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RECOMMENDATIONS FOR ELASTOGRAPHY-BASED IMAGING OF LIVER

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INTRODUCTION

Having diagnosed liver diseases, besides identifying the etiological agent, there is a necessity to determine the stage of liver damage. In fact, histopathological examination of tissue collected during liver biopsy or, less frequently, surgery was the only method used for years to assess the stage of hepatic fibrosis. Progress in medical technology, especially in ultrasound techniques, allowed for noninvasive assessment of liver damage stage, using elastography. Such techniques are applied globally. Currently, they are also more available in Poland. Examination results may be of decisive nature while selecting the management for patient and treatment regime. Therefore, it is required to unify the methods of patient preparation for examination as well as examination techniques and methods of result interpretation between centres.

CLASSIFICATION OF ELASTOGRAPHIC TECHNIQUES

Classification of elastographic methods was formulated by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB). Such classification is based on techniques assessing the stage of hepatic damage/fibrosis used in particular methods (1).

I. Shear-wave elastography (SWE).

This method allows for noninvasive **quantitative** assessment of hepatic damage/fibrosis stage, including:

a. transient elastography (TE);
b. point shear-wave elastography (pSWE):
- acoustic radiation force impulse imaging (ARFI);
- elastography point quantification (ElastPQ);

c. real-time shear-wave elastography*:*
- 2-D-shear-wave elastography (2D-SWE).

II. Quasi-static strain elastography (strain elastography - SE).

Such method allows exclusively for a **qualitative**, noninvasive, subjective assessment of fibrosis stage. For a quantitative assessment, it is required to apply additional computer-based tools.

Elastography is a useful method applied for diagnosing infectious and non-infectious liver diseases and monitoring the patients with a history of liver transplantation. Its use is recommended by the most prominent hepatological scientific societies (*European Association for the Study of the Liver*- EASL, *American Association for the Study of Liver Diseases*-AASLD, *Asian-Pacific Association for the Study of the Liver*- APASL) as well as Polish Group of Experts for HCV and HBV.

FibroScan

Transient elastography (TE) is the most widely adopted method in practice which is available in FibroScan device. Recommendations of the EASL (2), AASLD and APASL suggest this method to be the basic elastographic technique while qualifying the patient with chronic hepatitis C to treatment. Utility of transient elastography in clinical practice was confirmed by a number of studies including more than 13,000 patients (3). FibroScan, being a highly reproducible method assessing hepatic damage/fibrosis stage, is applied in the majority of currently conduced clinical trials. Furthermore, devices equipped with controlled attenuation parameter (CAP) allow for a quantitative assessment of hepatic steatosis. A list of advantages of this method includes simplicity of use, reproducibility of results and presence of system enabling automatic control of transducer pressure (which is not present in other devices used in elastography of liver). Average time of examination does not exceed 5 minutes. Reliability of results may be affected by morbid obesity (4,5), exacerbation of hepatitis (elevated aminotransferase activity) (6-10), ascites (11), cholestasis (12), congestive heart failure (13,14), eating in the period shorter than 6 hours prior to examination (15-17). Examination is contraindicated in pregnant women and persons with a history of pacemaker implantation.

RECOMMENDATIONS FOR FIBROSCAN

1. Preparation for examination

*Prior to examination, it is recommended to collect the data on the etiology of hepatic disease, concomitant diseases, time of the last meal as well as analyze the laboratory findings, especially alanine aminotransferase activity in present and past medical documentation.
*Presence of factors which may distort the results (meal, exacerbation of hepatic disease, intrahepatic cholestasis, ascites, congestive heart failure etc.) or constitute a contraindication for elastography (pregnancy, pacemaker etc.) should result in the resignation or deferment of examination until the discontinuation of circumstances which preclude its correct performance.
*Examination should be performed under fasting conditions or at least 6 hours following the last meal.
*Patient should be examined in the decubitus position with the right arm raised behind the head.
*Provided there are difficulties resulting from patient's anatomic characteristics, it is acceptable to put a roller under the lumbar region and slightly turn the patient's trunk.

