

## Screening for proximal deep venous thrombosis using B-mode venous ultrasonography following major hip surgery: implications for clinical management

J. WICKY<sup>1</sup>, O. BONGARD<sup>1,2</sup>, R. PETER<sup>3</sup>, S. SIMONOVSKA<sup>1</sup> and H. BOUNAMEAUX<sup>1</sup>

Venous thromboembolism (VTE) is a common complication following major orthopedic surgery. In the absence of prophylaxis, the incidence of deep vein thrombosis (DVT) exceeds 50% in many studies, of which about 20% are proximal [12, 15, 27, 43, 44]. Most of these DVTs are asymptomatic [3, 44] but they may result in fatal pulmonary embolism in 1-4% of the patients [7, 12, 43]. Several prophylactic regimens are effective to reduce postoperative VTE [4]. Subcutaneous fixed doses of unfractionated heparin reduce this risk by about two thirds [12] and, more recently, low-molecular weight heparins (LMWH) led to a further reduction of 25% of DVT [4, 36]. Alternatively, mechanical methods such as intermittent pneumatic compression also provide some protection against postoperative VTE. Nonetheless, incidence of overall DVT ranges in most series from 5% to 20% (up to 31% after LASSEN [27]) with 2.4%-8% proximal thrombosis (25.8% after LASSEN [27]). Moreover, prophylaxis for VTE remains underused in many hospitals, especially in the United States [3].

Because of this relatively high incidence of postoperative DVT despite prophylaxis, one might discuss the opportunity of a systematic postoperative screening in these high-risk patients. However, whereas effective diagnostic strategies are well established for patients with *symptomatic* DVT, detection of postoperative, mainly *asymptomatic* DVT remains a challenge. Several non invasive screening tests have been proposed for that purpose, including impedance plethysmography [21, 24, 34], continuous wave Doppler [39], radio-iodinated fibrinogen uptake

test (PUT) [21, 24], and liquid crystal contact themography [10]. However, these methods are quite insensitive and even combinations of some of them, e.g. PUT and impedance plethysmography, have been shown to miss more than 50% of the thromboses [13, 21]. At present time, ascending venography remains the «gold standard» for screening of asymptomatic DVT, but it is too invasive and expensive to be used as a screening test. In the past five years, real-time B-mode compression ultrasonography (US) has been shown to be very accurate for diagnosing proximal DVT in *symptomatic* patients, with both a sensitivity and a specificity of more than 95 %, as compared with ascending venography [6, 29, 48]. However, the accuracy of US in the detection of *asymptomatic* postoperative DVT seems to be far less good as suggested by several recent studies [1, 9, 19, 20, 32, 35]. Thus, a sensitivity of only 57% for a corresponding specificity of 99% for proximal DVT has been reported in a series of patients undergoing total hip arthroplasty [1]. Moreover, implementing color Doppler does not seem to improve significantly the sensitivity of ultrasonography with respect to the detection of proximal DVT in that setting [14].

With these shortcomings in mind, we set up the present study in order to evaluate prospectively the clinical usefulness of a systematic screening for proximal deep vein thrombosis using real-time B-mode venous compression ultrasonography in consecutive patients undergoing hip surgery.

## Patients and methods

### Patients

All patients who were consecutively admitted to the Clinic of Orthopedic Surgery of our institution between January 1 and March 31, 1993 for elective or emergency major hip surgery (hip arthroplasty, dynamic hip screw, or any operation on the hip or pelvis) were eligible for the study. Ongoing therapeutic anticoagulation or unwilling to give written informed consent were the only exclusion criteria.

