Multimodal thromboprophylaxis following primary hip arthroplasty

THE ROLE OF ADJUVANT INTERMITTENT PNEUMATIC CALF COMPRESSION

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We report a retrospective review of the incidence of venous thromboembolism in 463 consecutive patients who underwent primary total hip arthroplasty (487 procedures). Treatment included both total hip replacement and hip resurfacing, and the patients were managed without anticoagulants. The thromboprophylaxis regimen included an antiplatelet agent, generally aspirin, hypotensive epidural anaesthesia, elastic compression stockings and early mobilisation. In 258 of these procedures (244 patients) performed in 2005 (cohort A) mechanical compression devices were not used, whereas in 229 (219 patients) performed during 2006 (cohort B) bilateral intermittent pneumatic calf compression was used.

All operations were performed through a posterior mini-incision approach. Patients who required anticoagulation for pre-existing medical problems and those undergoing revision arthroplasty were excluded. Doppler ultrasonographic screening for deep-vein thrombosis was performed in all patients between the fourth and sixth post-operative days. All patients were reviewed at a follow-up clinic six to ten weeks after the operation. In addition, reponse to a questionnaire was obtained at the end of 12 weeks post-operatively.

No symptomatic calf or above-knee deep-vein thrombosis or pulmonary embolism occurred. In 25 patients in cohort A (10.2%) and in ten patients in cohort B (4.6%) asymptomatic calf deep-vein thromboses were detected ultrasonographically. This difference was statistically significant (p = 0.03). The regimen followed by cohort B offers the prospect of a low incidence of venous thromboembolism without subjecting patients to the higher risk of bleeding associated with anticoagulant use.

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The aetiopathogenesis of venous thromboembolism is multifactorial and includes the well-known Virchow's triad of hypercoagulability, venous stasis and endothelial damage. It is therefore appropriate to use a multimodal approach to thromboprophylaxis. The search continues for the ideal combination of agents and factors, whether chemical, mechanical, surgical or anaesthetic, that offers efficient thromboprophylaxis and is associated with the lowest incidence of adverse effects.

Reducing blood loss through hypotensive epidural anaesthesia[1,2] and effective local haemostasis is believed to have a beneficial effect on lowering the peri-operative hypercoagulable state. The debate regarding the ideal chemoprophylactic agent, however, has not yet been resolved.[3-5] Thrombin inhibition with heparin group or factor Xa inhibitors requires parenteral administration, and vitamin K antagonists such as warfarin need careful monitoring, both of which are logistically difficult after discharge from hospital. The risks of thrombus initiation and propagation, and of pulmonary embolism, continue well after the patient has left hospital.[6,7] The current trend for reduced length of stay adds to these difficulties and patient compliance with self-administered thromboprophylaxis is required.[8] In addition, chemical thromboprophylaxis increases the risk of bleeding, which can lead to wound complications, infection and intra-organ haemorrhage.[9]

Oral antiplatelet agents such as aspirin are easier to administer and do not need monitoring, and so they can be administered effectively over a longer period.[10]

The United Kingdom National Institute of Health and Clinical Excellence (NICE) has produced guidelines[11,12] that recommend the use of low molecular weight heparin (LMWH) or fondaparinux for thromboprophylaxis following elective hip operations. However, there were no accurate estimates of the risk of venous thromboembolism in the modern era when the guidelines were formulated. It was

acknowledged that as a consequence of changes in anaesthetic practice and earlier mobilisation, the current risk of venous thromboembolism is probably lower than that reported in the literature.

Mechanical measures such as initial exercises in bed, early weight-bearing mobilisation and the use of compression stockings prevent stasis and are widely practised.[13] Intermittent pneumatic compression devices are additional tools which are not so widely used.[13] NICE has recommended further research to assess the effectiveness of an adjuvant intermittent compression device in reducing the risk of objectively diagnosed venous thromboembolism.

We undertook a study to provide an accurate estimate of the incidence of venous thromboembolism in the modern era using only an antiplatelet agent in the absence of anticoagulants, and assessed whether the addition of an adjuvant mechanical measure in the form of intermittent pneumatic calf compression reduces the incidence of venous thromboembolism. Ultrasonographic Doppler scanning was used as an objective non-invasive test to screen all patients post-operatively.

