Gadolinium-ethoxybenzyl-diethylenetriamine (Gd-EOB-DTPA)-enhanced magnetic resonance imaging with various enhancement ratios: a correlation with clinical assessment of liver function using the Child-Pugh scoring system

Zastosowanie rezonansu magnetycznego z hepatotropowym środkiem kontrastowym (Gd-EOB-DTPA – kwas gadoksetowy) w ocenie funkcji wątroby u pacjentów z marskością – korelacja ze skalą Childa-Pugha

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Key words: liver cirrhosis, Gd-EOB-DTPA, Child-Pugh score, gadoxetate disodium, contrast enhancement ratio.

Streszczenie

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Streszczenie

Wprowadzenie: Marskość wątroby będąca zejściem wielu przewlekłych chorób tego narządu jest jedną z głównych przyczyn śmiertelności w krajach rozwiniętych. Biopsja wątroby uważana za złoty standard w rozpoznawaniu marskości wiąże się z wieloma powikłaniami, dlatego ostatnio podkreśla się rosnącą rolę rezonansu magnetycznego (MRI) w diagnostyce marskości.

Cel pracy: Określenie skuteczności MRI wątroby wzmocnionego Gd-EOB-DTPA (kwas gadoksetowy) w ocenie jej funkcji u pacjentów z marskością w odniesieniu do klinicznej skali Childa-Pugha.

Material i metody: Do badania włączono 126 pacjentów, u których w latach 2013–2016 wykonano MRI wątroby z hepatotropowym środkiem kontrastującym. Grupa badana składała się z 94 pacjentów z klinicznie rozpoznaną marskością,
Introduction

Liver cirrhosis is the final pathological result of many chronic liver diseases and an increasing cause of mortality in developed countries [1, 2]. Fibrosis which precedes cirrhosis is characterized by an increase in the number of fibroblasts and accumulation of collagen fibers resulting in progressive loss of hepatocytes and liver function impairment [3]. Liver biopsy, called “the gold standard” for liver fibrosis assessment, is invasive and carries a risk of complications and sampling errors [4–6], including a small tissue sample, inter-and intra-observer variability and post-procedure complications such as pain and bleeding, resulting in an overall low cost-effectiveness ratio [7, 8]. Over time it has become evident that this reference technique is inaccurate. Less invasive methods that would be safer, better tolerated by the patient and could be repeated as often as required have become more desirable [9, 10].

Recently, the increasing role of magnetic resonance imaging (MRI) in the diagnosis of liver cirrhosis has been emphasized. The most promising techniques are diffusion-weighted imaging (DWI), contrast enhancement (CE) MRI indexes utilizing hepatobiliary contrast agents and magnetic resonance elastography (MRE) [11–13].

DWI can evaluate restricted diffusion in cirrhotic liver caused by excessive accumulation of extracellular matrix, however susceptibility to motion artifacts and poor signal-to-noise ratio due to high b values used in this method are considered to be major limitations [14–16]. Several groups of investigators have reported that hepatocyte-specific contrast-enhanced MR imaging (Gd-EOB-DTPA-enhanced MRI) can be used for staging of liver fibrosis. Approximately 50% of Gd-EOB-DTPA is taken up by hepatocytes and excreted with bile; the more hepatocytes, the greater the uptake of the contrast agent, and thus the greater contrast enhancement of functional liver parenchyma in hepatobiliary phase [17]. For grading of liver fibrosis, different quantitative parameters have been utilized, including the contrast enhancement ratio (CER), contrast enhancement index (CEI), liver-to-muscle ratio (LMR), liver-to-spleen ratio (LSR), and liver-to-intervertebral disc SI ratio (LI) [17–20], however their usefulness has not yet been thoroughly investigated [21–24].

The potential advantage of parameters related to Gd-EOB-DTPA liver imaging over non-contrast enhanced indexes, including DWI derived apparent diffusion coefficient (ADC) values, is that they are not affected by deposition of fat and iron, as well as perfusion effect from blood vessels. Moreover, the use of Gd-EOB-DTPA-enhanced MRI provides not only morphological information but enables evaluation of the liver function, focal hepatic lesions and bile duct obstruction [25].