Routine perioperative antithrombotic prophylaxis consisted of one daily subcutaneous administration of low molecular weight heparin (LMWH) dalteparin sodium (Low-Liquemin®, Hoffmann-La Roche, Basel, Switzerland, which is identical to Fragmin®, Kabi Pharmacia, Stockholm, Sweden) with a dosage of 5000 IU (in patients with a body weight > 50 kg) or 2500 IU (body weight < 50 kg). The first injection was scheduled in the evening (i.e. 12 hours) before the operation and then each evening during 5 days. Subsequently, dalteparin was replaced either by oral acenocoumarol (Sintrom®, Ciba-Geigy, Basel, Switzerland, given from the 2nd postoperative day) with a target INR (International Normalized Ratio) of 1.5-2.0 or by an oral combination of aspirin and dihydroergotamin (DHE) (500 mg and 5 mg p.o. t.i.d, respectively, given from the 5th postoperative day) [46], depending upon the surgeon's decision. The prothrombin time was measured postoperatively on days 3, 7, 10 and 15. Anticoagulant effect was considered appropriate if INR on days 7, 10 and 15 was more than 1.5. Major hemorrhage were defined as those hemorrhages requiring blood transfusion, re-hospitalisation or re-operation. Leg circumference was measured on the day of venous ultrasonography at high (15 cm above the upper border of the patella), calf, and ankle (both largest circumference) levels. The study protocol was approved by the Ethical Committee of the Department of Surgery, University of Geneva.

### B-mode venous ultrasonography

Real-time B-mode ultrasonography (ALOKA 500 equipped with a 7.5 MHz linear probe) was performed postoperatively by one single experienced examiner (O. B) who was unaware of the clinical data and of the prophylactic regimen in use. This exam was performed at the bedside on the 15th postoperative day or earlier in case of earlier discharge from the hospital. Two proximal vein segments were systematically scanned in both legs: the common femoral vein in the groin and the popliteal vein in the popliteal fossa. The calf veins were not studied. Gentle but firm compression was performed with the transducer probe to test for presence of DVT. A vein was considered fully compressible if no residual lumen was seen. The absence of complete vein compressibility was adopted as criterion for the presence of a thrombus [41]. The result of ultrasonographic examination was scored as normal, indicative of DVT or inconclusive when the exam was not normal, but did not completely fulfill the criterion for DVT, or when the quality of the exam was poor.

If a patient developed symptoms or signs of DVT or pulmonary embolism during the study, the situation was managed according to usual diagnostic and therapeutic standards.

### D-Dimer plasma measurement

2.5 ml of blood was collected preoperatively as well as on the 15th postoperative day. Plasma was obtained by centrifugation for 10 min at 2500 g and stored in frozen aliquots until D-dimer, a highly sensitive marker for VTE [11], was assayed serially at the end of the trial using an ELISA assay. Its accuracy for diagnosing or predicting postoperative proximal DVT will be reported elsewhere [8].

### Statistical analysis

Data are displayed as median and range unless stated otherwise. Chi-square test was used for comparison of proportions. A p value equal or less than 0.05 was considered statistically significant. Sensitivity, specificity, and positive and negative predictive values were calculated according to standard methods.

## Results

### Clinical characteristics of the patients

Among the 772 consecutive patients admitted to the Clinic of Orthopedic Surgery of our institution over the three-month period of the trial, 207 patients were eligible. Twenty-nine did not complete the protocol because of inadvertent early discharge (n = 15), cancelled intervention (n = 11), refusal to participate (n = 1) or death (n = 2). Among the 173 patients who completed the study, 113 were women and 60 were men. The mean age was 72.5 years (range 22-105 years). Seventy-eight patients (45.5%) underwent elective total hip replacement for coxarthrosis and 95 patients (54.5%) underwent emergency surgery for hip fracture. The following operations were performed: hip arthroplasty in 109 patients, dynamic hip screw in 43 patients and miscellaneous hip or pelvis operations in the remaining 2 patients. The baseline characteristics of the patients with and without postoperative DVT are displayed in Table I. The mean operation time was 2.2 hours (range: 0.5-4.5 hours). General anaesthesia was used in 88 patients (51%) and spinal anaesthesia in 85 patients (49%). Identified risk factors for VTE were malignancy in 4 patients (2.3%), previous history of DVT or pulmonary embolism in 12 (7%), varicose vein in 40 (23%), overweight in 29 (17%) and family history of VTE in 21 (12%). None of the individual or surgical characteristics of the patient could help to predict or exclude DVT (Table I)

