Acute or subacute DVT - role of real time elastography for determining the age of thrombi

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Purpose

Lower-extremity deep venous thrombosis (DVT) is a life-threatening disease and should be treated in acute period (1). DVT can be extensive (iliofemoral vein) or confined to the popliteal vein (PV) but in both situation it can decrease the patient's life quality with the sequelae and complications such as post thrombophlebitis syndrome (PTS) and pulmonary embolism. Hence, DVT should be treated promptly when the diagnosis is confirmed (2). Thrombus age is crucial and determinative for choosing the therapy options. Patients with acute DVT are good candidates for such interventional procedures (3). Advanced gray-scale ultrasonography (US) technology enables the high-quality US, duplex Doppler US with color Doppler US (CDUS) images to diagnose DVT, but there are still overlaps to discriminate the thrombus age, and subacute DVT can be misdiagnosed as acute DVT by US findings alone (4). Real-time elastography (RTE), simply evaluates the stiffness of the tissue, may have a role to predict the thrombus age since thrombosis progress to fibrin bands and hardens with age (1,2). Although most of the studies found significant differences, they evaluated the thrombus elasticity of acute and chronic DVT in vitro or in animal models. There is a limited number of study on human subjects as far as we know. (5,6) Thus, there is still debate to predict the age of thrombus in vivo by means of elasticity. In this study, we aimed to display real-time elastography findings of thrombus in acute and subacute DVT and feasibility of the technique.

Methods and materials

All consecutive patients referred to outpatient Doppler ultrasonography unit for unilateral leg pain with swelling, and erythematous appearance between September 2015 and December 2015 were enrolled in the study. Inclusion criteria were having a DVT within a duration of 1-28 days from onset of symptoms and being a volunteer for the study. Patients with cellulitis, uni or bilateral superficial venous thrombosis, and chronic DVT were excluded from the study. Visualization of thrombus in the lumen of the common femoral vein (CFV), deep femoral vein (DFV), femoral vein (FV) or PV on the gray-scale US was used as a reference test for the diagnosis of lower-limb DVT (7). If symptoms were present less than 15 days, the patient was accepted as having acute DVT, and as subacute DVT if symptoms were present within 15-28 days. CDUS and RTE were performed respectively with the same US scanner (HI VISION Preirus, Hitachi Medical Corporation, Tokyo, Japan) by EUP-L54MA, 13-6 MHz linear probe in all patients.

Data Analysis

All gray scale US, CDUS, and RTE were performed by one observer. All elastographic images were recorded and evaluated with the consensus of two observers experienced
in US imaging for 10 and 12 years. Strain ratio of the thrombus was calculated by dividing the strain of thrombus (A) to the strain of the adjacent subcutaneous adipose tissue (B) which were obtained with the smallest ROIs including maximal thrombus and subcutaneous adipose tissue (Fig. 1 on page 3). The strain ratio (B/A), represented numerically, was calculated automatically.

**Statistical Analysis**

Patients were grouped into two as having acute or subacute lower-limb DVT on the basis of patient history, clinical findings, US and CDUS features. The thrombus echogenicity, compressibility, presence of recanalization, elastography pattern, and strain ratio of the thrombus in acute and subacute DVT were compared. Continuous variables were presented as mean (± SD), and nominal values were presented as number (%). The Shapiro-Wilks test was used to assessed the normality of strain ratio values. For comparison of US, CDUS and RTE findings the Mann-Whitney U or Student’s T-test were used. Statistical analysis was performed on a statistics program (MedCalc Statistical Software, version 12.7.7, MedCalc Software bvba, Ostend, Belgium, 2013).

**Images for this section:**
Fig. 1: A 60-year-old woman presented with right leg pain for five days. Thrombus in popliteal vein is hypo-iso echogenic on the gray-scale US image (white thin arrow). There is no blood flow and vein fails to compress. On the elastographic image, thrombus is mostly red and green indicating relatively soft in stiffness (white thick arrow). ROI in subcutaneous adiposse tissue is also shown (dashed arrow).

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Results

71 patients, consist of 47 patients with acute DVT and 24 patients with subacute DVT, were further evaluated by RTE. Among them, we could not perform RTE in 9 patients (16.67%) (6 patients with acute DVT and 3 patients with subacute DVT) due to improper position for evaluation or or excessive subcutaneous edema.

The mean age, duration, side and location of thrombus were presented in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Acute DVT (n=30)</th>
<th>Subacute DVT (n=19)</th>
<th>DVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>53.2 ± 15.32</td>
<td>53.14 ± 17.21</td>
<td></td>
</tr>
<tr>
<td>Duration (day)</td>
<td>7.14 ± 3</td>
<td>21.21 ± 3.68</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28 (68.3%)</td>
<td>12 (57.1%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>13 (31.7%)</td>
<td>9 (42.9%)</td>
<td></td>
</tr>
<tr>
<td>Side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right leg</td>
<td>17 (41.5%)</td>
<td>5 (23.8%)</td>
<td></td>
</tr>
<tr>
<td>Left leg</td>
<td>24 (58.5%)</td>
<td>16 (76.2%)</td>
<td></td>
</tr>
<tr>
<td>Location</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>To popliteal vein</td>
<td>13 (31.7%)</td>
<td>9 (42.9%)</td>
<td></td>
</tr>
<tr>
<td>Iliofemoral vein</td>
<td>28 (68.3%)</td>
<td>12 (57.1%)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. The demographic data and thrombus location in patients with acute and subacute DVT.

