0%, 11.9% respectively).

Velmahos, et al[9] looked at the ability of LDH and SCD or SCD alone in 200 critically injured patients who were then followed with biweekly Doppler exams to detect proximal lower extremity DVT. The incidence of DVT was 13% overall and not different between the two groups. The majority (58%) of DVT developed in the first two weeks. In a meta-analysis conducted under the auspices of the Agency for Healthcare Research and Quality, Velmahos and colleagues[10] looked at all randomized controlled and non-randomized studies on the use of LDH in trauma patients. In the four randomized control studies on the use of LDH in trauma patients showed no difference in the incidence of DVT between those receiving LDH vs no prophylaxis (OR, 0.965; 95% CI, 0.360, 2.965) there was again no difference (OR 1.33; 95% CI, 0.360, 2.965). In summary, to date, LDH has very little proven efficacy, in and of itself in the prevention of VTE following trauma.

V. Summary

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

VI. Future Investigation

There is enough accumulated data to warrant not using LDH in a trial in high risk trauma patients. Future studies should focus on the potential benefit of LDH in low risk trauma patients.

VII. References

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DEEP VENOUS THROMBOSIS (DVT) IN TRAUMA: A LITERATURE REVIEW

LOW DOSE HEPARIN

First Author	Year	Reference Title	Class	Conclusions
Clagett GP	1988	Prevention of venous thromboembolism in general surgical patients: Results of a meta-analysis. *Ann Surg 208:227-40*	I	Meta-analysis of various prophylactic methods used to prevent VTE in general surgical patients. LDH decreased DVT from 25.2% to 8.7% and PE from 1.2% to 0.5% ($p<0.001$) among treated general surgical patients.
Shackford SR	1990	Venous thromboembolism in patients with major trauma. *Am J Surg 159: 365-9*	III	177 high risk patients who received LDH, SCD, LDH & SCD or no prophylaxis. Non-randomized, uncontrolled study. VTE rate: LDH - 6%; SCD - 6%; SCD & LDH - 9%; no prophylaxis - 4%. There was no difference in VTE rate between groups.
Dennis JW	1993	Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high -risk groups. *J Trauma 35: 132-9*	III	Prospective, nonrandomized study of 395 patients with ISS > 9 who received LDH, SCD, or no prophylaxis. VTE rate: LDH - 3.2%; SCD - 2.7%; no prophylaxis - 8.8%. Sub-group analysis revealed no significant difference in VTE rate between LDH and no prophylaxis. Some randomization problems with study.
Ruiz AJ	1991	Heparin, deep venous thrombosis, and trauma patients. *Am J Surg 162:159-62*	III	Non-randomized 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 time period.
Knudson MM	1994	Prevention of venous thromboembolism in trauma patients. *J Trauma 37:480-7*	II	Randomized, prospective study of 251 patients receiving LDH, SCD or no prophylaxis. There was no significant benefit or VTE with prophylaxis. There was no significant benefit on VTE with prophylaxis except in the subgroup of neurotrauma patients in whom SCD seemed to offer protection.
Upchurch GR Jr	1995	Efficacy of subcutaneous heparin in preventi on of venous thromboembolic events in trauma patients. *AM Surg 61:749-55*	III	Meta-analysis on the use of LDH in 1102 trauma patients revealed no significant benefit on VTE rate: LDH - 10%, no prophylaxis - 7% ($p=0.771$).

LOW DOSE HEPARIN

First Author	Year	Reference Title	Class	Conclusions
Geerts WH	1996	A comparison of low-dose heparin and low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. *N Engl J Med 335:701-7*	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).
Napolitano LM	1995	Asymptomatic deep venous thrombosis in the trauma patient: Is an aggressive screening protocol justified? *J Trauma 39:651-9*	III	437 screened for DVT, nonrandomized. VTE rate: LDH - 8.6%, SCD - 11.6%, LDH & SCD - 8.0%, no prophylaxis - 11.9%. No difference in VTE rate between groups.
Velamahos 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? *J AM Coll Surg 187:529-533, 1998*	II	200 critically injured patients included received VT prophylaxis (L DH and/or SCD) 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.
Velamahos 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. *J Trauma 49:132-139, 2000*	I	Meta-analysis; 4 randomized control studies of LDH vs no prophylaxis; no difference in DVT rate (OR 0.965; 95% CI o.353, 2.636).

The Role of A-V Foot Pumps in the Prophylaxis of DVT/PE in the Trauma Patient

I. Statement of the Problem

Gardner and Fox,[1] in 1983, discovered a venous pump on the sole of the foot that consists of a plexus of veins that fills by gravity and empties upon weightbearing, thus increasing femoral blood flow without muscular assistance. A mechanical device, the 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 it to be used in patients with Jones dressings, casts, or externally fixed limbs that previously were unsuitable for SCD. 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%.[2]

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. There were eight articles specifically related to the use of A-V foot pumps in the trauma patient.

III. Recommendations

A. Level I

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

B. Level II

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

C. Level III

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

IV. Scientific Foundation

Most of the studies involving the use of A-V foot pumps are found in the orthopaedic literature, and many of these series involve small numbers of patients. Bradley et al.[3] in a randomized prospective trial of 74 patients undergoing total hip replacement assessed the additive effect of A-V impulse venous foot pump to prophylaxis with graduated compression stockings plus LDH plus hydroxychloroquine. All patients were submitted to bilateral ascending venography on the 12th postoperative day. The incidence of DVT was 6.6% in the pumped group and 27.3% ($p<0.025$) in the non-pumped group. Two patients developed pressure sores due to ill-fitting slippers in the pumped group. Stranks et al.,[4] in a randomized prospective trial of 82 patients treated for subcapital fractures, compared the A-V foot pump to no DVT prophylaxis. The incidence of DVT as assessed by Doppler ultrasound was 23% in the control group and 0% in those using the device ($p<0.0001$). Postoperative swelling was also decreased significantly in the treatment group as manifested by a decreased thigh circumference of 3.27cm ($p<0.001$) and thigh circumference of 1.55cm ($p<0.001$) in the pumped group relative to the control group. This study suffers somewhat in its design in that a control group which received no prophylaxis is probably not considered a standard treatment for hip fractures with its well known high propensity to develop venous thromboembolism complications. In addition, the comparability of the groups was not presented, and 93% of the DVTs were proximal (this is not sensible). A better comparison would be to compare A-V foot pumps to standard DVT prophylaxis such as subcutaneous heparin. Such a study was done

by Santori et al.[12] in 132 patients randomized to receive heparin vs. A-V footpumps. DVT was diagnosed in 23 patients (35.4%) in the heparin group vs. 9 (13.4%) in the A-V impulse group ($p<0.005$). In the heparin group there was one fatal PE, and 9 patients had excessive bleeding (13.8%) vs. none in the impulse group. Potential problems with this study include 1) the use of thermography and Doppler ultrasound as outcome measures, 2) the biased application of venography (48% vs 25% of patients), 3) unblinded DVT assessment, and 4) an unblinded bleeding assessment.

Fordyce and Ling[5] in a similar randomized prospective study compared the use of TED stockings with the A-V impulse system in 84 patients undergoing total hip replacement. Venographically-proved DVT was 40% in the TED group and 5% in the pumped group ($p<0.001$). Again, the study design was flawed in not providing more aggressive DVT prophylaxis in the control group. Also, they used only unilateral venography which underestimates the true DVT rates. In another prospective study[6] that included 59 patients undergoing elective knee replacement, venography showed a 19% incidence of proximal DVT in the control group and 0% in the group treated with A-V foot pumps. Westrich and Sculco[11] in a Level I study, compared 122 patients (164 knees) scheduled to undergo unilateral or bilateral knee replacement and were randomized to receive either aspirin alone or A-V foot pumps and aspirin. The prevalence of DVT was 27% (22 of 81 knees) in the A-V foot pump group vs. 59% (49 of 83 knees) in the aspirin group ($p>0.0 01$). Of note, no proximal thrombi were noted in any patient using the A-V foot pump vs. a 14% incidence ($p< 0.0003$) of popliteal or femoral DVT in the aspirin treated group. The authors also demonstrated that the total duration of time that the device was worn was related to whether or not the patient developed a DVT. Patients in whom a DVT did not develop used the device for a mean time of 96±23.4 hours while those who developed a DVT wore the device for 67±21.1 hours ($p<0.001$).

Although little has been done on the effects of the A-V impulse system 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 Fox[7] 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 paper, the authors hypothesized that the increased blood flow seen with the pumps is due to hyperemia mediated by endothelial-derived-relaxing factor (EDRF) which is liberated by the endothelium secondary to sudden pressure changes such as could be caused by the A-V pumps. This EDRF release could encourage the opening of critically closed capillaries, enabling reabsorption of fluid, hence the decrease in compartment pressures. In addition, there have been reports of A-V foot pumps improving arterial blood flow with the relief of ischemic rest pain.[8,9]
In a recently prospective randomized study by Knudson et al.,[10] A-V foot pumps were one arm of a number of prophylactic measures (low molecular weight heparin and sequential pneumatic compression devices 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 SCDs and 0.8% for the low-molecular weight heparin as determined on follow-up serial duplex ultrasound. Of note, severe skin changes, including blistering and wound problems, occurred in 8/53 patients who wore the foot pumps. This required three patients to be removed early from the study because of wound and skin problems.

