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Clinical applications of spleen ultrasound elastography – a review

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Abstract

In the last few years, notable technical progress has taken place in ultrasound elastography. Qualitative methods have been replaced by quantitative ones, such as: transient elastography, acoustic radiation force impulse and shear wave elastography. Owing to the fact that the spleen is superficially located, it is possible to obtain reliable measuring accuracy of its hardness using sonoelastography. Lately, many researchers have been investigating how spleen elasticity changes in patients infected with hepatitis B virus or hepatitis C virus and in patients suffering from liver fibrosis, portal hypertension, esophageal varices or myelofibrosis. In this article, we review the role and current status of accessible qualitative ultrasound elastography methods, including recent advances in the evaluation of spleen stiffness and its clinical utility. As study results demonstrate, spleen stiffness correlates with liver fibrosis and is helpful in determining the level of fibrosis in the METAVIR scoring system. In patients infected with hepatitis B virus or hepatitis C virus, spleen stiffness increases even when liver elasticity remains unaltered. Furthermore, it is useful in diagnosing portal hypertension or predicting existence of esophageal varices. Moreover, in patients suffering from biliary atresia after Kasai portoenterostomy, spleen sonoelastography may be helpful in selecting patients for liver transplantation as well as for choosing the best strategy for portal vein reconstruction before liver transplantation. In myelofibrosis, spleen stiffness correlates with bone marrow fibrosis and may be used to assess the response to treatment. Spleen sonoelastography is also useful in the monitoring of transjugular intrahepatic portosystemic shunt function.

Background

The spleen is the largest lymphatic organ in the human body. The capital functions of the spleen are connected with formation, storage and breakdown of blood cells as well as formation and storage of blood clotting factor VIII. Lymphocytes in splenic lymph follicles take part in antibody biosynthesis. The splenic pulp is responsible for lymphocyte formation, thrombocyte destruction, old red blood cell breakdown as well as keeping and releasing granulocytes[(1)].

Spleen function abnormalities, splenomegaly and hypersplenism usually result from systemic diseases. Spleen malfunction may be induced by infectious diseases, hemolytic anemia, myeloproliferative disorders, lymphoproliferative diseases, acute leukemia or autoimmune diseases. The splenic vein is directly connected to the portal vein. As a consequence, diseases that affect blood flow in the portal vein may also affect the spleen. Spleen stiffness examinations may therefore be useful in the diagnostic process of liver fibrosis, portal hypertension and esophageal varices.

Elastography is a relatively new non-invasive diagnostic method, which allows the assessment of tissue stiffness[2]. It is based on the assumption that pathologically changed tissue is harder than healthy tissue[3]. Studies on liver fibrosis, the musculoskeletal system as well as breast, prostate, testicular and thyroid nodules acknowledge this assumption[4–9]. There are two main different types of elastography: ultrasound elastography (EUS) and magnetic resonance elastography. EUS, for the sake of its simplicity, may be divided into qualitative and quantitative. The qualitative method, whereby elasticity values are obtained by exerting rhythmical pressure on the examined tissue, is the least technically advanced. Measurements may be also performed with the probe held motionlessly owing to the internal organs' physiological movements which generate strain images. Technical progress has resulted in the improvement of this method and led to the formation of quantitative elastography methods such as: transient elastography (FibroScan), acoustic radiation force impulse (ARFI) and shear wave elastography (SWE) (Fig. 1).

Spleen stiffness evaluation has been of interest to numerous researchers in the last few years. Since it is known that dynamic elastography methods produce reliable outcomes, they have been used to assess how the spleen hardness changes in different diseases. The aim of this review was to systemize the latest discoveries relating to spleen stiffness assessment carried out with quantitative ultrasound elastography techniques.

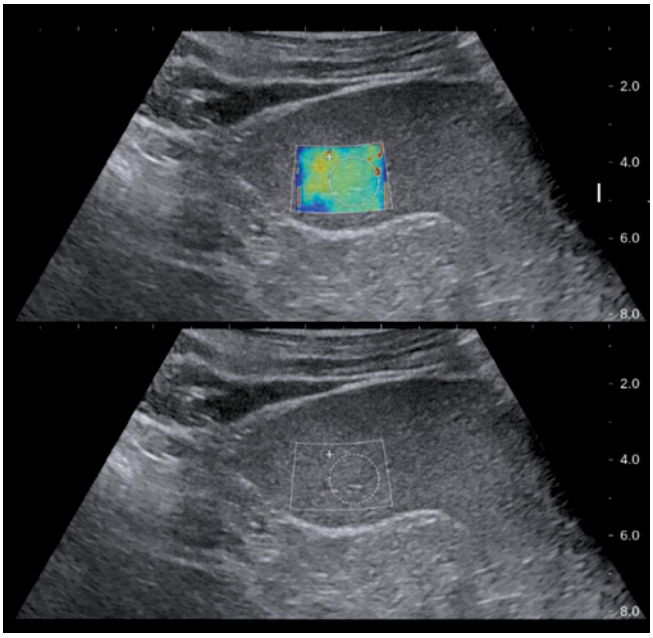

Fig. 1. *SWE view of the spleen in a healthy patient. ROI put at a site of homogeneous hardness*

