Deep-vein thrombosis in high-energy skeletal trauma despite thromboprophylaxis

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We report the incidence and location of deep-vein thrombosis in 312 patients who had sustained high-energy, skeletal trauma. They were investigated using magnetic resonance venography and Duplex ultrasound.

Despite thromboprophylaxis, 36 (11.5%) developed venous thromboembolic disease with an incidence of 10% in those with non-pelvic trauma and 12.2% in the group with pelvic trauma. Of patients who developed deep-vein thrombosis, 13 of 27 in the pelvic group (48%) and only one of nine in the non-pelvic group (11%) had a definite pelvic deep-vein thrombosis. When compared with magnetic resonance venography, ultrasound had a false-negative rate of 77% in diagnosing pelvic deep-vein thrombosis. Its value in the pelvis was limited, although it was more accurate than magnetic resonance venography in diagnosing clots in the lower limbs. Additional screening may be needed to detect pelvic deep-vein thrombosis in patients with pelvic or acetabular fractures.

Venous thromboembolic disease often follows blunt trauma,¹⁻¹³ manifesting as deep-vein thrombosis and/or pulmonary embolism. It is the most common cause of death more than seven days after traumatic injury,¹⁴ when patients are susceptible to Virchow's triad, namely intimal damage, venous stasis and hypercoagulability.¹⁵ Despite its prevalence the significance of venous thromboembolic disease after trauma is limited when compared with its importance in elective surgery, such as lower-limb arthroplasty.

There is controversy relating to many aspects of venous thromboembolic disease in trauma, such as its incidence,^{1-13,16-18} risk factors,^{3,9,12,16,19-23} diagnosis,^{3,5,6,9,10,13,16,24-28} the anatomical location of high-risk clots^{6,10,24,26-29} and the best prophylaxis.^{1,4-12,16} Among patients with orthopaedic injuries, those with high-energy skeletal trauma present the highest risk.

Venography is the method of choice for the diagnosis of deep-vein thrombosis of the lower limbs, but it is invasive, involves potentially hazardous contrast agents and is subject to interobserver variability and operator-dependent image quality. Its use is therefore limited to research in the less traumatised patient. Moreover, since its value in the imaging of pelvic clots is controversial^{6,9,10,27} its routine use in high-energy trauma is not considered to be practical. Non-invasive methods, such as mag-

netic resonance venography and Duplex ultrasound, can alternatively be used without risk for screening and diagnosis in all trauma patients.

Our prospective study aimed to document the prevalence of venous thromboembolic disease in high-energy, blunt, skeletal trauma despite thromboprophylaxis, to identify the location of clots and to investigate the value of magnetic resonance venography and ultrasound in this detection.

Patients and Methods

Between December 1997 and August 2002, 312 patients with high-energy, blunt, skeletal trauma admitted to the University of Alabama Hospital underwent two different regimes of prophylaxis for deep-vein thrombosis. The inclusion criteria were pelvic, acetabular, femoral or tibial fractures which either required surgical stabilisation or occurred in patients older than 55 years or in those with an abbreviated injury score for the head and neck of three or more, plus a fracture of a long bone. They received either mechanical compression or a pharmacological regime with enoxaparin (Aventis Pharmaceutical, Parsippany, New Jersey) and were included only if prophylaxis began within 72 hours of injury. Mechanical prophylaxis was initiated on admission and pharmacological prophylaxis at 24 to 72 hours after admission depending on haemodynamic

stability. Exclusion criteria were active uncontrolled bleeding, a history of previous venous thromboembolic disease, body habitus precluding magnetic resonance venography and non-compliance.

All patients underwent bilateral magnetic resonance venography and ultrasound in the 24 hours before discharge from hospital or earlier if there were symptoms or signs of venous thromboembolic disease. Duplex ultrasound examination was performed with an Acuson 128 XP, Sequoia System (Mountain View, California) or an Advanced Technology Laboratories 3000HD (Bothell, Washington) machine with high-resolution linear transducers and the use of colour and spectral Doppler vessel interrogation. It included standard compression and flow augmentation techniques from the groin to the popliteal fossa. The criteria for diagnosis of deep-vein thrombosis included observation of an intraluminal thrombus, loss of vessel compressibility and decreased blood flow.

