Review Article

Fundamentals of Liver Elastography

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Abstract

Chronic viral hepatitis is a major cause of liver fibrosis and liver fibrosis is an important risk factor for hepatocellular carcinoma. Management and prognosis of the patients with chronic liver disease depend on the extent of liver fibrosis. Liver biopsy is the gold standard for diagnosis and staging of liver fibrosis, however, it is limited by invasive nature. We present a review focused on fundamentals of ultrasound elastography techniques which is a novel non-invasive technique used to measure tissue stiffness

Key words: liver elastography, shear wave, ultrasonography

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Introduction

Asia has been considered as an endemic area of viral hepatitis infections.[1] There are five types of hepatitis viruses included A, B, C, D, E. Among these viruses, hepatitis B virus (HBV) and hepatitis C virus (HCV) are the major causes of chronic viral hepatitis (CVH).[1-2] The chronic infections cause hepatic fibrosis and are the important risk factors for hepatocellular carcinoma (HCC).[3] Most HCC patients present at intermediate or late stage at diagnosis.[2] Literature has shown that early detection of HCC decreases morbidity and mortality.[4] Therefore various guidelines have been developed for HCC surveillance.[4-5] According to Thailand Guideline, all cirrhotic patients should be surveilled.[5] Regarding this guideline, the criteria for the diagnosis of cirrhosis include; 1) pathologic diagnosis from liver biopsy reveals stage IV liver fibrosis according to METAVIR system[6], 2) clinical symptoms and signs plus radiologic imaging are compatible with cirrhosis, 3) another test that indicates stage IV liver fibrosis such as transient elastography.[5] Liver biopsy is the gold standard for diagnosis and staging of liver fibrosis.[7] However, it is invasive and sampling error occurs due to the small sample size in a heterogeneous process.[8] In clinical practice, non-invasive methods, both blood-based biomarkers and imaging-based techniques, to assess liver fibrosis are preferred. For imaging-based techniques, the tissue elasticity which is called elastography is measured either by ultrasound (US) or magnetic resonance imaging. Apart from the staging of liver fibrosis, elastography has been useful for follow-up changes in fibrosis in patients receiving antiviral therapy. There are several ultrasound methods to study tissue elasticity included; real-time elastography (RTE), transient elastography (TE), acoustic radiation force impulse imaging (ARFI) and 2D-shear wave elastography (2D-SWE).[9] Because the RTE method is mostly used for the measurement of breast lesions and the clinical evidence is scanty, this method is not discussed in this review.

This article aims to review basic technique of different ultrasound elastography methods and their performances with emphasized on SWE which has been growing in popularity.

Basic principles of elastography

There are two basic components of elastography including; applying force and tissue response. Three types of force have been used; 1) manual compression by palpation, cardiovascular pulsation or respiration, 2) acoustic radiation force impulse excitation, and 3) controlled external vibration.[10] The tissue response is expressed and measured in two different ways, strain elastography and shear wave elastography.

Strain elastography

When a pressure is applied to the tissue, tissue deformation is generated. The tissue displacement response relates to the difference in elasticity between a lesion and the surrounding tissue. The more stiffness of the lesion is, the less tissue displacement occurs. Strain elastography is displayed as strain image, called elastogram as illustrated in Figure 1. Thus it is a qualitative method or semiquantitative by measuring in relation to normal tissue. RTE is the example of this method.