Table I: Clinical characteristics of the patients and comparison of the patients with and without postoperative DVT.

|                            | N<br>(n = 173) | DVT<br>(n = 15) | no DVT<br>(n = 158) | p value |
|----------------------------|----------------|-----------------|---------------------|---------|
| <b>Risk factors</b>        |                |                 |                     |         |
| Malignancy                 | 4              | 0               | 4                   | n.s.    |
| Varicose veins             | 40             | 5               | 35                  | n.s.    |
| Previous DVT or PE         | 12             | 1               | 11                  | n.s.    |
| Overweight                 | 29             | 3               | 26                  | n.s.    |
| Familial history of VTE    | 21             | 4               | 17                  | n.s.    |
| <b>Type of anesthesia</b>  |                |                 |                     |         |
| General                    | 88             | 8               | 80                  | n.s.    |
| Spinal                     | 85             | 7               | 78                  |         |
| <b>Type of surgery</b>     |                |                 |                     |         |
| Total hip replacement      | 109            | 9               | 100                 |         |
| Dynamic Hip Screw          | 43             | 4               | 39                  | n.s.    |
| Miscellaneous              | 21             | 2               | 19                  |         |
| Emergency surgery          | 95             | 10              | 85                  | n.s.    |
| Elective surgery           | 78             | 5               | 73                  |         |
| <b>Clinical suspicion</b>  |                |                 |                     |         |
|                            | 7              | 2               | 5                   | n.s.    |
| <b>TJP* of prophylaxis</b> |                |                 |                     |         |
| <b>Perioperative</b>       |                |                 |                     |         |
| Dalteparin 2500            | 45             | 4               | 41                  | n.s.    |
| Dalteparin 5000            | 126            | 11              | 115                 |         |
| <b>Follow-up period</b>    |                |                 |                     |         |
| Acenocoumarol              | 123            | 9               | 114                 | n.s.    |
| Aspirin-DHE                | 31             | 3               | 28                  |         |
| Other                      | 19             | 3               | 16                  |         |

During the surveillance period, seven patients (4%) with clinical signs and symptoms of DVT, underwent a diagnostic procedure, and DVT was confirmed in only 2 patients. There was no clinical suspicion of pulmonary embolism and no relevant bleeding complication. The two deaths that occurred during the course of the study were unrelated to VTE (a 79-year-old woman died from a myocardial infarction and a 88-year-old man from a massive bronchoaspiration). The circumference of the operated limb, as measured on the 15th postoperative day, was slightly larger than that of the contralateral leg: the mean difference between the two legs was 1.5 cm at thigh level (range: -8.5 to 10 cm), 0.5 cm at calf level (range: -4.5 to 7.5 cm), and 0 cm at ankle level (range: -3 to 3 cm). Although there was a very large overlap between the circumferences measured in the patients with and without DVT, a circumference of the thigh in the operated leg equal or less than in the contralateral limb had a high predictive value for the absence of proximal DVT

(95%). However, a minority of the patients (23%) presented with that feature. Conversely, the specificity of a thigh circumference in the operated leg > 4 cm than in the contralateral limb was 81 %but the positive predictive value of this characteristic was only 14% (Table II).

Table II: Diagnostic performance of the thigh circumference measurement for the presence of ultrasonographic proximal vein thrombosis.

|                           | Thigh circumference                 |       |
|---------------------------|-------------------------------------|-------|
|                           | equal or less than<br>contralateral | > 4cm |
| Sensitivity               | 83%                                 | 42%   |
| Specificity               | 23%                                 | 70%   |
| Positive predictive value | 14%                                 | 7b    |
| Negative predictive value | 95%                                 | 7b    |

## *DVT prophylaxis*

Forty-five patients (26%) received one single daily subcutaneous injection of 2500 UI of dalteparin and 126 patients (73%) were given 5000 UI. Preoperative injection was given in only 44 patients (25%), because of emergency surgery and/or use of spinal anesthesia. One patient received unfractionated heparin (5000 UI t.i.d s.c.) and only one patient did not receive any prophylaxis because of severe liver disease. Following the immediate perioperative period, 123 patients (71%) were given acenocoumarol (Sintrom®). Thirty-one patients (18%) were given the combination Aspirin-DHE and 19 patients (11%) another or no prophylaxis at all. Among the 123 patients given oral anticoagulant, the INR was more than 1.5 in 66%, 85%, and 86% of them, on Day 7, 10, and 15, respectively. On 255 prothrombin time measurements, 277 (79%) were above the lower limit of prophylactic efficacy of an INR of 1.5. On the other hand, a considerable proportion of measurements (71/351, i.e. 20%) yielded INR values above 3.0, which is excessive in the prophylactic setting.