2. Examination

*Examination should be performed by operator who is trained by the device's producer and holds a proper certificate.
*Selection of transducer (M, XL or S) depends on patient's anatomic characteristics. Devices of newer generation are equipped with electronic system which assists the operator's decision.
*Transducer should be placed in an intercostal region at a height where the liver parenchyma is the thickest, avoiding measurement in the region of lower and upper edge of the liver (possible overstaging in the subcapsular region).
*Percussion or conventional ultrasound are used to select the proper region.
*Prior to examination, a proper amount of gel should be applied.
*Transducer should be positioned perpendicularly to skin surface. Its positioning should be controlled by vision prior to each measurement.
*On the screen displaying M-mode there should be a homogenous image of the liver of 6 cm in depth, without the presence of blood vessels or other structures which could interfere with wave propagation. Concurrently, A-mode image should be the closest to the linear array, without considerable curvatures.
*Each of the elastograms should be evaluated immediately after single measurement. A correct elastogram should have regular array, parallel to intermittent line drawn by the device. Curved, split (A waves), dilated (E waves) waves may lead to overstaging. Operator is responsible for identifying a problem, selecting different technique and issuing the final examination result out of the series of 10 valid measurements.

3. Examination result

*The final result of hepatic stiffness measurement is a median of all valid measurements.
*A recommended number of valid measurements performed at the same point should not be lower than 10.
*A measure of result dispersion is the interquartile range (IQR). Such ratio should not exceed 30%, if the final median of examinations is higher than 7.1 kilopascals (kPa). In case of the lower values of IQR, it does not affect the quality of examination (Tab. I)(4).
*According to the existing quality criteria, the percentage of valid measurements compared to its total number (success rate; SR) should be higher than 60%. The most current studies suggest that the success rate does not have a considerable impact on the diagnostic quality of examination.
*Results which do not meet the aforesaid quality criteria should not be distributed to patients. Provided subsequent attempts fail to provide valid results, another method assessing the hepatic damage/fibrosis stage should be considered.
*The final interpretation of the result obtained should include the etiology of disease and data on the present clinical status of patient.
*Result, which is issued to a patient, is an original hard copy printed from the device or programme for archiving, accompanied by interpretation of result and signature of operator.

Table I. Criteria for validity of TE result

Parameter	Value	Result validity
IQR	≤ 10%	Very high
IQR LS	11-30%, >30% <7.1 kPa	High
IQR LS	>30% >7.1 kPa	Low

4. Result archiving. Results obtained should be accessible in the centre performing the examination and possible to reproduce. It is recommended to apply an original programme for result archiving.
5. Technical indications. A regular calibration of transducer is required.

ARFI

Acoustic radiation force impulse elastography is available as an additional option (Virtual Touch TM) in conventional devices (USG Siemens Acuson S2000 and Acuson S3000). Its operation consists in assessing

the elastic properties of particular anatomic regions in B-mode, using the region of interest (ROI) defined with electronic cursor allowing for the selection of examination region. Graphic dimensions of the ROI are 10 mm in length and 6 mm in width. Measurements are expressed in meters per second in the range of 0.5 – 4.4 m/s and precision of ± 20%) [18,19]. Besides the examination result, the screen provides the depth at which the measurement is made. So far, the number of available publications discussing this method is considerably lower compared to TE. Contrary to FibroScan, the producer of device does not recommend particular quality criteria of measurements made. Studies conducted in Romania (19, 20), however, suggest that the application of the following technical parameters IQR <30 and ≥ 60 SR, derived from the recommendations for TE, significantly increased the accuracy of measurements. The advantage of this method is that it allows for a comprehensive ultrasonographic assessment of hepatic parenchyma, blood flow of the hepatic portal system and other organs of the abdominal cavity. ARFI lasts for about 15 minutes or longer if it is accompanied by the ultrasonographic assessment of abdominal cavity organs. Restrictions on the measurements are similar to those observed in TE (21). There are no contraindications for AFRI in pregnancy.

RECOMMENDATIONS FOR ARFI

1. Preparation for examination

* Prior to examination, it is recommended to collect the data on the etiology of hepatic disease, concomitant diseases, time of the last meal as well as analyze the laboratory findings, especially alanine aminotransferase activity in present and past medical documentation.
* Presence of factors which may distort the results (meal, exacerbation of hepatic disease, intrahepatic cholestasis, ascites, congestive heart failure etc.) should result in the resignation or deferment of examination until the discontinuation of circumstances which preclude its correct performance or interpretation of results.
* Examination should be performed under fasting conditions or at least 6 hours following the last meal.
* Patient should be examined in the decubitus position with the right arm raised behind the head.
* Provided there are difficulties resulting from patient's anatomic characteristics, it is acceptable to position him in the left lateral decubitus.

