Attenuation coefficient measurement (ACM) as a newest mode for ultrasound quantitative hepatic steatosis assessment

Poster No.: B-1245
Congress: ECR 2017
Type: Scientific Paper
Authors: O. Dynnyk, N. Kobyliak, A. Fedusenko; Kyiv/UA
Keywords: Abdomen, Liver, Pancreas, Ultrasound, CT, Elastography, Diagnostic procedure, Metabolic disorders
DOI: 10.1594/ecr2017/B-1245

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
Purpose

The most frequent of the chronic diffuse liver diseases (CDLD) is fatty liver disease (alcoholic (ALD) and non-alcoholic (NAFLD) etiology). NAFLD affects up to 30% of the adult western population [1-3]. Nowadays liver biopsy has been considered as the gold standard to confirm the clinical diagnosis, to assess the severity of steatosis, necro-inflammation and fibrosis, and to monitor the efficacy of treatments [4]. Liver biopsy is expensive, invasive and that's why associated with some potential adverse effects and complications [5].

Unlike fibrosis in the viral hepatitis and cirrhosis, steatosis poorly motivated patients and hepatologists to perform the liver biopsy procedure. Therefore there is an urgent need for the development and implementation of alternative, non-invasive methods of the liver steatosis diagnosis.

Recently, for the qualitative and quantitative assessment of degree steatosis became widely used along with a number of biochemical, radiological techniques such as ultrasound (US), computed tomography in native mode (CT) and magnetic resonance imaging (MRI - assessment of proton density and MR spectroscopy) [6].

However, re-examination of patients using CT and MRI to assess the effectiveness of treatment and the natural history NAFLD is difficult. According to this, US is a very promising diagnostic method as it is widespread, has no ionizing influence, not invasive, inexpensive and can be repeatedly re-used for patient monitoring. However, US is characterized by a significant operator-, machine- and patient-dependence in the diagnosis of CDLD and including FLD [7,8].

The presence of fat droplets in the hepatocytes (hepatic steatosis) increases the attenuation of US. It is shown that US B-mode is highly sensitive to the finding of a significant accumulation of fat in the liver. However, B-mode does not allow to identify the fatty liver when the presence of lesions is less than 20% of hepatocytes. This applies a Hamaguchi criteria and a hepato-renal index [9]. An exact quantification of fat in hepatocytes by the B-mode is not possible due to significant differences in echogenicity in the liver of healthy people and operator-dependent evaluation of Hamaguchi criteria [10]. Calculation of hepato-renal index and score histogram echogenicity of the liver did not find sufficient spread due to lack of B-mode standardization in the hepatic parenchyma visualization [11].

Later, for the US diagnosis of steatosis by B-mode the new technology of raw data analysis was offered. It is an acoustical structure quantification mode (ASQ). It has been proposed to use ASQ for quantification of DLD (fibrosis and steatosis) in an experiment and in a clinic [12].
Recently another US methods of evaluating steatosis have appeared as the alternative to B-method. Fat droplets scatter US wave and lead to its attenuation by liver parenchyma in the direction of wave propagation from the transducer to tissue and then return of the reflected wave back to the transducer. Throughout the path of US waves attenuation is uneven. It has been shown a correlation degree of US attenuation in liver tissue with the degree of steatosis morphological scales SAF/NAS [4, 5]. This is the basis of the Controlled Attenuation Parameter (CAP) in the Fibroscan (Echosens). The US attenuation scale for assessing the fat droplets accumulation in the hepatocytes was offered in decibels per meter - dB/m [13-15]. However in EASL guidelines is carefully noted that further accumulation of data is needed to assess the role of the CAP in the diagnosis of NAFLD [16]. Ukrainian developers in the past few years (2014-2016) offered a technology of 2 dimensions (2D) quantitative measurement in real-time of the fat droplets concentration for the US attenuation coefficient measurement (ACM) in the liver parenchyma [17].

Aim: Estimate ACM as a new 2D in real-time mode for US quantitative hepatic steatosis assessment.
Methods and materials

From total of 3274 patients who underwent to comprehensive abdominal US (2015-2016) in our clinic, 949 have been diagnosed with fatty liver according to Hamaguchi criteria. We provided ACM (dB/cm) measurement by SoneusP7 device (Ultrasign, Ukraine), with a 1-6 MHz convex transducer in the right lobes.

