concentrations of nifuratel obtained in the urine of treated subjects, so that the significance of our MIC findings for clinical practice is difficult to assess. The MICs of nifuratel of the three strains that were successfully eradicated from our patients were: 10 mg/l (*C albicans*), 25 mg/l (*C tropicalis*), and 50 mg/l (*C stellatoidea*). Most of the strains tested by us have had MICs in this range.

It seems reasonable to consider nifuratel as a possible choice for treating candidal urinary tract infection when the infection is thought to merit chemotherapy.

We are grateful to our colleagues, Mr D R Davies, Mr E Kirwan, and Professor A N Exton-Smith, for permission to treat patients under their care. Dr E Letley of Calmic Ltd and Dr A Salter of the Wellcome Foundation kindly supplied nifuratel tablets and powder. We are grateful for the meticulous care in specimen collection and follow-up shown by the nurses tending these patients.

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Preoperative prediction of postoperative deep vein thrombosis

J K CLAYTON,   J A ANDERSON,   G P McNICOL

Summary

A range of clinical data was obtained from 124 patients about to undergo operation and several coagulation tests were performed. No patient received prophylaxis for deep vein thrombosis, and isotopic scanning after operation showed that 20 patients had developed thrombosis. A simple prognostic index for predicting which patients would develop postoperative deep vein thrombosis was constructed using the clinical and coagulation data obtained before operation. The five variables with the best predictive power—euglobulin lysis time, age, presence of varicose veins, fibrin related antigen, and percentage overweight—produced an equation that identified 95% of those who developed deep vein thrombosis and misallocated only 28% of those who did not develop thrombosis. In view of the complications that low-dose heparin and dextran can cause, giving prophylaxis to under a third of the patients who will not develop deep vein thrombosis is clearly better than giving it to all.

Introduction

Recently impressive evidence has accumulated that the incidence of postoperative deep vein thrombosis can be reduced by prophylactic measures, particularly low-dose heparin and perioperative dextran 70.[1] [2] Both low-dose heparin and dextran may, however, significantly increase bleeding problems at the time of surgery,[3] [4] and our object was to try to identify before operation those patients particularly at risk of deep vein thrombosis in the hope that in future it would be unnecessary to give prophylactic treatment to patients in a low-risk group.

Patients and methods

One hundred and twenty-four patients undergoing major gynaecological surgery, both abdominal and vaginal, were investigated. The following clinical data were obtained: age; weight; height; length of stay in hospital before operation; preoperative haemoglobin level; smoking habits; presence of varicose veins on clinical examination; history of venous thromboembolic disease; the nature of the operation; and whether surgery was for benign or malignant disease.

Laboratory methods—Platelets were measured on a Coulter thrombocounter. Platelet factor III release was measured by the method of Spaet and Cintron,[5] fibrinogen by the method of Ratnoff and Menzie,[6] antithrombin III by the method of Howie et al,[7] factor VIII by a one-stage method of Breckenridge and Ratnoff,[8] euglobulin lysis time by the method of Nilsson and Olow,[9] serum fibrin related antigen (FR antigen) by the method of Merskey et al,[10] plasminogen by the method of Alkjaersig et al,[11] antiplasmin by the method of Howie et al,[12] activated partial thromboplastin time by the method of Langdell et al,[13] and thrombin time by the method of Eichelberger.[14] Platelet aggregation was measured to adenosine diphosphate (ADP) 1 μmol/l, 4 μmol/l, and 10 μmol/l; to collagen; and to adrenaline by the aggregometer method of Born and Cross.[15]

Diagnosis of deep vein thrombosis—All patients underwent preoperative isotropic scanning of the legs using the ^{125}I-fibrinogen technique with the criteria of Kakkar.[16] Routine postoperative scanning was performed on the first, third, and sixth days unless a significantly high count was obtained when daily scanning was started. None of the patients had received specific prophylaxis for deep vein thrombosis.

Results and comment

No patients had evidence of deep vein thrombosis before surgery. After operation 20 of the 124 patients developed isotopic evidence of deep vein thrombosis, which was confirmed by ascending venography in all of the 18 in whom this procedure was performed.

Clinical and coagulation data on the 104 patients without deep vein thrombosis after operation and the 20 with deep vein thrombosis are shown in the table.

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STATISTICAL ANALYSIS

The object of the statistical analysis was to produce a simple prognostic index that could be applied preoperatively to indicate those patients with a high chance of developing deep vein thrombosis. The 10 variables available preoperatively with the best chance of being useful in distinguishing between the positive and negative groups were (see table): (1) fibrinogen; (2) factor VIII; (3) euglobulin lysis time; (4) FR antigen; (5) age; (6) length of preoperative stay; (7) percentage overweight for height;[17] (8) presence of varicose veins; (9) cigarette smoking habits, recorded as "Yes" or "No" for the month before surgery; and (10) benign or malignant disease, as confirmed by postoperative histology. Variables 8 and 9 were scored 0 for absence and 1 for presence. Variable 10 was scored 0 for benign and 1 for malignant. Subsequently, x_1 represents the value taken by variable 1, x_2 the value taken by variable 2, and so on.