Patients and Methods

Cohort 'A' consisted of 244 of 251 consecutive patients who underwent 258 primary hip replacements performed by the senior author (DJWM) between January and December 2005. These patients did not receive intermittent pneumatic calf compression. Seven patients had been excluded as they required formal anticoagulation for existing medical problems (six patients received post-operative warfarin or intra-operative heparin, as they had a previous history of venous thromboembolism and one was on long-term warfarin for existing protein S deficiency). Birmingham Hip Resurfacings (BHR, Smith and Nephew Orthopaedics Ltd, Bromsgrove, United Kingdom) were undertaken on 156 patients (166 hips) and 88 (92 hips) underwent uncemented total hip replacements (THR). The BHR consists of a hydroxyapatite (HA)-coated porous uncemented acetabular component and a cemented femoral component. The THRs included 88 large diameter metal-on-metal devices, with a BHR acetabular component as above and a matching modular BHR femoral head fitted on a Synergy (Smith and Nephew) uncemented HA-coated proximally porous titanium alloy stem. In four hips the THR consisted of an uncemented Reflection (Smith and Nephew) acetabular component with a highly cross-linked polyethylene (Smith and Nephew) liner which articulated with an oxidised zirconium (Oxinium, Smith and Nephew) 32 mm femoral head on a Synergy stem. Osteoarthritis was the most common diagnosis in cohort A (243 of 258 hips).

Cohort 'B' comprised 219 of 228 consecutive patients who underwent primary hip replacement (229 procedures) between January and December 2006 and who received intermittent pneumatic calf compression in addition to a non-anticoagulant regimen of thromboprophylaxis which combined hypotensive epidural anaesthesia, early mobilisation, elastic graded compression stockings and aspirin (or other oral antiplatelet medication). Nine patients who required anticoagulation for existing medical problems were excluded. In this cohort, 139 patients (145 hips) underwent BHR and 80 (84 hips) underwent uncemented THR. These 84 THRs included 54 large-diameter metal-on-metal THRs (52 patients) and three Reflection acetabular component THRs (three patients), as described above. In the remaining 27 operations (25 patients) the Birmingham Mid Head Resection (Smith and Nephew) was used. It has the same bearing as a large-diameter metal-on-metal THR but the modular head is mounted on a short, uncemented proximal porous hydroxyapatite-coated titanium stem. Osteoarthritis was the most common diagnosis in cohort B (215 of 229 hips). Other diagnoses included rheumatoid arthritis, osteonecrosis of the femoral head, dysplasia, slipped capital femoral epiphysis and Perthes' disease.

The demographic data for the two cohorts are summarised in Table I. No statistically significant differences were observed.

All operations were undertaken in the lateral position through a posterior mini-incision approach,[14] under continuous hypotensive epidural anaesthesia administered through an epidural cannula and a syringe pump.[15] The objective was to maintain the mean arterial pressure between 35 mmHg and 60 mmHg for most of the operation. Meticulous diathermy haemostasis was achieved. The BHR and Birmingham Hip Mid Head Resection procedures included a negative suction vent applied at the level of the lesser trochanter during preparation and cementing of the femoral component to prevent elevation of intra-osseous pressure and systemic displacement of fat and marrow. In the THR a similar attempt was made to avoid systemic displacement of fat and marrow by frequent suction during preparation of the femoral canal. Two suction drains were used post-operatively, one in the hip joint and another deep to gluteus maximus.

Patients wore a full-length elasticated compression stocking (Credalast, Credenhill Surgical Hosiery Ltd, Ilkeston, United Kingdom) on the operated leg that was fastened above the hip with a waist band, and a below-knee thromboembolic deterrent stocking (T. E. D. stocking; The Kendall Company, Mansfield, Massachusetts) on the contralateral leg for six weeks post-operatively. Full weight-bearing mobilisation with a walking frame, followed by two elbow crutches, was started on the first day after surgery. Patients were discharged home between the fourth and sixth post-operative days, and made a gradual transition from elbow crutches to one walking stick.

The Sequential Compression Device (Tyco Healthcare UK Ltd, Gosport, United Kingdom) was used for intermittent pneumatic calf compression. The contralateral cuff was connected as soon as the patient was anaesthetised. On the operated side the cuff was attached and connected after the anti-embolism stocking had been applied post-operatively. The intermittent pneumatic calf compression was used continuously whenever the patients were not

Table I. Demographics of patients in cohorts A and B

	Cohort A	Cohort B	p-value
Mean age (range)	59.7 (35 to 84)	59.1 (19 to 85)	> 0.1
Gender distribution all implants			
Patients			
Male	179	142	> 0.05
Female	65	77	
Hips			
Male	187	151	> 0.1
Female	71	78	
Gender distribution by prosthesis*			
BHR			
Male	129	113	
Female	37	32	
THR			
Male	58	38	
Female	34	46	
Mean body mass index (kg/m^2)	26.2 (17.6 to 43.9)	26.8 (16.6 to 51.2)	> 0.1
Patients transfused (%)	13 (*5.3*)	9 (*4.1*)	> 0.1
Prosthesis used			
Patients			
BHR	156	139	> 0.5
THR	88	80	
Hips			
BHR	166	145	> 0.5
THR	92	84	
Unilateral *vs* bilateral procedures			
Patients			
Unilateral	230	209	> 0.5
Bilateral	14	10	
Hips			
Unilateral	230	209	> 0.1
Bilateral	28	20	

* BHR, Birmingham hip resurfacing; THR, total hip replacement

mobilising for at least four days after operation, or until they were discharged, whichever was earliest.

