Thromboembolism After Total Knee Arthroplasty: Intermittent Pneumatic Compression and Aspirin Prophylaxis

ABSTRACT: This is a study of two consecutive antithromboembolism regimens after total knee arthroplasty. In group 1, 131 patients were given aspirin prophylaxis alone (650 mg by mouth twice a day). In group 2, 123 patients were treated with aspirin, knee-high compression stockings, and intermittent knee-high pneumatic compression devices, which were started intraoperatively. The prevalence of deep vein thrombosis in group 1 was 15.9% (21 of 131 patients). One patient had a possible symptomatic nonfatal pulmonary embolism, and one patient had a symptomatic calf thrombus. Asymptomatic thrombi were detected in calf veins in 9 patients, popliteal vein in 6 patients, and femoral vein in 5 patients. In Group 2, the prevalence was 7.4% (9 of 123 patients). Asymptomatic thrombi were located in calf veins in 6 patients, popliteal vein in 1 patient, and femoral vein in 2 patients. There was a significant difference in the prevalence of deep vein thrombosis between the two groups. A history of previous thromboembolism was a significant risk factor for a new thrombus. The prevalence after bilateral one-stage knee arthroplasty was 24.3% for group 1 and 12.5% for group 2. Aspirin and knee-high intermittent pneumatic compression together are more effective than aspirin alone for prevention of deep vein thrombosis after primary and revision knee arthroplasty.

Thromboembolism continues to be a frequent postoperative complication of total knee arthroplasty. Without prophylaxis, thromboembolism has been reported to occur in 40% to 84% of patients having total knee arthro-

Christopher M. Larson, MD
Douglas P. MacMillan, MD
Paul F. Lachiewicz, MD
Chapel Hill, NC
plasty.1-6 Symptomatic pulmonary embolism after total knee arthroplasty has been reported to occur in 1.8% to 7.0% of patients without prophylaxis, with 0.2% to 2.0% of those being fatal.2-7,8 Controversy exists regarding optimal prophylaxis against thromboembolism after total knee arthroplasty. The various methods used have included aspirin, low doses of low molecular weight heparin with or without antithrombin III, warfarin, and intermittent pneumatic compression devices. In a recent review of trials, the reported prevalence of thromboembolism after knee arthroplasty with various methods of prophylaxis ranged from 11% to 79%.4

Intermittent pneumatic compression devices have been found to decrease venous stasis, accelerate emptying of the venous system, and increase systemic and local fibrinolysis.9,10 Two previous studies of 119 and 122 patients, respectively, reported a reduction in the incidence of thrombi after knee arthroplasty from 55% to 33% and from 59% to 27%, respectively, with the use of plantar compression devices and aspirin compared with aspirin alone.10,11 Another report of 61 patients having elective knee surgery noted a reduction in the rate of thromboembolism from 52% to 8% in a subset of patients taking aspirin with the use of intermittent calf compression.12 The purpose of the current study was to compare the efficacy of aspirin, knee-high compression stockings, and knee-high intermittent pneumatic compression devices versus aspirin alone for prophylaxis against thromboembolism after total knee arthroplasty.

**MATERIALS AND METHODS**

In this prospective study, 256 patients had 325 consecutive primary total knee arthroplasties between 1983 and 1996. All patients who had a primary or revision knee arthroplasty by one surgeon were included in the study. Two patients (2 knees) were excluded because of insufficient data. Thus, the study group consisted of 323 knees in 254 patients. Two prophylactic methods were used. Between 1983 and 1991, all patients having total knee arthroplasty received aspirin prophylaxis alone (group 1). Between 1991 and 1996, all patients received aspirin and wore knee-high compression stockings and intermittent knee-high pneumatic compression sleeves (group 2). All patients were given 650 mg of aspirin the night before surgery, and this dose was continued twice a day postoperatively for 6 weeks. In group 2, knee-high stockings (T.E.D. support stockings, Kendall Hospital Products, Boston, Mass) and intermittent knee-high compression sleeves (Kendall sequential compression device, Research Division of Kendall Corp, Barrington, Ill) were placed on the nonoperative leg in the operating room and continued postoperatively on both legs until discharge. Postoperatively, the compression devices were placed on the operative leg(s) in the operating room and were worn while the patient was recumbent and were removed only for daily hygiene and physical therapy sessions. The device has 3 chambers that inflate distal to proximal over 11 seconds and cycles every 60 seconds, with peak inflation pressures reaching 35 mm Hg to 55 mm Hg.