Significant preoperative clinical and coagulation data

Preoperative data	Postoperative leg scan	
	Positive (n = 20)	Negative (n = 104)
Clinical data		
Age (years)	58 ± 3	44 ± 2
% Overweight for height	13 ± 3	5 ± 1
Preoperative stay (days)	4 ± 1	2 ± 0·5
Cigarette smoking (% of group)	25	48
Presence of varicose veins (% of group)	45	20
Malignant disease (% of group)	20	1
Coagulation data		
Fibrinogen (g/l)	3·33 ± 0·13	2·96 ± 0·09
Factor VIII (% of normal)	127 ± 7	107 ± 3
Euglobulin lysis time (min)	412 ± 29	270 ± 14
Serum FR antigen (mg/l)	9 ± 1	5 ± 1

Linear prognostic and diagnostic indices have been used successfully,[18 19] and we selected this approach for the present study. The method of logistic discrimination[19] was used to estimate the coefficients of the prognostic index, I. All the above variables could have been fed into the system, but instead a more informative, stepwise approach was taken. The best single variable for prediction was found to be variable 3, euglobulin lysis time. Then the variable that added most to the prediction power of variable 3 was found to be variable 5, age. Proceeding in this stepwise fashion, variables 8, 4, and 7 (varicose veins, FR antigen, and percentage overweight for height) were added sequentially, in that order. No other variable significantly increased the prognostic power so we decided to restrict the prognostic index to these five variables. In all cases the statistical criterion used was a log-likelihood ratio test. The prognostic index based on these five variables as estimated from the observations of the 124 patients in the study is given in the following equation:

$$I = 11·3 + 0·0090x_3 + 0·22x_4 + 0·085x_5 + 0·043x_7 + 2·19x_8.$$

Large positive values of I are associated with a high risk of developing deep vein thrombosis and large negative values are associated with a low risk. Small values of I are equivocal.

This analysis does not imply that the variables not included in the equation are not prognostic for deep vein thrombosis. Rather, it means that after the information in the equation has been taken the remaining variables are redundant because they do not add anything further to the prognosis.

To find the value of the index, I, for a patient, the values of the five variables (3, 4, 5, 7, and 8) were substituted into the equation. The values of I for the 124 patients in the study are presented in the figure. Clearly, patients with and without deep vein thrombosis were well separated. Nevertheless, there was inevitably a "grey" zone where

prediction was less certain. When the cut-off point was taken at I = 0, 11 of the patients who developed deep vein thrombosis were correctly predicted, while two patients without deep vein thrombosis were incorrectly allocated. When the cut-off point was taken at −2·5 all but one of the positive patients were correctly allocated but the number of patients without deep vein thrombosis who were incorrectly identified rose to 29.

Discussion

Our results show that, by using three pieces of simple clinical information and the results of two laboratory tests, acceptable preoperative prediction of postoperative deep vein thrombosis is possible. Depending on the balance of importance attached to giving unnecessary prophylaxis to patients with a low risk of developing deep vein thrombosis and not treating patients with a high risk, a point on the scale can be selected to determine which patients should receive prophylactic treatment. At present the balance of benefit might suggest a cut-off point at −2·5, which would identify 95% of patients who will develop deep vein thrombosis, at the expense of unnecessarily treating 28% of those who will not. This is clearly a vast improvement on the outcome of routine universal prophylaxis—that is, the "unnecessary" treatment of all patients who will not develop deep vein thrombosis.

The data suggest that the addition of the laboratory data improved the separation and justified the extra effort needed.

Before the isotopic technique for diagnosing deep vein thrombosis became available, Hume and Chan[20] compared the results of several haematological tests performed postoperatively in 29 patients who had clinical evidence of postoperative deep vein thrombosis with those in a control group of preoperative patients. Using a stepwise discriminant analysis, they derived a discriminant function from platelet adhesiveness, packed cell volume, and partial thromboplastin time. Later Hume et al,[21] with a computer programme analysing clinical data, Doppler flowmeter assessment, a small panel of laboratory test results, and venography, correctly diagnosed thrombosis in 88% of the patients studied only after operation.

These studies from Hume and his associates differ from ours in that our prediction and classification was based on preoperative data in patients confirmed not to have deep vein thrombosis before surgery. Laboratory test results in blood taken after thrombosis have occurred may be a consequence of thrombosis or of surgery rather than related to predisposition to deep vein thrombosis.

Our approach is inevitably somewhat biased towards favourable results—the index was derived from our own patients and then reapplied to them—and it is essential to carry out a prospective study to examine the performance of the method with the same equation when applied to a new population of patients. Nevertheless, this approach to the selection of high-risk patients has considerable promise.