Magnetic resonance venography used a Sigma 1.5-T magnet (General Electric Medical Systems, Milwaukee, Wisconsin), and two-dimensional time-of-flight sequences with saturation of the arterial signal. The diagnostic criteria for deep-vein thrombosis included intraluminal signal-flow voids with abrupt narrowing or termination of the luminal signal which could not be explained by flow or magnetic susceptibility artefacts from internal or external fixation devices.

Two experienced radiologists reviewed the ultrasound and magnetic resonance venography images. These were initially read independently in a blinded fashion. Neither technique was treated as the method of choice. Both were evaluated independently as if in an isolated study. If there was any difficulty of interpretation between ultrasound and magnetic resonance venography this was resolved by consensus opinion after joint review.

Documentation of pulmonary embolism with a normal ultrasound of a lower limb was accepted as evidence of deep-vein thrombosis without a corroborating magnetic resonance venography if the patient was too unstable for transport to the MR scanner. In this position, the probable source of clot is in the pelvis which is very difficult to visualise by ultrasound.^{5,6,9,10,16,24,25,27,28} This presumptive evidence of a pelvic deep-vein thrombosis is consistent with previous published reports.^{4-6,10}

Results

Of the 312 patients, 90 had polytrauma without pelvic or acetabular fractures. The other 222 each had a pelvic or acetabular fracture among their injuries. A total of 36 patients (11.5%) developed venous thromboembolic disease despite prophylaxis. One developed late deep-vein thrombosis and pulmonary embolism approximately three months after injury. She was not included in the statistical analysis.

Nine of the 36 patients belonged to the non-pelvic group giving an incidence of venous thromboembolic disease of

10% in this group. Their injuries included fracture of the femoral neck (two), fracture of the femur (two), supracondylar fracture (two), dislocation of the knee (two), fracture of the tibial plateau (one), tibial fracture (one), pilon fracture (one) and fracture of the ankle (one). All these patients sustained at least one fracture on the same side as their deep-vein thrombosis. One developed a pelvic clot after a fracture of the femoral neck and shaft leading to a clot in an ipsilateral external iliac vein. Another developed pulmonary embolism with normal ultrasound but was too unstable to undergo magnetic resonance venography. Of the nine patients with non-venous thromboembolic disease and non-pelvic trauma, seven developed isolated lower extremity clots and one had a definite and another a presumed pelvic deep-vein thrombosis.

Of the 222 patients who each had a surgically-treated pelvic or acetabular fracture 27 (12%) developed venous thromboembolic disease. Of these, 13 (48%) had a definite pelvic deep-vein thrombosis, since a thrombus was identified in the pelvic vasculature, and coexistent lower extremity clots were found in four. Two patients (7.5%) had a presumed pelvic deep-vein thrombosis since they suffered pulmonary embolism with a negative ultrasound and were too unstable to undergo magnetic resonance venography. The other 12 (44.5%) had isolated lower extremity clots.

Statistical analysis of the patients with definite localisation of clots to the pelvis or lower extremity showed that there was a significant difference in the occurrence of pelvic clots between patients suffering pelvic and non-pelvic trauma (Fisher's exact test, $p = 0.056$). A similar trend was noticed when including the presumed pelvic deep-vein thrombosis but the difference was no longer statistically significant (Fisher's exact test, $p = 0.087$). There was no significant difference in the overall rate of venous thromboembolic disease between the pelvic and non-pelvic groups, probably because both had suffered high-energy trauma. Four patients had a pulmonary embolus (1.3%) which in three occurred after pelvic or acetabular fractures and in one after non-pelvic polytrauma. There were no deaths as a result of venous thromboembolic disease.

Of a total of 47 distinct clots in the 36 patients, 14 (30%) were in the pelvis, 30 (64%) were in the lower limbs and three (6%) were presumed to be pelvic since they presented with pulmonary embolism. Of the 36 patients, 19 (53%) had isolated lower extremity clots, four (11%) lower extremity and pelvic clots and 13 (36%) isolated or presumed pelvic deep venous thrombosis. The location of thrombi was as follows: common iliac vein (four), internal iliac vein (one), external iliac vein (nine), common femoral vein (21), femoral vein (five) and popliteal vein (four).