All total knee arthroplasties were done with the use of a tourniquet. A closed drainage system was inserted before closure of the wound, and a light dressing was applied to the knee, followed by the stocking and sleeve. The drain was usually removed on the second postoperative day and a progressive, continuous, passive motion and physical therapy protocol was started on the first or second postoperative days (usually before drain removal).

The Peripheral Vascular Laboratory of our hospital has had extensive experience since the late 1970s with noninvasive detection of leg thrombi, which has been previously validated.13-15 All patients were
prospectively monitored for deep vein thrombosis using Doppler vein examination between 1983 and 1986 and duplex ultrasonography between 1986 and 1996 on mean postoperative day number 5 (range, day 4 to 7). These studies were done by one of six registered vascular technologists (who are also registered nurses) with vascular laboratory experience ranging from 6 to 24 years. All scans were done with Acuson 128XP10 color flow ultrasound instruments (Acuson, Mountain View, Calif). Doppler signals were evaluated at the common femoral, popliteal, and posterior tibial levels. Compression to produce coaptation of the vein walls was applied sequentially and throughout the deep veins beginning at the inguinal ligament and proceeding in scanhead width increments through all 3 pairs of tibioperoneal veins, the sural veins, and the soleal sinuses. The greater saphenous vein was assessed at its confluence and for approximately 4 inches distally in asymptomatic patients and throughout its length if signs or symptoms of superficial phlebitis were present. The Doppler portion of the examination was considered normal when the signals showed equal, bilateral, spontaneous, and phasic flow in all veins (except the posterior tibial veins) and good augmentation in response to distal compression of the limb. The image was reported as negative when there was complete coaptation of the vein walls because of local compression. A Doppler study was considered positive (1) if distal limb compression produced no or reduced augmentation of flow in comparison with that in the contralateral limb; (2) if one common femoral vein Doppler signal showed decreased ventilatory phasicity as compared with the contralateral limb; or (3) if both common femoral vein Doppler signals were continuous. Color flow was used only as an adjunctive measure and not as a diagnostic criterion. Thrombi were classified as proximal if the popliteal or femoral veins were involved and distal if only the veins of the calf were involved.

If the duplex scan showed a calf vein thrombus and the patient was asymptomatic, the prophylaxis was continued and the scan was repeated in 1 week. In the asymptomatic patient with a popliteal or femoral vein thrombus, the prophylaxis was considered to have failed and anticoagulation was started with low molecular weight heparin or warfarin. Oral anticoagulation, with a goal of a prothrombin time of 15 to 18 seconds, was continued for 12 weeks. The symptomatic patients with a calf thrombus were treated according to the surgeon’s judgment, but the symptomatic patients with a popliteal or femoral thrombi routinely were given heparin followed by warfarin for 6 months. Symptomatic pulmonary emboli were confirmed with a ventilation/perfusion scan or pulmonary angiography, and the patients were treated with heparin and warfarin for 6 months.