2. Examination

* Operator should display the competence of ultrasonographist and be trained by the device's producer.
* Prior to examination, a proper amount of gel should be applied.
*Transducer (4C1) should be placed in an intercostal region at the right side, parallel to intercostals space, with minimal pressure on the thoracic wall, preferably during a breath hold (without breathing in or out – only motion hold) as to minimize the motion of breathing. It is not recommended to perform the examination via subcostal access. There is no objective control of transducer's pressure exerted by the operator on the thoracic wall in this method. Contrary to typical ultrasound, transducer should remain static.
*Operator places the electronic cursor of the ROI in the most representative, homogenous region of the liver, without great blood vessels, focal lesions and artefacts. ROI should not be placed subcapsularly.
*Measurements should be performed at 1-2 cm in depth below the hepatic capsular and exclusively in the right lobe as the values obtained in the left lobe of the liver are considerably higher due to the lack of protection from excessive pressure which is provided by the ribs for the right lobe. Preferably, examination should be performed in segments V and VIII (19-24).

3. Examination result

*It is recommended to perform 10 valid measurements and calculate the median.
*Similar to TE, it is recommended to apply quality parameters (IQR <30 and SR> 60) as to increase the accuracy of measurements.
*Results which do not meet the aforesaid quality criteria should not be distributed to patients. Provided subsequent attempts fail to provide valid results, another method assessing the hepatic damage stage should be considered.
*The final interpretation of the result obtained should include the etiology of disease and data on the present clinical status of patient.
*Result, which is issued to a patient, constitutes a series of photographs printed from the device. It should be accompanied by the description and interpretation of result provided by the operator and his signature.

4. Result archiving. Results obtained should be accessible in the centre performing the examination and possible to reproduce.

5. Technical indications. Device should be subject to maintenance service in line with producer's indications. Calibration of transducer is not required.

2D-SWE

2D-real-time shear-wave elastography is another elastographic technique used to assess the liver damage. So far, the number of available publications concern-

ing this method is considerable lower compared to TE. 2D-SWE is used in the Aixplorer® (SuperSonic). It also has a functionality of conventional ultrasound device. Its action consists in the registration of shear-wave propagated in tissues in real time and creation of colour-based map of elasticity of the observed region. This map is imposed on B-mode image. Device calculates maximum, minimum and mean liver stiffness (LS) within the ROI, whose dimension is modified by the operator, and standard deviation (1,26). Result is provided in kPa or m/s. Examination requires the operator to have the competence of ultrasonographist and additionally he should be trained by the device's producer. There are no unequivocal quality criteria of result. According to producer's recommendations, a valid measurement should be defined as an average of three valid measurement of approximate values. New reports suggest that 6 measurements increase the credibility of results. Similar to ARFI, the Aixplorer allows for a comprehensive assessment of liver parenchyma, blood flow of the hepatic portal system and other organs of the abdominal cavity. 2D-SWE lasts for about 10 minutes or longer if it is accompanied by the ultrasonographic assessment of abdominal cavity organs. Restrictions on the measurements are similar to those observed in TE with the exception of ascites, which according to producer's information does not limit SWE. Value of measurement may be decreased by the thrombosis of hepatic veins (Budd-Chiari syndrome) and peliosis hepatis. There are no data on the safety profile of 2D-SWE in pregnant women.

RECOMMENDATIONS FOR 2D-SWE

1. Preparation for examination

*Prior to examination, it is recommended to collect the data on the etiology of hepatic disease, concomitant diseases, time of the last meal as well as analyze the laboratory findings, especially alanine aminotransferase activity in present and past medical documentation.

*Presence of factors which may distort the results (meal, exacerbation of hepatic disease, intrahepatic cholestasis, ascites, congestive heart failure etc.) should result in the resignation or deferment of examination until the discontinuation of circumstances which preclude its correct performance.

* Examination should be performed under fasting conditions or at least 6 hours following the last meal.

* Patient should be examined in the decubitus position with the right arm raised behind the head.

* Provided there are difficulties resulting from patient's anatomic characteristics, it is acceptable to position him in the left lateral decubitus.

2. Examination

* Operator should be able to perform conventional ultrasound examinations and be trained by the device's producer.

* Prior to examination, a proper amount of gel should be applied.

* Transducer (SC6-1) should be placed in an intercostal region at the right side, parallel to intercostals space, leaning on the ribs and directing wave beam into intercostal spaces. It precludes excessive pressure of transducer on liver parenchyma. It is not recommended to perform the examination in the subcostal region. There is no objective control of transducer's pressure exerted by the operator on the thoracic wall in this method. Contrary to typical ultrasound, transducer should remain static.

