Technical Aspects of I-125 Fibrinogen Testing for Detection of Deep Venous Thrombosis

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Historically, the detection of deep venous thrombosis has been difficult because of the lack of a simple and accurate screening test. Recent technical advances have produced a number of sensitive procedures for confirming the presence or absence of thrombosis. For the past three years our institution has been using the radiolabeled fibrinogen procedure in the diagnosis of clinically suspected deep venous thrombosis of the lower extremities. We present and define the technical aspects of performing a radiolabeled fibrinogen test. Physiology, instrumentation, and data presentation are also discussed so that the technologist will have a working knowledge of this procedure.

Pulmonary embolism, a serious complication of deep venous thrombosis (DVT), continues to be an important cause of death, particularly for the in-hospital patient. It has been estimated that pulmonary embolism is responsible for approximately 50,000 deaths each year in the United States (*1*). Most thrombi responsible for such events are believed to originate in the deep venous system of the lower extremities. Detection of DVT has been difficult because of the lack of a simple and accurate screening test. Clinical diagnosis of deep venous thrombosis remains notoriously unreliable, yet early detection would permit prompt, appropriate therapy and might prevent embolization of large clots to the lung.

Traditional approaches to diagnosis of DVT have included clinical examination and contrast venography. Recent technical advancements provide a variety of new diagnostic aids, including impedance plethysmography; radioisotope venography; and radiolabeled fibrinogen.

Basic Concept

The radiolabeled fibrinogen procedure (RLF) involves intravenous administration of a small amount of human fibrinogen, which has been labeled with a suitable isotope, currently I-125. The key to this procedure is that during the coagulation process, radiolabeled fibrinogen behaves in the same manner as endogenous fibrinogen; thus it is incorporated into the developing clot where it can be detected by an external counting device. Figure 1 is a graphic representation of how radiolabeled fibrinogen fits into the coagulation process. Briefly, once the coagulation process is activated, prothrombin is converted to the enzyme thrombin, which then acts on circulating fibrinogen to form fibrin. Because of this naturally occurring process, both endogenous fibrinogen and radiolabeled fibrinogen are incorporated into a forming thrombus.

Method

The radiolabeled fibrinogen procedure involves four basic steps: blockade of the thyroid gland; administration of I-125 fibrinogen; marking of the precordium and legs; and counting and interpretation.

Blockade of the Thyroid. The estimated absorbed radiation dose to the unblocked thyroid of an average patient (70 kg) from an intravenous injection of 100 mCi of I-125 is 1.3 rad *(2)*. Unless the patient has a known sensitivity to iodides, a concentrated solution of iodide must be given to block the thyroid. The thyroid can be successfully blocked either by an oral administration of potassium iodide (250 mg) 24 hr prior to RLF injection, or by an intravenous administration of sodium iodide (100 mg) 1 hr before RLF injection. To assure that the blockade of the thyroid gland is maintained for an adequate period, an oral maintenance dose of saturated potassium iodide is given for approximately two weeks after the last injection of RLF. As a result of this procedure, the absorbed radiation dose to the thyroid will be approximately 0.02 rad *(2)*.

Administration of I-125 Fibrinogen. Once thyroid uptake is blocked, a standard dose of 100 μCi of I-125 fibrinogen (Abbott Laboratories, Chicago, IL) is injected into a peripheral vein. Equilibration is completed by 6 hr, at which time the first counts may be obtained.

Marking of the Precordium and Legs. In preparation

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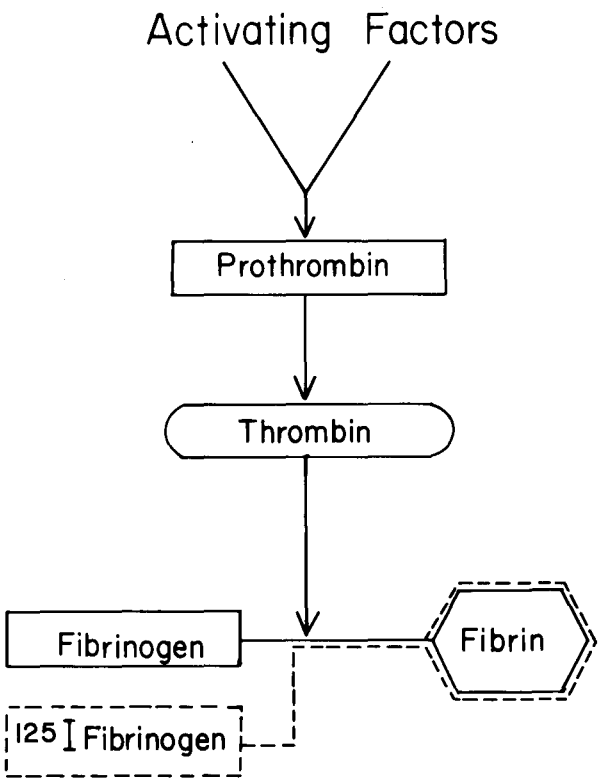

