CIRCULATION CLEARANCE RATE OF RADIOIODINE DURING FIBRINOGEN UPTAKE TESTS

J. G. Hardy and G. M. Newble

Essex County Hospital, Colchester, England

Scintillation counts, following administration of ^{125}I-labeled fibrinogen, were performed on the legs of medical and surgical patients. As part of the test procedure, precordial count rates were recorded and used in calculating the fibrinogen clearance rates. A short half-time for the circulating radioiodine was found to correlate well with the detection of venous thrombosis.

The diagnosis of venous thrombosis has proved difficult since the physical signs are notoriously unreliable (*1*). The diagnostic accuracy of the ^{125}I-labeled fibrinogen uptake test, however, is well established (*2*). In a recent study Browse et al (*3*) showed a clear connection between venous thrombosis, detected by fibrinogen uptake, and the incidence of pulmonary embolism.

The rate of ^{125}I-fibrinogen clearance from the circulation would be expected to be more rapid in patients undergoing active thrombus formation. By measuring the radioiodine concentrations of blood samples, this relationship has been established (*4,5*). The present study describes the calculation of the half-time of circulating radioiodine from precordial count rates.

MATERIALS AND METHODS

The patients were considered as two groups, medical and surgical. The 18 medical patients all exhibited physical signs that may have been indications of deep-vein thrombosis: for example, ankle edema, local leg tenderness, and positive Homans' sign. The 29 surgical patients underwent gynecologic operations, with the exception of one patient, who had a prostatectomy. All the surgical patients were considered to be "at risk," having severe varicose veins or a history of venous thrombosis or pulmonary embolism.

The technique employed was similar to that described by Evans and Negus (*2*). Each patient received an intravenous injection of 100 μCi of ^{125}I-human fibrinogen (Radiochemical Centre, Amersham, England). Thyroid uptake of the radioiodine was reduced by a daily oral dose of 120 mg of potassium iodide, begun before the ^{125}I-fibrinogen injection and continuing for 3 weeks. The equipment included a portable radiation monitor (MS-310 counter ratemeter, J & P Engineering, Reading)

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For reprints contact: J. G. Hardy, Essex County Hospital, Colchester, Essex CO3 3NB, England.

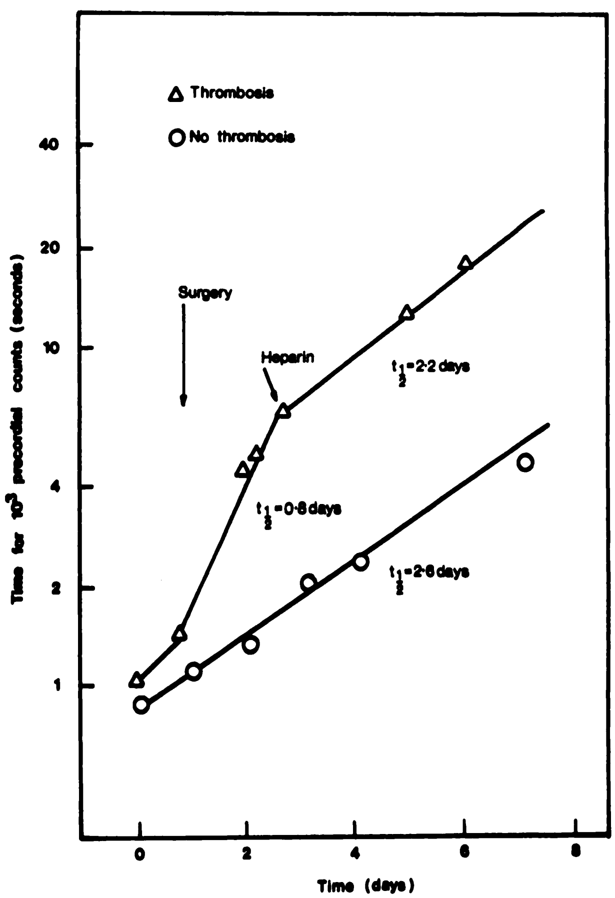

FIG. 1. Precordial counting times (per 1000 counts) during deep-vein thrombosis tests with ^{125}I-fibrinogen.

with a sodium iodide detector, 50 mm in diameter and 3 mm thick. The reliability of this instrument rendered recalibration unnecessary during individual patient studies; the chief source of error was in repositioning the detector over the counting sites.

