Prevention of thrombosis after hip arthroplasty

A prospective study of preoperative oral anticoagulants

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A prospective randomized study involving 101 patients undergoing total hip replacement was performed to find out whether prophylactic anticoagulation starting 4 days before the operation was more effective than starting on the eve of the operation. The postoperative level of anticoagulation was set at an INR of 2.1. There was no difference between the two groups in the incidence of proximal localized deep venous thrombosis. Blood loss did not depend on the level of peroperative anticoagulation. There were no postoperative hemorrhagic complications. No fatal pulmonary embolism occurred during the study. After discontinuation of the oral anticoagulants because of a negative venogram, nonfatal pulmonary embolism occurred in 3 out of 55 patients. A plea is made for low-dose anticoagulation for 3 months after total hip arthroplasty.

In our department, we used oral anticoagulants in hip surgery starting on the eve of the operation aiming at a Thrombotest level of 15 percent (INR 2.1). However, a pilot study with the aid of radionuclide venography revealed deep venous thrombosis in 1 out of 3 patients. After disappointing results of adding dextran infusions to this regimen to improve peroperative protection (Swierstra et al. 1984), we decided to investigate whether the high incidence of thromboembolic complications after elective total hip replacement could be reduced by earlier preoperative anticoagulation. A further part of the protocol was the use of low-dose postoperative anticoagulation to exclude hemorrhagic problems.

Patients and methods

The study concerned consecutive patients admitted for an elective, primary total hip replacement. Reasons to exclude patients were contraindications for oral anticoagulation and a second operation within the period of the study. Recorded data included age, sex, height, weight, and factors known to be associated with the occurrence of deep venous thrombosis in a positive or negative way (previous periods of thromboembolic disease, varicosis, diabetes, rheumatoid arthritis, use of nonsteroidal anti-inflammatory drugs).

Table 1. Clinical data for 101 randomized patients, who completed the study. The duration of preoperative anticoagulation was A 1 day or B 4 days

	Group A	Group B
Total number	51	50
women	44	37
men	7	13
Age, years (SD)	66 (10)	66 (11)
Weight, kg (SD)	67 (10)	69 (9)
Heigth, cm (SD)	166 (8)	167 (10)
Risk factors		
thromboembolic history	6	7
varicosis	7	5
diabetes	4	2
rheumatoid arthritis	8	6
NSAID[a]	22	17
adipositas[b]	7	6
Anesthesia time, min (SD)	175 (27)	178 (34)
Operation time, min (SD)	141 (25)	140 (32)

[a] Nonsteroidal anti-inflammatory drug.
[b] Weight–height +100 > 10.
No significant differences.

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In all, 131 patients were admitted for an operation. Thirty patients were excluded before randomization or during the study. The patients were divided at random into two groups. Both groups were identical regarding clinical data (Table 1). The prophylactic regimen (Table 2) in Group A was similar to our former regimen, and so this group acted as a control group. In Group B, oral anticoagulation was started 4 days preoperatively, aiming at a Thrombotest of 25–30 percent during the operation (INR 1.5–1.6). In both groups the postoperative Thrombotest level was set at 15 percent (INR 2.1). An anticoagulant unit was responsible for the anticoagulation throughout the study.

All the patients underwent a Charnley arthroplasty. The operations were performed through a lateral approach including a trochanter osteotomy. The wound was drained by two subfascial and one subcutaneous vacuum drains for 2 days. The patients were mobilized after the third postoperative day with crutches and minimal weight bearing.

Venous thrombosis was diagnosed on the basis of radionuclide venography with ^{99m}Tc-labeled macroaggregates of albumin, performed about 10 days after the operation. The presence or absence of hot spots after 20 min was the most important criterion for the diagnosis. The venograms were assessed independently by 3 observers for thrombosis in the calf or in the more proximal regions. Because of the limited reliability of radionuclide venography for calf vein thrombosis, only the incidence of proximal – localized in the popliteal and/or femoral and/or iliac vein – thrombosis will be given. Deep venous thrombosis was diagnosed when two or three positive assessments were made by the observers. The interobserver agreement was good, with kappa values between 0.75 and 0.88.

Peroperative blood loss was assessed by the amount of blood in the suction apparatus and the weight of the gauzes. Postoperative blood loss was estimated by the contents of the drain bottles. The number of blood transfusions during and after the operation was recorded.

The Mann-Whitney *U*-test and the chi-square test were used to compare the two independent groups. Multiple regression and Fisher linear discriminant analysis were used to investigate multivariate relationships.

Table 2. Thrombosis prophylaxis regimens

Group A		
day	−1	3 mg acenocoumarol
	0	3 mg acenocoumarol
	1 etc	dose acenocoumarol based on Thrombotest, target value 15 percent
Group B		
day	−4	3 mg acenocoumarol
	−3	3 mg acenocoumarol
	−2	dose acenocoumarol based on Thrombotest, aiming at 25–30 percent during operation
	−1	idem
	0	dose acenocoumarol based on Thrombotest, target value 15 percent

Acenocoumarol = SintromMitis®.
Day 0 = day of operation.