Spain et al[13] compared the use of A-V foot pumps to SCD in 184 consecutively injured patients. In this non-randomized study, patients who could not receive SCD because of lower extremity injuries were placed in A-V foot pumps. Overall, there was no significant difference in DVT rates between the two groups with SCD 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 SCD when lower extremity fractures preclude the use of SCD. Anglen et al[14] performed a randomized prospective trial comparing A-V foot pumps with SCE in high-risk orthopedic patients and followed them with serial ultrasound. In 124 patients, the overall incidence of DVT was 4% in the A-V foot pumps and 0% in the SCD. 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 postop. In another study by Anglen et al[15] in a trauma population of ICU and ward patients, the A-V foot

pumps were found to be applied properly and functioning correctly 59% of the time, a similar problem to that reported by Comerota et al[16] for SCD.

V. Summary

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

VI. Future Investigations

More 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.

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DEEP VENOUS THROMBOSIS (DVT) IN TRAUMA: A LITERATURE REVIEW

A-V FOOT PUMPS

First Author	Year	Reference Title	Class	Conclusions
Gardner AMN	1983	The venous pump of the human foot —preliminary report. *Bristol Medico-Chirurgical J 98:109-12*	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. *Phlebography 5:285-90*	III	This study demonstrated that A-V foot pump increases venous blood flow in popliteal vein by 250%.
Bradley JC	1993	The effectiveness of intermittent plantar venous compression in prevention of deep venous thrombosis after total hip arthroplasty: A randomized prospective trial. *J Arthroplasty 8:57-61*	II	74 patients undergoing total hip replacement compared SQ heparin to A-V foot pumps. SQ heparin - 27% DVT vs A-V foot pump - 6.6% DVT.
Stranks GJ	1992	The A-V Impulse System reduces deep-vein thrombosis and swelling after hemiarthroplasty for hip fracture. *J Bone Joint Surg 74B:775-78*	II	Prospective randomized trial of TED stockings ± A-V foot pumps. Control group had 23% DVT rate vs 0% in the A-V foot pump group.
Fordyce MJ	1992	A venous foot pump reduces thrombosis after total hip replacement. *J Bone Joint Surg 74B:45-9*	II	Randomized, controlled study of 84 patients with TED vs TED & A-V foot pump. Venography follow-up revealed 10% DVT rate in A-V foot pumped group and 40% in controls.
Wilson NV	1992	Thrombo-embolic prophylaxis in total knee replacement. Evaluation of the A-V impulse system. *J Bone Joint Surg 74B:50-2*	II	Prospective trial of 59 patients with no prophylaxis vs A-V foot pumps. Control DVT rate was 68.7% and A-V foot pump was 50% detected by venography, with major DVT in 59% vs 18%, respectively.

A-V FOOT PUMPS

First Author	Year	Reference Title	Class	Conclusions
Gardner AM	1990	Reduction of post-traumatic swelling and compartment pressure by impulse compression of the foot. *J Bone Joint Surg 72B:810-5*	III	Multicenter trial showe d decrease in pain and compartment pressures with the use of A-V foot pumps. Hypothesized that this was due to release of endothelial-derived relaxing factor in microcirculation.
Morgan RH	1991	Arterial flow enhanced by impulse compression. *Vasc Surg 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. *Eur J Vasc Surg 7:488-92*	III	A-V foot pumps increased transcutaneous oxygen and laser Doppler fluxemetry in patients with severe claudication.
Knudson MM	1996	The use of low molecular weight heparin in preventing thromboembolism in trauma patients. *J Trauma 41:446-59*	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 SCD, and there were complications with their use.
Westrich GH	1996	Prophylaxis against deep venous thrombosis after total knee arthroplasty. Pneumatic plantar compression and aspirin compared with aspirin alone. *J Bone Joint Surg 78A:826-33*	I	122 patients (164 knees) compared DVT with A-V foot pumps and aspirin (27%) vs aspirin alone (59%; $p<0.001$). No proximal DVT occurred with A-V foot pumps vs 14% with aspirin ($p<0.0003$). Length of time foot pump was used significant for development of DVT. Patients with no DVT wore foot pump for 96±23.4 hours. Patients with DVT wore foot pump for 67±21.1 hours ($p<0.001$).
Santori FS	1994	Prophylaxis against deep-vein thrombosis in total hip replacement. Comparison of heparin and foot impulse pump. *J Bone Joint Surg 76B:579-83*	I	132 patients randomized to receive subcutaneous heparin vs A-V foot pump with 35.4% vs 13.4% incidence of DVT ($p<0.005$). There was one fatal PE and nine patients (13.8%) with excessive bleeding in the heparin group vs none in the A-V foot pump group.
Spain DA	1998	Comparison of sequential compression devices and foot pumps for prophylaxis of deep venous thrombosis in high-risk trauma patients. *Am Surg 64:522-526*	III	Non-randomized study of 184 high risk patients, incidence of DVT was similar between groups (7% SCD; 3% A-V foot pumps) as was number of Pes (2 AV foot pumps, 1 SCD)
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. *Am J Ortho 33:53-57.*	II	Prospective, randomized controlled study of high risk or the patients followed with serial Duplex. DVT rates: 0% SCD 4% A – V foot pump
Anglen JO	1998	Foot pump prophylaxis for deep venous thrombosis: the rate of effective usage in trauma		Trauma population found that A – V footpumps were applied properly and

		thrombosis: the rate of effective usage in trauma patients. *Am J Ortho :580-582, 1998*	III	functioning only 59% of the time.
Comerota AJ	1992	Why does prophylaxis with external pneumatic compression for deep vein thrombosis fail? Am J Surg 164:265-8, 1992	III	A-V foot pumps increased transcutaneous oxygen and laser Doppler fluxemetry in patients with severe claudication.

The Use of Sequential Compression Devices (SCD) in the Prevention of DVT/PE

I. Statement of the Problem

The role of intermittent sequential compression devices (SCDs) for prophylaxis against DVT has been studied and increasingly utilized in general surgery patients,[1] orthopedic patients,[2-4] and trauma patients.[5-8]

Attacking the long-recognized risk factor of stasis, SCDs have been shown to increase mean and peak femoral venous blood velocities on the lower extremity.[9,10] Additionally, SCDs have been shown to have a direct effect on the fibrinolytic pathway acting to shorten the euglobulin lysis time, increase levels of coagulation cascade inhibitor molecules, as well as affecting the balance of plasminogen activation.[12-14] In a number of prospective, randomized studies, SCDs have been shown to reduce the incidence of both DVT and PE.[3,6,15,16] Unanswered questions regarding the use of SCDs include the mechanism by which SCDs act, the efficacy of SCDs worn on the upper extremities or a single lower extremity compared to both lower extremities, the nature of risk involved in discontinuing SCDs periodically during use, and the duration of SCD use. Reports suggest that SCDs should be worn with thromboembolism-deterrent stockings (i.e. TEDS), however, this practice has not been widely studied and is not standard. Complications of SCDs 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 articles were evaluated to formulate the following guidelines.

III. Recommendations

A. Level I

There are insufficient data to support a standard on this topic.

B. Level II

There is insufficient data at this time that SCD decreases the risk of VTE in multiply injured patients.

C. Level III

1. In the subset of spine-injured head-injured patients, SCD may have some benefit in isolated studies.

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

3.

IV. Scientific Foundation

Since their description in 1858 by Rudolf Virchow, 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 SCDs strongly suggest that the nature of their effect on DVT prophylaxis derives from their ability to increase mean and peak femoral vein velocity as well as their effect on the systemic coagulation and fibrinolytic mechanisms.

The sequential pattern of compression has been well described: chambers of the extremity garment are sequentially inflated from ankle to knee (or mid thigh) to a maximum pressure of 45-50mm Hg at the ankle, 35 mm Hg at the calf, and 30mm at the thigh (hence the term "gradient" compression). The duration of compression is 11 seconds with a 60 second relaxation period between compressions.

Keith et al.[9] measured peak venous velocity (PVV) at the common femoral vein in postoperative (non-trauma) patients and in healthy control subjects using Doppler ultrasound. In the control subjects, PVV was increased from a mean velocity of 23.8 cm/sec at rest to 45.5 cm/sec with knee-high SCDs and 53.2 cm/sec with thigh-high SCDs. In postoperative patients, the PVV was similarly raised from a resting velocity of 21.8 cm/sec to 55.1 cm/sec. In both of these evaluations, the differences were statistically significant when compared to controls and were not further augmented by the concomitant use of compression stockings (e.g. TEDS). Spectral recording of blood flow velocity during inflation and deflation of the SCDs reveal a temporal association with inflation and increased PVV which suggests a mechanical effect derived from inflation of the SCDs. Another study examined the role of SCDs on femoral vein flow velocity in patients undergoing laparoscopic abdominal procedures.[10] It was noted that the effect of pneumoperitoneum to lower the velocity of flow through the femoral vein could be abrogated with the use of lower extremity SCDs.

