Venous Thrombus Evaluation with Ultrasonographic Tissue Elasticity Imaging

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With increasing age venous clots undergo an organization process during which they become adherent to the vessel wall. Therefore, one important factor influencing the decision whether or not to perform thrombolysis or thrombectomy for venous thrombosis is the age of the thrombus. The aim of this study was to examine the diagnostic ability and an appropriate assessment procedure of this method for venous thrombus.

Methods: Conventional Ultrasonography (US) and Elastography were performed on 25 patients diagnosed with venous thrombosis in the lower extremities. All images were obtained with an Ultrasound Scanner EUB-8500 (HITACHI Medical Corporation) and analyzed by an external personal computer. First of all, we examined elasticity images obtained with different methods of compression and drew up a certain assessment procedure for evaluating venous thrombi. Secondly, we observed the venous thrombi with B-mode images, Color Doppler images and elasticity images. We estimated the age of thrombi by their appearance in conventional ultrasonographic images and divided them into three phases as follows: acute, sub-acute and chronic.

Results: 25 patients, 30 lesions were assessed. We could obtain stable images by vibrating the area of the thrombus after initial compression. It was recommended that the range of the region of interest (ROI) include muscle, and exclude bone and arteries. In general, thrombi in the acute phase were represented as soft elasticity images, and venous thrombi in the chronic phase were represented as hard elasticity images. Meanwhile, thrombi in the acute phase presenting anechoic lesions were not imaged clearly, and with mixed thrombi with a small amount of venous flow it was difficult to differentiate between fresh thrombi and venous flow.

Conclusion: Venous thrombi were imaged clearly with appropriate compression by Elastography. We will continue to improve elasticity imaging for assessing venous thrombus.

Key Words: Elastography, Venous Thrombus, Pulmonary Thromboembolism

1. Background

Deep venous thrombosis (DVT) is widely known as a disease sometimes accompanied by fatal pulmonary thromboembolism. Yearly advances in equipment and technology have brought changes to the methods used for its diagnosis. As a result, ultrasound is now widely used for detecting the presence of DVT.

The severity and indicated treatment differ widely for DVT depending on the site and timing of onset. When a thrombus is at the early stage of onset, the complication of pulmonary thromboembolism is more likely to occur and fibrinolytic therapy is effective. DVT diagnosis is expected to enable estimation of the risk of the complication of pulmonary thromboembolism and response to treatment by diagnosing not only the presence but also the state of a thrombus, particularly the timing of onset.

The time course changes by ultrasonography as a

thrombus with low echo intensity (hypoechoic) accompanied by distension of the vein when onset is early, with high echo intensity (hyperechoic) predicted to be shown when the thrombus becomes organized[1]. However, there have been few reports of detailed examination, and detailed evaluation of lesion characteristics by conventional ultrasonography appears to be limited. On the other hand, Emelianov et al. reported that the elasticity of a venous thrombus increases, transforming it from a soft to a hard thrombus in the course of organization[2]. It is anticipated that obtaining more detailed information of a venous thrombus by assessing its elasticity would enable estimation of its time of onset and mobility.

Tissue elasticity imaging yields new diagnostic information on the elasticity (hardness) of tissues whereas conventional ultrasonography images mainly show the shape of an organ by visualizing the intensity of echoes from the tissues. The usefulness of assessment of venous thrombus by means of tissue elasticity imaging has been reported but it has not yet been clinically applied[3]. Development of a clinically applicable device is still under way.

The EUB-8500 (Elastography) of HITACHI Medical Corporation used in this study is ultrasonography equipment developed by Ito et al. for the diagnosis of breast cancer through the clinical application of tissue elasticity imaging[4)5)]. It enables the use of most of the technologies of conventional ultrasonography and provides highly accurate elasticity images in real time. It is expected to be used increasingly for diagnosis in clinical settings.

In this study, we examined whether the images provided by Elastography are sufficiently stable for making diagnoses and whether the images are appropriate for clinical application when diagnosing venous thrombus.

2. Method

The subjects of this study were 25 patients with venous thrombi in 30 sites of the leg from whom informed consent was obtained. This study was performed with the approval of the ethical committee of Tsukuba University Hospital.