### *Result of postoperative venous ultrasonography*

Venous compression ultrasonography was performed on the 12th (median, range 8-16 days). The exam was considered normal in 159 patients (92%) and proximal DVT was diagnosed in 12 patients (7%) of whom only one had clinical signs. Two exams (1%) were inconclusive and led to venography, thereby disclosing two additional but distal (below the popliteal vein) thrombosis. In one additional patient with high clinical suspicion of DVT, venography was performed despite a negative ultrasound. This exam showed a 3-cm thrombus in the superficial femoral vein in addition to calf clots. Thus, a total of 15 DVT (8.6%) were diagnosed, 12 proximal DVT by ultrasonography and 3 DVT by venography (2 distal and 1 proximal). DVT was located in the operated leg in 10 patients (66%).

## **Discussion**

The present trial aimed at studying the usefulness of a systematic screening for proximal DVT in pa-

tients undergoing hip surgery using real-time B-mode venous ultrasonography. Proximal DVT was detected in 12 out of 173 (7%) patients with this technique. Although a thigh circumference in the operated leg equal or less than in the contralateral limb was highly predictive for the absence of DVT, none of the characteristics of the patients or the operations could really help to delineate the subgroup of patients with DVT. Moreover, the negative predictive value of the thigh circumference will be useful in a minority of patients. The relatively high incidence of proximal vein thrombosis in spite of active prophylaxis and the lack of valuable predictors for DVT emphasizes the need for screening of asymptomatic postoperative DVT in high-risk patients undergoing hip surgery. B-mode real-time ultrasonography has been shown to have both an excellent sensitivity and specificity, both about 95%, for diagnosing symptomatic DVT [6, 29, 48]. Since this technique is non-invasive, relatively easy, and can be performed at the bedside of the patient, it is particularly suited for screening for asymptomatic DVT in high-risk patients and preliminary studies reported promising results [2]. Unfortunately, several further studies have damped this initial enthusiasm by showing an unexpectedly much lower sensitivity in this population of patients [1, 5, 9, 32]. Thus, the sensitivity for the detection of proximal DVT was only 57% and 38%, respectively, in two recent phlebographi-

color pulsed Doppler in the latter [14]. The latter issue, however, is still debated. Anyway, the specificity was excellent in these two studies (99%). The low sensitivity of the diagnostic method represents the main limitation of the present trial and we can speculate that up to half of the proximal thrombi might have been missed by our examination. A possible explanation for this poor sensitivity might be the characteristics of the thrombi, which may be small and nonocclusive as illustrated by the only patient in our series with normal ultrasound examination and a proximal DVT proven by phlebography. Moreover, fresh clots that form despite active DVT prophylaxis might be so soft that they could be fully compressible by the transducer probe [14]. Nonetheless, in spite of its lack of sensitivity systematic venous ultrasound disclosed proximal DVT in 7% of our patients, from whom all bu

"Je

one were asymptomatic. Furthermore, distal, i.e. below the knee, DVTs were not screened for, but were certainly as frequent, as suggested by the distal thrombi found in all the three patients who underwent venography.

Several approaches may be proposed to reduce the consequences of DVT in patients after hip surgery. A more efficient prophylactic regimen might yield a further reduction of the incidence of DVT. However, LMWH, as used in the present trial, is a very efficient prophylaxis regimen and it is at least as effective as unfractionated heparin in preventing DVT [4, 31, 36]. In addition, LMWHs seem to be more effective in preventing proximal vein thrombosis [4] and are less likely to cause bleeding complications. Other perioperative prophylactic methods, such as adjusted-dose heparin therapy [4] and oral anticoagulant therapy [17] are about as effective, but have the inconvenience of laboratory monitoring [30].