Several studies in the selected bibliography[12-14] have evaluated in vivo fibrinolytic effects of SCDs. Inada et al.[12] reported a prospective study comparing euglobulin lysis times and a fibropeptide concentration in a cohort of cancer patients with and without SCDs. Both of these measurements are non-specific indicators of the relative activity of the fibrinolytic pathway in humans. They showed that the presence of SCDs vs. no-SCDs shortened the euglobulin lysis time and by the fifth postoperative day had increased the fibropeptide concentration suggesting increased plasminogen activity. In a well-designed study, Jacobs et al.[14] showed that euglobulin lysis times were not reproducible as a marker for fibrinolytic activation, and 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 SCD and postulated a (complex and incompletely proven) role of SCDs in the systemic balance of plasminogen activation and inhibition. In Jacob's study, they found that fibrinolytic activity begins to decay within minutes of discontinuing SCDs. This observation has important clinical implications in that SCDs must be worn continuously in order to avoid rapid decay in fibrinolytic activity. A recent study has documented patients in whom SCDs have been ordered, spent less than 50% of the time actually wearing the devices, possibly decreasing their effectiveness.[17] Another important finding in Jacob's study was that there appeared to be an incremental decrease in fibrinolytic activity when blood was sampled in sites remote form the area of placement of the SCDs. This difference in local and systemic effects has important implications on the ability of SCDs worn on the arms to prevent DVT in the legs.

Hoppensteadt et al.[13] studied levels of tissue factor pathway inhibitor (TFPI) in surgical patients before and after one hour of intermittent pneumatic compression. The authors describe TFPI as the key feedback inhibitor of the extrinsic activation of coagulation, a protease molecule which acts by binding to Factor Xa to inactivate the TF-FVIIa complex. They demonstrated a significant increase in TFPI concentrations in patients following pneumatic compression. The authors describe TFPI as being stored intima-bound on the endothelial cells, and suggest its release is mediated from these cells by the action of SCDs. This would represent a speculative

mechanism whereby SCDs have a direct inhibitory effect on thrombin generation as well as the primary effect on flow enhancement.

There is a paucity of studies specifically regarding the use of SCDs in the multiply-injured trauma patient. In a prospective study in which 113 trauma patients received either SCDs and TED stockings or low dose heparin (LDH), Knudson et al.[5] showed a 12% rate of venous thromboembolism (VTE) in the SCD vs. 8% in the LDH group, which was not significantly different. This study did not demonstrate that either method of attempted prevention (LDH or SCD) was better than no prophylaxis. Dennis et al.,[6] in a prospective, nonrandomized study of 395 trauma patients admitted with an ISS > 9 who received either SCD, LDH or no prophylaxis, demonstrated a VTE rate of 8.8% in the no prophylaxis group, 2.7% with SCD and 3.2% in the LDH group. There was no statistically significant difference in VTE rate in the prophylaxis groups, but there was a significant difference in those who received prophylaxis vs. no prophylaxis ($p<0.02$). Two very high risk groups seemed especially to benefit from prophylaxis were the head and spinal cord-injured patients. Overall risk reduction of VTE with prophylaxis was from 16.7% to 1.4% in head injured patients and from 27.3% to 10.3% in spinal cord-injured patients. The study suffers from the fact that there were randomization problems during the course of the study in which 67 patients (37%) originally assigned to receive no prophylaxis were switched to receive some sort of prophylaxis at the discretion of the attending surgeon. In a prospective trial, Knudson et al.[18] compared SCD, LDH and no prophylaxis. Neither LDH or SCD appeared to offer any protection to multiply-injured trauma patients, except in the specific subgroup of patients with neurotrauma in which SCD was more effective than control in preventing DVT ($p=0.057$). In contrast to Knudson's study, Gersin et al.[7] in a non-randomized prospective study, looked at the incidence of VTE in a group of 32 severely head-injured patients(GCS < 8). Fourteen patients received SCD and 18 did not because of concomitant lower extremity fractures. Within the group receiving SCD, four (28%) developed PE; 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 call into question the efficacy of SCD even in severe head-injured patients. In a group of 304 orthopaedic trauma patients with hip and pelvic fractures, SCDs were found to reduce thromboembolic events significantly over those who had no prophylaxis (11% vs. 4%; $p=0.02$). In subgroup analysis, SCD was 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 case reports of pressure necrosis from a too tightly fitted SCD have been reported.[19] Also peroneal palsy and compartment syndromes have been reported with SCDs.[20] A potential complication of SCD is to elevate intracranial pressure in those patients with severe head-injury. This question was addressed by Davidson et al.[21] in 24 severely brain-injured patients (mean GCS=6) who had intracranial pressure (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 at any time points studied with the use of SCDs, and concluded that SCDs 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 following trauma, Velmahos et al[25] found that SCD offered no benefit over no prophylaxis in both pooled randomized control studies (OR, 0.769; 95% CI, 0.265, 2.236) and in pooled non-randomized controlled studies (OR, 0.527; 95% CI, 0.190, 1.460). Velmahos et al[24] compared SCD, LDH and a combination of SCD 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 are sufficient in the high-risk patient.

Two studies have compared SCD to A-V foot pumps. Anglen et al[26] in a prospective, randomized, controlled study of 124 high risk orthopedic patients (pelvic, acetabular or femur fracture) were included in the study and followed with serial duplex ultrasound. The incidence of DVT was 0% in the SCD groups and 4% in A-V foot pump group. However, one patient in the A-V foot pump group suffered a nonfatal PE despite 3 negative duplex scans. Overall, the incidence of DVT seems low relative to other studies in similar high-risk population. Nevertheless, it is a Level I study because it is prospective, randomized, controlled trial. In a non- randomized

study of 184 high-risk patients, Spain et al[27] divided patients into SCD prophylaxis, or A-V foot pumps in patients with lower extremity fractures. The incidence of DVT was similar between groups (7% SCD; 3% A-V foot pump) as was the incidence of PE (2 A-V foot pump; 1 SCD).

V. Summary

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

VI. Future Investigation

More studies need to be done specifically related to the use of SCDs in trauma patients at risk for VTE. Questions regarding the efficacy of using the device on one lower extremity vs. two, and whether an arm vs. a leg provides equal protection, all need to be addressed. There are a number of commercial vendors of compression devices. Whether they all provide equal protection or one vendor is superior needs to be determined. Finally, the role of multimodality therapy (mechanical and pharmacologic) to provide any additional protection from VTE needs to be ascertained.

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DEEP VENOUS THROMBOSIS (DVT) IN TRAUMA: A LITERATURE REVIEW

SEQUENTIAL COMPRESSION DEVICES (SCDs)

First Author	Year	Reference Title	Class	Conclusions
Inada K	1988	Effects of intermittent leg compression for prevention of postoperative deep venous thrombosis with special reference to fibrinolytic activity. *Am J Surg 155:602-5*	II	Prospective, non-randomized study from Japan. Overall DVT incidence of 6.25% attributed to shortening of the euglobulin lysis time during first 48 hours postop and activating fibrinolysis.
Pidala MJ	1992	A prospective study on intermittent pneumatic compression in the prevention of deep vein thrombosis in patients undergoing to tal hip or total knee replacement. *Surg Gynecol Obstet 175:47-51*	III	Prospective but unfortunately uncontrolled study of SCDs in elective joint replacement surgery. Overall DVT incidence 4% by IPG with duplex confirmation. Authors believed, but did not prove that SCDs contributed to the low DVT incidence.
Knudson MM	1992	Thromboembolism following multiple trauma. *J Trauma 32:2-11*	II	Prospective comparison of 113 trauma patients prophylaxed with SCDs (76) or LDH (37). Thromboembolic complications occurred in 12% and 8%, respectively.
Lachmann EA	1992	Complications associated with intermittent pneumatic compression. *Arch Phys Med Rehabil 73:482-5*	III	Case report (x2) of SCD complications, both with SCDs worn during surgery. Peroneal nerve compression in setting of weight loss and compartment syndrome with legs in the lithotomy position.
Keith SL	1992	Do graduated compression stockings and pneumatic boots have an additive effect on the peak velocity of venous blood flow? *Arch Surg 127:727-30*	II	Good study demonstrates SCD effect of increased peak venous velocity in femoral vein not augmented by addition of graduated compression stockings.
Dennis JW	1993	Efficacy of deep venous thrombosis prophylaxis in trauma patients and identificatio n of high-risk groups. *J Trauma 35:132-9*	III	SCDs were comparable to the effect of LDH in significantly lowering DVT incidence compared to controls with no prophylaxis. Some randomization problems.

SEQUENTIAL COMPRESSION DEVICES (SCDs)

First Author	Year	Reference Title	Class	Conclusions
Caprini JA	1994	Prevention of venous thromboembolism in North America: Results of a survey among general surgeons. *J Vasc Surg 20:751-8*	III	Most recent ACS survey documents SCDs as the most frequently used prophylaxis (75% of respondents) with efficacy and safety cited as reasons why.
Knudson MM	1994	Prevention of venous thromboembolism in trauma patients. *J Trauma 37:480-7*	II	SCDs significantly reduced DVT complications vs control in neurotrauma group only.
Gersin K	1994	The efficacy of sequential compression devices in multiple trauma patients with severe head injury. *J Trauma 37:205-8*	III	Small numbers, and no description of randomization limits the value of this study.
Gibbons GH	1994	The emerging concept of vascular remodeling. *N Engl J Med 330:1431-8*	III	Excellent review article on humoral mediators, adhesion molecules, and neointima formation at the endothelial level.
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. *J Bone Joint Surg 73A:507-12*	II	The addition of aspirin or Coumadin to SCDs does not improve DVT or PE prophylaxis in elective hip replacement surgery.
Christen Y	1995	Hemodynamic effects of intermittent pneumatic compression of the lower limbs during laparoscopic cholecystectomy. *Am J Surg 170:395-8*	II	Femoral vein flow velocity, decreased by pneumoperitoneum, was restored by SCDs. SCDs did not restore normal vessel diameter or pressure.
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. *J Orthop Trauma 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.