The HITACHI EUB-8500 equipped with a 7.5 MHz Linear probe was used for ultrasonography. The presence or absence of thrombus and blood flow was diagnosed by B-mode, Color Doppler, and Power Doppler and Elastography was performed for patients diagnosed as venous thrombus of the leg. Raw data during Elastography imaging were transmitted from the equipment to an external computer to construct off-line elasticity images. This system was used initially to investigate a method providing stable images that could be used for evaluation. The appropriateness of the obtained images and the imaging ability of Elastography were then assessed.

3. Examination of imaging method

First, an appropriate imaging method was investigated. Because diagnosis is made by applying manual pressure, pressure should be applied as uniformly and as vertical to the ROI as possible to obtain suitable images for evaluation. Elastography images showing the characteristics of thrombi were judged to be stable, providing a suitable method for repeatedly obtaining the same results. The method of applying compression was evaluated by changing the degree of pressure and the amplitude and speed of the ultrasound signal. Since the obtained images show relative indications that compare the mean results of a randomly selected ROI and the surrounding tissues, settings for the ROI and the included surrounding tissues were investigated. Settings were adjusted so that the mean elasticity in the ROI is shown in green and areas softer and harder than that are shown in red and blue, respectively.

4. Evaluation of imaging ability

Next, the appropriateness of obtained images was compared with clinical findings and the results obtained from conventional ultrasonographic images. The clinical findings and results obtained from conventional ultrasonographic images were classified into the 3 phases of acute, sub-acute, and chronic, and images of thrombi at each phase obtained by Elastography were examined. The classification of Zwiebel et al. was referred to for the classification of conventional ultrasonographic images. Acute phase thrombus was defined as images showing regions of low brightness, venous dilatation, loss of compressivity, and free-floating sign. Compared to this, sub-acute phase thrombus was defined as images showing increased brightness, shrinkage of the thrombus itself or reduced venous diameter, and reperfusion of blood flow. Chronic phase thrombus was defined as an organized thrombus with fibrous tissue, which in conventional ultrasonographic images is shown as a thickened venous wall or bright regions. The time course from thrombus formation was estimated from clinical findings or conventional ultrasonographic images and the images of each phase obtained by Elastography were evaluated.

5. Results

5.1 Imaging method

It was possible to obtain stable images in this study, after stabilizing the ROI by initial compression, small amplitude vibrations were applied to enable application of uniform pressure. Fig. 1 shows two images. On the left is an image obtained with inappropriate pressure whereas

the right image shows stable imaging obtained with appropriate pressure indicated by a smooth red line extending along the peripheral muscle fibers. Because a certain diameter is required to apply uniform pressure to the ROI for long-axis imaging, evaluation using short-axis images would be desirable for an undilated vein. To achieve the most stability, it is thought that the range of ROI settings should exclude as much as possible bone, blood and arteries, and include surrounding muscle tissue for comparison because the displayed image is a relative image that compares the mean results within the ROI with the surrounding area.

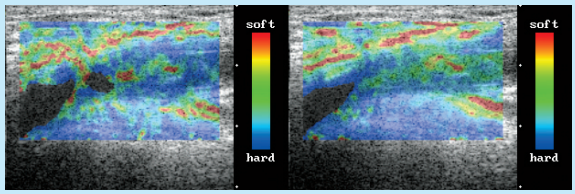

Fig. 1 : Compression method
On the left is an example of an image taken with inappropriate pressure. If pressure is not applied uniformly, both still and moving images are unstable. On the right is an example of an image taken with appropriate pressure. After determining the ROI with initial compression, it is possible to achieve stable images with small amplitude vibrations. The ROI includes peripheral muscle tissue, without including undesirable images of bone and arteries, for a suitable image for evaluation with a smooth red line extending along peripheral muscle fiber.

5.2 Imaging ability

Typical images at each phase are shown in Fig. 2.

Fig. 2-a shows the image of a thrombus soon after onset. It is an acute phase thrombus associated with venous dilatation and is shown with overall low brightness by B-mode. As can be seen on the right, it was shown as a red and green image by Elastography, indicating that it is soft.

