Impedance Plethysmography: The Relationship Between Venous Filling and Sensitivity and Specificity for Proximal Vein Thrombosis

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SUMMARY We investigated the hypothesis that the diagnostic accuracy of impedance plethysmography (IPG) for thrombosis of the popliteal, femoral or proximal veins increases with enhanced venous filling. Venous filling was increased by prolonging cuff occlusion and by sequential testing. IPG and venography were performed on 169 legs with and 317 legs without proximal vein thrombosis. The sensitivity and specificity of IPG rose significantly with increased venous filling. Changes in venous filling were associated with corresponding changes in emptying in normal legs, but not those with proximal vein thrombosis, so that the regression lines relating venous filling and emptying in normal and abnormal legs diverged significantly (P < 0.001). If the IPG sequence had been terminated after only a single 45 second occlusion time test, sensitivity would have deteriorated by 10% and specificity by 20%. These observations indicate that the accuracy of IPG can be significantly enhanced if optimal venous filling is obtained.

OCCLUSIVE CUFF IMPEDANCE plethysmography (IPG) is a sensitive and specific method for detecting thrombosis of the popliteal, femoral or proximal veins (proximal vein thrombosis).1-6 This technique quantitates the capacity of the venous system to fill and empty in response to temporary venous outflow obstruction.1-4 These changes in venous volume are influenced by a number of physiological determinants, including the anatomic capacity of the venous system, venous tone, venous pressure and venous distensibility.7-8 Volume changes are also influenced by pathological determinants, including reduced arterial inflow, increased central venous pressure and thrombotic or non-thrombotic obstruction of the proximal veins.1-4

The original method of impedance plethysmography, which used maximum inspiration or the Valsalva maneuver to delay venous return temporarily, was abandoned because it was inaccurate. The method was subsequently modified by replacing maximum respiratory effort with thigh cuff venous occlusion for up to 45 seconds but, even with this modification, its accuracy for detecting proximal vein thrombosis has varied.1-6,9 After documenting that a single 45-second occlusion sometimes led to both poor venous filling and failure to detect incompletely occlusive proximal thrombosis, we hypothesized that the accuracy of the test is influenced by the degree of venous filling occurring during cuff occlusion. To test this hypothesis, we altered the method to incorporate two maneuvers designed to produce increased venous filling: prolongation of cuff occlusion time to 120 seconds and repeated testing. Prolonged occlusion time was selected because venous filling, as reflected by change in impedance, often did not reach a plateau after only 45 seconds. Repeated testing was selected because it has been shown that repeated venous distension altered the physical properties of the venous bed (a phenomenon known as stress relaxation),8,10 resulting in increased venous capacity.

The present study tested the hypothesis that increased venous filling produces an increase in the sensitivity and specificity of the IPG test for proximal vein thrombosis.

Materials and Methods

Study Patients

The subjects were 324 consecutive patients who underwent both IPG and venography, in which the latter procedure was either normal or revealed proximal vein thrombosis. One hundred ninety-five patients had been referred for clinically suspected venous thrombosis, and the remaining 129 had suspected venous thrombosis on the basis of positive 125I-fibrinogen leg scans or positive IPGs following hip surgery.

Impedance Plethysmography

Impedance plethysmography was performed with the IPG 200 machine (Codman), using a procedure which has been described in detail elsewhere.4 In summary, each patient was tested while supine with the lower limb elevated 25–30°, the knees flexed 10–20°
and the ankle 8–15 cm higher than the knee. A pneumatic cuff 15 cm wide was applied to the mid-thigh and inflated to 45 cm H₂O), thereby occluding venous return. After a predetermined period of time (see below), the cuff was rapidly deflated and the changes in electrical resistance (impedance) resulting from alterations in blood volume distal to the cuff were detected by circumferential calf electrodes and recorded on an ECG strip. The changes in impedance during cuff inflation and deflation were measured and both the total rise during cuff inflation and the fall occurring in the first 3 seconds of deflation were plotted on a two-way IPG graph developed in a previous study and reported elsewhere. The changes in impedance were plotted as impedance units. One impedance unit was defined as a 1 mm deflection on the ECG paper which was obtained when the sensitivity was set so that 0.4% impedance units produced a 10 mm deflection. The graph included a “discriminant line” developed via a discriminant function analysis, which provided optimal separation of IPG results into those which corresponded with normal or abnormal venograms.