Thirteen patients had definite pelvic deep-vein thrombosis diagnosed by magnetic resonance venography but ultrasound was negative in ten of these. Based on consensus between the radiologists ultrasound had a false-negative rate of 77% when compared with magnetic resonance venography in the detection of pelvic clots. It was also

unable to demonstrate pelvic clots in the four patients with presumed pelvic deep-vein thrombosis. Of the 20 patients in whom lower extremity clots had been diagnosed by ultrasound, magnetic resonance venography was negative in eight, impracticable in three because of medical instability and positive in 12. All lower extremity clots with a discrepancy between magnetic resonance venography and ultrasound were resolved by consensus agreement between the radiologists. When compared with ultrasound, the false-negative rate for magnetic resonance venography was 40% (8 of 20). The main reason for this high rate was a metal implant or external fixator artefact since the tests were done post-operatively. This limits magnetic resonance venography to a significantly greater degree to the limbs rather than the pelvis.

Discussion

Patients with pelvic and acetabular fractures are at high risk of venous thromboembolic disease and present features not found in isolated trauma of a limb. An intrapelvic haematoma may compress the pelvic vasculature, surgical treatment is often delayed and post-operative rehabilitation slow. Numerous studies suggest that deep-vein thrombosis in the pelvic venous plexus is more common after pelvic and acetabular fractures.^{6,10,27} Pharmacological prophylaxis, mechanical prophylaxis and filters in the inferior vena cava have been advocated for such patients.^{2,6,9,10,13,14,18,27} Each technique has its complications and limitations, such as concern for delayed venous thromboembolic disease in young patients in whom a permanent filter is placed to deal with a short-term event.³⁰

Despite the use of differing prophylactic regimes, studies focusing on venous thromboembolic disease in pelvic trauma report rates of deep-vein thrombosis from 9% to 27% depending on the imaging techniques used.^{10,13,18} Review of the current literature shows that there is no ideal diagnostic test for deep-vein thrombosis in the pelvic vasculature. Although Duplex ultrasound is well accepted for that purpose in deep-vein thrombosis of a lower limb,^{4,5,9,16,25} it is significantly less sensitive in the pelvis.^{6,9,10,27,31-36} In one study, ultrasound was documented as missing clots in all eight patients with deep-vein thrombosis in the internal iliac system³⁵ and in another seven with isolated deep-vein thrombosis in pelvic veins.³⁴

Magnetic resonance venography is a relatively new technique which allows visualisation of the entire venous system, without contrast. One study of 85 patients undergoing contrast and magnetic resonance venography had a sensitivity of 100%, a specificity of 96%, a positive predictive value of 90% and a negative predictive value of 100%.²⁴ In another study of 75 patients in whom 34.7% had documented deep-vein thrombosis, magnetic resonance venography had a sensitivity of 100%, a specificity of 100% and an accuracy of 96%.²⁶ A third study comparing ascending venography with magnetic resonance venography using direct-puncture venography as the reference standard in

cases of discordance, found magnetic resonance venography to be 100% sensitive and 95% specific compared with ascending venography which had a sensitivity of 78% and specificity of 100%.²⁶ In a study of 30 patients, magnetic resonance venography detected pelvic deep-vein thrombosis in four but these had a negative result on contrast venography.²⁸ The authors noted that technical differences in image acquisition might have been a source of error, since three of the magnetic resonance venography images interpreted as positive had variations in technique. They stated that phase-contrast or cinemagnetic resonance was not used to reconcile any equivocal findings. Therefore interpretation of magnetic resonance venography could also be a possible source of error. It has been shown that contrast venography can be inaccurate in the pelvic system, especially for detecting clots in the internal iliac vasculature.^{6,9,10,16} It is invasive and can add to morbidity, especially in polytraumatised patients. Interobserver variability and operator-dependent image quality lead to inaccuracy. Review papers have concluded that ultrasound was the most appropriate screening and diagnostic test for the lower limbs, and that magnetic resonance venography had many advantages when imaging the pelvis.^{9,16,34,35,37} Their non-invasive nature is attractive in high-energy skeletal trauma.

