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Preoperative Identification of Patients at High Risk of Deep Venous Thrombosis Despite Prophylaxis in Total Hip Replacement

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Key words

Predictive index – Deep vein thrombosis – Total hip replacement – Surgery

Summary

Clinical and laboratory variables were measured on the day before operation in 111 patients who underwent total hip replacement prophylactically treated with acetylsalicilic acid or heparin-dihydroergotamine. Postoperative deep vein thrombosis (DVT) was deteced in 16 patients by ascending venography. Stepwise logistic discriminant analysis was used to identify DVT predicting factors. Three such factors, fibrinogen degradation products (FDP), plasminogen activator inhibitor (PA-inhibitor) and tissue type plasminogen activator (t-PA), were found to be significantly associated with DVT and were used to construct a predictive index. The predictive index, $I = -2.09 + 0.46$ (FDP) $+1.39$ (PA-inhibitor) -0.24 (t-PA), was 100% sensitive and 95% specific in the prediction of DVT. This index would allow for identification of those patients in whom routine prophylaxis would be sufficient and for selecting those in whom more effective prophylactic regimens would be necessary.

Introduction

The incidence of postoperative deep venous thrombosis (DVT) in hip surgery has been found to vary between 30 and 60 percent when ^{125}I-fibrinogen scanning or phlebography are used (1, 2). Pulmonary emboli still constitute a fatal complication in spite of prophylactic measures. It would, however, be helpful if patients at high risk of DVT could be identified preoperatively for selective prophylaxis. Many attempts have been made to establish different parameters for predicting the development of thrombosis (3–5) but difficulties have arisen in the elaboration of a prognostic index for application to patients undergoing hip surgery.

The aim of our study was to identify a predictive index of thromboembolism after total hip replacement by means of certain clinical and laboratory preoperative variables in patients given acetylsalicilic acid or heparin plus dihydroergotamine prophylaxis.

Patients, Materials and Methods

Patients

One hundred and eleven patients over 40 years undergoing total hip replacement were studied. All patients were hospitalized one day before the operation. Informed consent was obtained. Patients with bleeding disorders, on drugs interfering with haemostasis, previous pulmonary emboli, history suggestive of peptic ulcer or sensitivity to salicilates were excluded. Age, sex, overweight percentage, previous deep venous thrombosis, varicose veins, repeated surgery, heart disease, length of operation and malignancy were recorded before surgery in all cases.

Patients admitted to the trial were randomly allocated to one of the two treatment groups: Acetylsalicilic acid (ASA group) or dihydroergotamine-heparin (DHE-hep group).

Patients in the ASA group received 0.5 g acetylsalicilic acid twice daily orally or intramuscularly, starting 12 h preoperatively until the seventh postoperative day. Patients in the DHE-hep group received a combination of 5,000 IU sodium heparin plus 0.5 mg dihydroergotamine s. c., starting 2 h before operation and subsequently every 12 h during at least 7 postoperative days.

Methods

The ^{125}I-fibrinogen uptake test, as previously described (6), was used for diagnosis of DVT. Ascending phlebography was performed in those patients showing postive ^{125}I-fibrinogen test. Leg scanning and phlebography were interpreted by independent observers without knowledge of each other's results. The patient's treatment group was also unknown.

Blood samples were drawn on the day before surgery. Platelet count, platelet-crit, mean platelet volume (MPV), circulating platelet aggregates, platelet factor 4 (PF4), β-thromboglobulin (β-TG), fibrinogen, Xa, VIII : C, antithrombin III (AT III), fibrin monomers, euglobulin lysis time (ELT), fibrinogen degradation products (FDP), α_2-antiplasmin, tissue-type plasminogen activator (t-PA) antigen and plasminogen activator inhibitor (PA-inhibitor) were determined as previously described (7–9).

Data were statistically analyzed by using mean values, standard deviations, Student's t-test and chi square test. The BMDP7M-program for stepwise discriminant analysis was used to find out which factors influence the occurrence of DVT (10).

