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Heparin with and without graded compression stockings in the prevention of thromboembolic complications of major abdominal surgery: a randomized trial

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One hundred and seventy-six patients scheduled for elective major abdominal surgery were randomized to two prophylactic regimens to prevent postoperative thromboembolism. All patients were screened with the ^{125}I-labelled fibrinogen uptake test, and thromboembolism was verified by ascending phlebography and/or perfusion/ventilation lung scintigraphy. In the group of patients receiving low-dose heparin treatment (5000 units twice daily subcutaneously) 12 per cent developed thromboembolic complications. In the other group, where low-dose heparin treatment was supplemented with graded compression stockings only 2 per cent developed thromboembolism. It is concluded that the combination of low-dose heparin and the use of graded compression stockings is superior to heparin alone in preventing thromboembolism following major abdominal surgery.

Keywords: Thromboembolism, abdominal surgery, complications, heparin, compression stockings

Elimination of venous stasis and interference with coagulation have both been found effective in the prevention of postoperative thromboembolism[1]. Low-dose heparin sodium has gained wide acceptance, but in spite of this about 10 per cent of patients undergoing major abdominal surgery develop postoperative thromboembolic complications[2]. The use of elastic graded compression stockings has recently been shown to lower the incidence of postoperative thromboembolism[3] and one investigation indicated an additional effect when heparin and stockings were used simultaneously[4]. The purpose of this investigation was to compare the effectiveness of treatment with heparin and graded compression stockings with heparin alone, in preventing thromboembolic complications in major abdominal surgery.

Patients and methods

Between May 1982 and October 1983, patients scheduled for elective major abdominal surgery were included provided they fulfilled one of following criteria: age above 39 years, malignancy suspected, weight more than 19 per cent above normal[5], varicose veins of the lower extremities, diabetes mellitus, hypertension, previous thromboembolism or cardiac failure. Exclusion criteria were: hepatic disease with coagulation factors II, VII and X below 40 per cent, anticoagulation treatment, a history of peripheral arterial insufficiency and allergy to iodine. Informed consent was obtained. Randomization was carried out by random numbers the day before surgery.

The treatment was 5000 units of heparin sodium (Noparin) administered twice daily subcutaneously, starting one hour pre-operatively and continued for seven days or until discharge. Patients allocated to the combination treatment had thigh-length graded elastic compression stockings (TED stockings) fitted on both legs before surgery. The stockings were used day and night during the observation period. To ensure uniformity the heparin was from the same batch.

A fibrinogen uptake test was performed pre-operatively, immediately postoperatively, and on days 1, 3, 5 and 7 postoperatively[6]. Pre-operatively, 100 mCi of fibrinogen labelled with Iodine 125 was injected intravenously. When the count rate over the heart fell below 10 000 counts per minute, another injection of the same dose was given. The thyroid gland was blocked with iodine. Fibrinogen uptake test results were considered abnormal when one or more of the following changes persisted for more than 24 h: a 15 per cent increase in activity at one site in comparison with the corresponding site in the other extremity; a 5 per cent increase in activity at three consecutive sites compared with corresponding sites in the other extremity; a 15 per cent increase at one site in the lower leg and at the knee compared with previous scans; and a 15 per cent increase at two consecutive sites in the thigh compared with previous scans.

Whenever a fibrinogen uptake test was abnormal or when clinical signs were present, ascending phlebography and perfusion and ventilation scintigraphy of the lungs were performed. The criterion for deep venous thrombosis was an abnormal phlebogram, evaluated by a radiologist who was not aware of the patient's treatment group.

Perfusion scintigraphy was carried out using 3 mCi of ^{99m}Tc albumin aggregated. When focal perfusion defects were observed ventilation scintigraphy was performed using continuous breathing of ^{81}Kr. 300 000–500 000 counts were collected in anteroposterior, posteroanterior, and right and left posterioroblique positions with a gamma camera connected to a computer. The criterion for pulmonary embolism was a focal perfusion defect with intact ventilation, as obtained by scintigraphy and read blindly.

Discharged patients were followed with regard to causes of death within 30 days after surgery.

Patients were defined as having postoperative thromboembolism if they had deep venous thrombosis and/or pulmonary embolism diagnosed. If so treatment was started immediately.

The statistical tests were the χ^2 test and the Mann–Whitney U test with a level of significance of 0·05.

Results

Of the 196 patients allocated 20 were subsequently withdrawn (*Table 1*). This left 86 patients in the heparin–stocking group and 90 in the heparin group for evaluation. There was no significant difference between the two groups according to number and distribution of inclusion criteria, neither was a significant difference found in age, duration of operation or type of operation (*Table 2*). There were significantly more men allocated to the combination treatment.

There were 64 patients observed for less than 7 days, 2 died without suspicion of thromboembolism, 2 removed their stockings after 5 days and 60 were discharged. The median observation period of these 64 patients was 4 days with equal distribution in the two groups.