In group 1, 168 knee arthroplasties were done in 131 patients. There were 36 men (46 knees) and 95 women (122 knees). The mean patient age was 63.6 years (range, 30 to 83 years). Preoperative diagnosis was osteoarthritis in 74 patients (88 knees), rheumatoid arthritis in 46 patients (68 knees), and other (psoriatic arthritis, trauma, hemophilia, and osteonecrosis) in 11 patients (12 knees). Thirty-seven patients (74 knees) had bilateral one-stage knee arthroplasty. Four patients (5 knees) had a history of thromboembolism, and four patients (4 knees) had a history of varicose veins. The body mass index (BMI) was calculated (weight in kilograms divided by height in meters squared). A patient was considered to be of normal weight with a BMI less than 30 kg/m², obese with a BMI greater than 30 kg/m², and morbidly obese with a BMI greater than 40 kg/m². For group 1, the mean BMI was 28 kg/m² (range, 19 to 44 kg/m²). Ninety patients were of normal weight, 39 were obese, and 2 were morbidly obese. Of the 168 arthroplasties in this group, 140 (105 patients) were primary and 28 (26 patients) were revision arthroplasties.
In group 2, there were 155 arthroplasties in 123 patients—31 men (42 knees) and 92 women (113 knees). The mean patient age was 67.9 years (range, 22 to 84 years). The preoperative diagnosis was osteoarthritis in 89 patients (112 knees), rheumatoid arthritis in 26 patients (34 knees), and other in 8 patients (9 knees). Thirty-two patients (64 knees) had bilateral one-stage knee arthroplasty. Three patients (3 knees) had a history of thromboembolism, and two patients (3 knees) had a history of varicose veins. The mean BMI was 26 kg/m² (range, 17 to 45 kg/m²). Ninety-three patients were of normal weight, 27 were obese, and 3 were morbidly obese. In this group, 127 of the arthroplasties (99 patients) were primary and 28 (24 patients) were revisions.

Statistical evaluation was done by chi-square analysis and the two-tailed Fisher exact test.

### RESULTS

We found no statistically significant demographic differences between the patients or procedures in groups 1 and 2 (Table 1). However, this study did not evaluate total operative or tourniquet times, length of hospital stay, or physical therapy protocols. There were definite decreases in length of hospital stay during the period of the study because of cost-control pressures. These variables could not be reasonably analyzed and are beyond the scope of this study. The prevalence of thromboembolism in all patients having total knee arthroplasty in this study was 11.8% (30 of 254 patients) (Table 2). In group 1 (aspirin therapy alone), the prevalence of thromboembolism was 15.9% (21 of 131 patients), and in group 2 (aspirin, compression stockings, and intermittent pneumatic compression), the prevalence was 7.4% (9 of 123 patients) (P = .035). In group 1, asymptomatic thrombi were located in calf veins in 9 patients, popliteal vein in 3 patients, calf and popliteal veins in 3 patients, popliteal and femoral veins in 1 patient, a combination of all three veins in 3 patients, and calf and femoral veins in 1 patient. One patient in group 1 had a symptomatic calf vein thrombus on postoperative day 4. In group 2, asymptomatic thrombi were located in calf veins in 6 patients, calf and popliteal veins in 1 patient, and the femoral vein in 2 patients. No patient in group 2 had a symptomatic thrombus. Distal thrombi were seen in 10 patients (7.5%) in group 1 and 6 patients (5%) in group 2 (P = .57). Proximal thrombi (either the femoral or popliteal veins) were present in 11 patients (8.4%) in group 1 and 3 patients (2.4%) in group 2 (P = .069). One patient in group 1 had either a possible nonfatal pulmonary embolism or a cardiac ischemic event. No patient in group 2 had a symptomatic pulmonary embolism.

The entire group of patients was evaluated to detect possible risk factors for thromboembolism (Table 3). The prevalence of thromboembolism was significantly higher in patients having bilateral one-stage knee arthroplasty (13 of 69 patients, 18.6%) compared with unilateral knee arthroplasty (17 of 185 patients, 9.2%) (P = .04). The prevalence of thromboembolism after bilateral one-stage knee arthroplasty was 24.3% (9 of 37 patients) for group 1 and 12.5% (4 of 32 patients) for group 2 (P = .36). The prevalence of thrombi in patients with a history of thromboembolism was 71.0% (5 of 7 patients) compared with

