Prevention of deep vein thrombosis in neurosurgical patients: A controlled, randomized trial of external pneumatic compression boots

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A prospective, randomized clinical trial in 95 patients undergoing neurosurgical operative procedures was performed to investigate the efficacy of external pneumatic compression (EPC) of the calves as compared with results in a control group that received no specific form of prophylaxis for prevention of deep vein thrombosis (DVT). The diagnosis of DVT was established by the I^{125} fibrinogen scan and radiographic contrast phlebography. The data indicate that EPC provides significant protection against the development of DVT in comparison with results in the control group ($p < 0.05$). There were no known pulmonary emboli in any of the EPC-treated patients. There were no complications of EPC.

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Although low-dose heparin appears to be effective in reducing the incidence of deep vein thrombosis (DVT) and fatal pulmonary embolism in general surgical patients undergoing elective operations,[7] the possibility of intracranial bleeding in neurosurgical patients makes them poor candidates for drugs that interfere with hemostasis. External pneumatic compression of the calves is an extremely attractive alternative to the administration of anticoagulant drugs to protect such patients against the development of DVT.

The purpose of this prospective, randomized clinical trial in 95 patients undergoing neurosurgical operative procedures was to assess the effectiveness of external pneumatic compression of the calves as compared with results in a group that received no specific form of prophylaxis.

METHODS

Ninety-five patients undergoing neurosurgical operative procedures were admitted to this study. A few other patients declined to participate. After giving informed consent, patients were assigned to the control group or to an external pneumatic compression (EPC) group according to a table of random numbers. Patients randomized into the control group did not receive any specific form of prophylaxis to prevent deep vein thrombosis. Patients randomized into the EPC group received external pneumatic compression of both calves by means of inflatable boots (Anti-EM, Extremity Pump, Jobst, Toledo, Ohio), which produce an inflation cycle of 10 seconds of rapid inflation to 35 to 40 mm Hg, followed by slower deflation and recycling once per minute.[4] EPC was applied after induction of anesthesia and was maintained during the operative procedure and throughout the period of bed rest (up to 17 days after operation). The boots were removed for short periods to allow for a patient's comfort, nursing care, and ambulation. Occasionally EPC was discontinued prematurely because of a patient's intolerance of the boots.

The development of deep vein thrombosis was monitored by the I^{125} fibrinogen scan technique.[6] All patients were given 100 mg of sodium iodide on the day before operation and daily thereafter to prevent uptake of I^{125} by the thyroid gland. I^{125} fibrinogen

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(100 μCi) was given intravenously at least 30 minutes after the first dose of sodium iodide. Scanning of both legs was performed daily with a gamma detector to monitor any accumulation of I^{125}. Radioactivity at each site in the legs was expressed as a percentage of counts over the heart. A scan was judged to be positive for the development of thrombosis if any location was found to be 20 percentage points higher than adjacent sites on the same leg or the same site in the opposite leg on the same or previous day. Scanning was continued in most patients until the patient was discharged from the hospital. Reinjection of I^{125} fibrinogen was necessary in many patients because of the length of the hospital stay. A site judged to be positive on two consecutive hospital days was considered as an indication for contrast phlebography. Phlebography was performed by the technique of Rabinov and Paulin [14] in patients with a positive scan, except in two patients in whom this examination was refused by the patient or his physician.

Interpretation of the fibrinogen scans and phlebograms was made without knowledge of the group to which the patient had been assigned.

Specific diagnostic investigations for the presence of asymptomatic pulmonary embolism were not part of the protocol of this study.

Statistical analysis of the data was performed by the chi square test. This protocol was approved by the Committee on Clinical Investigations, New Procedures and Forms of Therapy of the Beth Israel Hospital.

RESULTS

The mean ± SD for the ages, duration of anesthesia, and duration of EPC treatment for the two groups are shown in Table I, where the data are subdivided according to whether the I^{125} scan was positive or negative. There was no statistically significant difference between the mean ages or duration of anesthesia. Although patients with negative scans in the EPC group received this therapy almost twice as long as did the scan-positive patients, this difference was not statistically significant; the trend presumably resulted from discontinuation of EPC once the diagnosis of DVT was made.

The types of operation performed in the two groups were comparable, except that twice as many craniotomies were performed for tumor in the control group (Table II). Seven of the 20 patients in the control group who underwent craniotomy for tumor developed DVT in comparison with one of 11 patients in the EPC group. The prevalence of malignancy in the entire control and EPC groups was somewhat higher in I^{125} scan-positive patients (Table III). A consideration of seven different risk factors in the entire group of 95 patients (Table III) shows that, with the exception of a history of varicose veins, the prevalence of other risk factors considered to favor the development of DVT was higher in patients who developed DVT.

