Impedance Plethysmography
Using the Occlusive Cuff Technique
in the Diagnosis of Venous Thrombosis


Summary
Impedance plethysmography using the cuff technique has been compared with venography in 346 consecutive patients with suspected venous thromboembolism. The limbs were classified according to the venographic results as no thrombosis, proximal (popliteal, femoral, or iliac) vein thrombosis, and calf thrombosis. A discriminant analysis was performed. The impedance plethysmographic result was normal in 386 of 397 limbs which were normal on venography, a specificity of 97%, and abnormal in 124 of 133 limbs which showed proximal vein thrombosis, a sensitivity of 93%. Seventy-three of 88 limbs with calf vein thrombi had a normal impedance plethysmographic result. The sensitivity in 29 limbs with asymptomatic proximal vein thrombosis was 83%. Impedance plethysmography is an accurate method for detecting proximal vein thrombosis but has limitations which include the possibility of false positive results due to arterial insufficiency and muscle tension.

Pulmonary Embolism is the commonest preventable cause of hospital death.1 The majority of clinically significant pulmonary emboli and most fatal pulmonary emboli are thought to arise from thrombi located in or proximal to the popliteal vein.2-4 Therefore, a sensitive method for detecting these proximal thrombi would be of potential value for the prevention of pulmonary embolism.

The clinical diagnosis of venous thrombosis is inaccurate.6-9 A number of studies have demonstrated that approximately 50% of patients with clinical signs compatible with venous thrombosis have a normal venogram10-12 and conversely that more than 50% of thrombi are not detected clinically.5, 13 While the majority of clinically silent thrombi are small, a significant proportion of these thrombi are situated in or proximal to the popliteal vein.14, 15

Venography is the most accurate diagnostic method currently available.16, 17 It is, however, invasive, not without morbidity and cannot be performed at the bedside.

125I-fibrinogen scanning has limitations as a diagnostic test as it may take up to 72 hours after the injection of isotope to show a positive finding in some patients with established thrombosis, while in others it never demonstrates the thrombosis. The method has fewer limitations when used to screen high risk patients but is relatively insensitive to proximal femoral vein thrombi and is insensitive to iliac vein thrombi.18, 19 Furthermore, it is unreliable over the operated thigh in patients who have had recent hip surgery20 because of leakage of labelled fibrinogen into the wound.

Plethysmography is a noninvasive method which has been used for the detection of venous thrombosis for a number of years. Several methods have been used for detecting changes in limb blood volume and these include the strain gauge,21 the air cuff22 (phleborheograph) and electrical impedance. Impedance plethysmography was introduced by Wheeler, who described its principles and clinical applications.23 In brief, the technique is based on blood volume changes in the calf produced by maximum respiratory effort or by inflation and deflation of a pneumatic thigh cuff which produce changes in electrical resistance (impedance) in areas of thrombosis. The original method, which relied on maximum respiratory effort, had shortcomings24, 25 because of the frequent inability of the patient to comply with the requirements of the test. The technique was then modified by replacing the respiratory method with the occlusive pneumatic thigh cuff method.26

The cuff method has been compared with venography in two studies.26, 27 Both reported that impedance plethysmography performed by this method was sensitive to proximal vein thrombosis. However, in neither study was assurance given that the two methods were assessed by independent evaluators. In addition, one study was relatively small26 and in the other, the group of patients was a selected one since phlebography was performed mainly when the impedance plethysmographic (IPG) result differed from the clinical impression.27 Because of the potential shortcomings of previous studies, we considered it important to re-evaluate impedance plethysmography using a blind design in a large consecutive series of patients referred for venography because venous thromboembolism was suspected either on clinical grounds or because the 125I-fibrinogen leg scan was positive.

Materials and Methods

Patients

Three hundred and forty-six consecutive patients (641 limbs) were investigated with both venography and impedance plethysmography. The patients’ age ranged from 17 to 101 (mean 59). There were 139 males and 207 females. The patients studied were hospitalized patients and included general medical, general surgical, orthopedic, and gynecological patients as well as patients in the respiratory, coronary, and intensive care units. Two hundred and sixty-nine (76%) of the patients were referred for venography because of a clinical suspicion of venous thrombosis and/or pulmonary embolism and 77 (24%) were referred for venography because they had a positive 125I-fibrinogen leg scan.
Patients in the latter group were being scanned prospectively because they were considered to be at high risk of developing venous thrombosis. Forty-four of the 346 patients had had hip surgery. The indication for venography in this group was clinical signs of thromboembolism in nine and a positive $^{125}$I-fibrinogen scan in 35.

Six patients with overt congestive cardiac failure were analyzed separately as it is known that cardiac failure may cause false positive impedance results.

Venography. Ascending venography was performed according to the method of Rabinov and Paulin in two hospitals and by a previously described method in the third hospital.