All patients received an oral antiplatelet agent, starting on the day of operation and continuing for 30 days after discharge. For most patients this comprised 300 mg of enteric-coated aspirin twice daily. Those who were intolerant of aspirin were given oral dipyridamole 100 mg three times daily (15 patients in cohort A and 21 in cohort B), and those who were intolerant of both aspirin and dipyridamole were given oral clopidogrel 75 mg a day (nine patients in cohort A and 17 in cohort B). In addition, all patients received an H_2 antagonist (ranitidine 150 mg twice daily) or a proton-pump inhibitor (omeprazole 20 mg once daily) to prevent potential upper gastrointestinal irritation from the antiplatelet agents. The volume of wound drainage collected in the vacuum suction bottles, blood transfusion rates and local wound problems were recorded for all patients.

Bilateral Doppler ultrasound scanning for deep-vein thrombosis (DVT) was performed on all patients between the fourth and sixth post-operative days by an experienced consultant vascular radiologist (MM), who was blinded to the use of calf compression. Those patients in whom there was no evidence of DVT were advised to continue the antiplatelet agent for 30 days after discharge. In 2005, those patients who were found to have DVT on Doppler screening were given warfarin for six weeks, with regular monitoring of their international normalised ratio at their local hospital, with the objective of maintaining it between 1.5 and 2. In 2006, asymptomatic patients with Doppler-detected below-knee DVTs were asked to continue with the non-anticoagulant therapy but advised to undergo repeat Doppler examination at two, four and six weeks post-operatively. Anticoagulation was considered necessary only in the event of propagation of the thrombus above the knee.

All patients were bearing weight prior to discharge and had been instructed in range of movement exercises. They were encouraged to increase their activities progressively to swimming or pool exercises and non-impact exercises at six weeks. All patients were followed up between the sixth and

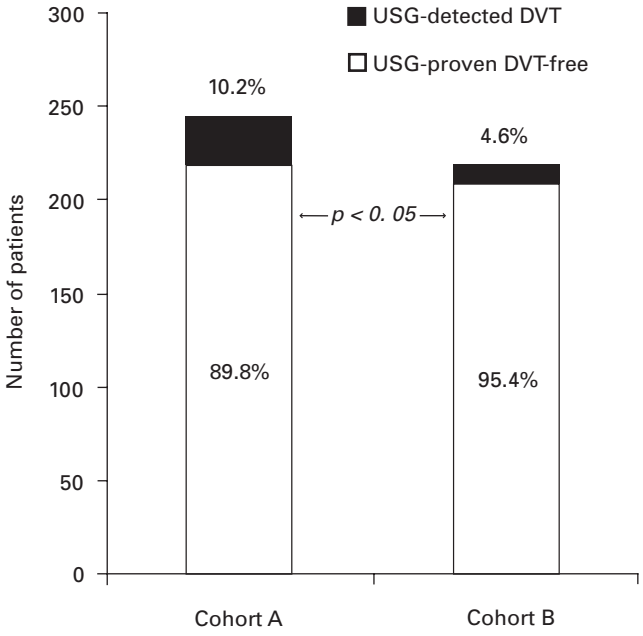

Fig. 1

Incidence of below-knee deep-vein thrombosis (DVT) in all hip arthroplasty patients who were managed with a multimodal regime of thromboprophylaxis with no anti-coagulants. In cohort A no mechanical compression devices were used and in cohort B intermittent pneumatic calf compression was used. There was no instance of femoral or popliteal DVT or symptomatic pulmonary embolism or post-thrombotic swelling in either group (USG, ultrasonographically).

tenth weeks with particular interest in a history, or clinical signs of, DVT or pulmonary embolism, and problems with wound healing. In addition, a questionnaire was sent to all patients at the end of three months, asking whether they had swelling of the lower limbs or been to hospital or their doctor with leg or chest symptoms. If the answer was 'Yes' further enquiries were made to establish the nature of the illness and to confirm deep venous or pulmonary embolism.

Statistical analysis of the results was performed using 95% confidence intervals, Student's *t*-test or Fisher's exact test, and a p-value ≤ 0.05 was considered significant.

Results

The Doppler study was performed at a mean of 4.9 days (95% confidence interval (CI) 4.78 to 5.02) after the operation in cohort A, and 4.8 days (95% CI 4.7 to 4.9) after the operation in cohort B. Mean hospital stay after the operation was 5.74 days (95% CI 5.58 to 5.9) in cohort A and 5.5 days (95% CI 5.3 to 5.7) in cohort B. There was no significant difference in the mean post-operative day on which the Doppler screening was performed (Student's *t*-test, p = 0.07) or the mean inpatient stay (Student's *t*-test, p = 0.55) between the two cohorts.

