Detection of Clinically Suspected Deep Vein Thrombosis Using Light Reflection Rheography

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Venography is the current standard for the diagnosis of deep vein thrombosis (DVT). Noninvasive tests have differing sensitivity and specificity, are technically demanding, and may be subject to variability in interpretation. Light reflection rheography (LRR) is a noninvasive method utilizing light-emitting diodes and a sensor to measure light reflected from the skin surface. The intensity of reflected light establishes a graphic pattern that indirectly quantifies parameters of venous function by measuring changes in the microcirculation.

Seventy-two patients who underwent contrast venography at our institution were also evaluated with LRR. Twenty-four patients were found to have DVT as demonstrated by venography. Of these, 23 also had DVT detected by LRR. No evidence of thrombus was seen in 45 patients studied by venography; in this group, 35 had normal venous emptying indicated by LRR.

Using LRR, a sensitivity of 96% was achieved in the evaluation of clinically suspected DVT. This sensitivity is comparable with other noninvasive tests. In addition, LRR is easy to operate, portable, inexpensive, and not technically demanding. Further investigation is needed to confirm these data and further define the role of LRR in the evaluation of clinically suspected DVT.

There is widespread agreement that the patient with clinically suspected deep vein thrombosis (DVT) must have confirmatory testing [1-3]. Contrast venography is the diagnostic standard for the detection of DVT [4]. This technique, however, is not without risk, which includes the potential for thrombogenesis and adverse reaction to intravenous contrast agents [5]. In some patients, the use of venography is also limited by poor venous access and edema.

A number of noninvasive methods that obviate the need for administration of contrast agents are currently available. Ideally, a noninvasive test should have several characteristics that would make its use desirable. These include accuracy, low risk of complications, ease of operation and interpretation, and low cost. Accessibility and portability would also add to its usefulness. These features combined in one modality may also facilitate wide application as a surveillance test in high-risk groups.

Impedance plethysmography (IPG) has been extensively evaluated in large cohorts of patients with adequate long-term follow-up [6,7]. High-resolution ultrasound (US) imaging with and without Doppler has also been studied [8-10]. These techniques have proven to be safe and effective for the diagnosis of occlusive proximal DVT. Despite their diagnostic accuracy, IPG and US have not been widely applied as screening tools; this is probably because obtaining adequate studies generally requires trained technical personnel in the setting of a vascular laboratory.

Light reflection rheography: Developed in West Germany, light reflection rheography (LRR) is a photoelectric technique similar to photoplethysmography (PPG). LRR does not require operator calibration and, unlike PPG, can quantitatively measure changes in the venous circulation. LRR measures reflected infrared light from the dermal microcirculation, which has been shown to correlate with invasively measured venous pressures [11,12].

Previous studies have verified LRR's accuracy as a noninvasive indicator of venous hemodynamics [11]. Currently in use for the evaluation and management of chronic venous insufficiency, it has thus far received little attention as a potential tool for detection of DVT [12].

Based on the hemodynamic parameters measured by LRR, we hypothesized that in the presence of occlusive DVT, a significant difference should be evident in the venous emptying and rate of venous emptying when measured in patients with DVT as compared with those patients with normal venous function of the lower extremities.
PATIENTS AND METHODS

Patients were referred for venography by their respective physicians when there was a clinical suspicion of DVT. They included outpatients and inpatients at the University of Miami/Jackson Memorial Medical Center. Twelve patients were enrolled in a pilot study between October 1987 and March 1988. Sixty patients were consecutively enrolled between August 1988 and January 1989. The study protocol was approved by the institutional review board.

Each patient scheduled for venography was interviewed and examined by one investigator after informed consent for the study was obtained. LRR was performed within 48 hours and in most cases on the same day as venography. If the LRR was performed after venography, the results of the contrast study were always unknown to the investigator.