### TABLE 1. Data on 254 Patients Having Total Knee Arthroplasty

<table>
<thead>
<tr>
<th>GROUP</th>
<th>NO. OF PATIENTS</th>
<th>NO. OF KNEES</th>
<th>MEAN AGE (YEARS)</th>
<th>NO. PATIENTS</th>
<th>BILATERAL ARTHROPLASTY (ONE STAGE)</th>
<th>UNILATERAL ARTHROPLASTY</th>
<th>REVISION ARTHROPLASTY</th>
<th>HISTORY OF DVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>131</td>
<td>168</td>
<td>64**</td>
<td>37</td>
<td>94</td>
<td>26</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>123</td>
<td>155</td>
<td>68**</td>
<td>32</td>
<td>91</td>
<td>24</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

*Aspirin alone as prophylaxis against deep vein thrombosis (DVT).
†Prophylaxis with combination of aspirin, compression stockings, and intermittent pneumatic compression.
**Age range (years): group 1, 30-83; group 2, 22-84.

No statistically significant differences between groups for any of these parameters.
10.1% (25 of 247 patients) in those without such a history \((P = .0003)\). A history of varicose veins was also a significant risk factor for the development of thrombi after total knee arthroplasty \((P = .022)\). There was no statistically significant correlation with sex \((P = .376)\), diagnosis \((P = .79)\), obesity \((P = .10)\), blood group \((P = .45)\), or revision versus primary total knee arthroplasty \((P = .22)\).

The prevalence of thromboembolism per knee arthroplasty in groups 1 and 2 also was evaluated and showed the same statistically significant difference as the prevalence per patient. The overall prevalence of thrombi per knee was 9.3% (30 of 323 knees). The prevalence of thromboembolism was 12.5% (21 of 168 knees) for group 1 and 5.8% (9 of 155 knees) for group 2 \((P = .027)\). In contrast to the prevalence per patient, there was no statistically significant difference in the rate of thromboembolism per knee between patients having bilateral one-stage knee arthroplasty (9.4%, 13 of 138 knees) and those having unilateral knee arthroplasty (9.2%, 17 of 185 knees) \((P = .97)\). The prevalence of thromboembolism after bilateral one-stage knee arthroplasty was 12.2% (9 of 74 knees) for group 1 compared with 6.3% (4 of 64 knees) for group 2 \((P = .39)\).

Duplex ultrasonography became the procedure of choice for detecting thrombi in 1986. Thus, the earlier patients in group 1 (1983 to 1986) had Doppler examination only and those treated after 1986 had a duplex examination. All patients in group 2 had duplex ultrasonography. Of the 131 patients in group 1, 44 (34%) had Doppler examination, and 87 (66%) had duplex examination. There was no significant difference in the prevalence of thrombi detected by Doppler (15.9%, 7 of 44 patients) versus duplex examination (16.1%, 14 of 87 patients) for patients in group 1 \((P = .96)\).

No major bleeding complication, defined as one that required additional transfusion or reoperation, occurred with the use of either aspirin alone or aspirin plus intermittent pneumatic compression prophylaxis. However, one patient in group 2 who had a thrombus and was treated with warfarin also required treatment for a late hemarthrosis.

There were no noticeable adverse affects, systemically or locally, as a result of wearing the intermittent knee-high pneumatic compression device.

**DISCUSSION**

Patients having primary or revision total knee arthroplasty have an increased risk for the development of thromboembolism. With-

---

**TABLE 2. Prevalence of Deep Vein Thrombosis (DVT)**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (Aspirin Alone)</th>
<th>Group 2 (Aspirin and Pneumatic Compression)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT (all)</td>
<td>15.9% (21 patients)</td>
<td>7.4% (9 patients)</td>
<td>.035</td>
</tr>
<tr>
<td>Proximal DVT</td>
<td>8.4% (11 patients)</td>
<td>2.4% (3 patients)</td>
<td>.069</td>
</tr>
<tr>
<td>Distal DVT</td>
<td>7.5% (10 patients)</td>
<td>5.0% (6 patients)</td>
<td>.57</td>
</tr>
<tr>
<td>Symptomatic DVT</td>
<td>.01% (1 patient)</td>
<td>0.0%</td>
<td></td>
</tr>
</tbody>
</table>

*Statistical significance defined as \(P < .05\).