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In the heparin group 3 patients did not have phlebography performed despite abnormal fibrinogen tests, because it was technically impossible. One was defined as a nonthromboembolic patient as pulmonary scintigraphy and a radionucleid venography were normal and no clinical signs were present. The other two were defined as thromboembolic patients as pulmonary scintigraphy was positive in one patient and pulmonary embolism caused the death of the second one 25 days postoperatively. One phlebogram was inconclusive but the patient had positive lung scintigraphy and symptoms of pulmonary embolism and was defined as thromboembolic.

According to the National Register no more of the 176 patients in the study died from pulmonary embolism during the first month after surgery.

Table 3 shows the incidence of positive fibrinogen uptake tests, the incidence of phlebographically verified deep venous thrombosis, the incidence of pulmonary embolism verified by scintigraphy or autopsy and the overall incidence of thromboembolic complications in the groups. Patients with the combination or low-dose heparin and graded compression stockings had a singificant lower incidence of deep venous thrombosis and thromboembolism, compared with low-dose heparin alone.

Table 1 *Patient withdrawals*

	Low-dose heparin $n=102$	Low-dose heparin/stockings $n=94$
Operation cancelled	0	2
Informed consent withdrawn	3	2
Clerical errors*	8	2
Pre-operative death	1	0
Incorrect drug administration	0	2
Patients left for evaluation	90	86

* Incomplete observation due to lack of sufficient fibrinogen scans: one patient developed emboli in the femoral artery, one patient fractured the neck of the femur, one patient was allergic to iodine, one received no fibrinogen pre-operatively, two patients were not scanned despite correct allocation and the scanner broke down during the admission of two patients. Two patients (one in each group) had no phlebography or lung scintigraphy performed despite positive fibrinogen uptake test

Table 2 *Patient characteristics*

	Low-dose heparin	Low-dose heparin/stockings
Male/female ratio	47/43	58/28
Median age and range (years)	59 (40–87)	61 (36–90)
Median duration of operation and range (h)	$2\frac{1}{2}$ ($\frac{3}{4}$–7)	$2\frac{3}{4}$ (1–8)
Biliary tract surgery, *n*	22	19
Gastric surgery, *n*	24	16
Pancreatic surgery, *n*	1	5
Colorectal surgery, *n*	37	40
Miscellaneous, *n*	6	6
Total	90	86

Discussion

The pathogenesis of postoperative thromboembolism is multifactorial, and it is still unknown whether intra- and postoperative changes in the haemostatic system or stasis in the lower extremities are more important. Low-dose heparin has been shown to lower the incidence of fatal pulmonary embolism[7] but some patients die from this complication despite heparin prophylaxis. Graded elastic compression stockings increase the venous blood flow velocity, not only in the legs but also in the pelvic veins and the inferior vena cava[8]. In our investigation the combination of stockings and low-dose heparin was superior to low-dose heparin alone in the prevention of thromboembolic complications following major abdominal surgery. This confirms the findings of Törngren[4] who used the stocking on one leg only. Deep venous thrombosis was not diagnosed in 5 cases of the 8 patients with pulmonary embolism. In 3 cases phlebography could not be performed or read due to technical problems, and phlebograms were normal in the last 2 patients. Whether this was due to inadequate visualization problems of veins by phlebography or lack of specificity of the pulmonary scintigrams we cannot tell, but we feel that pulmonary perfusion/ventilation scintigraphy and phlebography are the best available methods for diagnosing thromboembolism.

Most of the thromboembolic complications in our study were subclinical and only one pulmonary embolus was fatal. The clinical relevance of preventing subclinical episodes can be debated. As fatal pulmonary embolism, however, often occurs in patients without signs of deep venous thrombosis, and as it is known that even minor venous thrombosis from the calf can embolize[9] we believe that the prevention of even minor subclinical venous thrombosis is important. Furthermore all patients having thromboembolism diagnosed commenced anticoagulant treatment immediately and this perhaps explains why they remained without symptoms.

About one-third of the patients were discharged before the 7 day observation could be completed. These patients had mostly simple cholecystectomies and vagotomies, and as 85 per cent of the thromboembolic complications were diagnosed within the first 3 postoperative days we do not feel that the shorter observation period for these patients can have any influence on the final results. There were significantly more men in the combination-therapy group. Of the men in the investigation 9 per cent developed thromboembolism compared with 6 per cent of the women. This difference was not significant and we doubt that the skew in the sex-distribution can substantially modify our conclusion.

The graded compression stockings were well tolerated by the patients. The combination of these stockings and low-dose

Table 3 *Thromboembolic complications*

	Low-dose heparin	Low-dose heparin/stockings	Significance
Abnormal fibrinogen uptake test	12 (13 per cent)	5 (6 per cent)	n.s.
Deep venous thrombosis*	7 (8 per cent)	1 (1 per cent)	$P<0.05$
Pulmonary embolism†	6 (7 per cent)	2 (2 per cent)	n.s.
Thromboembolism‡	11 (12 per cent)	2 (2 per cent)	$P<0.05$
Fatal pulmonary embolism	1 (1 per cent)	0 (0 per cent)	n.s.

* Phlebographycally verified. † Verified at pulmonary scintigraphy or autopsy. ‡ Thromboembolism defined as deep venous thrombosis, pulmonary embolism or both

heparin in a superior method of prophylaxis of thromboembolic complications following major abdominal surgery.

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