LRR was performed using a simple bedside device (A-V 1000, Hemodynarnics, Inc., Boca Raton, Florida). The unit consists of an electronic sensor combined with an amplifier-recorder. The sensor contains three light-emitting diodes circumferentially arranged around a photodetector. Infrared light is beamed into the skin at depths of 0.5 to 1.5 mm where it is either absorbed by red blood cells or reflected back to the sensor. The quantity of reflected light is then converted to an electrical signal and recorded on a chart.

Lower extremity exercise performed during the testing procedure promotes venous emptying through the action of the musculovenous pump mechanism. The intensity of reflected light prior to initiating the exercise is defined as $R_0$. As venous emptying occurs and venous pressure diminishes, the amount of red blood cells in the microcirculation decreases with a resultant increase in the quantity of light reflected. At the completion of the exercise routine, venous emptying reaches a peak corresponding to maximal reflection ($R_{max}$). This is followed by a refill phase with return of blood to the lower extremity and a corresponding decrease in light reflection to a steady baseline. This period is designated the venous refill time (VRT). The amount of time needed to reach $R_{max}$ is measured from the beginning of the exercise routine and labeled T (seconds). Each light reflection rheography tracing was examined and the $R_0$, $R_{max}$, T, VRT, and AMP (average amplitude) of the deflections measured (Figure 1). The measured change in light reflection at $R_{max}$ is called delta $R$ ($R_{max}$ minus $R_0$) and the rate of change (slope) of light reflection (delta $R$/T) is calculated.

LRR was performed at the bedside in the sitting position, and when possible was also done in the supine and reverse Trendelenburg positions. Outpatients had the test performed while sitting comfortably in a chair. Patients sat so that the hip was extended slightly to an angle of approximately 120 degrees. The feet were positioned flat in front of the patient with a resultant angle at the knee of approximately 120 degrees. Using double-sided adhesive tape, the electronic photo sensor was placed approximately 10 cm above the medial malleolus of the leg to be tested.

The test procedure requires the completion of a simple exercise routine. The patients are instructed to perform 10 dorsiflexions of the ankle over 15 seconds. A built-in metronome that emits both an auditory and a light signal is used to guide the patient. A continuous graphic tracing is recorded throughout the procedure (Figure 1). Upon completion, the patient sits motionless until the tracing reaches a steady baseline. Multiple (three to five) LRR tracings were recorded for each subject. All tracings were independently reviewed by two of the investigators who had no knowledge of the patients' clinical status or veno-
gram results. The tracing of the best technical quality was selected for analysis in the study.

Ascending contrast venography was performed according to the methods of Rabinov and Paulin [4]. The criteria for the diagnosis of DVT were the presence of an intraluminal filling defect evident on two different projections or the absence of contrast in a venous segment. Venograms were interpreted independently by two vascular radiologists. The results of LRR were unknown to the radiologists interpreting the venograms. Three subsequent diagnostic categories were assigned based on the contrast venogram: no evidence of DVT, proximal (popliteal vein and above) DVT, and isolated calf or distal DVT. The methods used in this study adhere to criteria necessary for the evaluation of new testing procedures [13,14].

RESULTS

Seventy-two patients were enrolled in the study. Venography demonstrated proximal DVT in 22 patients (32%) and isolated calf (distal) DVT in 2 (3%). Forty-five patients (65%) were found to have no evidence of acute thrombosis. Three patients were excluded from the analysis due to technically imperfect venography. Because of the small number of subjects with distal DVT, these patients were combined with those having proximal vein thrombosis for analyses. The demographic profile of the study population is shown in Table 1. There was a difference in characteristics (sex) between the two study groups.

The quantity of venous emptying (delta R), and rate (slope) of venous emptying (delta R/T) are the parameters of LRR that best correlate with the presence of angiographically detected DVT. The mean values of these measurements in patients with positive venograms and those patients with negative venograms are detailed in Figures 2 and 3 (p = 0.0001). LRR also demonstrated a significant difference in VRT among patients in the two groups (not pictured, p = 0.0003). The AMP from the LRR graphic tracing was not significantly different (p = 0.21).