In this series of 463 patients, with 487 uni- or bilateral hip replacements for whom anticoagulants were not used, 35 DVTs (7.6%) were identified. There were no proximal DVTs in either of the cohorts. No patient had a symptomatic pulmonary embolism or experienced post-thrombotic swelling in the period up to three months following the operation, nor did any develop a haematoma requiring surgical drainage, or an intra-organ haemorrhage. The mean body mass index (BMI) of patients who did not develop a DVT was 26.2 kg/m^2 (SD 2.99) compared with a mean BMI of 28.5 kg/m^2 (SD 4.97) for those patients who developed a DVT, but the difference was not statistically significant (Student's *t*-test, p = 0.06). In cohort A there were 25 DVTs in 244 patients (10.2%) and in cohort B ten DVTs occurred in 219 patients (4.6%). This difference was statistically significant (Fishers exact test, p = 0.03).

All patients were able to tolerate the intermittent calf compression during their admission. As the full-length stocking was available only in the colour brown, and white thromboembolic deterrent stockings were supplied, a few women were reluctant to use such a combination. In addition, the full-length stockings were only available in four sizes, and were therefore unsuitable in very obese patients. This affected approximately 10% of these patients, for whom thromboembolic deterrent stockings had to be used.

Cohort A. Of the 25 patients with below-knee DVTs, 18 occurred in men and seven in women (Fig. 1). In total, 14 thrombi were found in the calf veins on the operated side, six were on the non-operated side, and five had thrombi in both calves. The rate of below-knee DVT was lower in patients who had a BHR (8.97%; 14 of 156) compared with those who had a THR (12.5%; 11 of 88), but the difference was not statistically significant (Fishers exact test, p > 0.1).

The blood transfusion requirement for symptomatic post-operative anaemia is presented in Table II and Figure 2.

The mean post-operative wound drainage in cohort A was 423 ml (100 to 990). There was no significant difference in the mean drainage between those who subsequently had a below-knee DVT (453 ml; 200 to 950) and those who did not, (420 ml; 100 to 990, Student's *t*-test, p > 0.1). There were no cases of wound dehiscence or deep infection. In 21 of 258 cases (8.1%) minor wound ooze continued for a mean of six days (2 to 21) after discharge from hospital. These patients were given prophylactic broad-spectrum antibiotics until the wound had completely healed.

Cohort B. In 2006, following the use of adjuvant intermittent pneumatic calf compression, ten below-knee DVTs (4.6%) were identified, which involved seven men and three women. Of these, six thrombi were found in the calf veins on the operated side, and four on the contralateral side. The rate of below-knee DVT was lower in patients who had a BHR (4.3%; 6 of 139) than in those who had a THR (5.0%; 4 of 80), but the difference was not significant (Fishers exact test p > 0.1).

Serial Doppler scans revealed complete resolution of these thrombi in seven patients at a mean of four weeks (2 to 6) after the operation. Three others did not show fur-

Table II. Rates of blood transfusion in different patient subgroups in cohorts A and B

Cohort*	Number of patients in subgroup	Number of patients who needed a blood transfusion (%)	Fishers exact test
Cohort A			
Unilateral			
BHR	146	2 (*1.4*)	p = 0.013
THR	84	7 (*8.3*)	
Bilateral			
BHR	10	2 (*20*)	
THR	4	2 (*50*)	
All patients in cohort A (unilateral and bilateral)	244	13 (*5.3*)	
Cohort B			
Unilateral			
BHR	133	3 (*2.3*)	p = 1.0
THR	76	2 (*2.6*)	
Bilateral			
BHR	6	1 (*16.7*)	
THR	4	3 (*75*)	
All patients in cohort B (unilateral and bilateral)	219	9 (*4.1*)	
Cohorts A and B			
Unilateral BHR	279	5 (*1.8*)	
Unilateral THR	160	9 (*5.6*)	
Bilateral BHR	16	3 (*18.8*)	
Bilateral THR	8	5 (*62.5*)	
All BHR	295	8 (*2.7*)	
All THR	168	14 (*8.3*)	
Unilateral arthroplasties	439	14 (*3.2*)	
Bilateral arthroplasties	24	8 (*33.3*)	
All patients	463	22 (*4.8*)	

* BHR, Birmingham hip resurfacing; THR, total hip replacement

ther progression; none of the patients needed to be anticoagulated.