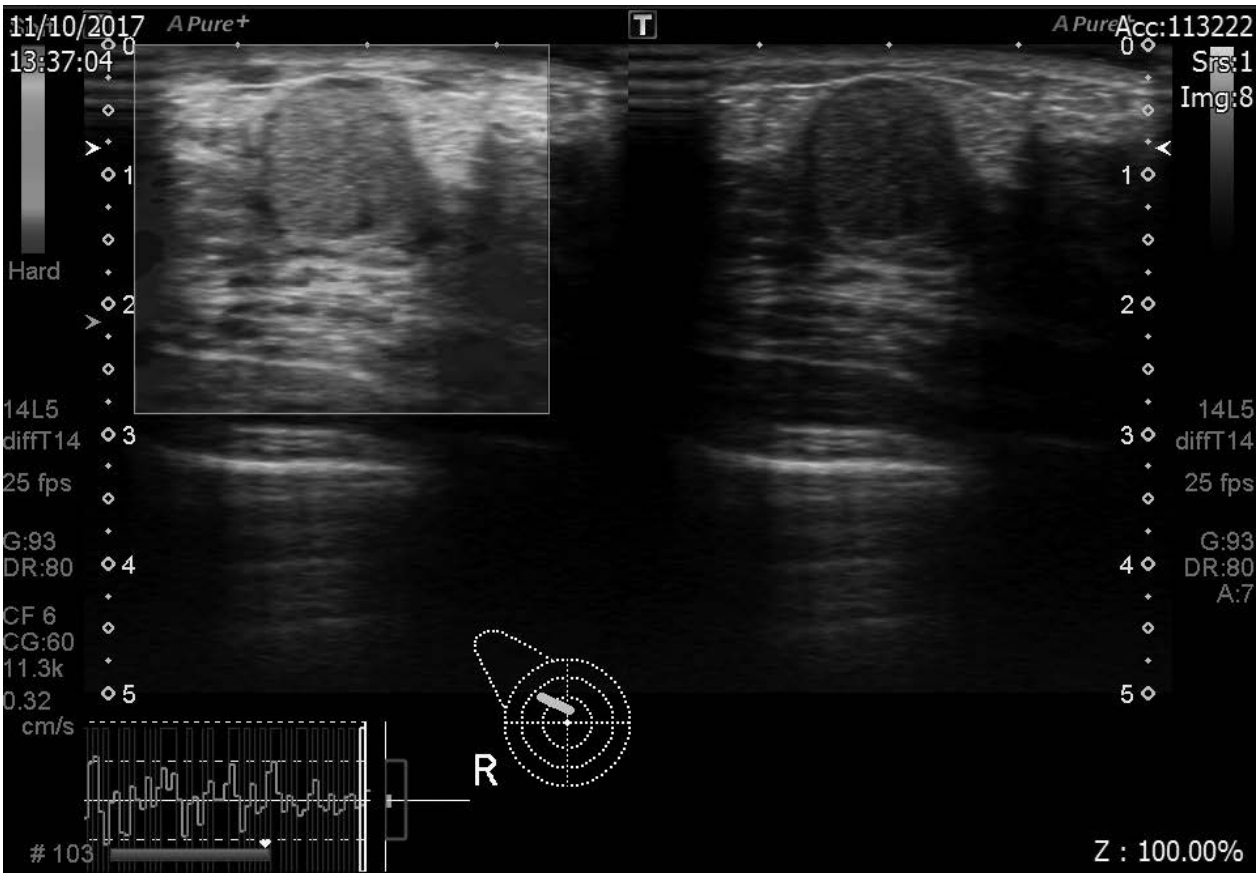

Figure 1 An illustration of an elastogram of the breast on the left screen, compared to gray- scale image on the right screen. Blue color indicates hard tissue whereas red color indicates soft tissue.

Shear wave elastography

When the force causes tissue deformation, it also induces elastic shear wave in the tissue. The more liver stiffness is, the faster the shear wave propagates. This method can be classified according to the type of forces into; 1) external force and 2) internal force.

1. External force

TE is the first commercially ultrasound method used to quantify liver fibrosis. Fibroscan (EchoSens, Paris, France) is the most popular used in the market. The force is produced externally at the skin surface. The shear wave speed is measured and calculated by Young modulus.[11] The outcome is expressed as a pressure in kilopascals (kPa) without B-mode image display. The normal value of liver stiffness on TE is 4.8 kPa - 6.9 kPa.[12] The cut-off values for the diagnosis of significant fibrosis (≥ grade 2) are ranging from 5.2 kPa - 8.7 kPa.[12] However, the cut-off values may vary according to the underlying disease as well as some conditions that may increase the TE values such as liver inflammation, postprandial state and portal hypertension.[12] This method is limited in obesity or ascites.[13] The failure rate is about 3.1%.[9]

2. Internal force

Acoustic radiation force impulse technology is used to generate shear wave internally. This method is incorporated into the high-end US machine. Hence operator is able to select an appropriate area to measure, using simultaneous B-mode scan. Therefore it allows visualization of the tissue during measurement. Thus it is superior to TE in terms of variable depths of tissue measurements and more promising results[14], and is not limited by ascites.[13] The outcome is expressed as a pressure

in kilopascal (kPa) or shear wave speed (m/s). Two techniques of measurement are used included point shear wave elastography (pSWE), and 2D-SWE.