The minimum time needed to accumulate 1000 precordial counts was measured. The number of counts obtained in this time was then determined at approximately 10-cm intervals along the patient's thighs and calves. With the surgical patients, the test was initiated on the day before the operation, thus providing two sets of readings for use as a reference distribution. Counts were undertaken daily for up to 7–10 days or until thrombus formation was detected. The test was considered positive if the count at any point showed a persistent increase of about 20% compared with those of the other points. Where anticoagulants were administered, monitoring was continued to assess the effect of the therapy.

RESULTS

On the basis of the leg counts, venous thrombosis was diagnosed in 17 (36%) patients, of whom seven (39%) were medical and ten (34%) surgical. The precordial counting times (per 1000 counts) were plotted on a logarithmic scale as a function of the time after injection. The half-times for the circulating ^{125}I-fibrinogen were determined from the slopes of the best-fit straight lines. Figure 1 shows the results obtained during two such investigations: the leg counts of one patient indicated thrombus formation less than 24 hr after hysterectomy, whereas the other patient showed no evidence of venous thrombosis. By the change in slope after heparin administration, the former plot (Fig. 1, triangles) also clearly shows the effect of anticoagulant therapy on the fibrinogen clearance rate. In general, the effect of anticoagulants was shown better by the change in slope of these plots than by the reduction in the rates of increase of the leg counts. Many patients who underwent surgery and did not develop venous thrombosis exhibited a gradual reduction in their fibrinogen clearance rates. In these cases the half-times were based on the precordial counts obtained during the first 3–4 days after operation. None of the surgical patients had a major hemorrhage, and no significant change occurred in the slope of the precordial plot immediately after operation for any patient who did not develop venous thrombosis.

The distributions of the half-times for both medical and surgical patients are given in Fig. 2; the uncertainty in the values was estimated from the effect on the slopes of the precordial plots of the counting statistics for individual rates. A statistical analysis of the data is summarized in Table 1.

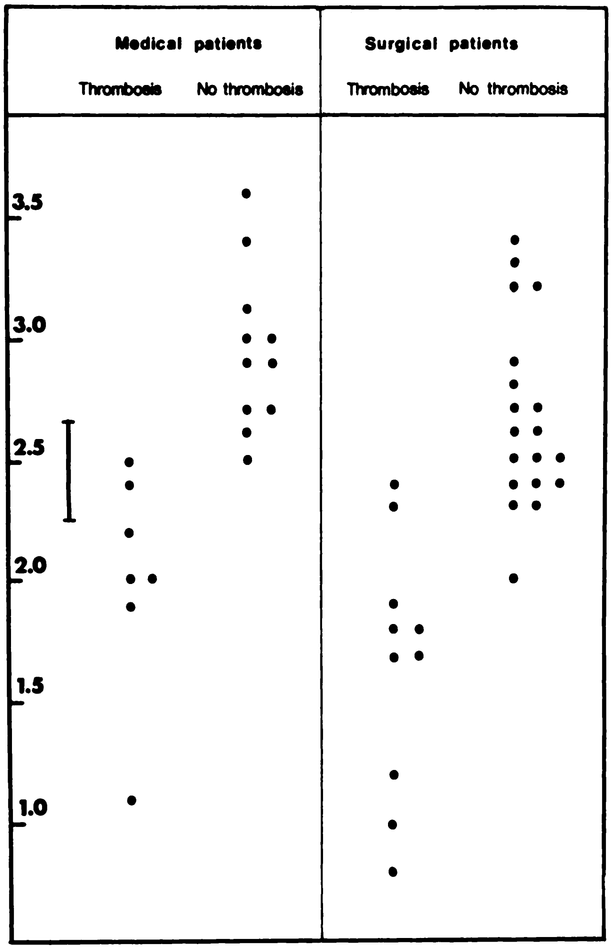

FIG. 2. Half-times (in days) for circulating ^{125}I-fibrinogen calculated from precordial count rates. Vertical bar represents uncertainty in values in region of overlap.