The transfusion requirements for symptomatic postoperative anaemia are shown in Table II. The mean postoperative wound drainage in cohort B was 412 ml (60 to 1000). There was no significant difference in the mean drainage between those who subsequently had a below-knee DVT (419 ml; 150 to 850) and those who did not (412 ml; 60 to 1000, Student's *t*-test, $p > 0.5$). There were no cases of wound dehiscence or deep infection. In total, 23 (10.5%) patients had minor wound ooze lasting for a mean of five days (2 to 21) after discharge from hospital; they were prescribed antibiotics until the wound had healed.

Discussion

Venous thromboembolism following joint replacement has the potential for two significant consequences. These are pulmonary embolism, which has been reported to be fatal in 0.1% to 0.2% of patients,[16] and symptomatic DVT, which is associated with acute morbidity and possible long-term sequelae. One series[17] of 1162 patients who received no routine chemoprophylaxis had an incidence of imaging-confirmed clinical pulmonary embolism of 1.2%, and a rate of fatal pulmonary embolism of 0.34%. The major groups of chemical thromboprophylactic agents currently in use to reduce these risks are vitamin K antagonists such as warfarin, antithrombin agents such as heparin and its fractionated forms, factor Xa inhibitors such as fondaparinux, and antiplatelet agents such as aspirin. The first three can be broadly grouped as anticoagulants and need either regular monitoring or parenteral administration, as opposed to the antiplatelet agents, which can be administered orally without the need for regular monitoring.

A meta-analysis[18] that included 130 000 patients showed that the incidence of fatal pulmonary embolism (0.1% to 0.2%) and the overall death rate (0.3% to 0.4%) were low, and remained relatively unchanged irrespective of the thromboprophylactic agent used. The benefit from the different agents used appears to be only in the incidence of DVT. It is important to note that although anticoagulants have been shown to reduce the incidence of DVT, their use has been associated with an increased risk of bleeding, which has the potential to outweigh the benefit of reducing the incidence of DVT. Another meta-analysis[19] comparing the risks of major bleeding episodes (death, intra-organ bleeding or re-operation) after THR shows this risk to be low in the groups managed with placebo or aspirin (0.6% and 0.70%, respectively) compared with warfarin (1.7%), LMWH (2.2%) or low-dose heparin (3.5%).[19]

A further difficulty with anticoagulant use is the potential risk of developing spinal haematoma in those patients where epidural anaesthesia is used.[20] This risk is increased

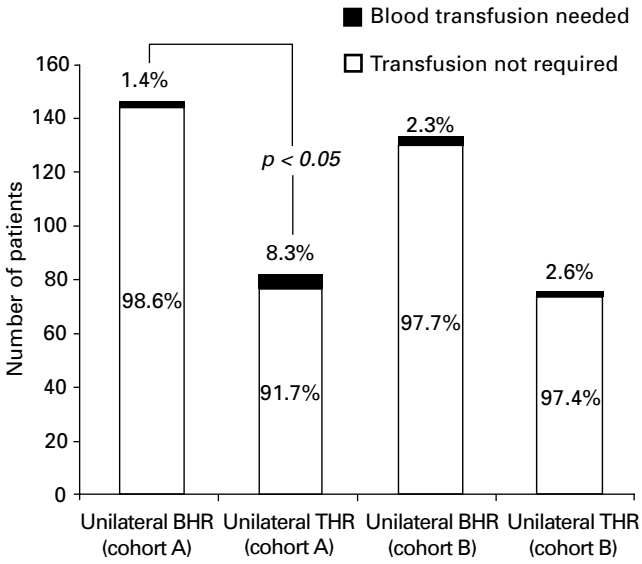

Fig. 2

Number of patients who required blood transfusion with Birmingham Hip Resurfacing (BHR) and those with total hip replacement (THR) in cohorts A and B (symptomatic anaemia was the trigger for transfusion). The difference in the rate of transfusion (6.9%) between BHRs and THRs in cohort A was statistically significant ($p < 0.05$). All other individual differences are not statistically significant.

in patients receiving LMWH, where the frequency of a spinal/epidural haematoma has been reported to be approximately 1 in 3000 among patients undergoing epidural anaesthesia.[21] In patients receiving pre-operative LMWH it is recommended that needle placement should occur at least ten to 12 hours after the last dose, and in those on post-operative LMWH the epidural catheter should not be removed within ten to 12 hours of the last dose.[22] With fondaparinux the actual risk is unknown, but the American Society for Regional Anesthesia[22] recommends that it should be used in patients undergoing spinal/epidural anaesthesia only under the conditions of a clinical trial which include a single needle pass, atraumatic needle placement, and the avoidance of indwelling epidural catheters, failing which, an alternate method of prophylaxis should be considered. There is some evidence that in patients receiving fondaparinux the addition of compression stockings does not add significant protection.[23]

Aspirin is an inexpensive, attractive oral thromboprophylactic agent which is generally well tolerated, requires no monitoring, and is associated with comparatively few bleeding complications. In addition, the benefit of aspirin continues after the first post-operative week, when other forms of chemoprophylaxis have usually been discontinued, at which stage the risk of venous thromboembolism is still high.[24,25] In the Antiplatelet Trialists' Collaboration[26] and the Pulmonary Embolism Prevention trial,[24,25] strong evidence has been forthcoming that aspirin reduces the risk of DVT and pulmonary embolism by approximately one-third in different groups of surgical and medical patients.