Five tests were performed at each examination. The durations of occlusion during these tests were 45, 45, 120, 45 and 120 seconds, respectively, and the time interval between them was 20–30 seconds. This sequence was performed so that the effects of prolonged occlusion time could be separated from the effects of repetitive testing.

Venography

Ascending venography was performed by the method of Rabinov and Paulin in two hospitals and by a previously described method in the other two. The radiographic criteria for proximal vein thrombosis were the presence of an intraluminal filling defect or the absence of one or more deep proximal veins in association with extensive collaterals involving the popliteal, femoral, external iliac or common iliac veins. If the external or common iliac veins were not visualized adequately at the first ascending venogram examination, this was repeated and, if necessary, a femoral venogram was performed. If the filling defect was not seen in all films or if any part of the proximal deep venous system was poorly visualized despite repeated attempts, the examination was coded as inadequate. Eleven patients were excluded from the analysis because the venograms were inadequate. These exclusions were made without knowledge of the impedance results.

Interpretation of the IPG and Venogram Results

The results of impedance plethysmography and of venography were interpreted independently of one another and without knowledge of the patient’s condition. The IPG was validated against the venogram and the comparison expressed in terms of sensitivity (proportion of patients with proximal vein thrombosis by venography who had positive IPG results) and specificity (the proportion of patients without deep vein thrombosis by venography who had negative IPG results).

Statistical Methods

The effect of occlusion time and sequential testing upon venous filling was assessed by the t test. Cochrane’s Q statistic was used to test for differences in sensitivity and specificity among the five individual tests of the sequence and also to partition the overall effects of the sequence into its two components of increased occlusion time and repeated testing. In order to determine the value of the additional information obtained with each subsequent test in the sequence, the cumulative sensitivity and specificity at each point in the sequence (based on that test with the greatest IPG rise and IPG fall) was compared with that obtained by inclusion of the next test, using Mc Nemar’s test statistic. The relationship between venous filling (IPG rise) and venous emptying (IPG fall) was evaluated by linear regression; a separate regression was computed for each patient and the slopes of the overall (mean) regression lines for patients with and without deep vein thrombosis were then compared.

Results

Effect of Occlusion Times
and Sequential Testing on Venous Filling

Figure 1 summarizes the effects of prolonging occlusion time and repeated sequential testing on venous filling. In the top half of the figure, adjacent tests with differing occlusion times are compared, revealing a consistent and substantial trend toward increased venous filling (as indicated by changes in impedance during occlusion) with the 120-second occlusion time. This increase in venous filling with longer occlusion was highly significant by paired t test ($P < 0.0001$). The bottom half of figure 1 compares tests with similar occlusion times and demonstrates that venous filling is also improved with sequential testing, but not to the extent observed with longer occlusion times. While changes in venous filling with sequential testing are statistically significant for patients free of venous thrombosis ($P < 0.01$), this trend was not significant for patients with venous thrombosis ($P > 0.05$).

Relationship Between Venous Filling and Emptying

Figure 2 shows the relationship between venous filling (IPG rise) and emptying (IPG fall) for patients with and without venographically-demonstrated proximal vein thrombosis. Among patients with proximal vein thrombosis, increasing degrees of venous filling (IPG rise) produce only modest changes in venous emptying (IPG fall); the mean slope for the regression of IPG fall on IPG rise is $0.14 \pm 0.018$ (SEM). However, among patients with normal venograms, venous
emptying (IPG fall) is augmented by greater venous filling (IPG rise); the mean slope for this regression is $0.61 \pm 0.021$. The slopes for the regression lines of these patients with and without thrombosis are significantly different ($P < 0.001$).