2.1 Point shear wave elastography

A single estimate of tissue is measured in a small region of interest (ROI). The measurement can be done at variable depths in contrast to TE where the measuring depth is fixed. Virtual touch quantification (VTQ; Siemens, Berlin, Germany) and Elastography point quantification (ElastoPQ; Philips Medical Systems, Bothell, WA, USA) are the two commercially used this technique. The previous article has shown that these 2 vendors had similar technical success rate and reliable measurements.[14] A recent prospective study has demonstrated a highly significant correlation between ElastoPQ values and METAVIR stage of liver fibrosis in HCV patients.[15] The cut-off values for cirrhosis are 1.75 - 2.00 m/s.[12] Apart from CVH, pSWE is proved to be useful in the evaluation of liver fibrosis from the other causes such as primary sclerosing cholangitis.[16]

2.2 2D-Shear Wave Elastography

2D-SWE is the latest technology of US elastography. The ROI is larger than the pSWE and can be adjusted up to 4 x 4 cm.[17] Three different displayed modes can be obtained after freezing the image (Toshiba Aplio 500 system, Tokyo, Japan) which include speed mode (m/s), elasticity mode (kPa) and propagation mode18 as shown in Figure 2. The whole elasticity map is demonstrated. The propagation mode displays the contour lines that allows the operator to select the area for measurement to obtain the higher reliable data.[18] The success rate is 98.7%.[19] A recent prospective study has demonstrated a high accuracy of 2D-SWE to assess liver fibrosis compared to liver biopsy.[17] Zeng et al.[19] compared the 2D-SWE with the liver biopsy results and reported a good diagnostic accuracy in staging liver fibrosis in patients with HBV infection. Previous literature has shown that 2D-SWE is highly accurate, compared to TE for staging liver fibrosis in HCV patients.[20 - 21] The previous article has demonstrated a concordance results between pSWE and 2D-SWE for the quantification of liver stiffness.[22] The cut-off value for cirrhosis is 8.1 - 10.4 kPa[9, 22] as demonstrated in Figure 3. Grgurevic et al[23] have proposed a cut-off value of 27 kPa for differentiating compensated from decompensated liver cirrhosis. Spleen stiffness measurement has been used as an alternative non-invasive method for measurement of portal hypertension when liver stiffness measurement is limited.[24] Yoon et al.[25] used 2D-SWE in the evaluation of rejection or recurrent hepatitis after liver transplantation. Their results have shown that the liver stiffness values in patients with the rejection of hepatitis are significantly higher than in patients without rejection. Three most common limitations of this measurement method are reverberations under liver capsule, respiratory/cardiac motion and vessel pulsation/loss of the SWE signal.[26]