---

**TABLE 3. Risk Factors and Overall Prevalence of Deep Vein Thrombosis (DVT)**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Group 1 (%)</th>
<th>Group 2 (%)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral arthroplasty</td>
<td>(18.6)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Obesity (7.6%)*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of DVT (71.0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of varicosities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoarthritis (13.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral (9.2%)*</td>
<td></td>
<td></td>
<td>.04</td>
</tr>
<tr>
<td>Not obese (15.8%)</td>
<td></td>
<td></td>
<td>.10</td>
</tr>
<tr>
<td>No history of DVT (12.2%)*</td>
<td></td>
<td></td>
<td>.0003</td>
</tr>
<tr>
<td>No history of varicose veins (12.7%)*</td>
<td></td>
<td>.022</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid arthritis (12.3%)</td>
<td></td>
<td></td>
<td>.79</td>
</tr>
</tbody>
</table>

*No significant difference in prevalence of DVT by sex, blood group, or primary vs revision arthroplasty.

*Statistically significant difference, \(P < .05\).
out prophylaxis, the overall prevalence of thromboembolism has been reported to range from 40% to 84%, with proximal thrombi in 9% to 24% of patients. Symptomatic pulmonary embolism has been reported to occur in up to 7% of patients having total knee arthroplasty without prophylaxis, being fatal in 2% of them. Most surgeons recommend routine prophylaxis against thromboembolism, but the optimal method is controversial. The prevalence of thromboembolism after knee arthroplasty with aspirin prophylaxis alone (at various doses) has ranged from 55% to 79% in several studies using a variety of end points (venography, ultrasound, clinical evaluation). However, one study reported an 8% prevalence of thrombi after knee arthroplasty with the use of 1.3 mg of aspirin 3 times daily, but this study included only 12 patients and one of them had a major gastrointestinal hemorrhage. Lotke et al compared low-dose aspirin (325 mg daily) and “low-dose” warfarin (international normalized ratio not specified) in 179 patients having knee arthroplasty and found no difference in the prevalence of thrombi detected by venography. Despite the high rate of thrombi reported with aspirin alone, it remains a popular prophylaxis because no monitoring is required and bleeding complications are minimal. The Antiplatelet Trialists’ Collaboration evaluated more than 9,000 surgical and medical patients treated with aspirin for thromboembolism prophylaxis and reported a 49% reduction in the rate of thrombi among patients who had an elective orthopaedic procedure (hip or knee arthroplasty) and a 64% reduction in the rate of pulmonary embolism for all patients reviewed. In addition, a recent study of 13,356 patients who had an operation for a fracture of the neck of the femur and 4,088 who had elective total hip arthroplasty showed that, compared with placebo, aspirin produced significant reductions in total thromboembolism, as well as total pulmonary embolism and deep vein thrombosis.

Several studies have evaluated the efficacy of low molecular weight heparins and warfarin for prophylaxis against thromboembolism after total knee arthroplasty. Although Hull and Raskob reported no significant difference in the rate of thrombi after knee arthroplasty in 317 patients treated with warfarin (55%) or low molecular weight heparin (45%), others have found low molecular weight heparin to be more effective than warfarin after knee arthroplasty. Fitzgerald reported that 25% of patients treated with enoxaparin had a deep vein thrombosis compared with 45% of patients given warfarin (P < .05). Spiro et al, in a multicenter trial, reported the incidence of venous thromboembolic disease was 25% with enoxaparin and 45% with warfarin (P < .001). The RD Heparin Arthroplasty Group compared once and twice daily low molecular weight heparin with low dose warfarin and found a significant reduction in the rate of thrombi with both regimens of low molecular weight heparin.