Table 3. Thrombotest during operation in Group B

Thrombotest (percent)	Number of patients
> 35	9
31–35	6
25–30[a]	18
20–24	11
15–19	4
< 15	2

[a] Target values.

Results

Anticoagulation. In Group B the Thrombotest during operation was 30 percent or less in 35/50 patients (Table 3). After the operation the Thrombotest was not always inside the desired range (Figures 1 and 2). Therefore, a separation was made arbitrarily between patients with a satisfactory and patients with an insufficient level of postoperative anticoagulation. The anticoagulation level was defined to be satisfactory when at least two thirds of the Thrombotest values on the second up to and including the tenth postoperative day were less than 20 percent. An identical number of patients in both groups turned out to have satisfactory anticoagulation levels (Figures 3 and 4).

Proximal thrombosis. No difference in the incidence of proximal thrombosis could be found between groups. A tendency towards reduction of the incidence in Group B existed only in combination with a satisfactory anticoagulation level (Table 4). During further statistical analysis, no

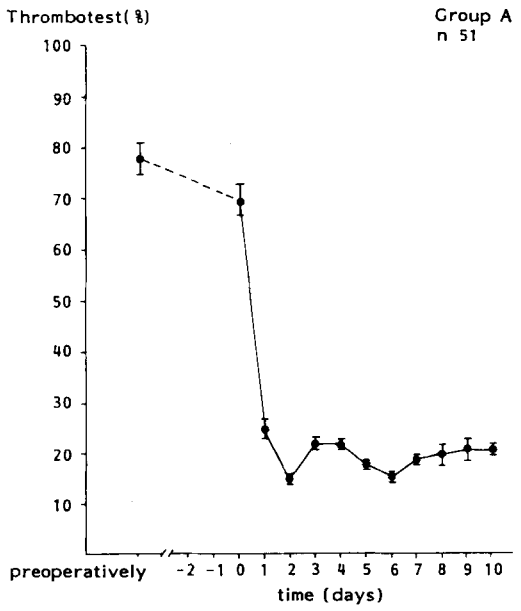

Figure 1. Mean Thrombotest (± SEM) of the patients in Group A.

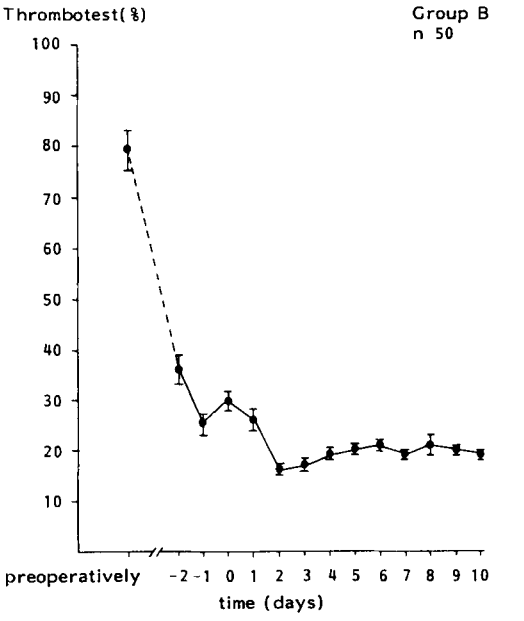

Figure 2. Mean Thrombotest (± SEM) of the patients in Group B.

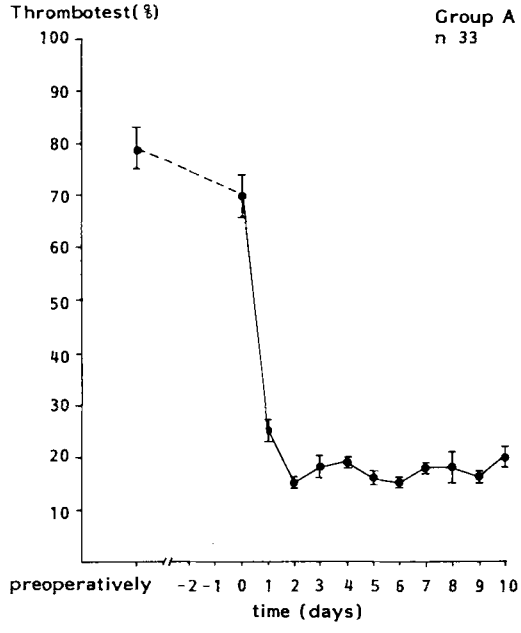

Figure 3. Mean Thrombotest (± SEM) of the patients in Group A with a satisfactory postoperative anticoagulation level.

