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Rapid-Inflation Intermittent Pneumatic Compression for Prevention of Deep Venous Thrombosis

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**Background:** Current treatment regimens that are designed to prevent deep venous thrombosis in patients undergoing orthopaedic procedures rely predominantly on drug prophylaxis alone. The purpose of this randomized clinical study was to evaluate the effectiveness of a mechanical adjunct to chemoprophylaxis that involves intermittent compression of the legs.

**Methods:** During a twenty-two month period, 1803 patients undergoing a variety of orthopaedic procedures were prospectively randomized to receive either chemoprophylaxis alone or a combination of chemoprophylaxis and mechanical prophylaxis. Nine hundred and two patients were managed with low-molecular-weight heparin alone, and 901 were managed with low-molecular-weight heparin and intermittent pneumatic compression of the calves for varying time periods. Twenty-four percent of the patients underwent total hip or knee joint replacement. Screening for deep venous thrombosis was performed on the day of discharge with duplex-color-coded ultrasound.

**Results:** In the chemoprophylaxis-only group, fifteen patients (1.7%) were diagnosed with a deep venous thrombosis; three thromboses were symptomatic. In the chemoprophylaxis plus intermittent pneumatic compression group, four patients (0.4%) were diagnosed with deep venous thrombosis; one thrombosis was symptomatic. The difference between the groups with regard to the prevalence of deep venous thrombosis was significant (p = 0.007). In the chemoprophylaxis plus intermittent pneumatic compression group, no deep venous thromboses were found in patients who received more than six hours of intermittent pneumatic compression daily.

**Conclusions:** Venous thrombosis prophylaxis with low-molecular-weight heparin augmented with a device that delivers rapid-inflation intermittent pneumatic compression to the calves was found to be significantly more effective for preventing deep venous thrombosis when compared with a treatment regimen that involved low-molecular-weight heparin alone.

**Level of Evidence:** Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.

Deep venous thrombosis is a common complication in patients undergoing a variety of orthopaedic procedures, and its prevalence can be reduced substantially through the use of prophylactic measures. Typically, these measures consist of anticoagulant drugs such as low-molecular-weight heparin, anti-inflammatory drugs, early postoperative physiotherapy, and compressive stockings. Intermittent pneumatic compression of the limbs has been postulated to reduce venous stasis by increasing the velocity of venous return. It has been shown to be effective not only for prophylaxis against

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deep venous thrombosis but also for the treatment of lymphedema, leg ulcers, posttraumatic swelling, congestive heart failure, and other conditions. Earlier intermittent pneumatic compression devices used low pressure and slow inflation of an air bladder that was applied to the leg. More recent devices produce graduated, sequential, rapid inflation of multiple air chambers within the applied cuffs. This latter approach has been shown to improve the hemodynamic response when compared with relatively slow, low-pressure inflation.

At our institution, the prevalence of deep venous thrombosis during the use of low-molecular-weight heparin for prophylaxis against deep venous thrombosis has been reported to range from 1.5% among patients with skeletal and soft-tissue trauma to 2.5% among those managed with elective orthopaedic surgery. The positive effect of walking and weight-bearing on venous flow in the superficial femoral vein has been investigated previously. Because intermittent pneumatic compression can simulate the effects of walking and weight-bearing on the venous system, the present study was initiated to test the hypothesis that the results of chemoprophylaxis alone could be improved significantly if intermittent pneumatic compression was incorporated into the treatment regimen.

Materials and Methods
The present study was approved by our institutional ethical review committee. Between January 2001 and October 2002, 1803 consecutive inpatients who were to undergo orthopaedic trauma surgery or elective orthopaedic surgery were recruited and ultimately enrolled in the study. The inclusion criteria included an age of between twenty and eighty-six years and a surgical site in an area other than the upper extremity. Approximately 24% (439) of the 1803 procedures involved total joint arthroplasty. Other major procedural categories included knee ligamentous and meniscal repair, tumor resection, and open fixation of traumatic fractures (Fig. 1). The remainder of the procedures primarily involved elective osteotomies to correct deformities of the femur, tibia, foot, and ankle and to treat high-impact contusion injuries of the lower extremity, pelvis, abdomen, spine, and chest. The exclusion criteria included a location of surgery that would interfere with the application of the pneumatic compression cuff and one otherwise eligible patient was excluded because of an existing acute deep venous thrombosis. None of the eligible patients declined to participate. The operative procedures were performed predominantly with the patient under general anesthesia. The deep venous thrombosis prophylaxis regimen was randomly assigned in the operating theater at the time of completion of surgery, and the randomization was stratified by age.