The American College of Chest Physicians Multidisciplinary Panel 2004[27] recommends that after hip or knee replacement, patients should receive one of three thromboprophylactic agents, LMWH, fondaparinux or warfarin, with a target international normalised ratio of 2.5. They strongly advise not to use aspirin alone. These recommendations and those of NICE[11] are based on what is described as 'available evidence', on which basis the NICE guidelines have been criticised.[28] Meta-analyses and reports comparing aspirin with anticoagulants suffer from bias against the efficacy of aspirin, as the recent studies of LMWH and fondaparinux enjoy the added benefits of modern anaesthetic and operative techniques, and those of mechanical adjuncts, whereas more studies with aspirin are older and were undertaken before these advances.[19]

One weakness of the pulmonary embolism prevention trial[24,25] was that only symptomatic patients were investigated. It was therefore unable to detect asymptomatic DVT. Our study was based on duplex and colour Doppler ultrasound screening of both lower limbs and the pelvis in all patients four to six days after the operation, and overcomes that weakness. Modern ultrasonography, with its ability to assess venous compressibility and blood flow, has been shown to have high levels of sensitivity (93%), specificity (98%), and accuracy (95.5%) in terms of overall detection of DVT when used by experienced radiologists.[29] All ultrasound examinations in the present series were performed by an experienced consultant radiologist with a special interest in the procedure in orthopaedic patients. Two objectively proven findings emerge from this study. First, a low incidence of venous thromboembolism is possible with this multimodal regimen of non-anticoagulant thromboprophylaxis without the increased risk of bleeding associated with anticoagulant use. Second, a statistically significant reduction in the incidence of DVT was achieved through the addition of intermittent pneumatic calf compression to the regimen, which we have accordingly incorporated into our standard care in all arthroplasty patients.

Although this is a small series of 487 procedures, its strengths include the following: no patient was lost to follow-up; ultrasound Doppler scanning of all patients enabled us not to miss asymptomatic DVTs; being a single-surgeon series the confounding variables of operative and anaesthetic techniques and surgeon experience were kept to a minimum. We accept that one weakness of the study was that the cohorts were not contemporary. However, the patient demographics, including age, gender, BMI, diagnoses, implant types and unilateral/bilateral procedures were similarly distributed in the two cohorts. In cohort A, there was a statistically significant difference ($p = 0.013$) between the transfusion requirements in resurfacing procedures (1.4%) and THRs (8.3%). However, there was no difference ($p = 0.07$) in the overall transfusion rates between cohorts A and B showing that intermittent pneu-

matic calf compression had no deleterious effect. The inclusion of both resurfacing and THR in both cohorts ensures that these data are generalised to other groups.

Multimodal regimens similar to ours have been reported from other centres.[30,31] One regimen comprised a single intra-operative intravenous injection of heparin in addition to either aspirin or warfarin.[30] In another, aspirin was started only after ultrasonography had excluded a DVT.[31] The incidence of symptomatic pulmonary embolism in these reports was 0.6%[30] and 0.7%,[31] respectively.

Our series did not contain any patients with symptomatic pulmonary embolism. Displaced fat and marrow content are known to initiate the clotting cascade and lead to pulmonary embolism.[32,33] The operative steps we took to minimise systemic displacement of marrow contents in both the resurfacings and the replacements may have contributed to reducing the incidence of pulmonary embolism. It seems likely that the extended duration of thromboprophylaxis after discharge from hospital, made possible through the ease of administration of oral antiplatelet agents, would also have played a role. The objectively proven low incidence of distal DVT and the absence of proximal DVT and symptomatic pulmonary embolism in this series are comparable with the results from other series with anticoagulant use.[19]

Distal DVT has been defined as that involving the infrapopliteal veins including the posterior tibial, peroneal, anterior tibial and muscular calf veins (soleal or gemellar veins).[34] The management of asymptomatic distal DVT is far from clear and is usually based on empirical therapy. One important concern with distal DVT has been that of proximal clot propagation. One study has shown that up to 40% of calf vein thrombi are confined to the veins that drain the gastrocnemii and soleus muscle.[35] When left untreated, the risk of proximal clot propagation has been reported as 3% when the initial thrombus had been in the gastrocnemius or soleus veins.[36] In cohort B none of the distal clots detected with ultrasound examination extended beyond the popliteal vein or became symptomatic or embolised. Current evidence suggests that there are insufficient data to support anticoagulation in distal DVT, and that treating asymptomatic distal DVT detected by ultrasound entails the risk of over-treatment.[34,37]