The drawback of our study is that it is open to selection bias because of the inclusion criteria used to isolate high-energy trauma and the tertiary referral nature of our practice. Since our sample contained a larger proportion of patients with pelvic trauma, extrapolation of the results to trauma patients in a general orthopaedic practice may not be tenable. Nevertheless, we feel that relevant conclusions which have a direct bearing on the management of polytrauma can still be drawn.

Our results indicate that deep-vein thrombosis is common in high-energy, blunt trauma, with an incidence of 11.5% despite prophylaxis. Also, pelvic deep-vein thrombosis is significantly more frequent after pelvic than non-pelvic trauma. Our study confirmed that magnetic resonance venography was better than ultrasound for detecting pelvic clots whereas ultrasound was the better technique for lower extremity clots.

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References

1. Anglen JO, Bagby C, George R. A randomized comparison of sequential-gradient calf compression with intermittent plantar compression for prevention of venous thrombosis in orthopedic trauma patients: preliminary results. *Am J Orthop* 1998;27:53-8.
2. Buerger PM, Peoples JB, Lemmon GW, McCarthy MC. Risk of pulmonary emboli in patients with pelvic fractures. *Am Surg* 1993;59:505-8.
3. Geerts WH, Code KI, Jay RM, Chen E, Szalai JP. A prospective study of venous thromboembolism after major trauma. *N Engl J Med* 1994;331:1601-6.
4. Knudson MM, Morabito D, Paiement GD, Shackelford S. Use of low molecular weight heparin in preventing thromboembolism in trauma patients. *J Trauma* 1996;41:446-59.
5. Knudson MM, Collins JA, Goodman SB, McCrory DW. Thromboembolism following multiple trauma. *J Trauma* 1992;32:2-11.