Nine hundred and two patients were managed with chemoprophylaxis alone, and 901 were managed with the same chemoprophylaxis regimen augmented with rapid-inflation intermittent pneumatic compression (Fig. 1). The perioperative regimen for all patients consisted of intravenous intraoperative and postoperative hydration, analgesic drugs

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**Fig. 1**

Histogram illustrating the category of surgery and the type of prophylaxis. A total of 902 patients were managed with chemoprophylaxis alone (white columns), and 901 patients were managed with chemoprophylaxis augmented with intermittent pneumatic compression (IPC) (black columns). The “Other” group comprised primarily patients who had osteotomies for the treatment of acquired deformities of the femur, tibia, foot, and ankle, and high-impact contusion injuries.
(Novaminsulfon [metamizole]; twenty drops administered three times per day), anti-inflammatory drugs (diclofenac; 50 mg administered three times per day), low-molecular-weight heparin (cetoparin), and compression stockings. Low-molecular-weight heparin was administered subcutaneously in doses of 3000 anti-factor Xa (aXa) units twelve hours before surgery and twelve hours after surgery. Subcutaneous low-molecular-weight heparin administration was continued with a single dose of 3000 aXa units daily during hospitalization.

Patients in the intermittent pneumatic compression group had the intermittent pneumatic compression system applied to both calves in the recovery room shortly after the completion of surgery. The VenaFlow system (Aircast, Vista, California) uses calf cuffs containing two overlapping air chambers located posteriorly on the leg (Fig. 2). As the device cycles, the distal chamber inflates to 52 mm Hg over a 0.5-second period. During the last 0.2 second of this period, the proximal chamber inflates and reaches 45 mm Hg. After six seconds of inflation the cuff deflates, and the cycle is repeated every minute. A mean increase in peak venous flow velocity of 240% to 300% during the inflation of this device has been documented, compared with the 80% to 140% increase found with other intermittent pneumatic compression systems.

In the intermittent pneumatic compression group, 132 patients were assigned to receive compression for one to two hours daily; 154, for more than two to four hours daily; 394, for more than four to six hours daily; sixty-one, for more than six to eight hours daily; 101, for more than eight to ten hours daily; and fifty-nine, for more than ten hours daily. Thus, a total of 680 patients received intermittent pneumatic compression for six hours per day or less, and 221 patients received intermittent pneumatic compression for more than six hours a day. Intermittent pneumatic compression therapy was applied daily during the time that the patient was confined to bed postoperatively, and it was terminated at the time that the patient was able to walk. The average duration of application of postoperative intermittent pneumatic compression was three days (range, one to sixteen days).

On the day of discharge, all patients were screened for deep venous thrombosis in both legs with use of duplex-color-coded ultrasound. The personnel who performed the deep venous thrombosis screening were not blinded to the treatment regimens. Several variables were documented for each patient, including age, gender, risk factors, the location of surgery, whether or not deep venous thrombosis was detected with ultrasound (and, if it was detected, whether or not it was symptomatic), the duration of daily intermittent pneumatic compression, and the perceived comfort of the intermittent pneumatic compression cuffs. The patients were asked to report comfort on a visual analog scale of 1 to 10, with 1 being designated as very uncomfortable and 10 being designated as very comfortable. Symptomatic deep venous thromboses were defined as those accompanied by fever, swelling, or local pain (either spontaneous or in response to compression). Risk factors included a history of deep venous thrombosis, venous insufficiency, a body mass index of >30, an age of greater than forty years, and smoking.

**Statistical Methods**

Statistical comparison of the rates of deep venous thrombosis in the chemoprophylaxis-only group and intermittent pneu-
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Fig. 3
Bar graph illustrating the prevalence of deep venous thrombosis (DVT) in the chemoprophylaxis-only group (n = 902) and the intermittent pneumatic compression (IPC) group (n = 901). The difference between the groups was significant (p = 0.007).

Fig. 4
Bar graph illustrating the prevalence of deep venous thrombosis for patients undergoing total hip arthroplasty (n = 306) and total knee arthroplasty (n = 133). IPC = intermittent pneumatic compression.

Results
There was no significant difference between the groups when the number of thromboembolic risk factors per patient was analyzed (see Appendix).

In the chemoprophylaxis-only group, fifteen (1.66%) of the 902 patients were found to have a deep venous thrombosis (Fig. 3). These patients included eight women and seven men with a mean age of sixty-two years (range, twenty-six to eighty-six years). Ten deep venous thromboses were associated with hip and knee joint replacements; one, with anterior cruciate ligament reconstruction; two, with tumor resection; and two, with open fracture fixation. One tumor was located in the femur, and the patient underwent total femoral replacement with a modular prosthesis. The second tumor was located in the pelvis. The open fractures were located in the distal part of the femur and the pelvis and were treated with plate fixation. Five deep venous thromboses were located in...
the femoral vein and, of these, two were symptomatic. Ten deep venous thromboses were located in the calf and, of these, one was symptomatic.

In the intermittent pneumatic compression group, four (0.44%) of the 901 patients were found to have a deep venous thrombosis. These patients included one female patient and three male patients with a mean age of sixty years (range, forty-two to seventy-six years). No deep venous thromboses were detected among patients managed with total hip replacement, and three deep venous thromboses were detected among patients managed with total knee replacement. The fourth deep venous thrombosis occurred in a patient who had undergone meniscal repair. Three of the deep venous thromboses (two of which were located in the calf and one of which was located in the thigh) were asymptomatic, and one (located in the calf) was symptomatic.