The etiology was unknown in 16 patients (11 acute DVT, 5 subacute DVT), immobilization in 25 patients (15 acute DVT, 10 subacute DVT), pregnancy related or postpartum complications in 10 patients (6 acute DVT, 4 subacute DVT), trauma in 1 patient with acute DVT, coagulation disorders in 6 patients (4 acute DVT, 2 subacute DVT), and previous history of DVT in 4 patients with acute DVT. The mean serum D-dimer level was 4664.21 ± 5081.34 in acute DVT, and 2385 ± 2274.38 at subacute DVT (p = 0.190). The hypoechoic and incompressible thrombus, and absence of recanalization were all significant for acute DVT (p = 0.0003, p < 0.00001, and p < 0.00001 respectively). The diagnostic performance of the US and CDUS parameters were presented in Table 2. The thrombus in acute DVTs had mostly intermediate stiffness, while subacute DVTs were mostly hard (p = 0.2). Also, the mean strain ratio of acute DVT (1.391 ± 2.01) was lower than the mean strain ratio of subacute DVT (1.835 ± 2.72) indicating a softer thrombus in acute DVT (p = 0.343).
<table>
<thead>
<tr>
<th>Feature</th>
<th>Hypoechogeticity</th>
<th>Incompressibility</th>
<th>Absence of Recanalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.76 (0.61 - 0.87)</td>
<td>0.82 (0.68 - 0.91)</td>
<td>0.76 (0.62 - 0.87)</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>93.33 (77.93 - 99.18)</td>
<td>100 (88.43 - 100)</td>
<td>100 (88.43 - 100)</td>
</tr>
<tr>
<td>Specificity</td>
<td>57.89 (33.50 - 79.75)</td>
<td>63.16 (38.36 - 83.71)</td>
<td>52.63 (28.86 - 75.55)</td>
</tr>
<tr>
<td>PPV</td>
<td>77.77 (61.99 - 88.283)</td>
<td>91.08 (64.84 - 92.04)</td>
<td>76.92 (28.86 - 75.55)</td>
</tr>
<tr>
<td>NPV</td>
<td>84.61 (57.765 - 95.674)</td>
<td>100 (73.54 - 100)</td>
<td>100 (69.15 - 100)</td>
</tr>
<tr>
<td>Accuracy</td>
<td>79.59</td>
<td>85.71</td>
<td>81.63</td>
</tr>
</tbody>
</table>

**Table 2.** The diagnostic performance of US and CDUS features

**Images for this section:**

![Images showing various medical imaging techniques and measurements.](image-url)
Fig. 2: A 63-year-old man presented with left leg pain for four days. Thrombus in popliteal vein is hypo-iso echogenic on the gray-scale US image. There is no blood flow and vein fails to compress. On the elastographic image, thrombus is green indicating intermediate stiffness (white arrow). ROI within the adipose tissue is also seen (dashed arrow).

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Fig. 3: Same patient in Fig.2 after 14 days. On elastography images; the thrombus is more blue in color, representing harder than acute phase (white arrow).

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Conclusion

DVT is a common vascular disease with a prevalence of 1/1000 person in a year (4). Acute thrombus is soft and fragile whereas chronic thrombus is hard, fully organized and have strong attachment with the vein wall (2, 6). Effective therapies for DVT include catheter-directed thrombolysis and percutaneous mechanical thrombectomy which can be applied only in the acute DVT (3). Thus, information about thrombus age is essential for therapy decision and for patients especially in incorporable or in bedridden patients (4,8). In this study, we primarily aimed to evaluate the RTE findings of acute and subacute thrombus in lower-limb DVT and found that there was no difference regarding thrombus stiffness. On the other hand, US and CDUS features were significantly different between acute and subacute DVT.

Limitations

Our study group was relatively small. We could call back the patients with acute DVT and evaluated them in subacute phase to increase the number of patients. But the design of our center is not appropriate for such control imaging. We had to classify the DVT as acute and subacute on the basis of patients' history which is a poor predictor for thrombus characteristics, but a simple way to classify DVT (9). We performed RTE by applying external force concerning the quality factor. But still, we don’t know the compression force which may change the elastographic pattern of thrombus (10).

In conclusion, thrombus in acute DVT is softer than in subacute DVT in terms of tissue stiffness, however RTE has no role in the differentiation of the acute DVT from subacute DVT.

Personal information

References