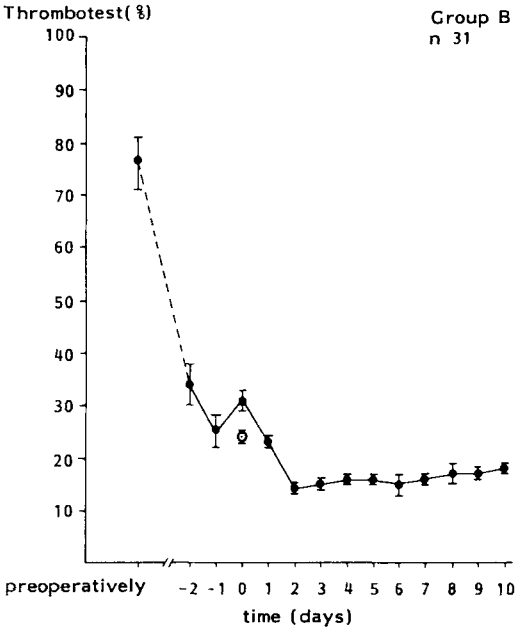

Figure 4. Mean Thrombotest (± SEM) of the patients in Group B with a satisfactory postoperative anticoagulation level. ⊙ Mean Thrombotest (± SEM) of the patients with a perioperative value ≤ 30% as well (n 22).

relationship could be revealed between the development of proximal thrombosis and the Thrombotest during operation, the clinical characteristics as presented in Table 1, blood loss, number of blood transfusions, or site of operation.

Pulmonary embolism. Fatal pulmonary embolism did not occur during the study. Fifty-five patients showed no thrombosis on their venograms, neither in the calf nor proximally, and oral anticoagulation was discontinued on discharge from the hospital. In 3 of these patients, nonfatal pulmonary embolism diagnosed by scintigraphy occurred later.

Blood loss. The blood loss during and after the operation was similar in both groups (Table 5). There was no statistical relationship to the level of anticoagulation during and after the operation. The number of blood transfusions was also identical in both groups. Bleeding complications (as a result of too intensive anticoagulation) did not occur during the postoperative period.

Table 4. Proximal thrombosis

	Total	Thrombosis
Group A	51	11
Group A[b]	33	8
Group B	50	12
Group B[a]	35	7
Group B[b]	31	5
Group B[ab]	22	3

[a] Peroperative Thrombotest ≤ 30 percent.
[b] Satisfactory postoperative anticoagulation level.
No significant differences.

Table 5. Blood loss during and after operation. L (SD)

	Number of patients	Peroperatively	Postoperatively
Group A	51	1.21 (0.63)	0.58 (0.33)
Group B	50	1.11 (0.52)	0.60 (0.41)
Group B[a]	35	1.19 (0.58)	0.66 (0.46)

[a] Peroperative Thrombotest ≤ 30 percent.
No significant differences.

Discussion

In this study the incidence of proximal thrombosis after elective total hip replacement could not be reduced by preoperative anticoagulation. A tendency towards reduction in Group B appeared only in combination with a satisfactory level of postoperative anticoagulation. A possible explanation can be given when comparing Figures 3 and 4. In Group A a transient elevation of the Thrombotest appeared during the thrombogenetically important first postoperative days. In addition, the Thrombotest value during the first days of anticoagulation is mainly the result of a decrease in factor VII, whereas the full antithrombotic effect may be delayed until the other vitamin K-dependent factors are sufficiently decreased. In individual cases, this can have led to insufficient protection.

Our results are less favourable than those of Francis et al. (1983), who found a proximal thrombus in only 1 out of 53 patients after preoperative anticoagulation. However, they applied another detection method (radiocontrast phlebography) before the end of the first week. Further, these authors aimed at a more intensive anticoagulation (INR 2.7); they described two bleeding complications, and each was associated with an excessively prolonged prothrombin time. Sevitt and Innes (1964) showed that more intensive anticoagulation was accompanied by more hemorrhagic problems. This has been confirmed more recently by Hull et al. (1982), who found a mean INR of 2.1 to be equally successful as a mean INR of 3.7 in preventing rethrombosis during long-term anticoagulation, coupled with a strong reduction of bleeding complications. We showed that low-dose anticoagulation administered by an anticoagulant unit is able to avoid these complications in hip surgery.

An important finding in our study was the occurrence of nonfatal pulmonary embolism after discontinuation of the oral anticoagulants after a negative venogram. This points out a delayed onset of the thrombosis, which has also been described under other prophylactic regimens, i.e., subcutaneous heparin (Hampson et al. 1974), intermittent pneumatic compression (Sikorski et al. 1981), heparin-dihydroergotamine (Kakkar et al. 1985).

At the moment, no prophylactic method really prevents deep venous thrombosis in hip surgery. Hence, we suggest that oral anticoagulation be continued for 3 months in all patients after total

hip replacement. There is now evidence that a sensitive control technique in combination with an international normalized ratio of 2.0–2.5 is safe and efficient in venous thrombosis (Poller 1985). We are well aware that such a regimen can only be fully implemented in countries with a well-functioning thrombosis service, like the Netherlands.

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