**Effect of Test Order on Sensitivity and Specificity**

The upper portion of table 1 shows the sensitivity and specificity of each of the five IPG tests in the sequence. Statistical comparisons between these individual test results revealed two features. First, the duration of occlusion had a definite effect upon the ability of the IPG to detect venous thrombosis; the two 120-second tests (3 and 5) generated higher levels of both sensitivity and specificity than the three 45-second tests ($P < 0.0001$), and both the sensitivity and specificity of the third 45-second test (4) were lower than those generated by the preceding first 120-second test (3). Second, sensitivity and specificity tended to rise with repeated testing. Among the three 45-second tests (1, 2 and 4), specificity rose 13% ($P < 0.0001$), although sensitivity rose only 3% ($P > 0.13$). Between the two 120-second tests (3 and 5), sensitivity rose 4% ($P = 0.02$) and specificity rose 3% ($P < 0.08$).

**Table 1. Individual and Cumulative IPG Test Results**

<table>
<thead>
<tr>
<th>Test</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of occlusion</td>
<td>45 sec</td>
<td>45 sec</td>
<td>120 sec</td>
<td>45 sec</td>
<td>120 sec</td>
</tr>
<tr>
<td>Individual results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Sensitivity</em></td>
<td>82%</td>
<td>81%</td>
<td>87%</td>
<td>85%</td>
<td>91%</td>
</tr>
<tr>
<td><em>Specificity</em></td>
<td>76%</td>
<td>82%</td>
<td>93%</td>
<td>89%</td>
<td>96%</td>
</tr>
<tr>
<td>Cumulative results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Sensitivity</em></td>
<td>82%</td>
<td>82%</td>
<td>88%</td>
<td>88%</td>
<td>92%</td>
</tr>
<tr>
<td><em>Specificity</em></td>
<td>76%</td>
<td>82%</td>
<td>93%</td>
<td>93%</td>
<td>96%</td>
</tr>
</tbody>
</table>

*169 legs with proximal vein thrombosis by venography (positive venograms). 1317 legs without venous thrombosis by venography (negative venograms).*

A clearer delineation of the effect of repeated IPG testing is presented in the bottom portion of table 1 in the cumulative sensitivity and specificity achieved along the five-test sequence. Cumulative sensitivity rose 6% between tests 2 and 3 ($P < 0.01$), and was 4% higher after five tests than after only three ($P < 0.05$). Cumulative specificity improved between tests 1 and 2 ($P < 0.001$) and again between tests 2 and 3 ($P < 0.001$) and rose 3% between tests 3 and 5 ($P < 0.01$). The only test which failed to raise cumulative sensitivity and specificity was test 4, the third 45-second test.

**The Effect of Venous Filling Upon the Sensitivity and Specificity of the IPG**

The relationship between venous filling and sensitivity and specificity in patients with and without proximal vein thrombosis is summarized in table 2. The improvement in venous filling which occurred between tests 2 and 3 and between tests 4 and 5 (upper half of table 2) was accompanied by an increase in sensitivity and specificity, while the deterioration in venous filling which occurred between tests 3 and 4 was accompanied by a loss in both sensitivity and specificity. Similarly, the improvement in venous filling noted with sequential tests of identical occlusion times (tests 1, 2, 4 and tests 3 and 5) was also accompanied by an increase in both sensitivity and specificity (lower half of table 2).

**Discussion**

The results of this study support our hypothesis that increased venous filling produces an increase in the sensitivity and specificity of the IPG test for proximal vein thrombosis. The relationship between venous filling and emptying is such that, as filling increases, there is a proportionate increase in the rate of emptying. However, if there was obstruction to venous outflow from proximal vein thrombosis, increased venous filling was not accompanied by a corresponding increase in the rate of emptying. Consequently, with increased venous filling, the regression line describing the relationship between filling and emp-
tying in normal and abnormal legs diverge. This study evaluated two approaches which improved venous filling: prolongation of cuff occlusion time from 45 seconds to 120 seconds and repetitive testing. Both maneuvers improved venous filling, but the prolonged occlusion time produced greater improvements in the sensitivity and specificity of the IPG, so this maneuver is likely to be of more practical value. It is possible, therefore, that the sensitivity and specificity may be equally as good if two tests using a 120-second occlusion time were used, but this was not formally tested in this investigation.