Mechanical methods of prophylaxis against thromboembolism after total knee arthroplasty include continuous passive motion and intermittent pneumatic compression devices. Continuous passive motion could theoretically reduce the prevalence of thrombosis by stimulating venous flow. However, a prospective randomized trial found no difference in the rate of thrombosis. Intermittent pneumatic compression accelerates the emptying of the venous system, reduces venous stasis, and possibly affects fibrinolysis. Several studies have found this prophylaxis to be effective in a variety of clinical settings. Haas et al found that, in unilateral total knee arthroplasty, the incidence of deep vein thrombosis was 22% with compression boots and 47% with aspirin alone (P < .03). Westrich and Sculco reported 27% deep vein thrombosis with pneumatic plantar compression and aspirin compared with 59% with aspirin alone (P < .001). Hull et al reported a decrease in the
prevalence of thrombi after total knee arthroplasty from 66% to 6% using pneumatic compression, compared with a control group. In their study, pneumatic compression further reduced the prevalence of thrombi from 52% to 8% in a subset of patients receiving aspirin. McKenna et al19 prospectively assigned patients to one of four groups after total knee arthroplasty. Thrombi occurred in 10% of patients treated with pneumatic compression, 8% of patients given high-dose aspirin therapy (1.3 g tid), 75% of patients treated with a lower dosage of aspirin (325 mg tid), and 78% of patients given a placebo. In this study, the prevalence of deep vein thrombosis was reduced significantly after total knee arthroplasty when knee-high compression stockings, knee-high pneumatic compression, and aspirin were used together, as compared with aspirin alone.

The risk of thromboembolism after bilateral one-stage arthroplasty continues to be controversial. Morrey et al30 found no statistically significant difference in the incidence of pulmonary embolism or clinically significant thrombophlebitis between 290 bilateral and 501 unilateral total knee arthroplasties. However, Stulberg et al31 reviewed 638 total knee arthroplasties and found a significant increase in the rate of thromboembolism after simultaneous bilateral total knee arthroplasty (74%) compared with unilateral total knee arthroplasty (51%). Haas et al11 also found a statistically significant increase in risk of thromboembolism for one-stage bilateral total knee arthroplasty (57%) compared with unilateral knee arthroplasty (35%). In that study, although the prevalence of thromboembolism for each knee after simultaneous bilateral arthroplasty was comparable to that for unilateral arthroplasty, one-stage bilateral total knee arthroplasty doubled the risk of thromboembolism per patient.

The standard for the detection of thrombi has been venography. Duplex ultrasonography has been shown to have a lower sensitivity than venography for detecting calf thrombi.29 However, in other reports, ultrasonography has had a sensitivity of 93%, specificity of 99%, and accuracy ranging from 93% to 99%.32-34 Duplex ultrasonography has been used exclusively at our institution for the detection of deep venous thrombosis for the past 12 years.12-14 All scans were done by registered vascular technologists with extensive experience. One limitation of the study is that approximately one third of patients in group 1 (aspirin alone) had only a Doppler examination, since Duplex ultrasonography was not introduced at our institution until 1986. However, there was no difference, with the small numbers available, in the prevalence of thrombi detected by Doppler examination versus duplex examination within that group.

In conclusion, the combination of knee-high compression stockings, knee-high intermittent pneumatic compression, and aspirin is a safe and effective method of prophylaxis against thromboembolism after total knee arthroplasty. We found a significantly lower prevalence of deep vein thrombosis with this combination than with aspirin prophylaxis alone. A history of thromboembolism, preexisting venous disease, and bilateral one-stage total knee arthroplasty were significant risk factors for the development of deep vein thrombosis despite this prophylaxis. Additional studies are necessary to determine the optimal prophylaxis for these high risk groups.

References


**EDITORIAL PERSPECTIVE:** Although analyzing venous thrombosis by ultrasonography is controversial, the two groups studied are reasonably comparable in that all patients had monitoring for deep vein thrombosis with either Doppler or duplex scans. One concern is that the study covered such a long period (some 13 years), during which a number of changes might have occurred in the rehabilitation protocols. However, given the data in this paper, one can reasonably conclude that the use of aspirin in combination with pneumatic compression devices is better than aspirin alone when assessed by ultrasonography.