The difference between the chemoprophylaxis-only group and the intermittent pneumatic compression group with regard to the rate of deep venous thrombosis was significant (p = 0.007) (Fig. 3). Following total hip replacement, deep venous thrombosis was diagnosed in six of 116 patients in the chemoprophylaxis-only group compared with zero of 190 patients in the intermittent pneumatic compression group; this difference was also significant (p < 0.001) (Fig. 4). Following total knee replacement, deep venous thrombosis was diagnosed in four of fifty-four patients in the chemoprophylaxis-only group compared with three of seventy-nine patients in the intermittent pneumatic compression group; again, the difference was significant (p = 0.038) (Fig. 4).

There were no instances of deep venous thrombosis in patients who received intermittent pneumatic compression for six hours or more per day. In contrast, there were four instances of deep venous thrombosis in patients who had intermittent pneumatic compression for six hours per day or less. This difference was significant (p < 0.006). There were no significant differences in the prevalence of deep venous thrombosis when the group receiving intermittent pneumatic compression for more than two to four hours was compared with the group receiving intermittent pneumatic compression for more than four to six hours (Fig. 5).

The majority of patients found the cuffs comfortable. The mean comfort score was 7.6 (range, 1 to 10).

Discussion

While most physicians accept the concept that early patient mobilization greatly enhances venous return, venous flow augmentation in recumbent patients after surgery was problematic until the advent of pneumatic devices that provide cyclic compression of the limbs.

A number of intermittent pneumatic compression devices are currently available. They vary with respect to the site of application, the rates of inflation and deflation, the pressure amplitude, and the chamber inflation sequence. Recently introduced intermittent pneumatic compression designs combine rapid inflation to relatively high pressures and graduated, sequential inflation of adjacent chambers in order to achieve optimal flow velocity and volume. Intermittent pneumatic compression of the calf has been shown to be superior to intermittent pneumatic compression of the foot. We believe that the device that we used in the present study incorporates the optimal characteristics to provide a level of venous flow enhancement that exceeds that achievable with other designs.

Rather than simulating contraction of the underlying muscles, intermittent pneumatic compression devices, when applied to the calf, produce their effect by simulating calf mus-
cle stretching. Elongation of the calf muscles concomitant with dorsiflexion of the foot increases the flow in the superficial femoral vein fourfold. It has been proposed that the kneading motion produced by rapid, sequential inflation such as that achieved with the device used in the present study is particularly effective because of the resulting shear stresses generated in the vascular endothelium.

The antithrombotic effect of intermittent pneumatic compression has been attributed to both the reduction of venous stasis and enhanced fibrinolysis. Intermittent pneumatic compression results in an increase in plasma tissue factor pathway inhibitor and a decline in the amount of t-PA (activated factor VII of the coagulation cascade). Inhibition of the tissue factor pathway, the initiating mechanism of blood coagulation, is a possible mechanism for the antithrombotic effect.

In addition, nitric oxide release from the vascular endothelium has been shown to increase in response to intermittent pneumatic compression. Formerly known as endothelium-derived relaxing factor, it is an important inhibitor of the coagulation cascade. Endogenous nitric oxide synthase appears to be elevated only during the period during which intermittent pneumatic compression is applied.

Because intermittent pneumatic compression has few contraindications and few deleterious side effects, we hypothesized that combining it with pharmacologic measures that have been shown to be effective for prophylaxis against deep vein thrombosis would confer additional protection to our patients. This combination has been shown to be effective in other clinical studies. While the present study did not address the use of intermittent pneumatic compression as a replacement for chemoprophylaxis, there is sufficient evidence to warrant exploring that possibility. The benefit of intermittent pneumatic compression described in the present study was most clear when its application exceeded six hours daily.

In the present study, a specific chemical prophylaxis regimen was compared with the same regimen augmented by a specific intermittent compression device. Additional studies will be required to determine whether these findings can be generalized to other chemoprophylaxis regimens and other intermittent compression devices.

On the basis of earlier work and the large randomized clinical study presented here, we believe that there are distinct advantages to augmenting chemoprophylaxis regimens with intermittent pneumatic compression, particularly among patients undergoing pelvis, knee, and hip surgery. Because it does not pose an increased risk of postoperative bleeding, intermittent pneumatic compression may be used safely to augment conventional prophylactic measures. The findings of the present study indicate that the use of a device that incorporated rapid inflation and graduated, sequential pneumatic compression in combination with chemoprophylaxis with low-molecular-weight heparin was effective for accomplishing these goals. The local comfort and ease of application of this intermittent pneumatic compression device are features that are likely to promote patient acceptance and compliance.

Appendix

A figure showing the number of risk factors per patient is available with the electronic versions of this article, on our web site at jibs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

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