Fig. 2-b shows a thrombus about 3 weeks after onset. It is a sub-acute phase thrombus tending to shrink and increase in brightness as shown by B-mode. In the Elastography image on the right, it is shown as mainly green.

Fig. 2-c shows a chronic phase mural thrombus. The entire mural thrombus region is shown with high brightness by B-mode. Blood flow indicating reperfusion can be seen in the surrounding tissues. Elastography showed the entire thrombus in blue, indicating that it was hard.

As seen in the typical images above, thrombi showed a tendency to gradually harden after onset but the imaging did not agree with the clinical course in some patients. Fig. 3 shows changes over time of a venous thrombus in a soleus muscle vein. As time progressed, the entire thrombus was shown in red (soft) due to the development of blood flow caused by recanalization. This suggests that evaluation of the thrombus itself becomes difficult due to blood flow in the ROI. In the right image of Fig. 3, the sur-

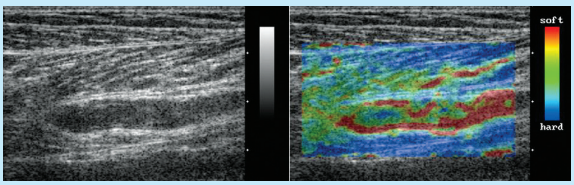

Fig. 2-a : Acute phase thrombus
Case of a hard thrombus in a soleus muscle vein. In a conventional ultrasonographic image (left), showing hypoechoic, and vein dilatation and blood flow inside the thrombus are not detected. With Elastography (right), a red and green image indicates the thrombus is soft.

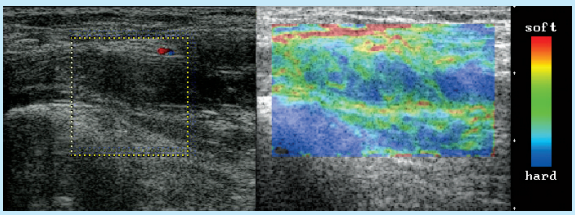

Fig. 2-b : Sub-acute phase thrombus
A case of femoral vein thrombus. About 3 weeks after onset, a conventional ultrasonographic image (left) shows the thrombus as a brighter area. With Elastography (right), a red and blue image indicates the thrombus is hard.

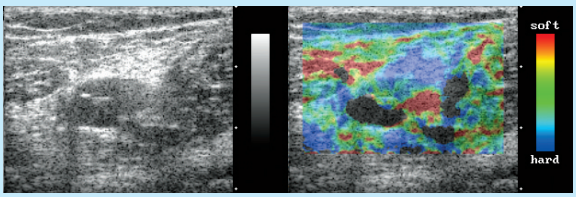

Fig. 2-c : Chronic phase thrombus
A mural thrombus remaining in a vein in the soleus muscle. This is a case with a clinical course of about 2 years after onset. A conventional ultrasonograpic image (left) shows the mural thrombus as a very brighter area. On the other hand, with Elastography (right), the thrombus shows as blue (hard).

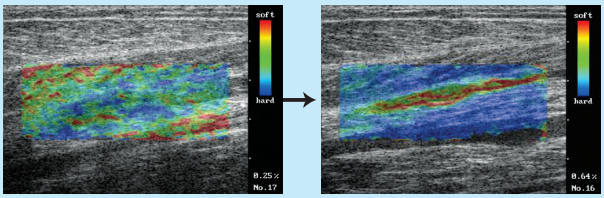

Fig. 3 : Case of soleus muscle vein thrombus at a later time
This a thrombus that formed in a vein of the soleus muscle, but after time, due to the influence of renewed blood flow resulting from recanalization, the thrombus shows as red (soft). In this case it was difficult to visualize the thrombus itself. Elasticity in the ROI was also influenced by blood flow, with all peripheral tissue showing as blue (hard).

rounding tissues are shown entirely blue (hard) because the mean elasticity in the ROI tended to become soft due to blood flow.

6. Discussion

An appropriate method of imaging venous thrombi by Elastography and its imaging ability were investigated in this study. The principle of Elastography is visualization of tissue elasticity based on the difference in the degree of change of different tissues in response to applied compression. Because this equipment shows relative imaging by comparing the amount of change (elasticity) with the surrounding tissues upon the application of manual pressure, an index for selecting the surrounding tissues for comparison purposes is required. It is also desirable to apply pressure as uniformly as possible to the ROI.