*Operator positions the ROI (here referred to SWE-box) in the region of homogenous echogenicity, without great blood vessels and other structures distorting the measurement in a distance ranging from 2 to 8 cm below the hepatic capsular. Optimal quality of measurement can be achieved in parenchyma located between 3 and 7 cm below the hepatic capsular.

*Prior to measurement, the patient should hold his breath for at least 4 seconds, which ensures the image stabilization.

*Region, in which the measurement is made (Q-box), should be placed in the centre of the SWE-box whose diameter is usually 15-20 mm.

*It is not recommended to perform the measurement in the left lobe of the liver due to the lack of protection from excessive pressure which is provided by the ribs for the right lobe.

3. Examination result

It is recommended to perform at least 3 valid measurements of approximate values and calculate the median which is then issued as the final result. If the values of these measurements are not convergent, they should not be distributed to patients. Provided subsequent attempts fail to provide convergent results, another method assessing the hepatic damage stage should be considered.

*The final interpretation of the result obtained should include the etiology of disease and data on the present clinical status of patient.

*Result, which is issued to a patient, constitutes a series of photographs printed from the device. It should be accompanied by the description and interpretation of result provided by the operator and his signature.

4. Result archiving. All results obtained should be accessible in the centre performing the examination and possible to reproduce.

5. Technical indications. Device should be subject to maintenance service in line with producer's indications. Calibration of transducer is not required.

ELASTPQ

ElastPQ is an integrated system of elastography and conventional ultrasound (Philips, EPIQ7 with xMATRIX,). It is comparable to 2D- SWE, however, the EFSUMB classified it together with ARFI into the group of point SWE methods. Its action consists in generating ultrasound wave-induced pressure which is then propagated by tissues. Doppler effect, using the changes in the frequency of ultrasound wave dependent on motion direction, is applied for imaging. As with AFRI-based elastography, shear waves spread within the ROI of the following dimensions: length - 15 mm and width - 5 mm. Shear wave speed is displayed on the screen. Operator may select whether the results are to be expressed in m/s or kPa. It is a relatively new technique. Due to a few publications available, there are no unequivocal indications with regard to its execution and cut-off points for particular stages of fibrosis. Thus, this method cannot be currently recommended for a routine diagnosis of hepatic diseases.

Strain elastography

Such elastographic technique is available in the majority of conventional ultrasound systems. It is referred to as quasi-static elastography. Generally, it is applied for the diagnosis of focal lesions, especially in superficial organs. As the assessment of differences in the elasticity of tissues is here of the qualitative nature (e.g. imaging of tumour tissue of cohesion other than surrounding normal organ parenchyma), this technique is of low utility in the assessment of liver damage stage, which requires an objective, quantitative evaluation of liver stiffness. The number of publications on the use of this method in the assessment of fibrosis stage is relatively low, thus, this method cannot be currently recommended for a routine diagnosis of hepatic diseases.

Table II. Suggested range of result values by fibrosis stage and elastographic technique (Polish guidelines)

Etiology	TE (kPa)		2D SWE (kPa)		ARFI (m/s)	
Healthy	2.5 – 5.0		up to 5.7		1.0 – 1.2	
HCV	F≥1	5.1 – 7.0	F≥1	5.8 – 7.0	F≥1	1.21 -1.3
	F≥2	7.1 – 9.5	F≥2	7.1 – 8.6	F≥2	1.31-1.5
	F≥3	9.6 – 12.5	F≥3	8.7 – 10.3	F≥3	1.51-1.9
	F=4	≥ 12.6	F≥4	≥ 10.4	F=4	≥ 1.91
HBV	F≥1	5.1 – 7.0	F≥1	5.8 – 7.0	F≥1	1.21 -1.3
	F≥2	7.1 – 8.0	F≥2	7.1 – 8.0	F≥2	1.31-1.5
	F≥3	8.1 – 11.5	F≥3	8.1 – 10.0	F≥3	1.51-1.9
	F=4	≥ 11.6	F=4	≥10.1	F=4	≥ 1.91
NAFLD	F≥1	5.1-7.0	F≥1	N.A.	F≥1	≥ 1.10
	F≥2	7.1- 10.5	F≥2		F≥2	≥ 1.16
	F≥3	10.6 – 11.5	F≥3		F≥3	≥ 1.48
	F=4	≥ 11.6	F=4		F=4	≥ 1.63

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