Exclusions from the Study. Eight patients were not entered into the study either because they refused venography or because the radiologist was unable to insert the needle into the dorsal foot vein. Twelve patients were excluded from the analysis because technical difficulties resulted in poor opacification of the veins above the knee. These exclusions were made without knowledge of the impedance results.

$^{125}$I-Fibrinogen Leg Scanning. $^{125}$I-fibrinogen leg scanning was performed as previously described.

Impedance Plethysmography. A model 100 Impedance Plethysmograph (Cintor) equipped with a rapid release wide low pressure thigh cuff (6 inches in width) was used throughout the study. The cuff was inflated to 45 cm H2O.

The principle of impedance plethysmography has been described by Wheeler. In brief, a mid-thigh pneumatic cuff is applied and inflated to occlude venous return, and after a period of time, rapidly deflated. The changes in blood volume of the calf resulting from these maneuvers produce changes in electrical resistance (impedance) which are detected by a pair of electrodes which are applied to the calf. The changes in impedance during the period of cuff inflation and deflation are traced by a recorder. During cuff inflation, the tracing rises and after deflation it falls. The rise at the end of inflation is then expressed as a function of the fall at the end of three seconds of deflation and the point obtained is plotted onto a graph. If there is obstruction to venous return, the fall in three seconds will be reduced and there will be a variable reduction of the rise depending on the severity of obstruction. The method used in this study was based on that described by Wheeler but was modified. Each patient was tested in the supine position and the lower limb was elevated to 25-30° with the knee flexed to 10-20° and with the ankle 3-6 inches higher than the knee. This position provided optimal emptying of the limb before starting the test and thus allowed large volume changes to occur during inflation and release of the thigh cuff. Furthermore, this position was found suitable for testing patients with hip fractures and hip surgery.

Experience during a pilot study showed that the sensitivity and specificity of the test were enhanced by obtaining maximal filling during cuff occlusion. It was found that maximal filling rarely occurred until the limb was subjected to 3 or 4 cycles of inflation and deflation and that filling was impaired if leg muscles were not freely relaxed. Accordingly, five consecutive tests were performed on each limb — three with a 45 second occlusion time and two with a 2 minute occlusion time. Each test was plotted on a graph and the point used to represent the patient’s impedance plethysmography (IPG) result was that which showed the highest rise and greatest fall. In the rare instance when the greatest rise and fall did not occur in the same test of a sequence, the examination was regarded as inadequate and was repeated.

Comparison of Impedance Plethysmography and Venography. In 91% of cases impedance plethysmography and venography were performed within 24 hours of each other and in 98% of these instances impedance plethysmography was performed before the venogram. Of the remaining 9%, 6% were performed on the next day and 3% within 48 hours of venography.

Care was taken to insure that impedance plethysmography was performed and interpreted without knowledge of the venogram results and that interpretation of the venogram was carried out without knowledge of impedance plethysmographic (IPG) results.

The patients were classified into three categories on the basis of venographic results; no thrombosis, proximal vein thrombosis (popliteal, femoral, or iliac vein thrombosis), and calf vein thrombosis only. The results in the normal limbs without thrombosis and those limbs with proximal vein thrombosis for patients entered into the study between September 1974 and mid-January 1975 were subjected to a discriminant analysis. This produced a line of best discrimination between normal and proximal vein thrombosis.

This procedure was validated by applying this estimated discriminant prospectively to the data from patients who were entered into the study from mid-January 1975 to May 1975.

Results

Adequacy of Venography

Of the 618 venograms compared with impedance testing, 508 (82%) showed visualization of the deep calf veins, popliteal, superficial and common femoral veins and the external and common iliac veins.

One hundred and ten (18%) showed good visualization of the deep venous system including the common femoral but poor visualization of the external and common iliac veins.

Initial Analysis

On the basis of the discriminant analysis, 168 of the IPG results were classified as normal and 73 as abnormal. One hundred and seventy-two limbs were normal on venography and 69 had proximal thrombi. Table 1 and figure 1 show the correspondence between the venographic and IPG results in these 241 limbs. Of the 172 limbs which showed no evidence of thrombosis by venography, 164 were classified as normal on the basis of the IPG assessment. Thus, specificity was

| Table 1. Initial Analysis. The Correspondence between the Venographic and IPG Results in 241 Limbs of Patients Entered into the Study from September 1974 to mid January 1975 |
|---|---|---|
| Venogram | PVT | Norm |
| IPG | Abn | 65 | 8 |
| Norm | 4 | 164 |

Abbreviations: IPG = impedance plethysmography; PVT = proximal vein thrombosis; Norm = normal; Abn = abnormal.
95%. Sixty-nine limbs were demonstrated by venography to have proximal vein thrombosis and of these the IPG result was abnormal in 65 limbs. Thus, the sensitivity for proximal vein thrombosis was 94%.