Whether our multimodal method of thromboprophylaxis can be recommended for general application in primary hip replacement is unclear. Adopting hypotensive epidural anaesthesia with minimised blood loss is likely to have been one of the factors responsible for the low incidence of DVT in this study. Further, the stems of the THRs were uncemented and the BHR, although it has a cemented femoral component, is designed to restrict the cement into a closed space under the femoral head and not allow it to spread around the stem. It has been shown that intra-operative activation of the clotting cascade and intra-operative subclinical pulmonary embolism are more common when a cemented stem is used.[38] It is yet to be established whether non-anticoagulant thromboprophylaxis would yield similar results with other modes of anaesthesia and with cemented stems. The low incidence of venous thromboembolism seen in the present series merits further investigation of these questions through multicentre randomised controlled trials.

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References

1. **Lieberman JR, Huo MM, Hanway J, et al.** The prevalence of deep venous thrombosis after total hip arthroplasty with hypotensive epidural anesthesia. *J Bone Joint Surg [Am]* 1994;76-A:341-8.
2. **Lieberman JR, Hsu WK.** Prevention of venous thromboembolic disease after total hip and knee arthroplasty. *J Bone Joint Surg [Am]* 2005;87-A:2097-112.
3. **Callaghan JJ, Dorr LD, Engh GA, et al.** Prophylaxis for thromboembolic disease: recommendations from the American College of Chest Physicians: are they appropriate for orthopaedic surgery? *J Arthroplasty* 2005;20:273-4.
4. **Kwong LM.** Deep vein thrombosis prophylaxis: better living through chemistry in the affirmative. *J Arthroplasty* 2005;20(Suppl 2):12-14.
5. **Lotke PA, Lonner JH.** Deep venous thrombosis prophylaxis: better living through chemistry: in opposition. *J Arthroplasty* 2005;20(Suppl 2):15-17.
6. **Howie C, Hughes H, Watts AC.** Venous thromboembolism associated with hip and knee replacement over a ten-year period: a population-based study. *J Bone Joint Surg [Br]* 2005;87-B:1675-80.
7. **Bjørnarå BT, Gudmundsen TE, Dahl OE.** Frequency and timing of clinical venous thromboembolism after major joint surgery. *J Bone Joint Surg [Br]* 2006;88-B:386-91.
8. **Watts AC, Howie CR, Simpson AHRW.** Assessment of a self-administration protocol for extended subcutaneous thromboprophylaxis in lower limb arthroplasty. *J Bone Joint Surg [Br]* 2006;88-B:107-10.
9. **Imperial TF, Speroff T.** A meta-analysis of methods to prevent venous thromboembolism following total hip replacement. *JAMA* 1994;271:1780-5.
10. **Parry M, Wylde V, Blom AW.** Ninety-day mortality after elective total hip replacement: 1549 patients using aspirin as a thromboprophylactic agent. *J Bone Joint Surg [Br]* 2008;90-B:306-7.
11. **No authors listed.** Venous thromboembolism: reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in in-patients undergoing surgery. Quick reference guide. Issued by the National Institute of Health and Clinical Excellence, UK, April 2007. http://www.nice.org.uk/nicemedia/pdf/CG046quickrefguide.pdf (date last accessed 12 March 2008).
12. **No authors listed.** Venous thromboembolism. Reducing the risk of venous thromboembolism (deep vein thrombosis and pulmonary embolism) in inpatients undergoing surgery. Guideline 46. Issued by the National Institute for Health and Clinical Excellence, UK, April 2007. http://www.nice.org.uk/nicemedia/pdf/CG046NICEguideline.pdf (date last accessed 12 March 2008).
13. **Anderson FA Jr, Hirsh J, White K, Fitzgerald RH Jr.** Temporal trends in prevention of venous thromboembolism following primary total hip or knee arthroplasty 1996-2001: findings from the Hip and Knee Registry. *Chest* 2003;124:349-56.
14. **McMinn DJ, Daniel J, Pynsent PB, Pradhan C.** Mini-incision resurfacing arthroplasty of hip through the posterior approach. *Clin Orthop* 2005;441:91-8.
15. **Westrich GH, Farrell C, Bono JV, et al.** The incidence of venous thromboembolism after total hip arthroplasty: a specific hypotensive epidural anesthesia protocol. *J Arthroplasty* 1999;14:456-63.
16. **Salvati EA, Pellegrini VD Jr, Sharrock NE, et al.** Recent advances in venous thromboembolic prophylaxis during and after total hip replacement. *J Bone Joint Surg [Am]* 2000;82-A:252-70.
17. **Warwick D, Williams MH, Bannister GC.** Death and thromboembolic disease after total hip replacement: a series of 1162 cases with no routine chemical prophylaxis. *J Bone Joint Surg [Br]* 1995;77-B:6-10.
18. **Murray DW, Britton AR, Bulstrode CJ.** Thromboprophylaxis and death after total hip replacement. *J Bone Joint Surg [Br]* 1996;78-B:863-70.
19. **Freedman KB, Brookenthal KR, Fitzgerland RH Jr, Williams S, Lonner JH.** A meta-analysis of thromboembolic prophylaxis following elective total hip arthroplasty. *J Bone Joint Surg [Am]* 2000;82-A:929-38.