SEQUENTIAL COMPRESSION DEVICES (SCDs)

First Author	Year	Reference Title	Class	Conclusions
Hoppensteadt DA	1995	The role of tissue factor pathway inhibitor in the mediation of the antithrombotic actions of heparin and low-molecular-weight heparin. *Blood Coagul Fibrinolysis 6:S57-S64*	III	TFPI, tissue factor pathway inhibitor, inhibits the extrinsic pathway of coagulation. SCDs worn for 1 hour doubles the TFPI concentration in volunteers' blood.
Ramos R	1996	The efficacy of pneumatic compression stockings in the prevention of pulmonary embolism after cardiac surgery. *Chest 109:82-5*	II	Prospective, randomized study of cardiac patients. The addition of SCD s to LMWH vs LMWH alone significantly reduced PE rates.
Hull RD	1996	Intermittent compression for the prevention of venous thromboembolism (Editorial). *Chest 109:6-9*	III	An editorial summary of SCD evidence and a critique of Ramos' paper in the same volume.
Jacobs DG	1996	Hemodynamic and fibrinolytic consequences of intermittent pneumatic compression: Preliminary results. *J Trauma 40:710-7*	II	A well-designed and well-described study of the effect of SCDs on the plasma levels of various compounds involved in the regulation of fibrinolysis. The discussion in the paper describes these components well.
Velmahos GC	1998	Inability of an aggressive policy of thromboprophylaxis to prevent deep venous thrombosis (DVT) in critically injured pat ients: are current methods of DVT prophylaxis insufficient? *J Am Coll Surg 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. *J Trauma 49:132-139*	I	Meta-analysis of SCD vs. no prophylaxis revealed SCD offered no benefit over no prophylaxis in both pooled randomized control 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)
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. *Am J Ortho 33:53-57*	II	Prospective, randomized controlled study 124 high risk ortho patients followed with serial Duplex. DVT rate 0% SCD 4% A-V foot pump.
Spain DA	1998	Comparison of sequential compression devices and foot pumps for prophylaxis of deep venous thrombosis in high-risk trauma patients. *Am Surg 64:522-526*	III	Non-randomized study of 184 high-risk patients, incidence of DVT was similar between groups (7% SCD; 3% A-V foot pump) as was number of Pes (2 A-V footpump; 1 SCD)

The Role of Low Molecular Weight Heparin (LMWH) in Venous Thromboembolism (VTE) Prophylaxis in Trauma Patients

I. Statement of the Problem

The use of LMWH has gained popularity for reducing the risk of VTE over the last 20 years. In trauma patients, LMWH has better efficacy than unfractionated heparin (UH) and similar efficacy to sequential compression, with similar bleeding risk when used for VTE prophylaxis.[19,21,30] Specifically, in trauma patients with an ISS > 9, LMWH was shown to be more efficacious than unfractionated heparin (UH) in preventing DVT (venogram). However, the LMWH group had more bleeding but this was not statistically significant. In another large study of trauma patients, LMWH was found to have similar efficacy to SCDs in preventing DVT (duplex ultrasound), however, the overall DVT incidence for all groups was only 2%. The orthopedic literature has several studies noting that LMWH outperforms UH for VTE prophylaxis and is more efficacious than oral anticoagulants in knee replacement surgery.[11,24,34,39,41,49,52,56] The general surgery literature is more variable but two studies show clear efficacy of LMWH over UH for VTE prophylaxis.[3,15] Except for two recent studies examining one-month prophylaxis in hip replacement surgery, duration of prophylaxis was generally 7 to 14 days while patients were hospitalized.[5,51]

II. Process

Medline searches and personal review of the literature revealed hundreds of articles examining the use of LMWH in VTE prophylaxis. Two meta-analyses, both published in 1992, regarding the "older" literature on the use of LMWH in general surgery and orthopedic surgery populations were summarized.[35,42] The important recent Class I studies that have appeared in the English literature were reviewed.

III. Recommendations

A. Level I

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

B. Level II

Low molecular weight heparin (LMWH) could 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); 2) complex lower extremity fractures (defined as open fractures or multiple fractures in one extremity) requiring operative fixation or prolonged bed rest (> 5 days); 3) spinal cord injury with complete or incomplete motor paralysis. 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.

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

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

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

4. LMWH should not be in use when epidural catheters are placed or removed.

IV. Scientific Foundation

The use of LMWH for VTE has gained popularity over the last 10 to 20 years. There are two LMWHs approved for VTE prophylaxis in the US. Enoxaparin is approved for use in orthopedic joint replacement surgery, and dalteparin has been approved for use in general surgery. There is now Class I data in trauma patients for the use of enoxaparin. A landmark study done by Geerts et al. reported in the *New England Journal of Medicine*,[19] and the study by Knudson et al. recently published in the *Journal of Trauma*[30] advocate for the use of enoxaparin as VTE prophylaxis in trauma patients.

LMWHs vary in size from 2000 to 9000 Daltons. They contain the unique pentasaccharide which is required for specific binding to antithrombin III but in a lower proportion than that contained in the parent UH. LMWHs have proportionally more anti-factor Xa activity compared to anti-factor II activity because they are less able to bind thrombin and ATIII simultaneously to accelerate the inactivation of thrombin by ATIII. However, they retain their ability to catalyze the inhibition of factor Xa by ATIII. In general, LMWHs have anti-factor Xa to anti-factor II ratios between 4:1 and 2:1. LMWHs have superior bioavailability to unfractionated heparin and produce less bleeding for equivalent antithrombotic doses. This is probably the result of the different effects on platelet function and vascular permeability.[25] However, the relationship between in vitro and in vivo studies has to be carefully examined when looking at LMWHs. While their 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.[54] Overall, LMWHs are clearly superior to placebo for VTE prophylaxis in general surgery, orthopedic surgery, and medical patients with small to minimal bleeding risk.

More studies are needed in trauma patients to give a Level I recommendation for the use of enoxaparin. However, three of these studies report good efficacy when enoxaparin was given bid in moderate to high risk trauma patients (Table 6). In a prospective trial of trauma patients who were considered high risk for DVT, Knudson et al. showed that enoxaparin resulted in a DVT rate of only 0.8%, though it was not significantly less than sequential compression or AV impulse pumps.[30] Geerts et al. showed that, in trauma patients with an ISS>9, enoxaparin was superior to UH and resulted in less overall and proximal DVT rates. There were more bleeding incidents in the enoxaparin group but this was not statistically significant. This landmark study showed that enoxaparin was more effective than low-dose heparin in preventing VTE after major trauma and that both interventions were safe.[19] A pilot study has been done comparing three modes of prophylaxis: enoxaparin vs UH vs sequential compression in patients with ISS>9 considered to be at high risk for DVT.[21] The DVT rate in the enoxaprin group was lower than that in both the UH and sequential compression group, however, this did not reach statistical significance because of sample size. These studies would support the use of enoxaparin in trauma patients at moderate to high risk for VTE with an acceptable bleeding risk.

There is one study that clearly shows Logiparin 3500 units q8 hr is superior to UH 5000 units q8 hr in spinal cord injury patients. Event rates (DVT and bleeding) were 0/20 in the Logiparin group and 7/21 in SH group. [20]

There have been three studies which have examined the cost-effectiveness of using a relatively expensive therapy, ie LMWH, in hip replacement surgery. Taking into account the reduction in DVT with similar or lower bleeding risk and the ability to administer LMWH without following coagulation, it has been shown to be more cost-effective than SH.[1,39,44]

In their meta-analysis on the prevention of venous thromboembolism after injury, Velmahos et al[61] showed that there was no difference in PE rate when LMWH was compared to SCH (OR 3.010:9% CI: 0.585, 15,485). However, the confidence intervals were wide and the authors concluded that a significant difference cannot be excluded.

V. Summary

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

VI. Future Investigation

There are many unresolved issues concerning VTE prophylaxis of trauma patients that need to be studied in a multicenter fashion. There is one multicenter trial being formulated at this time, which will address the use of LMWH in trauma patients and address not only efficacy of LMWH but also bleeding complications. This Class I data will more clearly define the role of LMWH in VTE prophylaxis in trauma patients. When these studies are completed, the Class I data will more clearly define the role of LMWH in VTE prophylaxis in trauma patients. Hopefully, the multicenter trials will also establish a risk factor scoring tool for clinicians to better quantify VTE risk in their patient population. Until prospectively validated risk assessment tools are available, we urge that each institution adopt local guidelines for VTE risk and establish guidelines among the trauma, orthopedic, and neurological surgeons for bleeding risk after trauma.

Table 2
Low Molecular Weight Heparin in Trauma

STUDY	PROPHYLAXIS REGIMEN	DVT DIAGNOSIS	DVT INCIDENCE	BLEEDING INCIDENCE
Green[20] (spinal cord injury)	logiparin 3500u qd x 8w (n=20) UH 5000u tid x 8w (n=21)	serial non-invasive screen then venogram	0% "event rate"^ 35% "event rate"	0% "event rate" 35% "event rate"
Geerts[19]	enoxaparin 30mg bid (n=171) UH 5000u bid x (n=173)	Venogram	31%* 44%	5 episodes p<0.12 1 episode
Knudson[30]	enoxaparin 30mg bid (n=120) sequential compression (n=199) AV impulse pumps (n=53)	duplex q5-7 days until dc	0.8% 2.5% 5.7%	one bleeding complication "potentially related to enoxaparin
Greenfield[21]	enoxaparin 30mg bid (n=11) UH 5000u bid (n=7) sequential compression (n=20) venous foot pumps (n=15)	duplex day 3 and q week x 3 or until dc	27% 58% 44% 40%	no difference in bleeding among groups

* p<0.05, ^ "event rate" = DVT+bleeding, dc=discharge

VII. References

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21. Velmahos GC, Kern J, Chan LS, Oder D, Murray JA, Shekelle P. 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. J Trauma 2000;49:132-139.