6. **Montgomery KD, Geerts WH, Potter HG, Helfet DL.** Thromboembolic complications in patients with pelvic trauma. *Clin Orthop* 1996;329:68-87.
7. **Muntz JE.** The risk of venous thromboembolism in non-large-joint surgeries. *Orthopedics* 2003;26(Suppl):237-42.
8. **Norwood SH, McAuley CE, Berne JD, et al.** A potentially expanded role for enoxaparin in preventing venous thromboembolism in high risk blunt trauma patients. *J Am Coll Surg* 2001;192:161-7.
9. **Rogers FB.** Venous thromboembolism in trauma patients: a review. *Surgery* 2001;130:1-12.
10. **Stannard JP, Riley RS, McClenney MD, et al.** Mechanical prophylaxis against deep-vein thrombosis after pelvic and acetabular fractures. *J Bone Joint Surg [Am]* 2001;83-A:1047-51.
11. **Turpie AG, Eriksson BI, Lassen MR, Bauer KA.** A meta-analysis of fondaparinux versus enoxaparin in the prevention of venous thromboembolism after major orthopaedic surgery. *J South Orthop Assoc* 2002;11:182-8.
12. **Velmajos GC, Kern J, Chan L, et al.** Prevention of venous thromboembolism after injury: an evidence-based report: part I: analysis of risk factors and evaluation of the role of vena caval filters. *J Trauma* 2000;49:132-8.
13. **White RH, Goulet JA, Bray TJ, et al.** Deep-vein thrombosis after fracture of the pelvis: assessment with serial duplex-ultrasound screening. *J Bone Joint Surg [Am]* 1990;72-A:495-500.
14. **Webb LX, Rush PT, Fuller SB, Meredith JW.** Greenfield filter prophylaxis of pulmonary embolism in patients undergoing surgery for acetabular fracture. *J Orthop Trauma* 1992;6:139-45.
15. **Virchow RLK.** Virchow's triad: gesammelte abhandlungen zue wissenschaftlicher medizin, von meidinger sohn. *Frankfurt-ann-Main* 1856.
16. **Rogers FB, Cipolle MD, Velmahos G, Rozycki G, Luchette FA.** Practice management guidelines for the prevention of venous thromboembolism in trauma patients: the EAST practice-management guidelines work group. *J Trauma* 2002;53:142-64.
17. **Devlin JW, Tyburski JG, Moed B.** Implementation and evaluation of guidelines for use of enoxaparin as deep vein thrombosis prophylaxis after major trauma. *Pharmacotherapy* 2001;21:740-7.
18. **Russell GV Jr, Nork SE, Chip Routt ML Jr.** Perioperative complications associated with operative treatment of acetabular fractures. *J Trauma* 2001;51:1098-103.
19. **Jacoby RC, Owings JT, Holmes J, et al.** Platelet activation and function after trauma. *J Trauma* 2001;51:639-47.
20. **Meissner MH, Chandler WL, Elliott JS.** Venous thromboembolism in trauma: a local manifestation of systemic hypercoagulability? *J Trauma* 2003;54:224-31.
21. **Peet D, Hafner G, Hansen M, et al.** Dose adjusted thrombosis prophylaxis in trauma surgery according to levels of D-Dimer. *Thromb Res* 2000;98:473-83.
22. **Trottier SJ, Veremakis C, O'Brien J, Auer AL.** Femoral deep vein thrombosis associated with central venous catheterization: results from a prospective, randomized trial. *Crit Care Med* 1995;23:52-9.
23. **Wilson D, Cooke EA, McNally MA, et al.** Altered venous function and deep venous thrombosis following proximal femoral fracture. *Injury* 2002;33:33-9.
24. **Carpenter JP, Holland GA, Baum RA, et al.** Magnetic resonance venography for the detection of deep venous thrombosis: comparison with contrast venography and duplex Doppler ultrasonography. *J Vasc Surg* 1993;18:734-41.
25. **Cipolle MD, Wojcik R, eislove E, Wasser TE, Pasquale MD.** The role of surveillance duplex scanning in preventing venous thromboembolism in trauma patients. *J Trauma* 2002;52:453-62.
26. **Evans AJ, Sostman HD, Witty LA, et al.** Detection of deep venous thrombosis: prospective comparison of MR imaging and sonography. *J Magn Reson Imaging* 1996;6:44-51.
27. **Rubel IF, Potter H, Barie P, Kloen P, Helfet DL.** Magnetic resonance venography to evaluate deep venous thrombosis in patients with pelvic and acetabular trauma. *J Trauma* 2001;51:622.
28. **Stover MD, Morgan SJ, Bosse MJ, et al.** Prospective comparison of contrast-enhanced computed tomography versus magnetic resonance venography in the detection of occult deep pelvic vein thrombosis in patients with pelvic and acetabular fractures. *J Orthop Trauma* 2002;16:613-21.
29. **Ouriel K, Green RM, Greenberg RK, Clair DG.** The anatomy of deep venous thrombosis of the lower extremity. *J Vasc Surg* 2000;31:895-900.
30. **Decousus H, Leizorovicz A, Parent F, et al.** A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *N Engl J Med* 1998;338:409-15.
31. **Voci SL, Gottlieb RH.** Doppler respiratory patterns in the femoral veins with pelvic vein obstruction. *Clin Imaging* 1999;23:172-6.
32. **Della Valle CJ, Steiger DJ, DiCesare PE.** Duplex ultrasonography in patients suspected of postoperative pulmonary embolism following total joint arthroplasty. *Am J Orthop* 2003;32:386-8.
33. **Spritzer CE, Arata MA, Freed KS.** Isolated pelvic deep venous thrombosis: relative frequency as detected with MR imaging. *Radiology* 2001;219:521-5.
34. **Dupas B, el Kouri D, Curtet C, et al.** Angiomagnetic resonance imaging of iliofemoro-caval venous thrombosis. *Lancet* 1995;346:17-19.
35. **Dorfman GS, Cronan JJ.** Venous ultrasonography. *Radiol Clin North Am* 1992;30:879-94.
36. **Laissy JP, Cinqualbre A, Loshkajian A, et al.** Assessment of deep venous thrombosis in the lower limbs and pelvis: MR venography versus duplex Doppler sonography. *AJR Am J Roentgenol* 1996;167:971-5.
37. **Evans AJ, Sostman HD, Knelson MH, et al.** Detection of deep venous thrombosis: prospective comparison of MR imaging with contract venography. *AJR Am J Roentgenol* 1993;161:131-9.