FIG. 1. Diagram of the coagulation process involving endogenous and radiolabeled fibrinogen.

for counting, the patient is placed in the supine position; the legs and precordium are marked. Starting at the point of inguinal ligament, the legs are marked (Fig. 2) at 5-cm intervals along the medial aspect of the thigh to the knee, and at 5-cm intervals from the popliteal fossa to the ankle. The number of points will vary depending on the length of the appendage. For proper identification of the precordium, survey area around the left fourth intercostal space with the detector until the highest counting rate is observed and marked. All markings should be done with an indelible marking pen to insure reproducible probe placement for the duration of the procedure.

Counting and Interpretation. The counting procedure involves the use of a portable scintillation detector interfaced to either a scaler and timer or a rate meter. In 1972, Browse (*3*) demonstrated that there is no difference in the results obtained with these two different types of counting systems. There are a variety of commercial systems for both types that read directly in percent, thus eliminating time consuming calculations. Additional features such as an angled probe and hard copy printout further reduce the time required to perform the procedure.

Because of the low energy levels associated with I-125, the results of this test are invalid in the presence of excessive background radiation. To reduce background radiation caused by venous pooling, the patient's legs are elevated approximately 30° for 15 min. In addition, a background count should be taken prior to the study and the patient's chart reviewed for concommitant radionuclide procedures.

After venous drainage is complete, the patient is ready to be counted. The precordium is counted and the resulting counting rate equals 100%. Counting then proceeds down each leg with the counting rate at each marked position expressed as a percentage of the precordial rate. As each site is scanned, the data are recorded on a work sheet (Fig. 3) for subsequent interpretation. At our institution we are using the criteria for positivity as determined by Browse (*3*); i.e., a positive result is reported whenever a given counting site shows a counting rate 15% higher than either an adjacent site (above or below) on the same leg, or on the same location on the contralateral leg, and this difference maintained for at least 24 hr. Other protocols require a 20% increase for positivity (*4*).

Results

When compared with classical contrast venography, the correlation between the RLF test and venography is cited by various investigators as between 83 and 100% (*5,*

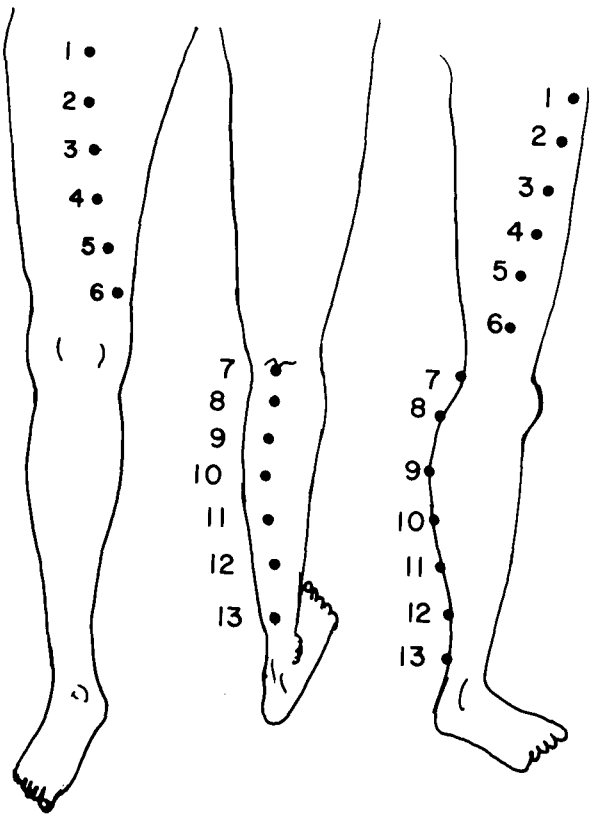

FIG. 2. Anterior (left), posterior (center), and lateral views (right) of the leg marked at 5-cm intervals.