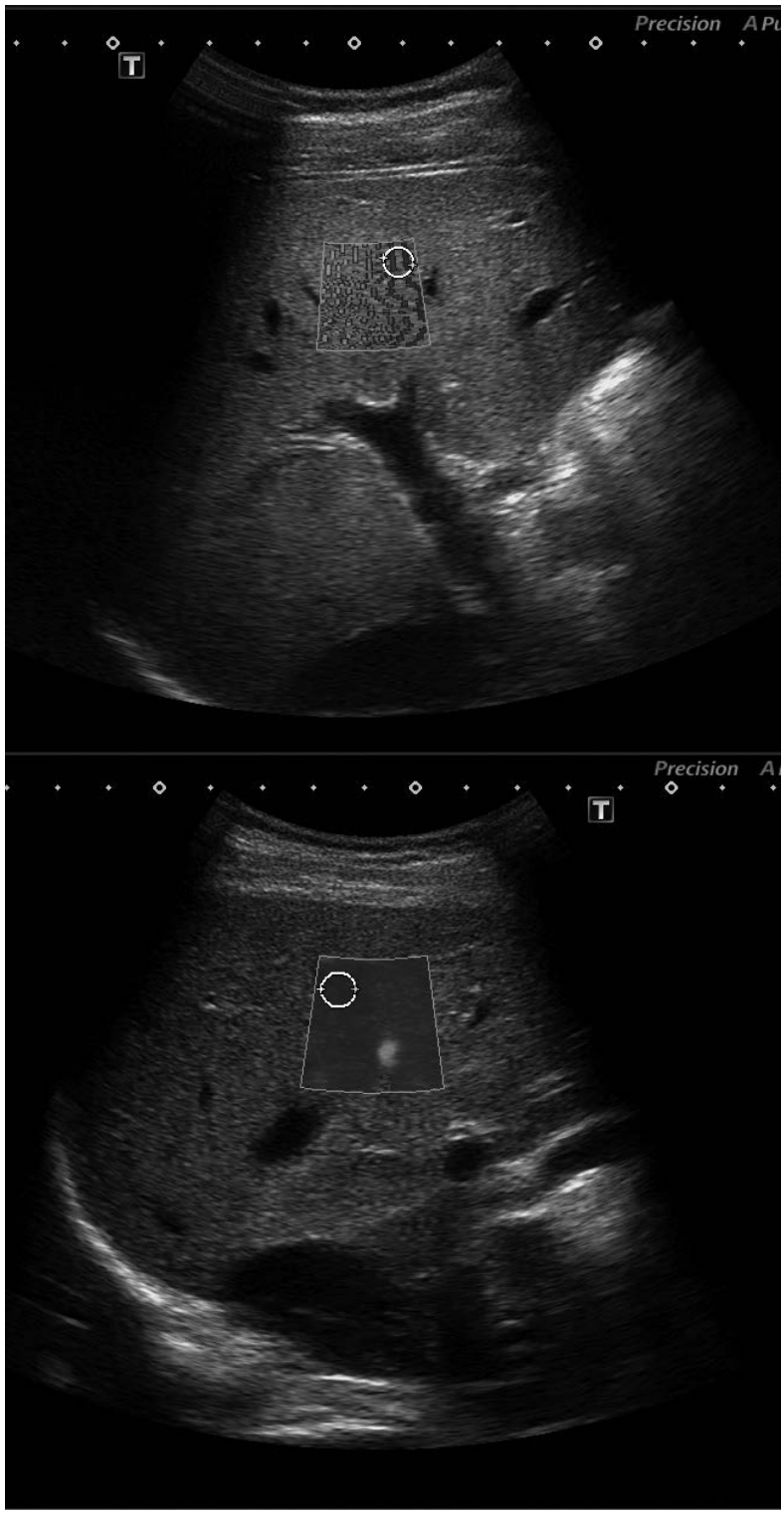

Figure 2 Upper image reveals propagation mode and lower image reveals elasticity mode limitations.