Prognostic index (I) for deep vein thrombosis (DVT).

o Patients with DVT
▲ Patients without DVT

Prognostic index

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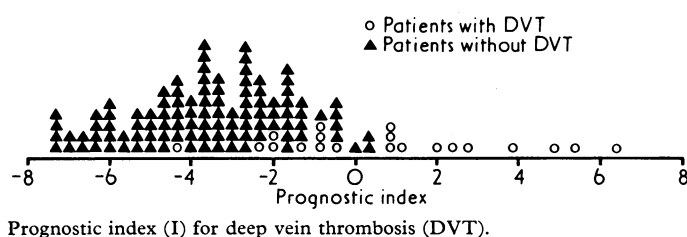
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Virus-like particles in paraspinal muscle in scoliosis

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Summary

Biopsy material from the skeletal muscle (paraxials) of 21 patients with scoliosis was examined by light and electron microscopy. Virus-like particles, 17 nm in diameter with a crystalline structure, were identified in the skeletal muscle fibres of four patients. Associated changes in the sarcoplasm included swelling of mitochondria, presence of lipid droplets, and vesicular structures. Serological studies and culture for virus isolation gave negative results. An excess of lipid (predominantly in type 1 fibres) was noted in the skeletal muscle of several other cases. The significance of these findings is obscure, but the morphology of the paraxial muscles of patients with scoliosis and controls is currently being investigated in greater detail.

Introduction

Idiopathic scoliosis is a crippling and distressing disorder of childhood, most cases occurring in young girls. Pathological studies of the musculoskeletal system have not succeeded in elucidating the cause of the condition.[1] Scoliosis secondary to neurological disease or myopathic processes is well recognised,[2] and it is therefore tempting to speculate that an undisclosed disorder affecting muscles of the spine might be responsible for causing the condition. Nevertheless, clinical[3] and traditional histological methods have failed to show any important abnormalities. Hirano[4] in an electronmicroscopical study has described degenerative changes in the back muscles of patients with idiopathic scoliosis. It was suggested on the basis of these findings that a myopathic process might be implicated in the aetiology of the condition.

Patients and methods

Through the kindness of colleagues at the Princess Margaret Rose Orthopaedic Hospital, Edinburgh, we have had the opportunity of examining biopsy specimens of skeletal muscle (taken from paraspinal muscles: rotators and multifidus) from 21 patients with scoliosis; 12 had idiopathic disease, seven had congenital scoliosis, and two had neurofibromatosis. At open exposure of the spine for intra-articular fusion, or at revision, blocks of muscle tissue were taken from each side from the deeper parts of the paraspinal muscles at the apex of the curve. Frozen sections were cut for histological and histochemical study, and 1-mm³ pieces of tissue were fixed in 2·5% buffered glutaraldehyde for electron microscopy.

Results

No definite histological abnormality was observed in the muscle on light microscopy and no appreciable changes were seen in the type 1 and type 2 fibres, as shown by the dihydronicotinamide adenine dinucleotide diaphorase and myosin adenosine triphosphatase (at pH 9·4) methods. In some cases a slight excess of intracellular lipid was noted, mainly in type 1 fibres. This was confirmed on electron microscopy (fig 1).

A wholly unexpected finding in four patients (see table) was the presence of virus-like particles within the muscle fibres (fig 2). They consisted of uniform electron-dense particles aggregated into a
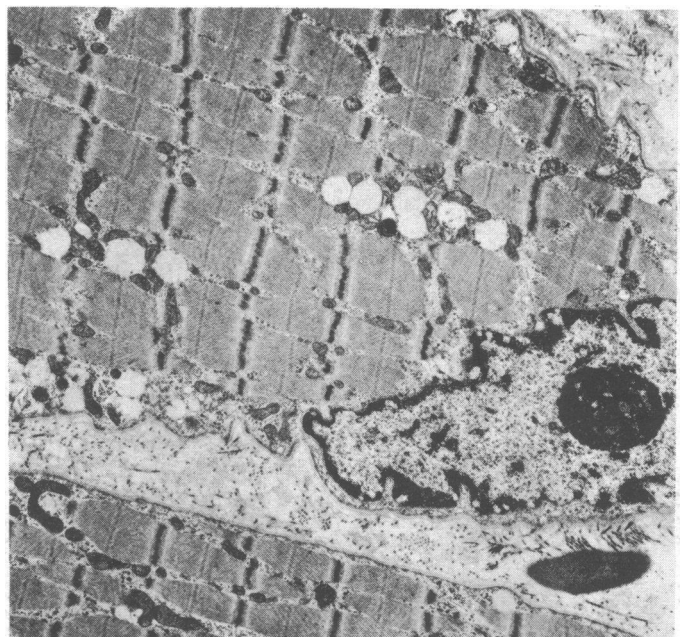
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FIG 1—Electron micrograph of skeletal muscle showing lipid droplets between myofibrils and beneath sarcolemmal membrane. (× 5957.)