Results

One hundred and eleven patients were included in the analysis. No patients showed evidence of DVT before surgery. Fifty-six patients were assigned to the DHE-hep group and 55 patients to the ASA group. Results of preoperative clinical and analytical parameters studied were similar in both groups (data not shown). After surgery 20 out of 111 patients developed isotopic evidence of DVT, which was confirmed by ascending venography in 16. Twelve of these (21.4%) were in the DHE-group and 4 (7.2%) in the ASA group and thus a statistically significant difference was observed ($p < 0.05$). Clinical data and results of preoperative hemostasis analyses on the 95 patients without postoperative DVT and the 16 with DVT are shown in Table 1. Only five of the twenty-five preoperative measurements showed a significant correlation with DVT after surgery.

Preoperative variables with the best chance of being useful in distinguishing the positive and negative groups, listed in descending order were as follows: FDP ($p < 0.0001$), PA-inhibitor ($p < 0.0001$), t-PA ($p = 0.0095$), ELT ($p = 0.01$) and PF4 ($p = 0.021$). FDP, PA-inhibitor and t-PA were found to be the best

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Table 1 Results of preoperative clinical and hemostasis analysis

Variable	DVT (n = 16)	No DTV (n = 95)	p
Age (years)	61,5±5	61±10	NS
Male/female	6/10	50/45	NS
Overweight for height	8±9	8±9	NS
Previous DVT (%)	0	6	NS
Presence of varicose veins (%)	31	27	NS
Repeated surgery (%)	21	17	NS
Heart disease (%)	18	11	NS
Duration of surgery >3 h (%)	6	2	NS
Malignant disease (%)	0	1	NS
Platelet count ($x10^9$/l)	314±73	330±103	NS
Platelet crit (%)	0.29±0.03	0.28±0.08	NS
MPV (fl)	8.8±0.8	8.9±1.4	NS
Platelet aggregate (ratio)	0.96±0.11	0.95±0.18	NS
PF4 (ng/ml)	13±7	21±14	0.021
β-TG (ng/ml)	38±15	47±28	NS
Fibrinogen (mg/dl)	282±62	286±80	NS
Factor Xa (%)	99±17	103±15	NS
Factor VIII: (%)	125±30	125±62	NS
AT III (%)	99±28	106±32	NS
Fibrin monomers (μg/ml)	16±11	17±14	NS
ELT (min)	277±48	334±85	0.010
FDP (μg/ml)	4.9±2.0	1.5±1.4	<0.0001
α_2-Antiplasmin (%)	114±28	111±34	NS
t-PA (ng/ml)	6.7±2.8	8.3±2.1	0.0095
PA-inhibitor (U/ml)	3.4±0.4	2.0±0.6	<0.0001

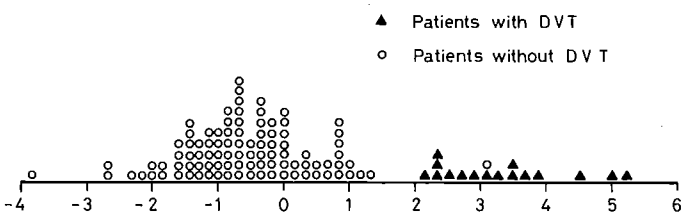

Fig. 1 Prognostic index for deep vein thrombosis (DVT)

variables for predicting DVT. Proceeding in stepwise fashion, no other variable significantly increased the prognostic power, so the prognostic index was restricted to these three variables.

The predictive index based on the variables as estimated from observations made on the 111 patients is given in the following equation:

$I = -2.09 + 0.46\,(a) + 1.39\,(b) - 0.24\,(c)$

where, I = risk score for DVT; a = FDP (μg/ml); b = PA-inhibitor (U/ml); c = t-PA antigen (ng/ml).

Large positive values of I are associated with a high DVT risk and large negative scores are associated with a low risk (Figure 1). When the cut-off point was arbitrarily taken at I = +1, the predictive index had correctly identified 100% of patients (sensitivity 100%) who had postoperative DVT, and wrongly allocated 5 patients (5%, specificity 95%) without DVT to the high-risk group. When the cut-off was taken at I = +2 the predictive index had correctly identified 100% of patients who had postoperative DVT and wrongly allocated 1 patient (1%, specificity 99%) without.

Discussion

Whereas in general surgical patients, postoperative DVT can be predicted by using different indexes (3–5, 11, 12), no information concerning the preoperative prediction of DVT in patients undergoing total hip replacement is available, in spite of its being the surgical procedure with the highest documented incidence of thromboembolic complications (1, 2). Despite prophylaxis there is still a relatively larger number of cases of thromboembolism. Our present data indicate that several clinical or analytical variables are useful even when prophylactic regimens with aspirin or DHE-Hep are used. One interesting finding was that a combination of these variables allowed us to formulate a prognostic index for the prediction of DVT under prophylaxis in an individual patient. Patients undergoing total hip replacement in whom simple prophylaxis with aspirin or DHE-Hep is insufficient can be identified.