Maximum sensitivity and specificity were obtained with test 5, which was also the test that produced the greatest increase in venous filling. The 8% frequency of falsely negative results was accounted for by non-occlusive asymptomatic thrombi. All symptomatic proximal vein thrombi in the study produced an abnormal impedance plethysmographic result, even though many were associated with collaterals on

![Figure 2](http://circ.ahajournals.org/)

**Figure 2.** The relationship between venous filling (IPG rise — horizontal axis) and venous emptying (IPG fall — vertical axis) in patients with and without proximal vein thrombosis. The numbers on the horizontal and vertical axes refer to impedance units (10 impedance units = 0.4% impedance change). The regression line expressing the relationship between venous filling and venous emptying is significantly different for patients with and without venous thrombosis (P < 0.001). The broken lines indicate 95% confidence limits.

<table>
<thead>
<tr>
<th>Test comparisons</th>
<th>In patients with positive venograms (169 legs)</th>
<th>In patients with negative venograms (317 legs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ΔRise*</td>
<td>ΔSens.†</td>
</tr>
<tr>
<td>To determine the effect of the duration of occlusion:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#2 (45 sec) to #3 (120 sec)</td>
<td>+14.2 (1.55)†</td>
<td>+6%</td>
</tr>
<tr>
<td>#4 (45 sec) to #5 (120 sec)</td>
<td>+12.3 (1.62)†</td>
<td>+6%</td>
</tr>
<tr>
<td>#3 (120 sec) to #4 (45 sec)</td>
<td>−10.7 (1.76)†</td>
<td>−2%</td>
</tr>
<tr>
<td>To determine the effect of repeated tests:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#1 (45 sec) to #2 (45 sec)</td>
<td>+0.3 (1.05)†</td>
<td>−1%</td>
</tr>
<tr>
<td>#2 (45 sec) to #3 (45 sec)</td>
<td>+3.5 (1.33)†</td>
<td>+4%</td>
</tr>
<tr>
<td>#3 (120 sec) to #5 (120 sec)</td>
<td>+1.7 (1.37)†</td>
<td>+4%</td>
</tr>
</tbody>
</table>

*Change in venous filling (as indicated by impedance) between the first and second IPG tests in the comparison. The values are expressed in impedance units.
†Mean and SEM.
‡Change in sensitivity or specificity between the first and second IPG tests in the comparison.
venography. Termination of the IPG sequence even after two 45-second occlusion time tests would have decreased this specificity by 14%. Furthermore, if the common practice was followed of terminating the IPG series after one normal result with 45 seconds of occlusion, a 10% deterioration in sensitivity would have occurred. These observations emphasize the practical importance of achieving optimal venous filling and also provide a physiological basis for standardizing impedance plethysmography.

References

Arterial Insufficiency of the Hand
Evaluated by Digital Blood Pressure
and Arteriographic Findings

MASAFUMI HIRAI, M.D.

SUMMARY In 80 hands with arterial occlusive disease, systolic blood pressure at the wrist and in all fingers was measured by photoelectric plethysmography. The correlation of such pressures with angiographic evidence of organic obstruction or the development of digital ischemic signs was studied. Digital blood pressure was normal in all 184 fingers in which there was at least one obstruction-free arterial path to and through the finger. Ischemic signs developed in only one. Of 203 fingers with occlusion in vessels in or leading to both sides of the finger, a decreased pressure was seen in 173 and a normal pressure in 30. Ischemic signs were observed in 132 of 173 fingers with a decreased pressure, and in two of 30 with a normal pressure. The clinical significance of measurement of digital blood pressure in arterial occlusive disease is discussed.

IN THE EVALUATION of arterial insufficiency of the hand, the five fingers should be studied separately, since the degree of ischemia is often different in each finger. Especially in the early stage of the disease, only one or two fingers may be involved. Arteriography may be used for this type of study. However, arterial occlusion in arteriograms does not always indicate digital ischemia. During recent years there has been an increasing interest in measuring the blood pressure of the limbs, because blood pressure values correlate with the function of the collaterals and the clinical findings. By using strain gauge or photoelectric plethysmography with a blood pressure cuff, blood pressure measurement can be carried out in all fingers. However, there has not yet been a detailed study regarding clinical significance of blood pressure measurement in all fingers. Downs et al. reported the correlation of digital blood pressure with arteriographic findings in hands with arterial occlusion, but they did not deal with the development of digital ischemia.

In the present study, systolic blood pressure at the
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