LOW MOLECULAR WEIGHT HEPARIN

Trauma

First Author	Year	Reference Title	Class	Conclusions
Green D	1990	Prevention of thromboembolism after spinal cord injury using low-molecular-weight heparin. *Ann Intern Med 113:571-4*	I	Compared Logiparin 3500 units daily for 8 weeks (n=20) vs SH 5000 units tid q8 hr for 8 weeks (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 & complete motor paralysis, and is superior to SH.
Geerts WH	1996	A comparison of low-dose heparin with low-molecular-weight heparin as pr ophylaxis against venous thromboembolism after major trauma. *N Engl J Med 335:701-7*	I	Landmark study of trauma patients with ISS ?9 who could receive anti-coagulants. 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 to 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. *J Trauma 41:446-59*	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 SCDs 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 *J Trauma 42:100-3*	II (pilot study)	Small pilot study of 53 patients compared enoxaparin vs SH vs SCDs 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 SCD groups, though not statistically significant due to 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. *J Trauma 49:132-139.*	I	SCH 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, CI were wide and a significant difference couldn't be excluded.

The Role of the Vena Cava Filter in the Prophylaxis and Treatment 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. Patients with ongoing bleeding or those with recent brain, spinal cord or ocular injury will not tolerate even minor amounts of bleeding. Furthermore, multiply injured patients often have extremity injuries which preclude the use of sequential compression devices (SCDs). The decision to place a "prophylactic" vena cava filter in a trauma patient requires a fundamental understanding of the risk:benefit ratio. The data included in this review indicate the risk:benefit ratio is favorable in a high-risk trauma patient. Therefore, the problem becomes defining the "high-risk" patient and the short and long-term complication rates of vena caval interruption.

The literature is somewhat difficult to interpret because each author differs in their definition of a "prophylactic" vena cava filter. It is probably more accurate to use the terms "traditional" and "extended" indications for vena cava filter placement. This review is designed to examine the data available for the use of vena cava filters for "extended" indications in the trauma patient, that is, filter placement early after injury, before the patient has clinical or radiographic evidence of a DVT or PE.

II. Process

A Medline search from 1980 to 1999 showed ten articles when "vena cava filter" was cross-referenced with "trauma". An additional personal review of the literature revealed seven additional articles and two abstracts that address extended indications of vena cava filter placement in trauma patients. Also, there were four articles that specifically addressed complications and long-term follow up with vena cava filters which are included in this review.

III. Recommendations

A. Level I

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

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

B. Level II

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

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

C. Level III

Insertion of a "prophylactic" vena caval filter should be considered in very high risk trauma patients.

1. Who cannot receive anticoagulation because of increased bleeding risk, and

2. Have one or more of the following injury patterns:
    a. Severe closed head injury (GCS < 8),
    b. Incomplete spinal cord injury with para 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 intraabdominal organ injury (ie. 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 due to injury, medication, or congenital/hereditary.

IV. Scientific Foundation

The placement of a vena cava filter in a trauma patient who does not have an established DVT or PE is certainly controversial. There is no question that vena cava filters are efficacious. They prevent the occurrence of PE from lower extremity DVT with about a 98% success rate.[1] The real issue is defining who should receive these filters, and whether it is without significant complications and cost-effective. There is no data at this point to address the latter, and some recent papers do address the risk factor issue.

Several recent studies have reported on the use of vena caval filters for extended indications. Golueke and coworkers[2] reported on 21 filters placed prophylactically before total joint replacement. All patients also received low dose heparin, aspirin, and, when possible, graduated compression stockings. There were no filter-related complications or episodes of PE in this group. Likewise, Webb et al. in 1992 reported their results of using a "prophylactic" filter in 24 of 52 patients undergoing acetabular fracture repair with sufficient risk factors.[3] They had no insertion complications. Four patients had leg edema, one with phlegmasia, and no PEs. In the 27 patients who did not receive a filter, there were 2 PEs, one of which was fatal. Rohrer and coworkers reported on the use of vena caval filters for "extended" indications in 66 patients (many of whom were trauma patients).[4] There was only one fatal PE in this group, and 22 patients had no documented DVT before filter insertion. The recurrent nonfatal PE rate was 3%, and symptomatic occlusion of the IVC occurred 4.5% of the time in this study. Major limitations of this study include the retrospective design, inability to distinguish outcomes in the 21 patients with VCF used as prophylaxis from the 45 others, and unspecified follow-up duration. Jarrell and coworkers[5] reported a favorable experience with 21 Greenfield filters that were placed in spinal-cord-injured patients with documented DVT or PE and a "traditional" indication for filter insertion. There was only one PE death in this group and two instances of IVC thrombus, both of which were well tolerated.

There are now several reports in the literature of the use of "prophylactic" vena caval filters for extended indications in trauma patients. [5,6,8,9,10,11,12,13,14,15,20,22,23,24,25,26] To date. 14 studies have reported on inferior vena cava (IVC) filter insertion in trauma patients. Five of these studies [8,9,10,22,23] demonstrated a demonstrated a significant reduction in the indicence of PE in their trauma population compared to historical controls. None of these studies were Level I studies, however. Further McMurty et al [25] 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 to historical controls. There have been minimal insertion and short-term complications reported; one-year patency rates ranged from 82% to 96%,[9,11] and two-year patency rates have been reported in 96%[9] of prophylactic filters inserted in trauma patients. Moreover, there does not seem to be a higher DVT rate in prophylactic filter patients compared to non-filter patients.[7,8] A recent followup study with a minimal of 5 years followup in 199 patients showed that the filters are well tolerated, patients can go on to active life, and their was a minimal migration or caval thromboses in the patients studied.[26] The efficacy of vena

cava filters preventing PEs is not an issue. The long-range complications and cost-effectiveness of this therapy does need to be studied.

The decision to place a prophylactic filter in a trauma patient requires a fundamental understanding of its risk-benefit ratio. The data would indicate that the risk-benefit ratio is favorable in the high-risk trauma patients. The problem is defining the high-risk patient. One trauma study[14] identified four injury patterns that accounted for 92% of PEs: (1) spinal cord injury with paraplegia or quadriplegia, (2) severe closed head injury with a Glasgow Coma Score ? 8, (3) age > 55 years with isolated long bone fractures, and (4) complex pelvic fractures associated with long bone fractures. Another retrospective review including 9,721 patients[12] 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 would have utilized a prophylactic filter in these 2% of patients, there would have been a very dramatic reduction in PE. They suggested that patients with an estimated risk of PE of 2% to 5%, despite prophylaxis, are reasonable candidates for prophylactic vena caval filter placement, especially if conventionalprophylactic 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%. [7] These are reasonable complication rates, but multiplied over the lifetime of a young patient, these rates could become important. There is one study that indicates a significant amount of chronic venous insufficiency in long-term follow up of prophylactic filter patients.[15] However, there was no non-filter group to compare to, so it is not clear if the filter was the cause of this chronic venous insufficiency in this very high risk group.

More recently, interest and experience have been gaining for the many types of retrievable filters. Muchof this early work has been done in Europe.[27,28,29] The use of retrievable filters are particularlyh appealing to trauma surgeons whose patients are at high risk for PE for a relatively short period of time. Technical problems with the retreivable 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 ($P < .01$) prophylactic filter placement from 29% to 53%.

V. Summary

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

VI. Future Investigation

There is an obvious need of Class I randomized, prospective controlled data to either support or refute the use of vena caval interruption in trauma patients. Such studies need to enroll only high risk patients with a sufficiently high enough PE rate to attempt to prove filter efficacy and improve outcome in the patients who receive a truly prophylactic vena cava filter. This study would need to be large and multicenter in nature. The pilot portion of such a study has been completed, and the large multicenter trial should involve many investigators from trauma associations. Other important unresolved issues include the following:

- Do vena cava filters significantly reduce the incidenceof 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 vena cava filter insertion used as primary prophylaxis in trauma patients?

- Is vena cava filter insertion cost-effective?