An acquisition of the acoustic data of the US attenuation magnitude was in the sample volumes (SV). While scanning within region of interest (ROI ACM) was selected an array of SV. The standard method for determining the US attenuation coefficient derived from the well-known exponential attenuation law [19] in which to improve the accuracy of measurements used information from a plurality of the SV in the ROI [17].

Calculation of the US AC in real-time averaging of data from a plurality of the SV. Therefore ROI mapping at US steatography/steatometry must exclude from the area reverberations by operator.

To navigate the ROI ACM in US equipment we proposed to use of the AC graph as a profilogram. It screen displays the graph of the logarithmic amplitude of depth. We did not include data from the place of the ROI, where the attenuation is not consistent with a linear relationship. Accordingly, we positioned the ROI in the liver, where there are no strong reflectors in the anatomical B-mode. Attenuation mapping algorithm and ACM is able to excluded from the selection the small portal tracts and hepatic veins branches up to 10 mm in diameter. Fig.1, 2.

For diagnostic accuracy assessment we used CT as references method and comparison with CAP by Fibroscan (Echosens, France) we included 142 patients for subanalysis.
Fig. 1: The liver steatography/steatometry. An each colored dot in the ROI is the ACM SV. The results table shows the average values of ACM in the ROI for different US frequencies: 2.0; 2.73 and 3.53 MHz - accordingly 1.20; 1.60 and 1.91 dB/cm.

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2015
**Fig. 2:** Patient without liver steatosis. ACM - 1.62 dB/cm. Graph of the US attenuation profilogram allows to carry out the correct positioning ROI in the direct segment by operator.

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2016
Results

Depending on the stage of steatosis according to B-mode median, 25 and 75 quartiles for ACM were as follows: control group 1.57 (1,32-1,85); S1 - 1,86 (1,78 - 2,11); S2 - 2,26 (2,20-2,49) and respectively for S3 - 2,7 (2,40-2,82) dB/cm. Fig.3-6.

ACM value increase parallel the hepatic steatosis progression (p <0.001), which was also accompanied with presence of very strong correlation between these parameters (r = 0,814, p <0.001).Fig.7.

The ACM value significantly correlated with Controlled Attenuation Parameter (CAP). Fig.8.

The AUROC of ACM for steatosis diagnosis was 0,919 (95%CI 0,854-0,985). The optimal cutoff point was >1,99 dB/cm, with sensitivity, specificity, PPV and NPV respectively 96,3%, 74,4%, 72,2% and 96,6%.Fig.9.

ROC-curve for ACM.Fig.10.
**Fig. 3:** Patient with mild steatosis. ACM - 2.24 dB/cm.

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2016
Fig. 4: Patient with middle steatosis. ACM - 2,40 dB/cm.

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2016
Fig. 5: Patient with severe steatosis. ACM - 3.02dB/cm.

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2016
Fig. 6: Stages of steatosis. Compliance with data of the ACM and B-mode. The top of the bottom of the boxes are the first (25) and third (75) quartiles, respectively. The length of the box represents therefore the interquartile range (IQR) including 50% of the values. The line through the middle of each box represents the median. The error shows the minimum and maximum values (range).

© Department of Endocrinology, Bogomolets National Medical University, Kyiv, Ukraine, 2016
Fig. 7: Correlation between ACM value and degree of steatosis (r - Spearman's rank correlation coefficient)

© Department of Endocrinology, Bogomolets National Medical University, Kyiv, Ukraine, 2016
Fig. 8: Correlation between ACM and CAP value (r - Pearson correlation coefficient)

© Department of Endocrinology, Bogomolets National Medical University, Kyiv, Ukraine, 2016
<table>
<thead>
<tr>
<th>Parameters</th>
<th>NAFLD vs control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optimal cutoff point</td>
<td>&gt;1,99</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>96,3</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>74,4</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>96,6</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>72,2</td>
</tr>
<tr>
<td>AUROC</td>
<td>0,919</td>
</tr>
<tr>
<td>95% CI</td>
<td>0,854-0,985</td>
</tr>
<tr>
<td>P (AUROC)</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>

**Fig. 9:** Diagnostic accuracy of ACM for steatosis detection when CT used as references method. AUROC - Area under Receiver Operating Characteristic; 95%CI - 95% confidence interval for AUROC.