^{125}I FIBRINOGEN WORK SHEET

Patient _____ Hospital Number _____

Date of Inj. _____ Time of Inj. _____ Dose _____ Lot No. _____

Date of Scan															
Position	R	L	R	L	R	L	R	L	R	L	R	L	R	L	
1															
2															
3															
4															
5															
6															
Etc.															
Precordial Rate															
Background															
Technologist															

Comments:

FIG. 3. An example of an I-125 fibrinogen worksheet with appropriate information; precordial and background rates are expressed in counts per sec.

6). False negative studies do occur and are related to inactivity of the thrombus. In order to incorporate RLF, a clot must be in the process of converting fibrinogen to fibrin. Thrombi that are inactive because of age (completely formed) or the presence of adequate amounts of anticoagulant will not pick up circulating labeled fibrinogen. False positive studies are encountered in those diseases where fibrinogen accumulates locally in abnormally high concentrations. These include superficial thrombophlebitis, hematomas, surgical wounds, gross edema, and Baker's cysts. Any acute inflammatory condition such as arthritis will also result in a local deposition of fibrinogen. Knowledge of the patient's clinical condition is essential when interpreting the causes of positive RLF studies. Therefore, whenever any of the above conditions are observed during the scanning procedure, they should be indicated next to the appropriate counting site on the worksheet. Finally, the RLF test is not suitable for detecting pelvic thrombi because of the high degree of background radiation from the bladder and larger vessels in the area.

Discussion

The radiolabeled fibrinogen test has proven to be a reliable procedure that has two major areas of application. First, it is a sensitive method of confirming clinically suspected, actively forming, deep venous thrombosis. This takes a minimum of 24 hr because of the time required for equilibration of labeled fibrinogen and for a repeat scan. Second, the procedure is useful in the identification of high risk subgroups of patients who would benefit from prophylactic therapy. If the physician requires proof of DVT before institution of therapy, this would necessitate a 24-hr delay in heparinization. Such decisions must be made by the individual physician. Recently we have found an incidence of DVT as detected by RLF of 75% in patients recovering from hip surgery (7) and of 90% in those who have recently suffered spinal cord trauma (8).

A potential application of the RLF test is in the monitoring of anticoagulant therapy in proven deep venous thrombosis. Our graph (Fig. 4) represents eight days of continuous monitoring of the left leg and each day's activity is expressed as a percent of the previous day's count. The vertical axis represents the percent of previous day's count. The horizontal axis is time in days and the black band is the 15% margin for positivity. Prior to the administration of radiolabeled fibrinogen, this patient was started on 1000 units/hr of heparin for

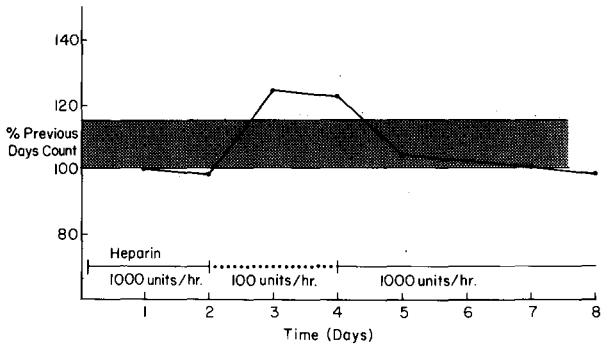

Fig. 4. Potential use of the RLF procedure in monitoring of anticoagulant therapy.

suspected deep venous thrombosis. His negative studies on the first and second days indicate the lack of active venous thrombosis owing either to inactivity of underlying disease or successful therapy with heparin. On the third day his study became positive, indicating active venous thrombosis. This was coincident with the inadvertent decrease of heparin to 100 units/hr, a less than therapeutic dose, which occurred after the scan of the second day and prior to the scan on the third day. The patient was then given the correct dose of heparin, 1000 units-hr. Scans on subsequent days remained positive and the degree of positivity did not increase. This would be in keeping with the successful blockage of further labeled fibrinogen incorporating into the thrombus and indicates a more satisfactory level of heparin therapy.

The radiolabeled fibrinogen procedure is a sensitive, reliable, and noninvasive method for detecting clinically suspected deep venous thrombosis. It is a bedside procedure that requires minimal patient cooperation. In addition, the simplicity of the procedure and the availability of equipment permits it to be used in community hospitals as well as in larger medical centers.

Acknowledgment

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