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DEEP VENOUS THROMBOSIS (DVT) IN TRAUMA: A LITERATURE REVIEW

Vena Cava Filters

First Author	Year	Reference Title	Class	Conclusions
Carabasi RA III	1987	Complications encountered with the use of the Greenfield filter. *Am J Surg 154:163-8*	II	200 filters in 193 patients, unspecified long -term follow-up. Complications: venous anomalies 2.5%; insertion compilations 9.2%; Postoperative: 2.5% minor, 4.1% major; 0.5% m ortality secondary to distal migration. Stress importance of preop venography, visualization of thrombus, marking of renal veins, diagnosing venous anomalies, knowing accurate size of vena cava.
Greenfield LJ	1988	Twelve-year clinical experience with t he Greenfield vena cava filter. *Surgery 104:706-12*	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.
Greenfield LJ	1992	Late results of suprarenal Greenfield vena cava filter placement. *Arch Surg 127:969-73*	III	Review of 71 patients who had suprarenal placement of Greenfield filter. 60 available for follow-up, mean=53 months (18 months -16 yrs). 24 deaths, none secondary to recurrent embolism or renal failure. Recurrent embolism rate was 4% which is identical to infrarenal experience. Duplex exam (n=22) showed all filters were patent. 16 patients (41%) had lower extremity edema that predated filter insertion. Filter fracture in 2 patients and distal migration in 2 patients with no clinical symptoms. Suprarenal placement of Greenfield filter is safe and effective for thrombus e xtending above renal veins and for pregnant patients or women of childbearing age.
Ferris EJ	1993	Percutaneous inferior vena cava filters: Follow -up of seven designs in 320 patients. *Radiology 188:851-6*	III	324 filters placed over 7 yrs. No placement-related mortality or morbidity. Average follow-up=404 days (1-2392). 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.

VENA CAVA FILTERS - "Traditional" Indications

First Author	Year	Reference Title	Class	Conclusions
Jarrell BE	1983	A new method of management using the Kim -Ray Greenfield filter for deep venous thrombosis and pulmonary embolism in s pinal cord injury. *Surg Gynecol Obstet 157:316-20*	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 p opulation 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.
Leach TA	1994	Surgical prophylax is for pulmonary embolism. *Am Surg 16:292-5*	II	205 vena cava filters placed for indications that were outlined prospective -ly, although many were inserted for "traditional" indications. No PEs in these filter patients and minimal insertion complications.
"Extended" Indications: Ortho				
Golueke PJ	1988	Interruption of the vena cava by means of the Greenfield filter: Expanding the indications. *Surgery 103:111-7*	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 months (1-60) in 65 patients. Complications: 3% recurrent PE, 9% leg edema, 7.5% caval occlusion, 92.5% patency. No PEs in prophylactic group that received anti -platelet and sequential compression therapy. Indications should be extended for vena cava filter to help reduce preventable deaths secondary to PE.
Webb LX	1992	Greenfield filter prophylaxis of pulmonary embolism in patients undergoing surgery for acetabular fracture. *J Orthop Trauma 6:139-45*	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 preop filter; 2 PEs in this group, 1 fatal. All patients had SQ heparin and aspirin.
Rogers FB	1993	Prophylactic vena cava filter insertion in severely injured trauma patients: Indications and preliminary results. *J Trauma 35:637-42*	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).

VENA CAVA FILTERS - "Extended" Indications: Trauma

First Author	Year	Reference Title	Class	Conclusions
Rogers FB	1995	Routine prophylactic vena cava filter insertion in severely injured trauma patients decreases the incidence of pulmonary embolism. *J Am Coll Surg 180:641-7*	II	Continued follow-up from J Trauma '93. 63 prophylactic vena cava filters 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).
Wilson JT	1994	Prophylactic vena cava filter insertion in patients with traumatic spinal cord injury: Preliminary results. *Neurosurgery 35:234-9*	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 (9-5993). 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. *J Trauma 37:600-6*	III	8-year retrospective registry review at Level 1 trauma center (9721 patients). Overall PE rate=37%. 29 prophylactic vena cava filters 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 plus long bone fracture (12%); multiple long bone fracture (10%). Patients with estimated risk of PE, despite prophylaxis of > 2 -5%, are reasonable candidates for prophylactic vena cava filter placement, especially if conventional measures cannot be used.
Rosenthal D	1994	Use of the Greenfield filter in patients with major trauma. *Cardiovasc Surg 2:52-5*	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.
Zolfaghari D	1995	Expanded use of inferior vena cava filters in the trauma population. *Surgery Annual 27:99-105*	III	Retrospective analysis of 45 filters placed in 3005 patients. 38/45 had extend-ed 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.
Cipolle M	1995	Prophylactic vena caval filters reduce pulmonary embolism in trauma patients [Abstract]. *Critical Care Medicine 23:A93.*	III	Review of 43 high risk trauma patients who had vena cava filters placed, 16 for "traditional" indications and 27 for "extended" indications. 0 PEs in prophylactic group and 5 PEs in "traditional" indications group. Overall PE rate was 11.6%.

VENA CAVA FILTERS : "Extended" Indications: Trauma

First Author	Year	Reference Title	Class	Conclusions
Patton JH Jr	1996	Prophylactic Greenfield filter: Acute complications and long-term follow-up. *J Trauma 41:231-7*	II	Follow-up of prophylactic filters placed between 1991-1994. 69 filters with 9% insertion rate. 15 patients died. 30 patients were locate d and 19 returned for follow-up evaluation (35%). Average follow-up was 770 days (246-1255). No caval thrombosis. 14 patients had chronic DVT. 11/14 had chronic venous insufficiency. No long -term caval thromboses. Not clear, however, if filter caused chronic venous insufficiency because there was no nonfilter group.
Rodriguez JL	1996	Early placement of prophylactic vena cava filters in injured patients at high risk for pulmonary embolism. *J Trauma 40:797-804*	II	40 vena cava filters placed in cons ecutive 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.
Greenfield LJ	1996	Posttrauma thromboembolism prophylaxis. *8th Annual American Venous Forum*	I	Pilot study for large, multicenter trial. 53 patients randomized to receive SCD, LMWH, or unfractionated heparin and 1/2 randomized to receive vena cava filter. 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 groups. 12 DVTs in nonfilter pat ients and 11 DVTs in filter patients.
Nunn CR	1997	Cost-effective method for bedside insertion of vena cava filters in trauma patients. *J Trauma 45:752-758*	III	Ultrasound-guided IVC filter insertion in 55 trauma patients. 49 successful; 6 failed.
Tola JC	1999	Bedside placement of inferior vena cava filters in the intensive care unit. *American Surg. 65:833-837*	III	25 patients underwent prophylactic IVC filters in the ICU with digital C -arm with no postop or intraop complications. Average s aving of $1844 when filters were placed in ICU vs. OR.
Khansarinia S	1995	Prophylactic Greenfield filter placement in selected high-risk trauma patients. *J Vasc Surg 22: 235-236*	I	108 filters placed in high risk trauma patients over a two -year period with injury matched controls who did not receive a filter. OPEs 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. *Ann Vasc Surg 11:100-105*	II	99 prophylactic filters placed in high risk trauma population over 2 year period. This decreased PE in trauma population to 1.6% from 4.8% in historical controls (p<0.045 Fischer's Exact).
Headrick JR	1997	The role of ultrasonography and inferior vena cava filter placement in high -risk trauma patients. Am Surg 1997;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 to historical controls.

McMurtry AL	1999	Increase use of prophylactic vena cava filters in trauma patients failed to decrease overall incidence of pulmonary embolism. *J Am Coll Surg; 189:314-20.*	III	Review of 299 patients with prophylactic filters over an 8 year period, yeilded no demonstrable decrease in PE incidence compared to historical controls.
Sekharan J	2000	Long term follow up of prophylactic greenfield filters in multisystem trauma patients. *J Trauma 49: 374*	III	5 year followup study of 199 patients showed that filters are well-tolerated in trauma patients with minimal migration on caval thrombosis
"Extended" Indications: Medical/Surgical				
Rohrer MJ	1989	Extended indications for placement of inferior vena cava filters. *J Vasc Surg 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 due to poor cardiopulmonary reserve; 3) large ileofemoral 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.

TEMPORARY FILTERS:

First Author	Year	Reference Title	Class	Conclusions
Lorch H	2000	Current practice of temporary vena cava filter insertion: a multicenter registry. *J Vasc Interv Rad 11:83-88*	III	188 patients (Antheor filter 54%, Guenthe r 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. *Cardiovasc Intervent Radiol 20:10-16.*	III	83 patients implanted with retreivable Tulip filter; 3 filter insertion problems, 1 fatal recurrent PE; 2 non -fatal PE; 8 caval occlusions.
Bovyn G	1997	The tempofilter: a multicenter study of a new temporary caval filter implantable for up to six weeks. *Ann Vasc Surg 11:520-528.*	III	66 patients at high risk for PE had filter implanted for up to 6 weeks. Filter migration occurred in 7.5 of the cases.

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 for treatment to be initiated, thus decreasing the frequency of complications. Ultrasound scanning has the advantage as a diagnostic tool in detecting DVT because it is non-invasive, 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 employs real time B-mode sonography which produces a two-dimensional image using high frequency sound waves and Doppler ultrasound. It is important for the reader to distinguish between these two technologies in the accuracy of ultrasound to detect DVT. Further, in the critical review of ultrasound technology to detect DVT, a dichotomy exists in the sensitivity of ultrasound to detect DVT in symptomatic vs. asymptomatic patients.

II. Process

A Medline search from 1966 to present revealed several thousand articles related to the ultrasound diagnosis of DVT. Several of the more seminal articles and review articles related to the ultrasound diagnosis of DVT in the non-trauma patient are included to provide a perspective on the current state of the technology. A total of 16 articles related to the ultrasound diagnosis of DVT in the trauma patient are discussed in this review.

III. Recommendations

A. Level I

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

B. Level II

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

C. Level III

1. Hand-held Doppler ultrasound may be used to assess **symptomatic** trauma patients with suspected DVT. Confirmatory venography may be needed in patients who screen positive for DVT with Doppler ultrasound.