**Validation**

Table 2 and figure 2 show the venographic and IPG results in 289 limbs analyzed prospectively using the discriminant function derived from the preliminary analysis. The IPG was normal in 222 of the 225 limbs which were normal on venography. Thus, the specificity was 99%. The IPG was abnormal in 59 of the 64 limbs which were demonstrated by venography to have proximal vein thrombosis. Thus, the sensitivity for proximal deep vein thrombosis was 92%.

**Total Results**

Table 3 shows the venographic and IPG results in 618 limbs which represents the total population studied. The IPG was normal in 386 of the 397 limbs which were normal on venography, a specificity of 97%. One hundred and thirty-three limbs were demonstrated by venography to have proximal vein thrombosis and the IPG was abnormal in 124, a sensitivity of 93%.

Twenty-nine of the 133 limbs with proximal vein thrombosis were asymptomatic. The IPG result was abnormal in 24 of these 29 limbs. Thus, the sensitivity for asymptomatic proximal thrombosis was 83%.

Forty-one of the proximal thrombi were nonocclusive, that is, dye was seen between the vessel wall and the thrombus for its total length. Nine of these nonocclusive thrombi were not detected by the IPG. These nine thrombi were small and measured 0.5 to 1.0 cm in width and up to 5 cm in length. Thus, the sensitivity of the IPG for nonocclusive thrombi was 78%.

Seventy-three of 88 limbs with calf vein thrombi had a normal IPG. Fourteen of the 15 calf vein thrombi that were detected by the IPG were large, five involved the proximal one-third of the calf and nine involved more than one-half of one of the deep veins of the calf. On the other hand, 52 calf vein thrombi of similar dimensions were not detected by the IPG.

**Patients in Congestive Cardiac Failure**

Six patients were in overt congestive cardiac failure. The IPG result was bilaterally abnormal in these patients. Venography showed proximal vein thrombosis in two limbs, calf vein thrombosis only in three limbs, and normal findings in the remainder.

**Expectant 125I-Fibrinogen Leg Scanning**

The results of the IPG were also analyzed separately in patients who were scanned expectantly with 125I-fibrinogen and who had venograms performed because venous thrombosis was suspected. Many of the patients had bilateral venograms performed so it was possible to compare the IPG results with venography in 77 scan positive limbs and 63 scan negative limbs. Venography showed proximal vein thrombosis in 37 limbs, calf vein thrombosis in 36 limbs, and no evidence of thrombosis in 67 limbs. The IPG was abnormal in 32 of the 37 limbs with proximal vein thrombosis, five of the 36 limbs with calf vein thrombosis, and three of the 67 limbs with no evidence of thrombosis. Thus, the sensitivity for proximal thrombosis was 86% and specificity was 96%.

**Patients With Hip Surgery**

Forty-four of the 346 patients had hip surgery. On the operated side, 17 of these had proximal vein thrombi detected by venography, eight had calf vein thrombi and 19 patients had a normal venogram. The IPG was abnormal in 15 of the 17 limbs with proximal vein thrombosis and was

**Table 2. Validation. The Correspondence between the Venographic and IPG Results in 289 Limbs of Patients Entered into the Study from mid January to May 1975**

<table>
<thead>
<tr>
<th>Venogram</th>
<th>PVT</th>
<th>Norm</th>
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<tbody>
<tr>
<td>IPG</td>
<td>Abn</td>
<td>59</td>
</tr>
<tr>
<td></td>
<td>Norm</td>
<td>5</td>
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See table 1 for abbreviations.
normal in 16 of the 19 normal limbs. Thus, the sensitivity for proximal vein thrombosis was 88% and specificity 84%. Only two of the eight calf vein thrombi were associated with an abnormal IPG.

Relationship of False Positive IPGs to Adequacy of Venography

Ninety-six of the venograms which were read as "normal" had inadequate visualization of the external and common iliac veins. In 91 the IPG was normal and in five the IPG was abnormal. The remaining 301 normal venograms showed good visualization of the external and common iliacs and of these, the IPG was normal in 294 and abnormal in six. Thus, there was little difference in the incidence of false positive IPGs between the two groups suggesting that the results were not biased by lack of visualization of the iliac veins.

Discussion

The results of this study confirm previous investigations\textsuperscript{28, 29} which have shown that impedance plethysmography is a sensitive and specific method for the detection of proximal vein thrombosis. Our study evaluated impedance plethysmography in a large number of limbs with symptomatic venous thrombosis, in a large number of limbs without clinical or venographic evidence of venous thrombosis, and in a smaller number of limbs with asymptomatic venous thrombi. The test was most sensitive for symptomatic, totally occluding proximal vein thrombi and was highly specific in the limbs without venous thrombosis. However, the IPG also detected 83% of asymptomatic proximal vein thrombi and 78% of nonobstructing proximal thrombi. The proximal vein thrombi that were not detected varied in size from approximately 0.5 cm in width to 1–5 cm in length.