Spleen elastography in healthy subjects

Spleen examination with sonoelastography requires determination of normal values for healthy individuals. Different studies have been conducted to assess the mean value of spleen stiffness and standards for its examination. The measurements of spleen stiffness are obtained with the patient in the supine position; in most cases, the examination has been conducted with the left arm in maximum abduction and by placing the probe in the left intercostal space[10–15]. Increased spleen stiffness on deep breaths in adults has been confirmed[12]. In order to minimize respiratory motion, it is common to instruct patients to hold their breath[4,14]. This enables one to obtain a stable homogeneous elastogram with complete filling, both spatially and temporally. In children, who cannot control breathing, the measurements are performed during free respiration and are not invalidated by breathing or other motions[10–11]. The measurements can be taken using a linear or convex probe. Research has proven that there is no significant difference in the mean values obtained using the two types of probes, but a higher variability was observed when using a convex transducer[10]. Moreover, Mi-Jung Lee *et al*. have proven that ARFI measurements are feasible for solid abdominal organs in children using high- or low-frequency probes[11].

The spleen is the organ with the highest rigidity as measured by ARFI in the abdominal viscera in adults[10,16]. According to Pawluś *et al*. the mean value of spleen stiffness is 16.6 ± 2.5 kPa: in men (N = 25) it is 17.3 ± 2.7 kPa, and women ($N = 34$) 16.1 ± 2.2 kPa. Leung *et al*. obtained similar values at a level of 17.3 ± 2.6 kPa[4,14]. The mean ARFI-derived velocity for the spleen in adults equals 2.46 ± 0.35 m/s[12,16]. No correlation between gender and elasticity of the spleen has been detected, although there are studies suggesting that gender may influence ARFI SWVs[10–11,13–14]. Authors have also assessed the dependence of the dimensions of the spleen on its stiffness and did not find any interconnections[13–14]. The data on spleen stiffness dependence on age are divergent in various studies. The results of research in adults are independent of age, while studies in children show age-related correlations[10–11,13–14]. Spleen stiffness in elastography techniques increases after food intake. Patients may be misclassified with higher stages of fibrosis if they are assessed within less than a three-hour fasting period[15].

Spleen stiffness in liver fibrosis

One of the applications of spleen elastography is the assessment of liver fibrosis and determining its METAVIR score. As it is known, the spleen is one of the extrahepatic

Author	Spleen stiffness in kPa				
	F0	F1	F2	F3	F4
Leung *et al.*	17.3 ± 2.6	19.4	19.8	20.6	22
Rewisha *et al.*	19.41 ± 3.63	25.56 ± 5.36		46.19 ± 16.29	
Giunta *et al.*	–	–	36	–	46
Grgurevic *et al.*	–	23	24		35

Tab. 1. *METAVIR score of liver fibrosis based on spleen elastography*

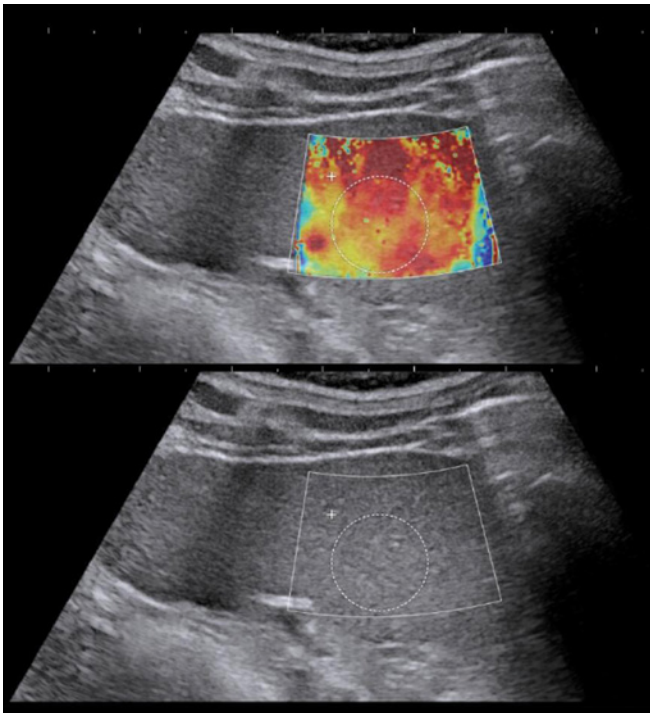

Fig. 2. *SWE view of the spleen in a patient with advanced liver fibrosis. ROI put at a site of increased hardness*

reservoirs of hepatitis C virus and extrahepatic hepatitis B virus replication sites[17–19]. Studies have provided evidence that spleen stiffness correlates with the progression of liver fibrosis[4,20–25]. The more advanced the liver fibrosis, the stiffer the spleen (Tab. 1, Fig. 2)[4,20–25]. The dependence is stronger in significant liver fibrosis (METAVIR ≥2). Worth mentioning is the fact that spleen hardness increases in patients infected with HBV or HCV, even when liver elasticity remains unaltered[25].