2. Serial duplex ultrasound imaging of high-risk asymptomatic trauma patients to screen for DVT may be cost-effective and decrease the incidence of PE. However, the use of ultrasound in screening asymptomatic patients is burdened by a low sensitivity when compared to venography in the short term.

IV. Scientific Foundation

A. Ultrasound Diagnosis of DVT in the Non-Trauma 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 as an outpatient. The accuracy is very much dependent on the experience of the user.[1] Comerota et

al.[2] compiled a meta- analysis of 23 studies examining the accuracy of Doppler ultrasound compared to venography. Overall, in symptomatic patients Doppler ultrasound had a sensitivity of 85% (722/847) and a specificity of 88% (1,415/1,615) to detect proximal DVT.

2. Duplex Ultrasound

Duplex ultrasound employing both real-time B-mode scanning and Doppler ultrasound allows for non-invasive 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 absence of Doppler flow sounds. Again, the technical quality of the study is very much user-dependent. In patients who present with symptoms of DVT (symptomatic), 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% (1,132/1,178) and a specificity of 96% (1,384/1,450).[2] In the 10 series in which duplex was used to diagnose calf DVT in symptomatic patients, it had a sensitivity of 80% (122/153).

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 their success rates. Most of these studies have been performed in orthopedic patients undergoing elective surgery. Agnelli et al.[3] 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 in every patient, 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 1 summarizes these results:

Table 1: Sensitivity and Specificity of Duplex ultrasound in asymptomatic patients in which it was used to screen for DVT according to experimental design.

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

95% confidence intervals in parentheses
(adapted from Agnelli et al. [3] 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

There are several studies on the use of ultrasound to screen for DVT in asymptomatic patients at high risk for DVT. Unfortunately, most of these studies had significant methodological flaws, and few, if any, employed 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. Nevertheless, these ultrasound studies do offer a glimpse of the incidence

of the occult DVTs that occur in high risk trauma patient, 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.[4] did a comprehensive color Doppler ultrasound exam twice weekly of all major venous structures in 57 patients classified as high risk during an eight-month period. Both upper and lower extremities were examined as well as the internal jugular, subclavian and axillary veins, the inferior vena cava, and common iliac, internal and external veins. Twelve high-risk trauma patients (21%) were identified as having occult DVT. In 23% of patients, they were unable to get a complete ultrasound exam. No confirmatory study was performed in those who tested positive on ultrasound. Of note, there were 2 PEs in this group of high risk patients (confirmed by pulmonary angiogram), and both patients at the time had screened negative for DVT. Napolitano et al. [5] retrospectively reviewed the results of biweekly duplex screening in 458 trauma patients admitted to their ICU over a five-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. There was no confirmatory study employed in those patients who tested positive for DVT, and a PE occurred in this population. In a commentary which accompanied the article, Dr. M. Knudson pointed out several methodological flaws with the study. At issue were the timing of the scans performed, 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 which may not need ICU admission.

Meythaler et al.[6] performed a cost analysis of routine screening for proximal DVT using color-Doppler ultrasound in 116 head-injured patients being admitted to a rehab 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 ($129,527.83/43.5years). This compared favorably to the $8,280 per year of life saved for biennial mammograms for women age 50-59 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, there are a number of underlying assumptions which 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.[7] performed serial duplex ultrasound 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 6 were proximal and two were distal (calf). All were asymptomatic for DVT. There was one PE 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 ultrasounds, and all had positive venograms. There was one patient who had a negative duplex but a positive venogram. Overall, the predictive value of a positive duplex in this study population was 100% (11 out of 11) and that of a negative duplex ultrasound, 95% (21 of 22).

Chu et al. [8] looked at the 21 spinal cord injured patients admitted to a rehab unit over an 11-month period who were screened with Doppler ultrasound and IPG on alternate weeks. Only two patients developed DVT during an 8-week period, and both were detected clinically prior to 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%. [9,10] It also should be noted that the authors of this study used Doppler ultrasound with an unknown sensitivity and specificity as a screening procedure in the asymptomatic patient.

Meredith et al.[11] looked at the incidence of DVT with femoral vein catheterization using 8.5F 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 different study of 96 elderly patients with isolated hip fractures Dorfman et al.[12] used compression sonography (i.e. Doppler ultrasound) perioperatively and every 3 days until discharge. Positive ultrasounds were confirmed with venography, and venography was performed on all patients at discharge. There were 18 patients (19%) who had a diagnosed DVT. Of these, 5 were diagnosed on the pre-discharge venogram. This gives ultrasound a sensitivity of 73% and specificity of 100% in this series of patients.

Jongbloets et al.[13] in a series of 100 patients undergoing craniotomy compared serial Doppler ultrasound and contrast venography. Venography demonstrated proximal DVT in 13 patients (13%). Doppler ultrasound also identified DVT in 5 of these patients (sensitivity 38%, 95% CI 8-69%). In the 87 patients without proximal DVT on venography, Doppler ultrasound gave four false positive results (specificity 95%, 88-99%).

In a study examining modes of prophylaxis in 281 high risk trauma patients, Dennis et al.[14] scanned for DVT on admission and every 5 days thereafter with a duplex scanner or Doppler ultrasound. Approximately 25% were scanned using duplex and 75% employed 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 exams there was an incomplete study. 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 3 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 which was 100% accurate. Overall, there was approximately a 10% DVT rate, but again there were 4 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.[16] 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, the rest were occult. Again, two patients developed PE, one of which was fatal, following repeated negative ultrasound exams.

The low sensitivity of ultrasound to detect asymptomatic DVT seen in the general medical population is also mirrored in the trauma population. In a meta-analysis reviewing contrast venography to ultrasound in 2000 patients who had orthopedic surgery, [18] ultrasound was found to have a sensitivity of only 62% in detecting asymptomatic proximal DVT compared with venography. Likewise, Davidson et al[19] prospectively assessed asymptomatic high risk patients following hip surgery with both venography and color Doppler ultrasonography and found that the sensitivity of Doppler was only 38% in detecting asymptomatic DVT.

In a similar analysis, Brasel et al[20] examined the cost effectiveness of biweekly ultrasound screening versus placement of prophylactic vena cava filters 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 $46,3000 vs $97,000. However, ultrasound screening became more expensive than VCF when the anticipated length of stay was greater than or equal 2 weeks. Again there are a number of assumptions that underlie such a decision tree analysis that may not reflect clinical

reality. In contrast, Satiani et al[21] 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 non-trauma literature attest to the overall accuracy of both Doppler and duplex ultrasound in the detection of DVT in the symptomatic patient. The overall accuracy of screening ultrasound in the asymptomatic patient is less clear. Many reports on the use of screening ultrasound, (either Doppler or duplex), lack corroboration of accuracy with contrast venography. Of concern is that many of these studies report on PEs in the presence of negative screening ultrasound exams, leading one to speculate on the ability of duplex to detect clinically significant DVT.

VI. Future Investigation

A prospective study with adequate sample size and appropriate power calculation, possibly multi-institutional, (with standardization of ultrasound techniques) should be undertaken to determine the accuracy (i.e. sensitivity, specificity, positive predictive, negative predictive) of screening duplex ultrasound when compared to the standard venography in trauma patients. It is not cost-effective to serially screen all trauma patients for DVT, therefore, the high-risk trauma patient who is prone to develop DVT likewise needs to be identified.

VII. References

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DEEP VENOUS THROMBOSIS (DVT) IN TRAUMA: A LITERATURE REVIEW

ULTRASOUND (U/S)

First Author	Year	Reference Title	Class	Conclusions
Wheeler HB	1995	Diagnostic methods for deep vein thrombosis. *Haemostasis 25:6-26*	I	Review article summarizing series examining U/S (duplex and Doppler) comparing results in symptomatic and a symptomatic patients. Compared U/S to other diagnostic modalities for DVT.
Comerota AJ	1993	Venous duplex imaging for the diagnosis of acute deep venous thrombosis. *Haemostasis 23:61-7*	I	Review of meta-analysis of cumulative series comparing U/S to phlebography. Sensitivity, specificity, positive predictive value and È are reported on symptomatic and asymptomatic patients with DVT.
Agnelli G	1995	Diagnosis of deep vein thrombosis in asymptomatic high -risk patients. *Haemostasis 25:40-8*	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.
Burns GA	1993	Prospective ultrasound evaluation of venous thrombosis in high -risk trauma patients. *J Trauma 35:405-8*	III	58 high risk trauma patients underwent total body bi -weekly 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? *J Trauma 39:651-9*	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. *Arch Phys Med Rehabil 77:1-5*	II	8.5% of head-injured patients admitted to rehab 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. *J Bone Joint Surg 72A:495-500*	III	60 pelvic fractures screened with duplex U/S. 15% DVT rate; 1 PE noted in patient who became positive on dup lex that day.