Using a stepwise discriminant analysis, FDP, PA-inhibitor and t-PA antigen were the variables which contributed most to the prediction of DVT, suggesting an important role for the fibrinolytic system. Various studies have shown that a relationship exists between different pre- and postoperative fibrinolytic parameters and the development of DVT but in general non-specific methods were used (13, 14). Our index was mainly constructed on the basis of recent methods for t-PA and PA-inhibitor and has a 100% sensitivity for correctly predicting patients with postoperative DVT.

A further prospective evaluation using a new group of patients undergoing elective total hip replacement is required in order to confirm the validity of this predictive index. Since fibrinogen scans may miss some cases of DVT limited to the femoral veins (15), the application of this predictive index in patients in whom routine venography is to be performed would be necessary. Nevertheless, this index has considerable promise for identification of those patients in whom routine prophylaxis would be sufficient and for selecting those in whom more efficacious prophylactic regimens would be necessary.

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References

1 Nillius A S, Nylander G. Deep vein thrombosis after total hip replacement: A clinical and phlebographic study. Br J Surg 1979; 66: 324–6.
2 Sikorski J M, Hampson W G, Staddon G E. The natural history and etiology of deep vein thrombosis after total hip replacement. J Bone Joint Surg 1981; 63B: 171–7.
3 Clayton J K, Anderson J A, McNicol G P. Preoperative prediction of postoperative deep vein thrombosis. Br Med J 1976; 2: 910–1.
4 Lowe G D O, Osborne D H, McArdle B M et al. Prediction and selective prophylaxis of venous thrombosis in elective gastrointestinal surgery. Lancet 1982; 1: 409–12.
5 Sue-Ling H M, Johnston D, McMahon M J, Philips P R, Davies J A. Pre-operative identification of patients at high risk of deep venous thrombosis after elective major abdominal surgery. Lancet 1986; 1: 1173–6.
6 Alfaro M J, Páramo J A, Rocha E. Prophylaxis of thromboembolic disease and platelet related changes following total hip replacement: A comparative study of aspirin and heparin-dihydroergotamine. Thromb Haemostas 1986; 56: 53–6.
7 Páramo J A, Rocha E. Changes in coagulation and fibrinolysis after total hip replacement and their relations with deep vein thrombosis. Haemostasis 1985; 15: 345–52.
8 Páramo J A, Rocha E. Deep vein thrombosis and related platelet changes after total hip replacement. Haemostasis 1985; 15: 389–94.
9 Páramo J A, Alfaro M J, Rocha E. Postoperative changes in the plasmatic levels of tissue-type plasminogen activator and its fast-acting inhibitor. Relationship to deep vein thrombosis and influence of prophylaxis. Thromb Haemostas 1985; 54: 713–6.
10 BMDP statistical software, University of California Press, Berkeley 1981.

11 Kjaergaard J, Esbensen K, Wille-Jørgensen P et al. A multivariate pattern recognition study of risk-factors indicating postoperative thromboembolism despite low-dose heparin in major abdominal surgery. Thromb Haemostas 1985; 54: 409–12.
12 Veth G, Meuwissen O J A Th, Van Houwelingen H C, Sixma J J. Prevention of postoperative deep vein thrombosis by a combination of subcutaneous heparin with subcutaneous dihydroergotamine or oral sulphinpyrazone. Thromb Haemostas 1985; 54: 570–3.
13 Sautter R D, Myers W O, Ray III J F, Wenzel F J. Relationship of the fibrinolytic system to postoperative thrombotic phenomena. Arch Surg 1973; 107: 292–6.
14 Knight M T N, Dawson R, Melrose D G. Fibrinolytic response to surgery. Labile and stable patterns and their relevance to postoperative deep vein thrombosis. Lancet 1977; 1: 370–3.
15 Turpie A, Levine M N, Hirsh J et al. A randomized controlled trial of low-molecular-weight heparin (enoxaparin) to prevent deep-vein thrombosis in patients undergoing elective hip surgery. N Eng J Med 1986; 315: 925–9.

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