Receiver-operator curve (ROC) analysis [15,16] was used to better characterize LRR in the two study groups. The ROC curve for the slope and the delta R are shown in Figures 4 and 5. Using a slope of less than or equal to 0.17 mm/second as indicating the presence of DVT (positive LRR), a sensitivity of 83% and specificity of 89% are achieved. If the slope threshold for a positive LRR is set at a value of less than or equal to 0.31 mm/second, a sensitivity of 96% with a specificity of 78% is demonstrated. Using delta R, thresholds of 6 mm or less or 3 mm or less yield sensitivities of 96% and 83%, respectively, with specificities of 71% and 89%.

Of the 69 patients included in the analysis, all had LRR performed in the sitting position. In addition, 39 LRR tracings were analyzed with patients supine, and 26 with patients positioned in reverse Trendelenburg. ROC analysis showing comparable areas under the ROC curves for the patients tested with LRR in the different positions is demonstrated in Figure 6.

| TABLE 1
Demographic Profile of Study Patients |
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<tr>
<td>Positive Venogram (n = 24)</td>
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</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Age (yrs)</td>
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<tr>
<td>Race</td>
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<td>White</td>
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Figure 2. A significant difference in the mean slope of venous emptying as measured by LRR is evident in patients with and without DVT. The numbers represent means of each group. Each boxplot center line represents the median, the gray area represents 95% confidence intervals for the median, and the box itself indicates the 25% to 75% confidence interval with the whiskers representing range.

Figure 3. Boxplots of delta R show the significant difference of statistical parameters for this variable in patients with and without DVT. The box depicts the 25% to 75% confidence interval while the gray area represents the 95% confidence interval for the median depicted by the center line in the box. Numbers again represent mean values in each patient group.
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Figure 4. Receiver-operator characteristics curve for the range of threshold values for slope (sitting position). The sensitivity and specificity at thresholds of 0.31 or less and 0.17 or less are illustrated. The point at which the specificity increases to 89% is more favorable for the use of LRR as a diagnostic test. As the slope approaches 0, the specificity would favor more accuracy of LRR as a diagnostic test at the expense of lower sensitivity.

Chi-squared analysis of the contingency table comparing the slope of LRR (positive less than or equal to 0.31 mm/second) with venography revealed that 23 of 24 patients with DVT were correctly identified (Figure 7). Of 45 patients with no evidence of acute DVT, there were 10 false-positive results by LRR. The prevalence of DVT in this study was 35%, thus the positive predictive value of LRR using slope less than or equal to 0.31 mm/second was 70%. The negative predictive value of LRR with a slope greater than 0.31 mm/second was 97%.

Of the 10 patients with false-positive results by LRR, 7 had confounding factors responsible for impeding venous outflow (Table II). The patient with a false-negative LRR had superficial and calf phlebitis with significant collateral flow allowing adequate venous emptying.

COMMENTS

This study comparing contrast venography with LRR demonstrates a useful clinical application for this photoelectric technique. As hypothesized, venous emptying and the rate of venous emptying are highly sensitive in identifying patients with occlusive DVT. Using ROC analysis, a sensitivity of up to 96% was achieved. This sensitivity is comparable with that of other noninvasive techniques currently in use [6-10]. LRR was easy to operate and interpret using the criteria we derived from measurements taken directly from the tracings.

The unit used in this study is lighter and more compact than other noninvasive devices. Combined with its ease of operation and relatively low equipment cost (approximately $7,000), this may allow its widespread application in many patient care settings. These factors and its high sensitivity may define LRR as an excellent alternative in screening patients. In this role, LRR may influence clinical decisions in emergency settings by identifying patients who require further study and possible hospital admission. Conversely, the high negative predictive value of 97% achieved with LRR makes a diagnosis of occlusive DVT unlikely and may affect the cost of unnecessary admissions and exposure to risky therapy. With its char-

Figure 5. Receiver-operator characteristics curve for the range of threshold values for delta R (sitting position). The sensitivity and specificity at sample points on the ROC curve are illustrated.