ULTRASOUND (U/S)

First Author	Year	Reference Title	Class	Conclusions
Chu DA	1985	Deep venous thrombosis: Diagnosis in spinal cord injured patients. *Arch Phys Med Rehabil 66:365-8*	III	Systematic clinical exam for DVT was successful in diagnosing 2 DVTs out of 21 patients. Both were confirmed with Doppler U/S.
Myllynen PM	1985	Deep venous thrombosis and pulmonary embolism in patients with acute spinal cord injury: A comparison with nonparalyzed patients immobilized due to spina l fractures. *J Trauma 25:541-3*	II	23 patients with acute spinal cord injury had a 100% incidence of DVT diagnosed with ^{125}I-labeled fibrinogen and confirmed with venography.
Brach BB	1977	Venous thrombosis in acute spinal cord paralysis. *J Trauma 17:289-92*	III	9/10 patients had DVT by ^{125}I-labeled fibrinogen and 7 were confirmed with venography.
Meredith JW	1993	Femoral catheters and deep venous thrombosis: A prospective evaluation of venous duplex sonography. *J Trauma 35:187-91*	III	Serial B-mode duplex U/S showed a 14% incidence of ileofemoral DVT on the side of 8F femoral venous catheter.
Dorfman GS	1990	Lower-extremity venous thrombosis in patients with acute hip fractures: Determination of anatomic location and time of onset with compression sonography. *AJR Am J Roentgenol 154:851-5*	II	Serial compression sonography revealed 19% DVT rate (all occult) which were confirmed with venogram.
Jongbloets LM	1994	Limitations of compression ultrasound for the detection of symptomless postoperative deep vein thrombosis. *Lancet 343:1142-4*	II	U/S had only 38% sensitivity in detecting DVT in postop craniotomy patients when compared to venography. Authors conclude that U/S is not useful in screening for DVT in high risk asymptomatic postop patients.
Dennis JW	1993	Efficacy of deep venous thrombosis prophylaxis in trauma patients and identification of high risk groups. *J Trauma 35:132-9*	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.
Knudson MM	1992	Thromboembolism following multiple trauma. *J Trauma 32:2-11*	II	Prospective U/S evaluation in 113 patients identifying risk factors for DVT (age, # days immobilized, # transfusions, abnormal admission clotting studies).
Wells PS	1995	Accuracy of ultrasound for the diagnosis of deep venous thrombosis in asymptomatic patients after orthopedic surgery: A meta-analysis. *Ann Intern Med. 122:47-54.*	I	Meta-analysis comparing contrast venography to ultrasound in 2000 Orthopedic patients, ultrasound found on ly to have a sensitivity of 62% in detecting proximal asymptomatic DVT.
Davidson BL	1992	Low accuracy of color Doppler ultrasound in the detection of proximal leg vein thrombosis in asymptomatic high -risk patients. The RD Heparin Arthroscopy Group. *Ann Intern Med. 117:735-738.*	I	Ultrasound was only 38% sensitive in detecting asymptomatic DVT compared to venography in high risk hip surgery.

Brasel KJ	1997	Cost effective prevention of pulmonary embolus in high -risk trauma patients. *J Trauma 42:456-463.*	II	Cost-effectiveness study of biweekly ultrasound vs. prophylactic vena cava filter in high risk trauma patients using decision tree analysis. Ultrasound cheaper if length of stay <2 weeks, but VCF more cost effective if length of stay >2 weeks.
Satiani B	1997	Screening for major deep venous thrombosis in seriously injured patients. A prospective study. *Ann Vasc Surg. 11:626-629.*	III	Cost of routine screening ($18,586 per DVT identified) did not justify its use in patients receiving routine prophylaxis.

The Role of Venography in the Diagnosis of DVT in Trauma Patients

I. Statement of the Problem

Venography is the diagnostic modality to which all other invasive or non-invasive diagnostic modalities for DVT are compared. It is often referred to as the "gold standard" for the diagnosis of DVT in trauma patients.

II. Process

A Medline search from 1966 to 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.

III. Recommendations

A. Level I

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

B. Level II

1. Ascending venography should be used as a confirmatory study in those trauma patients who have an equivocal IPG or ultrasound for DVT.

2. Ascending venography should not be used to screen asymptomatic trauma patients at high risk for DVT. There may be a role for ascending venography in research studies on the incidence of DVT in trauma patients.

C. Level III

1. Magnetic resonance venography many 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).

IV. Scientific Foundation

Ascending contrast venography as a diagnostic modality has been around since the 1920s but was considered to be unreliable or even dangerous until Rabinov and Paulin[1] standardized the technique in 1972. When this proper technique is utilized by a skilled radiologist, the entire lower extremity venous system should be visualized in a normal patient. Rabinov and Paulin[1] described the four cardinal signs of DVT: 1) constant filling defects 2) abrupt termination of the dye column 3) non-filling of the entire deep venous system or portions thereof, and 4) diversion of flow. Despite improvements in technique several logistical problems remain for venogram. A venogram requires transport of the patient to the radiology suite which is often difficult in critically ill trauma patients. Venography requires a cooperative patient who can be examined in a semi-erect position on a tilting fluoroscopy table. Venous access is not always possible especially in those with massive leg swelling. Usually 150-300cc of contrast material is required for adequate visualization of the deep venous system. With the use of nonionic contrast agents, the risk of allergic reactions and nephrotoxicity is very uncommon. Although the possibility of contrast-induced DVT exists,[2] the risks of this complication are unknown but 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 "gold standard" in DVT

diagnostic imaging, up to 30% of venograms will fail to visualize some segment of the venous system.[3] Due to 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.[4] 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.[5] 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.[6] In this study, all patients admitted with
ISS>9 were assessed with contrast venography for evidence of DVT. No patient received any DVT prophylaxis. DVT was found in 201/349 patients (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 - how many were nonocclusive, or were small and confined to single venous segments below the knee. This has been a criticism of venography in that it may detect small isolated thrombi such as those on valve cusps that are clinically insignificant.[3] It can be difficult to predict which ones will emerge as one of the 5-30%[7] that go on to propagate an extensive, proximal (dangerous) thrombi. A decision to treat these patients is not insignificant as anticoagulant treatment can be associated with substantial morbidity in the trauma patient. Brathwaite et al.,[8] in a cohort of 70 trauma patients treated with full anticoagulation, found a 36% complication rate requiring termination of anticoagulation. In a study of 39 immobilized patients, Kudsk et al.[9] evaluated the lower extremities with venography between 7-12 days after injury. They found 63% of patients immobilized for 10 days or longer developed DVT, with thrombi extending above the knee in 50% of these patients. All but one of these DVTs were clinically silent. In 1967, Freeark et al.[10] studied 124 trauma patients admitted for hospital stays of 3 weeks or longer. They found 44 (35%) had venographic signs of DVT. Less than one third of these patients had any clinical signs and symptoms related to a DVT. Although this study was performed prior to refinement in technique by Rabinov and Paulin it was one of the first to draw attention to the high rate of DVT in immobilized trauma patients. Likewise, serial lower limb venography was performed in 127 spinal cord injured patients by Yelnik et al.[11] They found a 33% incidence of DVT on first examination with another 13.8% developing DVT on subsequent exam.

Magnetic resonance venography (MRV) has been used to diagnose DVT in patients with acute pelvic trauma. Montgomery et al[12] used MRV in 45 consecutive patients with displace acetabular fracture and diagnosed 24 asymptomatic DVT, 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 exam, requires transport to the MR suite and requires a dedicated radiologist with an interest in this technique.

V. Summary

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

VI. Future Investigation

A study comparing venography to other non-invasive imaging for DVT such as duplex ultrasound should be performed.

VII. References

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DEEP VENOUS THROMBOSIS (DVT) IN TRAUMA: A LITERATURE REVIEW

VENOGRAPHY

First Author	Year	Reference Title	Class	Conclusions
Rabinov K	1972	Roentgen diagnosis of venous thrombosis in the leg. *Arch Surg 104:134-44*	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. *Radiology 165:113-6*	II	Multi-institutional study comparing ionic and non -ionic contrast material for venography. Demonstrated 9% post-venography DVT by ^{125}I-fibrinogen scanning.
Wheeler HB	1995	Diagnostic methods for deep vein thrombosis. *Haemostasis 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. *Lancet ii:716-9*	III	50 patients with suspected DVT underwent numerous diagnost ic 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. *Clin Chest Med 16:253-68*	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. *N Engl J Med 331:1601-6*	II	Major incidence study of DVT following trauma in patients who received no prophylaxis. Diagnosis of DVT was made by contrast venography.

P

VENOGRAPHY

First Author	Year	Reference Title	Class	Conclusions
Kakkar VV	1970	Deep vein thrombosis of the leg. Is there a "high risk" group? *Am J Surg 120:527-30*	III	Radioactive fibrinogen study that demonstrated a significant number of calf emboli extend proximally.
Brathwaite CE	1993	Complications of anticoagulation for pulmonary embolism in low risk trauma patients. *Chest 104:718-20*	III	Study demonstrated anticoagulation had a high bleedi ng complication rate (36%) even in low risk trauma patients.
Kudsk KA	1989	Silent deep vein thrombosis in immobilized multiple trauma patients. *Am J Surg 158:515-9*	III	Incidence study of DVT employing venogram as diagnostic modality. 63% of immobili zed patients for 10 days or longer developed DVT.
Freeark RJ	1967	Posttraumatic venous thrombosis. *Arch Surg 95:567-75*	II	Early study employing venogram in 124 trauma patients in hospital 3 weeks or longer. 35% incidence of DVT in this population.
Yelnik A	1991	Systematic lower limb phlebography in acute spinal cord injury in 147 patients. *Paraplegia 29:253-60*	II	Serial venogram revealed a significant rate of DVT in spinal cord injured patients.
Montgomery KD	1995	Magnetic resonance venography to evaluate the deep venous system of the pelvic in patients who have an acetabular fracture. *J Bone and Joint Surg. 77A:1639-1649*	III	45 patients with acetabular fracture; MRV detected 24 asymptomatic DVT, 7 in internal iliac vein, an area not seen on ultrasound or venography.