On the other hand, the risk of VTE is still present after the immediate perioperative period and even after hospital discharge [26, 38, 45]. A recent survey in general abdominal surgery has shown that about one fourth of symptomatic PE following general surgery do occur in the month after hospital discharge [22]. DVT prophylaxis after hip surgery is usually limited to 3 weeks, as it is the case in our hospital. Since the risk may persist up to 6 weeks after orthopedic surgery [18, 26], it has been therefore suggested to prolong the prevention [37, 40].

O'MEARA et al. [37] concluded in a recent overview that low to moderate doses of vitamin K antagonists would be the most suitable modality for VTE prevention in total hip replacement patients after hospital discharge. In addition, the major advantage of the use of oral anticoagu-

lants in the postoperative period over other regimens is to provide an efficient treatment to the patients with undiagnosed DVT [23]. Unfortunately, this regimen is not widely used because of the fear of bleeding [28]. However, this risk may be considerably lowered by using «low-intensity» anticoagulation, i.e. with a target INR of 1.5-2.0 and by performing frequent monitoring early in treatment [16]. Moreover, moderate intensity oral anticoagulation has been shown to be efficient in the treatment of established DVT and PE with a low rate of bleeding complication of only 3.2% in a recent trial [42]. In the present study, oral anticoagulation level was within the therapeutic range in 79% of the patients who received acenocoumarol and no major bleeding complication was recorded.

Thus, one possible practical approach for the management of patients undergoing hip surgery could be to systematically prolong perioperative prophylaxis (with low-dose heparin or LMWH or intermittent pneumatic compression) by «low-dose» oral anticoagulation. Then, real-time B-mode venous ultrasonography might be performed before hospital discharge in order to detect proximal DVT (Fig. 1). Should this examination disclose proximal DVT, the anticoagulation period would be prolonged for 3 months, as recommended by the Third American College of Chest Physicians Consensus Conference on Antithrombotic Therapy [25]. Otherwise, it would be stopped after 6 weeks, a treatment duration that should be sufficient even in patients with asymptomatic, undiagnosed calf vein DVT.

Because of the relatively high incidence of proximal DVT in patients undergoing major hip surgery, screening for proximal DVT in these patients using venous compression ultrasonography

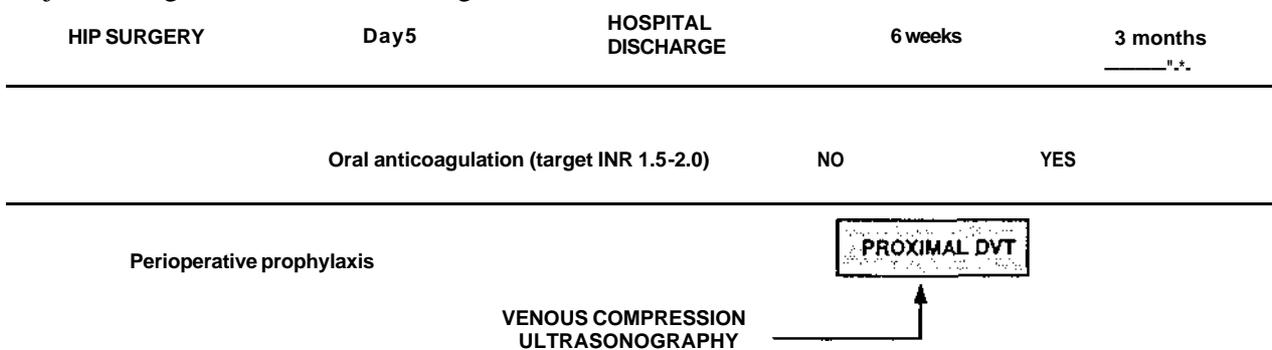


Fig. 1: Antithrombotic management of patients undergoing major hip surgery: a practical approach. (For explanations, see text.)