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Figure 6. Comparison of ROC curves for slope in patients tested in various positions illustrating similar characteristics and thus reliability independent of position, as shown by the comparable shape and areas under each curve.

Chi Squared = 31.10
(Fischer's exact test)
p < .0001

Figure 7. Two by two comparing LRR results with venography as the "gold standard." Using slope of 0.31 or less, 23 of 24 patients with DVT were correctly identified, resulting in a sensitivity of 96% and a negative predictive value of 97%.

Table II: Confounding Conditions in Patients with False-Positive Results on Light Reflection Rheography (by slope)

<table>
<thead>
<tr>
<th>LRR SLOPE D/R</th>
<th>VENOGRAm</th>
<th>Positive</th>
<th>Negative</th>
<th>Chi Squared</th>
<th>Fischer's exact test</th>
</tr>
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<tbody>
<tr>
<td>≤ 0.31</td>
<td>Positive</td>
<td>23</td>
<td>10</td>
<td>31.10</td>
<td>p &lt; .0001</td>
</tr>
<tr>
<td>≥ 0.31</td>
<td>Negative</td>
<td>1</td>
<td>35</td>
<td></td>
<td>97%</td>
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1. Knee effusion
2. Deep muscle abscess of calf
3. Pelvic mass with iliofemoral vein compression
4. Pregnancy
5. Superficial phlebitis with chronic deep vein thrombosis
6. Suprapatellar collection with knee effusion
7. Pregnancy
8. Pelvic mass with iliofemoral vein compression
9. Ineffective dorsiflexion
10. Chronic deep vein thrombosis with lumbar irregularities
acteristics as an effective and simple screening device, LRR can also be applied by hospital or office staff without specialized training to provide surveillance for DVT in high-risk patients.

The use of LRR as a diagnostic test, as opposed to a screening test, will require further studies that may identify a "probability scale" of disease depending on the observed abnormality in the venous emptying or rate of emptying. For example, varying the threshold for a positive study to a slope less than 0.17 improves specificity to 89%, with a corresponding decrease in sensitivity to 83%. This threshold maximizes the likelihood ratio (7.54) of a positive test result and significantly improves diagnostic accuracy. Further studies with modified techniques may be necessary for improvement in the specificity of LRR, although in comparison to IPG and US, it has achieved better early results [10,17-19]. IPG and US also required revisions in early testing protocols to achieve their current level of accuracy [6,8,20].

The confounding factors that affected LRR results were related to nonthrombotic disruption of venous outflow and may also influence results of other tests that rely on flow for a diagnosis of DVT. Of 10 patients with no DVT and a positive LRR, all except 1 had a clinical condition that could directly or indirectly influence venous hemodynamics. However, the aim of the present study was to establish the usefulness of LRR in detecting DVT as compared to venography, and we did not directly compare IPG and US with LRR. A direct comparison of LRR with other noninvasive techniques is clearly necessary.

In this study, two patients were found to have distal DVT by venography; in both, DVT was also detected using LRR. This observation in only two patients is not sufficient to conclude that LRR is reliable in the diagnosis of calf DVT. It does, however, indicate the need for further evaluation in studying the potential use of LRR in this group of patients.

We conclude that in our population of patients with clinically suspected DVT, LRR is a highly sensitive technique for detecting angiographically confirmed deep vein thrombosis. It is a simple, reproducible, technician-independent, inexpensive, and portable noninvasive method. These features potentially make LRR an ideal screening test. Further studies are necessary to better define the role of LRR in evaluating patients with suspected DVT.

Progressively less invasive and simultaneously more definitive testing seems very much a part of contemporary medicine. How this relates to real clinical illness remains to be fully defined.

REFERENCES