20. **Hantler C, Despotis GJ, Sinha R, Chelly JE.** Guidelines and alternatives for neuraxial anesthesia and venous thromboembolism prophylaxis in major orthopedic surgery. *J Arthroplasty* 2004;19:1004-16.
21. **Wysowski DK, Talarico L, Bacsanyi J, Botstein P.** Spinal and epidural hematoma and low-molecular-weight heparin. *N Engl J Med* 1998;338:1774-5.
22. **No authors listed.** American Society for Regional Anesthesia Consensus Statements. Second consensus conference on neuraxial anesthesia and anticoagulation April 25-28, 2002. Regional Anesthesia in the anticoagulated patient: defining the risks. http//www.asra.com/consensus-statements/2.html (date last accessed 17 May 2007.
23. **Cohen AT, Skinner JA, Warwick D, Brenkel I.** The use of graduated compression stockings in association with fondaparinux in surgery of the hip: a multi-centre, multinational, randomised, open-label, parallel-group comparative study. *J Bone Joint Surg [Br]* 2007;89-B:887-92.
24. **No authors listed.** Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention (PEP) trial. *The Lancet* 2000;355:1295-302.
25. **Collins R, Rodgers A, Prentice C, MacMahon S.** PEP trial. *The Lancet* 2000;356:250-1.
26. **No authors listed.** Collaborative overview of randomised trials of antiplatelet therapy. III: reduction in venous thrombosis and pulmonary embolism by antiplatelet prophylaxis among surgical and medical patients: Antiplatelet Trialists' Collaboration. *BMJ* 1994;308:235-46.
27. **Geerts WH, Pineo GF, Heit JA, et al.** Prevention of venous thromboembolism: the Seventh ACCP conference on Antithrombotic and Thrombolytic Therapy. *Chest* 2004;126:338-400.
28. **Atkins RM.** NICE work. *J Bone Joint Surg [Br]* 2007;89-B:849-50.
29. **Pitto RP, Hamer H, Fabiani R, Radespiel-Troeger M, Koessler M.** Prophylaxis against fat and bone-marrow embolism during total hip arthroplasty reduces the incidence of postoperative deep-vein thrombosis: a controlled, randomized clinical trial. *J Bone Joint Surg [Am]* 2002;84-A:39-48.
30. **González Della Valle A, Serota A, Go S, et al.** Venous thromboembolism is rare with a multimodal prophylaxis protocol after total hip arthroplasty. *Clin Orthop* 2006;444:146-53.
31. **Lachiewicz PF, Soileau ES.** Multimodal prophylaxis for THA with mechanical compression. *Clin Orthop* 2006;453:225-30.
32. **Pitto RP, Koessler M, Kuehle JW.** Comparison of fixation of the femoral component without cement and fixation with use of a bone-vacuum cementing technique for the prevention of fat embolism during total hip arthroplasty: a prospective, randomized clinical trial. *J Bone Joint Surg [Am]* 1999;81-A:831-43.
33. **Hofmann S, Huemer G, Salzer M.** Pathophysiology and management of the fat embolism syndrome. *Anesthesia* 1998;53(Suppl 2):35-7.
34. **Righini M, Paris S, Le Gal G, et al.** Clinical relevance of distal deep vein thrombosis: review of literature data. *Thromb Haemost* 2006;95:56-64.
35. **Labropoulos N, Webb KM, Kang SS, et al.** Patterns and distribution of isolated calf deep vein thrombosis. *J Vasc Surg* 1999;30:787-91.
36. **Macdonald PS, Kahn SR, Miller N, Obrand D.** Short-term natural history of isolated gastrocnemius and soleal vein thrombosis. *J Vasc Surg* 2003;37:523-7.
37. **Righini M.** Is it worth diagnosing and treating distal deep vein thrombosis? : No. *J Thromb Haemost* 2007;5(Suppl 1):55-9.
38. **Sharrock NE, Go G, Harpel PC, et al.** The John Charnley Award: thrombogenesis during total hip arthroplasty. *Clin Orthop* 1995;319:16-27.