© Department of Endocrinology, Bogomolets National Medical University, Kyiv, Ukraine, 2016
**Fig. 10:** ROC-curve for ACM

© Department of Endocrinology, Bogomolets National Medical University, Kyiv, Ukraine, 2016
Conclusion

In this study, we found that directly correlated the ACM value and the steatosis degree (CAP and CT values).

Sasso et al. assessed CAP diagnostic accuracy in a large cohort (n=615) of biopsy-proven patients with chronic hepatitis C (CHC) virus. In multivariate analysis, CAP was related to steatosis (P < 10(-15) ) independently of fibrosis stage (which was related to LSM). The areas under ROC curves using CAP to detect steatosis were 0.80 (95% CI, 0.75-0.84) for S ≤ S(1) , 0.86 (0.81-0.92) for S ≤ S(2) and 0.88 (0.73-1) S = S(3) . CAP exhibited a good ability to differentiate steatosis grades (Obuchowski measure = 0.92) [19].

In multi-center prospective cohort study from China a total of 152 patients were recruited, including 52 (34.2%) patients with NAFLD and 100 (65.8%) with CHB virus infection. After adjustment, the steatosis grade (OR = 37.12; 95%CI: 21.63-52.60, P < 0.001) and body mass index (BMI, OR = 6.20; 95%CI: 2.92-9.48, P < 0.001) were found independently associated with CAP by multivariate linear regression analysis. CAP was not influenced by inflammation, fibrosis or etiology [20].

Limitation.

There are not any limitations to this study. The ACM availability was similar to the B-mode. But it should be noted the importance of the ROI navigation and the possibility of influence on the ACM result of the reverberations.Fig.11, 12.

We have proposed a step-by-step algorithm for performing real-time US steatography/steatometry for ACM:

Step 1. Selection of a window for acoustic access in the B-mode without noise and reverberation.

Step 2. Navigation. The ROI position depth should not be close to the liver capsule than 1.5 - 2 cm (area reverberation and noise) and farther than 10 cm. The US wave needs running optimally at least 4 cm deep for the measure US attenuation. The width of the ACM ROI was in the range of 2-3 cm. It should not include in ROI: liver capsule and hilum, diaphragm, gall bladder and intestinal gas. Special algorithm automatically excludes from the measurement of the portal tracts and hepatic veins and it do not affect the result of the ACM. The reference measurement position: a direct segment of the attenuation graph on the profilogram. Choice (position and size) of the ROI and the ACM occurs in real time. This allows the operator to optimize the ROI, using fan-shaped and rotary motions of the transducer.
Step 3: ROI optimization without noise. For the ACM do not matter: a deep breath, liver compression by transducer, etc. Therefore, the operator can be traditional for B-mode imaging to improve by deep inspiration and straining, as well as subcostal access.

Step 4: Measurement. Requires at least 3 times of the ACM for averaging the results. The steatometry of the right liver lobe is preferred.

Step 5: Evaluation of ACM. The scale of the US attenuation unit of the equipment is calibrated by a steatometry phantom. The steatometry results were evaluated on a scale of US attenuation for steatosis proposed by [19].

The ACM as novel real time ultrasound approach can be used for noninvasive hepatic steatosis diagnosis and allows clinicians to follow up FLD progression and response to treatment.
**Fig. 11:** The presence of ascites was no obstacle to the ACM (ACM - 1,92 dB/cm).

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2016
**Fig. 12:** The reverberations in the liquid are a source of false attenuation measurements. ACM - 8.78 dB/cm. It is an artifact of the steatometry.

© Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine, 2016
Personal information

1. Dynnyk Oleg, M.D., Ph.D. Department of Clinical Pathophysiology, Bogomolets Institute of physiology of the Ukrainian National Academy of Sciences, Kyiv, Ukraine. E-mail: obdynnyk@gmail.com.

2. Kobyliak Nazarii, M.D., Ph.D. Department of Endocrinology, Bogomolets National Medical University, Kyiv, Ukraine.

E-mail: nazariikobyliak@gmail.com.

3. Fedusenko Oleksandr, M.D., Ph.D. Department of Radiological Diagnostics, National Medical Postgraduate Academy, Kyiv, Ukraine. E-mail: ctus@li.ru.
References


5. Kobyliak N, Abenavoli L. The role of liver biopsy to assess non-alcoholic fatty liver disease. Reviews on Recent Clinical Trials 2014; 9(3):159-169.