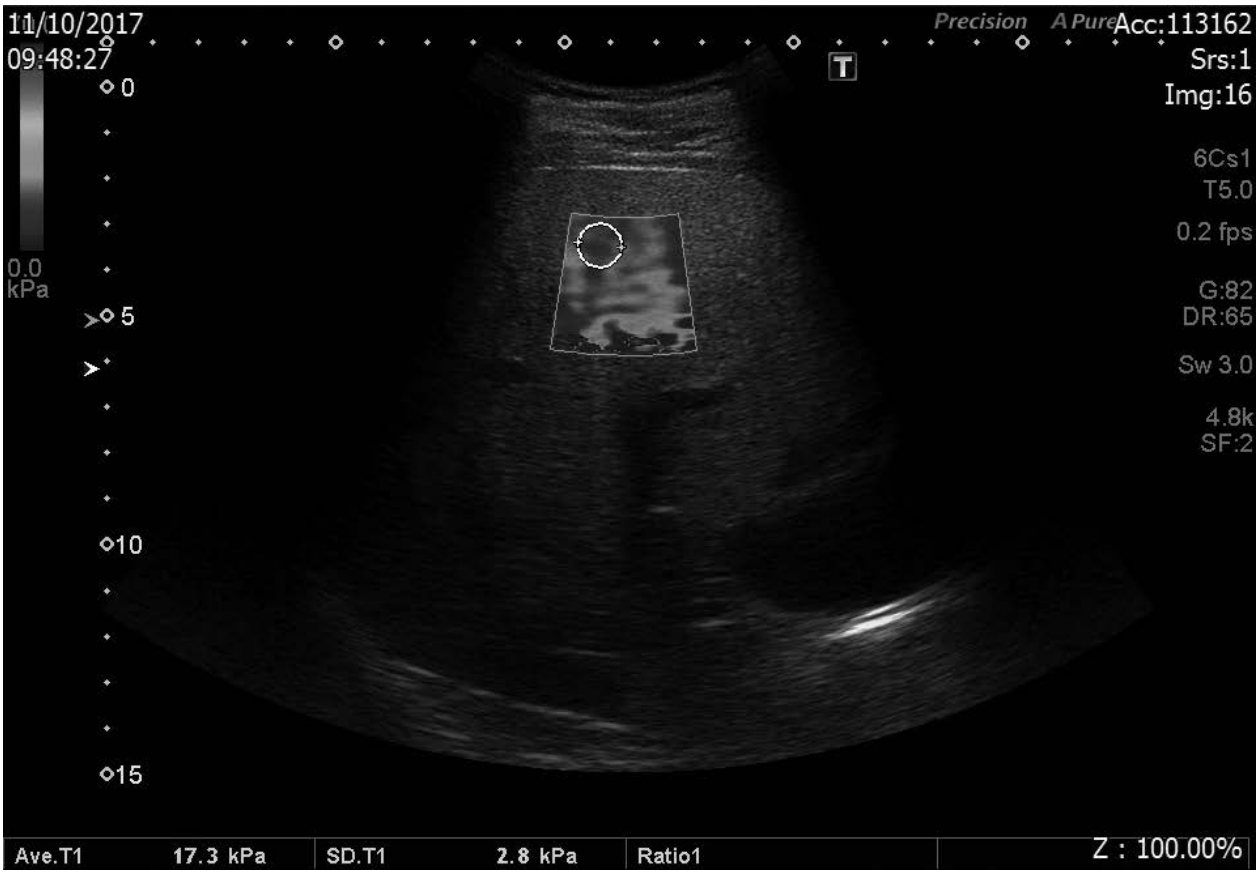

Figure 3 A 48-year-old man with chronic viral hepatitis B and cirrhosis. The 2D shear wave elastography value is 17.3 kPa.

There are two aspects of limitations, limitations from liver conditions and limitations from US technique. The liver stiffness may increase in many conditions such as liver inflammation, cholestasis, liver congestion, portal hypertension and postprandial state and may decrease in post-transplant liver.[7] US limitations that can compromise in the evaluation are general US limitations; for example a large-sized patient, poor acoustic window and operator dependency.

Abbreviations:

HBV = Hepatitis B virus
HCV = Hepatitis C virus
CHV = Chronic viral hepatitis
HCC = Hepatocellular carcinoma
US = Ultrasound
RTE = Real-time elastography
ARFI = Acoustic radiation force imaging
2D-SWE= 2D-shear wave elastography
ROI = Region of interest

Discussion

US elastography is a non-invasive method for measurement of liver fibrosis. The field of US elastography has evolved rapidly and become widely available. The use of liver elastography has the potential for change in clinical practice. However, the clinician should keep in mind that different US elastography techniques or machines give different values, as well as the liver stiffness values from different underlying liver diseases, which are not identical.

Conflict of interest

The author has no relevant conflict of interest to disclose.

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บทคัดย่อ

หลักการพื้นฐานของเครื่องคลื่นเสียงความถี่สูงในการวัดสภาพการเกิดพังผืดของเนื้อตับ

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ภาวะตับอักเสบเรื้อรังจากเชื้อไวรัสเป็นสาเหตุหลักที่ทำให้เกิดพังผืดของเนื้อตับซึ่งเป็นปัจจัยความเสี่ยงที่สำคัญของมะเร็งตับ การดูแลรักษาและการพยากรณ์โรคในผู้ป่วยที่มีภาวะตับอักเสบเรื้อรังจากเชื้อไวรัสขึ้นกับความรุนแรงของการเกิดพังผืดของเนื้อตับ วิธีมาตรฐานเพื่อประเมินความรุนแรงของการเกิดพังผืดของเนื้อตับคือการเจาะตับแต่เป็นวิธีที่ก่อให้เกิดความเจ็บปวดแก่ร่างกายและอาจเกิดภาวะแทรกซ้อนได้ บทความฉบับนี้นำเสนอหลักการพื้นฐานและคุณสมบัติของเครื่องคลื่นเสียงความถี่สูงชนิดต่างๆ ตั้งแต่ในอดีตมาถึงปัจจุบันในการนำมาใช้วัดความรุนแรงของการเกิดพังผืดของเนื้อตับ โดยมุ่งเน้นที่เครื่องรุ่นล่าสุดที่นิยมใช้ในปัจจุบัน นอกจากนี้ท้ายบทความได้นำเสนอข้อจำกัดและข้อควรระวังในการแปลผลค่าความรุนแรงของการเกิดพังผืดของเนื้อตับที่ได้จากเครื่องคลื่นเสียงความถี่สูงชนิดต่างๆ

คำสำคัญ: การวัดความรุนแรงของการเกิดพังผืดของเนื้อตับ, คลื่น shear wave, เครื่องคลื่นเสียงความถี่สูง