Seventy-four percent of all patients studied received at least one drug known to interfere with platelet function during the preoperative or postoperative course. The four most common platelet-active drugs ingested, in order of decreasing frequency, were prochlorperazine (Compazine) (27 patients), oxycodone combined with aspirin, phenacetin, caffeine (Percodan) (19 patients), acetylsalicylic acid (aspirin) (15 patients), and diphenhydramine (Benadryl) (14 patients). The frequency of ingestion of these drugs was not significantly

Table I

*Group and scan results**	*No. of patients*	*Age† (yr)*	*Duration of anesthesia† (min)*	*Duration of EPC treatment† (hr)*
Control:				
Scan (−)	37	48 ± 17	377 ± 194	—
Scan (+)	11	51 ± 15	501 ± 302	—
Boot:				
Scan (−)	44	49 ± 18	419 ± 263	132 ± 102
Scan (+)	3	50 ± 28	311 ± 121	76 ± 42

Legend: EPC, external pneumatic compression boots.
*Scan (+) patients had confirmatory (+) venograms.
†Refers to mean ± standard deviation.

Table II

Type of operation	*Group* Control*	EPC
Craniotomy	25 (10)	20 (2)
Aneurysm	3 (2)	4 (1)
Tumor	20 (7)	11 (1)
Other (including head injury)	2 (1)	5
Laminectomy:	23 (1)	27 (1)
Cervical	2	11 (1)
Thoracic	3	1
Lumbar	18 (1)	15
Total	48 (11)	47 (3)

Legend: See Table I.
*Figures in parentheses refer to patients who developed DVT as judged by (+) scans with confirmatory (+) venograms.

Table III

Risk factor	Control* Scan (+) (%)	Control* Scan (−) (%)	EPC* Scan (+) (%)	EPC* Scan (−) (%)
1. Previous DVT	1 (9)	1 (3)	—	2 (5)
2. Previous PE	1 (9)	—	1 (33)	2 (5)
3. Obesity	7 (63)	9 (24)	2 (67)	17 (39)
4. Varicose veins	—	3 (8)	—	5 (11)
5. Age over 60 yr	3 (27)	10 (27)	1 (33)	12 (27)
6. Birth control pills	—	—	1 (33)	2 (5)
7. Malignancy	4 (36)	10 (27)	1 (33)	8 (18)

Legend: EPC, external pneumatic compression boots. DVT, deep vein thrombosis. PE, pulmonary embolism.
*Figures in parentheses refer to the percentage of patients in each scan group having that particular risk factor.

Table IV

Diagnostic criteria for DVT	Group: Control		Group: Boot	
1. Scan (+), venogram (+)	11	25%	3	8.5%
2. Scan (+), no venogram	1		1	
3. Scan (+), venogram (−)	2		3	
4. Scan (−)	34		40	
Total	48		47	

Groups compared	1+2 vs. 3+4 X^2	1+2 vs. 3+4 p value	1 vs. 3+4 X^2	1 vs. 3+4 p value	1 vs. 4 X^2	1 vs. 4 p value
Control vs. boot	4.62	< 0.05	5.18	< 0.025	5.01	< 0.05

different in the control or EPC groups. Moreover, the prevalence of ingestion of platelet-active drugs was similar in the I^{125} scan-positive and scan-negative groups.

If the diagnosis of DVT is defined as a positive scan and positive phlebogram or a positive scan and no venogram, 12 patients in the control group (25%) and four patients in the EPC group (8.5%) developed DVT ($p < 0.05$) (*Table IV*). If the two patients with positive scans and no phlebograms (one in each group) are excluded from the statistical analysis, the statistical difference between phlebographically positive and negative patients in the control group and EPC group is even more in favor of a positive benefit to EPC ($p < 0.0025$).

Of the 21 patients in this study who developed a positive I^{125} scan, five had negative venograms. The incidence of false-positive scans in this study, therefore, was 24%. If these patients are excluded from the analysis, the difference in favor of EPC remains significant (Table IV).

No patients in the current study developed symptomatic evidence of pulmonary embolization during the period of hospitalization. One control patient in the I^{125} scan-negative group underwent lumbar laminectomy and died on the 18th day after operation; he had segmental pulmonary arterial embolism at postmortem examination. Pneumonia, rather than pulmonary embolism, was considered to be the major reason for his death. A second control patient whose postoperative I^{125} scan was negative after craniotomy for aneurysm was discharged for home on the 16th day after operation. He was readmitted 1 day later because of pulmonary embolization and underwent placement of an umbrella in the inferior vena cava.