TABLE 1. STATISTICAL ANALYSIS OF ^{125}I-FIBRINOGEN CLEARANCE DATA

	Medical patients		Surgical patients	
	Venous thrombosis	No thrombosis	Venous thrombosis	No thrombosis
Number of patients	7	11	10	19
Mean half-time (days)	2.0	2.9	1.7	2.7
Range (days)	1.1–2.5	2.5–3.6	0.8–2.4	2.0–3.4
Standard deviation (days)	0.46	0.34	0.52	0.38

Significance of the differences (using Student's t-test) between:
- medical patients with and without thrombosis: $p < 0.001$
- surgical patients with and without thrombosis: $p < 0.001$
- medical and surgical patients without thrombosis: $p < 0.005$
- medical and surgical patients with thrombosis: $0.2 < p < 0.3$

DISCUSSION

The test results (Fig. 2) showed a significant ($p < 0.001$) difference between the half-time distributions of circulating ^{125}I-fibrinogen for patients with and without venous thrombosis. This applied both to the medical and surgical patients, although the division was clearer within the medical group. For patients with normal leg counts there was a clear difference ($p < 0.005$) in the fibrinogen half-times between the two groups. For patients who developed venous thrombosis the difference was not significant ($0.2 < p < 0.3$), but this may be due to the number of patients investigated. The fibrinogen half-times for the surgical patients were shorter, on the average, than for the medical patients. This is not surprising, since some clotting must inevitably occur postoperatively.

Takeda (*6*) investigated the catabolism of ^{125}I-fibrinogen in 12 healthy men. From blood samples he obtained a mean fibrinogen half-time of 3.36 days (range 2.78–3.65 days), with a more rapid clearance during the first day. In a study of 46 geriatric patients, Denham et al (*5*) found that the fibrinogen half-times formed two well-separated groups: patients without venous thrombosis had values greater than 3.0 days, while patients with fibrinogen half-times below 2.5 days had a high incidence of venous thrombosis. In a study of geriatric patients with hemiplegia (*7*), 25 patients who did not develop venous thrombosis had an average fibrinogen half-time of 3.5 days (95% range, 2.2–4.6 days), whereas the corresponding mean half-time for 22 patients with thrombosis was 2.0 days (95% range, 1.1–2.9 days). An investigation by Jeyasingh et al (*4*) of seven medical or surgical patients without venous thrombosis yielded a mean fibrinogen half-time of 3.11 days, whereas for a group of five patients with venous thrombosis this value was 1.68 days. These figures were calculated by referring the radioiodine count rate of each blood sample to that of a specimen taken only 15 min after injection. Therefore, the half-times obtained by Jeyasingh contain contributions from the faster-clearance components and should be slightly lower than those obtained by the other workers (*5–7*). For comparison with the present results, the times obtained by counting blood samples should be reduced by about 0.1 day to allow for radioactive decay.

The use of the precordial counting technique as an indicator of deep-vein thrombosis is not applicable to patients with myocardial infarction. Simmons et al (*8*) were unable to show a correlation between the plasma clearance rates of ^{125}I-fibrinogen and the incidence of venous thrombosis in such cases. Warlow and Terry (*9*) showed that, following myocardial infarction, abnormally high precordial count rates may occur due to mural thrombosis. None of the patients included in the current study had any history of myocardial infarction.

The fibrinogen half-time values of the present investigation (Table 1) are in a good agreement with those of previous studies, indicating that in the absence of cardiac thrombi the precordial counting technique is comparable with that of counting blood samples. None of the patients exhibited rapid radioiodine clearance in the absence of increased leg counts. Such a finding, if present, would be a strong indication for further investigation of the patient, for example, by phlebography. Labeled fibrinolytic agents (*10*) may also prove to be of value in such cases, although their use would normally involve moving the patient to a scintillation camera, which might not be convenient.

CONCLUSION

The calculation of the half-time of circulating ^{125}I-fibrinogen provides a useful adjunct to routine leg counting for the diagnosis of venous thrombosis. The precordial counting technique results in no additional inconvenience to the patient and can even be used alone where leg counting is contraindicated.

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