The IPG was abnormal in 11 of 397 (2.8%) limbs in which thrombosis was not detected by venography. In five of these 11 venograms the iliac vein was not well visualized and it is possible that an isolated iliac vein thrombus was present in some of these. Although venography is the current standard with which other methods must be compared, it too is subject to the possibility of falsely positive and negative results. When this possibility is considered, the agreement found in this study between the venogram and the IPG for proximal vein thrombosis was remarkably good.

The IPG also detected 15 of the 17 proximal vein thrombi in the operated limbs of 44 patients evaluated after hip surgery. However, false positive results were more frequent in this group (3 of 22) than in patients without hip surgery. Although the findings in patients with hip surgery are promising, our study is too small to enable firm conclusions to be made regarding the value of impedance plethysmography in this group of patients.

The test procedure used was rather tedious, required dedication and persistence on the part of the technologists, and required a certain amount of patient cooperation. Our early experience with the test indicated that the accuracy of the test is likely to suffer if the method is greatly simplified or if the test is performed by inexperienced or poorly trained technologists. Because of this, the use of impedance plethysmography should probably be limited to centers with sufficient resources and commitment to provide adequate quality control.

The major limitation of the IPG is that it is insensitive to calf vein thrombi. In addition, the test is unable to distinguish between venous thrombosis and other factors affecting venous filling or outflow such as arterial insufficiency, right heart failure, compression of the major veins by an external mass or failure of muscle relaxation.\textsuperscript{28, 29} Since completion of the study, we have performed impedance plethysmography in five patients with long standing venographically proven iliac or iliofemoral vein thrombosis. The results were normal in three cases and in all of these, there were multiple large collaterals. Thus, the IPG is likely to lose sensitivity in the weeks to months that follow an acute episode of proximal vein thrombosis.

What then is the place of the IPG in the practical management of patients with venous thromboembolism? Our results indicate that over 90% of patients with an abnormal IPG result have a venographically demonstrable thrombus. Although it is likely that venography will remain the standard diagnostic method, this test is not available in many community hospitals and cannot always be performed on short notice. In addition, it cannot always be performed because of technical difficulties or because of difficulty in transporting the patient to the radiology department, and may be contraindicated because of iodine allergy. Under these circumstances, an abnormal IPG result would be a clinically useful finding on which therapeutic decisions could be based. On the other hand, a negative result does not exclude calf vein thrombosis or nonocclusive proximal vein thrombosis and therefore cannot be used to make therapeutic decisions.

The IPG correctly identified 86% of the proximal thrombi that were detected venographically in patients who had been scanned prospectively with $^{131}$I-fibrinogen. This suggests that the test may prove useful in planning the management of high risk but asymptomatic patients who are having leg scans.

At present there is a considerable difference of opinion regarding the most appropriate approach to the management of patients with a positive $^{131}$I-fibrinogen leg scan. Kakkar and associates\textsuperscript{30} advocated that scan-detected calf vein thrombosis should not be treated because they are associated with a small or negligible risk of clinical pulmonary embolism. They suggested that such patients should be followed with leg scanning and treatment be given only if there is evidence of extension into the popliteal vein or above. Adar and Salzman\textsuperscript{31} have suggested that all scan-detected thrombi should be treated because of the possibility that they may be associated with a proximal vein thrombosis which is not detected by scanning. They also pointed out that venography performed at the time of the positive scan may not totally exclude this possibility since proximal vein

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**Table 3. Total Results. The Venographic and IPG Results in the 618 Limbs of the Total Population Studied**

<table>
<thead>
<tr>
<th>Venogram</th>
<th>PVT</th>
<th>Norm</th>
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<tbody>
<tr>
<td>IPG</td>
<td>Abn</td>
<td>124</td>
</tr>
<tr>
<td></td>
<td>Norm</td>
<td>9</td>
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See table 1 for abbreviations.
thrombi undetected by leg scanning could develop some time after venography. However, since between 20 and 30% of patients undergoing abdominal surgery develop scan-detected thrombi in the early postoperative period,8 most of which are small calf vein thrombi, it would be desirable to selectively treat those patients who are at risk of pulmonary embolism.

Our results suggest that in patients with scan-detected thrombi it should be possible to detect subsequent extension or development of noncontiguous proximal vein thrombosis by following the patient with both leg scanning and impedance plethysmography. Limiting heparin treatment to patients who show evidence of proximal thrombosis would provide a safe approach to the management of a positive leg scan in postoperative patients who are at risk of bleeding.

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