In our investigation of a method of compression, after stabilizing the ROI by initial compression, small amplitude vibrations were applied to enable application of relatively uniform pressure. It was considered desirable to exclude bone and arteries, and to include muscle tissue when selecting the surrounding tissues and establishing the ROI. A smooth red line extending along muscle tissue in images is currently accepted as an index for the selection of images appropriate for evaluation.

It was possible to capture the changes from a soft thrombus in the acute phase to a hard thrombus in the chronic phase of a venous thrombus by Elastography using these methods of pressure application and diagnosis. It is considered to show the changes associated with organization of a clot.

Meanwhile, one of the obvious problems at present is the difficulty in evaluating a thrombus itself, as in the case of recanalization indicated in Fig. 3, because the mean results tend to show a soft region when blood flow is clearly included in the ROI. An imaging method for excluding the apparent blood flow was examined, the results of which are shown in Fig. 4. Fig. 4-a shows the blood flow detected by Color Doppler in red (soft) whereas an image of tissue elasticity in the region of distinct blood flow is not shown in Fig. 4-b. It is difficult at present to exclude extremely slow blood flow but the distribution of elasticity in the ROI can be relatively standardized by using this method. Blood flow is likely to develop in a venous thrombus over time and the use of this imaging method is recommended for evaluation under conditions as standardized as possible.

Elastography is a diagnostic technique that visualizes tissue elasticity and it is anticipated that it will show more detailed tissue characteristics than conventional ultrasonography. A venous thrombus is transformed into granulation tissue from a clot consisting mainly of erythrocytes

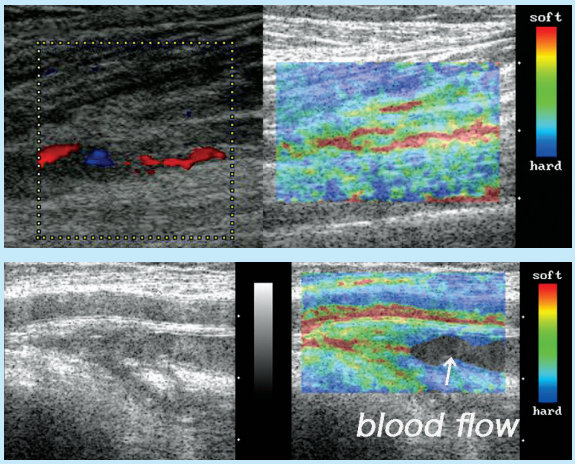

Fig. 4-a, b : Blood flow indication and exclusion
Blood components show as red (soft). Since blood, which is extremely elastic, that is included in the ROI tends to result in an image indicating overall softness, it is difficult to evaluate the thrombus itself. For this reason, settings were created to exclude distinct regions of blood flow as shown in Fig. 4-b.

and fibrinogen at an early phase[6]. It has been reported that the elasticity of each component tissue differs and that a thrombus become harder with organization. Tissue characteristics of a venous thrombus can be evaluated by accurately displaying the difference in elasticity. It was also reported that a venous thrombus in acute phase responds to fibrinolysis therapy and is likely to become a source of embolism due to its high mobility. It is therefore anticipated that evaluation by Elastography would enable prediction of therapeutic effect or the risk of a thrombus becoming an embolic source. In other words, it could enable prediction of complications of pulmonary thromboembolism.

The methods of diagnosis and evaluation by Elastography have not yet been objectively assessed. It has also been pointed out that the application of pressure manually leads to difficulty in determining the degree of pressure applied and inconsistency of evaluation criteria. To establish the diagnostic technique of Elastography, it is necessary to establish an objective index, develop a quantitative method for applying pressure, verify inaccuracy among operators, and conduct comparisons with tissue specimens.

7. Conclusion

With the use of an appropriate method of visualization, Elastography would be useful for evaluating the tissue characteristics of venous thrombi, enabling selection of the treatment method and forecast of complications. Further review is desired.

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