Correlation between portal hypertension, esophageal varices and spleen stiffness

Cirrhosis is the last stage of liver fibrosis and may be induced by many factors such as: liver viral infections, chronic alcohol abuse, autoimmune hepatitis, congenital and acquired metabolic diseases, chronic biliary tract diseases accompanied by cholestasis and chronic treatment with certain drugs (e.g. methotrexate, amiodarone, isoniazid). Portal hypertension and esophageal varices are the consequences of advanced liver fibrosis. The portal vein is directly connected with the splenic vein, and therefore, disorders in the portal vein blood flow may affect the spleen. The superiority of spleen elastography over liver elastography results from the fact that the spleen is not affected by the disease that is the primary cause of portal hypertension. This suggests that spleen stiffness may be a more accurate parameter for the detection of portal hypertension and esophageal varices than liver stiffness. In cirrhotic patients, screening for esophageal varices is highly recommended and extremely important. As a few studies have proven, spleen stiffness correlates with the presence of portal hypertension[26–32], but this dependence is not precise enough to assess its degree. Nevertheless, study results show that spleen elastography could be used to suggest the presence of clinically significant portal hypertension[26–32]. The values of spleen stiffness obtained in patients with clinically significant portal hypertension were between 35.6–75 kPa[26–32].

A meta-analysis conducted by Ma *et al*. proves that spleen elastography may be applicable in identifying patients with esophageal varices, and there is evidence concerning its superiority over liver elastography in this particular disease[27]. However, Park *et al*. demonstrates that the usefulness of spleen elastography in detecting esophageal varices depends on the cause of cirrhosis. According to this study spleen elastography is not a reliable predictor of esophageal varices induced by alcoholic cirrhosis[33]. According to available studies, spleen elastography is not useful in assessing the grade of esophageal varices[27,33–35]. Single studies show that spleen stiffness correlates with clinical history of variceal bleeding[36–37], but its utility in determining the risk of bleeding from esophageal varices requires further investigation.

Other applications

Sonoelastography of the spleen is also used to diagnose and evaluate other medical conditions. Spleen stiffness correlates with the portal vein diameter, portal hypertension and liver dysfunction in patients suffering from biliary atresia after Kasai protoenterostomy[38]. According to Uchida *et al*., spleen elastography in these patients could be used to assess the severity of portal hypertension and liver dysfunction in a non-invasive way, and may be helpful in selecting patients for liver transplantation, as well as for choosing the best strategy for portal vein reconstruction before liver transplantation[38].

Patients suffering from myelofibrosis can be distinguished from healthy individuals by FibroScan and SWE of the spleen. However, these measurements have little ability to distinguish between patients with myelofibrosis and cirrhosis of the liver[39]. Other authors suggest that Transient Elastography is a user-friendly approach to the evaluation of spleen stiffness in primary myelofibrosis patients as a marker of the bone marrow fibrosis status and as a means of monitoring their response to innovative myelofibrosis therapies[40]. Another example of spleen elastography utilization is monitoring of transjugular intrahepatic portosystemic shunt (TIPS) function; it has been proven that splenic SWV is compatible with splenoportal venous velocity in the quantitative monitoring of the TIPS function and in determining TIPS dysfunction[41].

To conclude, spleen sonoelastography is useful in miscellaneous groups of disorders, *inter alia* those that cause splenomegaly, including infections, deposition diseases and lymphoproliferative disorders. However, there are few publications available on this subject, which makes it an interesting field for new research.

Conclusion

Even though spleen elastography is not widely applied, it has been proven to be clinically helpful. Firstly, it might be used for non-invasive liver fibrosis assessment. As research reveals, spleen stiffness changes earlier than liver hardness in patients infected with HCV or HBV without significant liver fibrosis. Secondly, it correlates with blood flow changes in the portal vein, which helps detect portal hypertension. Additionally, spleen stiffness is helpful in the prediction of esophageal varices. Several studies have shown the value of spleen elasticity assessment as a supplementary tool in the treatment of biliary atresia and in myelofibrosis (diagnosis, bone marrow fibrosis assessment and evaluation of the treatment response). The practical usefulness of spleen elastography in other hematological diseases remains unclear and requires further investigation.

Conflict of interest

There are no financial or other relations that could lead to a conflict of interest.

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