DISCUSSION

A variety of physical methods to prevent DVT in the postoperative period have been described. These include elevation of the legs,[11, 13] the application of elastic stockings,[10, 17] and the use of mechanical devices that compress the calves[2, 15] or stimulate the contraction of the calf muscles.[12, 16] Of these methods, EPC of the calves by inflatable plastic boots appears to be the technique which is most promising for clinical use in terms of its combination of efficacy and simplicity.

Although it has been accepted generally that the special appeal of EPC is that this method does not interfere with the hemostatic mechanism, there is evidence that EPC of the calves does increase systemic fibrinolytic activity.[1] The authors of a report of a recent prospective randomized trial of 128 cancer-free patients over 50 years of age suggested that intermittent pneumatic compression of the arms is associated with a significant and persistent increase in the fibrinolytic activity of free-flowing blood obtained from the arm veins in comparison with control patients not receiving intermittent compression until the third day after operation.[9] Since the mean plasma fibrinogen levels in the control and treated groups were the same in the latter study, they concluded that the highly significant differences in the euglobulin clot lysis times of the two groups reflected real differences in fibrinolytic activity. A significant difference in the incidence of DVT (32% in control group vs. 14% in the treated group [$p = 0.029$]) also was noted in the latter study. It was suggested that, despite the presence of venostasis in the lower limbs, the release of fibrinolytic activity may be necessary for the prophylactic action of pneumatic leggings.[9]

Notwithstanding these studies, it is the absence of a major effect on hemostasis which makes this method particularly suitable for patients undergoing urological[3] or neurosurgical[18] operative procedures.

The present randomized trial of 95 patients undergoing neurosurgical procedures showed that EPC was associated with a significant reduction of DVT when the diagnosis of DVT was defined as a positive I^{125} scan and positive phlebogram or a positive scan and no phlebogram. (Table IV) ($p < 0.05$). These results are in agreement with those of Turpie and co-workers,[18] who found a transient protective effect of EPC in 128 patients who had craniotomy for brain tumor, subarachnoid hemorrhage, or subdural hematomas. In the latter study the incidence of DVT was initially reduced from 18.4% to 1.9% in 103 patients in whom calf compression was begun after craniotomy. However, the treatment period was only 5 days, and continued scanning to 14 days after surgery or injury revealed the frequent late development of DVT. Some patients received EPC in our study for as long as 17 days. The mean treatment period for scan (+) patients was approximately 3 days (Table I), in comparison with a mean of approximately 5 days in the scan(−) patients (p = NS). In the present study no scan (−) patients in the treated group are known to have developed DVT in the late period. However, because of the possible development of late DVT, we agree with the suggestion of Gallus and Hirsch[5] that neurosurgical patients who remain bedridden for more than 5 days should receive EPC or some other form of effective prophylaxis against DVT until they become fully ambulatory.

Although the number of patients in the current trial is insufficient to provide reliable statistical data concerning the incidence of risk factors predisposing to the development of DVT (Table III), the trends are similar to those reported by Kakkar and coworkers,[8] who showed that patients with a previous history of DVT or pulmonary embolism, varicose veins, obesity, age over 60 years, and the presence of malignancy had a higher incidence of DVT. In the current trial the ingestion of birth control pills also was a significant risk factor for DVT, but the presence of varicose veins was not.

False-positive results were obtained in 24% of positive scans in the present study, a higher figure than that reported for general surgical patients undergoing intra-abdominal operations,[19] but approximately the same as that found in a recent trial comparing low-dose heparin vs. EPC in urological patients.[3]

Two patients in the control group of the present study are known to have developed pulmonary embolism, one proven at postmortem examination and the other verified by lung scan. Since routine examinations to detect the presence of asymptomatic pulmonary emboli were not part of the design of this study, it is possible that other pulmonary emboli may have occurred.

The results of this trial strongly suggest that intermittent calf compression by inflatable plastic boots is an effective measure to prevent deep vein thrombosis in patients undergoing neurosurgical operative procedures in whom anticoagulant drugs specifically are contraindicated because of the risk of hemorrhage. The effect of EPC was particularly striking in patients who underwent craniotomy for tumor. This beneficial result of EPC also was observed in an earlier study of patients undergoing open urological operations,[12] a group in whom the use of anticoagulant drugs is also of concern.

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