The Child-Pugh (CP) scoring system was originally designed to predict mortality in patients with cirrhosis. Based upon five clinical and laboratory criteria: ascites, neurological disorder, serum bilirubin, serum albumin and prothrombin time, patients are divided into three categories: A – good hepatic function, B – moderately impaired hepatic function, and C – advanced hepatic dysfunction [26, 27]. It has a major clinical importance as it enables to assess the prognosis, helps in choosing optimal treatment and predicting the expected survival rate in these patients. To date there have been only a few publications discussing the association between functional Gd-EOB-DTPA-enhanced MRI and the Child-Pugh scoring system in the assessment of patients with liver fibrosis [28–30].

Aim of the research

The purpose of this study was to determine the efficacy of quantitative Gd-EOB-DTPA-enhanced MRI for assessing the liver function impairment in cirrhotic patients in correlation with the clinical assessment using the Child-Pugh scoring system.

Material and methods

Patients

Our retrospective study was approved by the local institutional review board. We researched and selected 332 patients who underwent hepatocyte-specific contrast-enhanced MRI in our department in 2013-2016, on account of evaluation of chronic liver disease or a suspected focal liver lesion. The inclusion criteria for the control group were as follows: clinically healthy liver, no history of chronic liver disease nor liver cirrhosis. The factor that determined allocation
to the study group was clinically diagnosed cirrhosis. The exclusion criteria were incomplete data and MRI study without Gd-EOB-DTPA. Finally, 126 patients were enrolled in this study (94 in the study group and 32 in the control group).

The study group (n = 94) comprised patients with cirrhosis and the most common underlying disease was chronic hepatitis C (VHC). The classes of the diagnosis of liver disease in the study group are listed in Table 1. The mean age in this group was 60.4 ± 12.63 years, median 60 (55–69) years (Figure 1).

Thirty-two patients without liver cirrhosis comprised the control group. The most common underlying disease was a benign, clinically insignificant focal liver lesion (Table 2). The mean age in this group was 52.2 ± 15.52 years, median 51 (39.5–62.5) years (Figure 2).

In the study group the diagnosis of cirrhosis was made using standard abdominal ultrasound and clinical findings: presence of ascites, gastroesophageal varices, icterus and hepatic encephalopathy. Based on the Child-Pugh scoring system these patients were subsequently divided into 3 subgroups, according to the severity of liver function impairment. Subgroup A (CP-A, n = 62) comprised patients with 6 points or less in the 15-point Child-Pugh scale, subgroup B (CP-B, n = 21) patients with 7–9 points and subgroup C (CP-C, n = 11) patients with 10 points or more (Figure 3). Furthermore to assess the possible impact of biochemical parameters on contrast enhancement ratio values, laboratory blood tests were performed in all patients, including following serum parameters: bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), γ-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), serum albumin, hemoglobin, thrombocytes and creatinine.

**MRI technique and evaluation**

MRI was performed with a 1.5 Tesla (T) MRI scanner using phased-array multicoil system. For the acquisition of hepatobiliary phase images we used the generalized autocalibration partially parallel acquisition (GRAPPA) algorithm with volumetric interpolated breath-hold examination (VIBE). The parameters of T1 VIBE sequence were consistent with our standard abdominal scanning protocol: TR 2.97 ms, TE 1.1 ms, average 1, voxel size 1.9 × 1.4 × 1.8 mm, slice thickness 1.8 mm, flip angle 10 deg., and phase oversampling 30%.

Besides the hepatobiliary phase, the imaging protocol consisted of the following sequences: axial breath-hold T2-weighted TSE sequence, axial and coronal respiratory-triggered T2-weighted TSE sequence with fat-saturation, axial breath-hold in-and-out-of-phase spoiled gradient echo sequence with double echo, coronal trueFISP sequence and axial T1 VIBE sequence for dynamic contrast-enhanced images.

The dynamic study and hepatobiliary phase images were obtained after an intravenous administration of gadoxetic acid disodium (Gd-EOB-DTPA) followed by a 20 ml saline infusion. The contrast medium was injected at a dose of 0.025 mmol/kg body weight. Hepatobiliary phase images were acquired at 20 min after the contrast injection in axial and coronal planes.

**Analysis of MRI**

All signal intensity (SI) measurements were made on a standard workstation, by placing a 1 cm² circular...
region of interest (ROI) on liver, muscle and spleen parenchyma, avoiding large blood vessels, liver capsule and areas of fatty infiltrations of paraspinal muscles, possibly at the same slice on pre-enhanced and enhanced MR images (Figure 4). Mean SI was used as a datum.

For the purposes of this study, we divided liver into four sections: left lateral section, comprising segments 2 and 3, left medial section (segments 4a and 4b), right anterior section (segments 5 and 8) and right posterior section (segments 6 and 7). To obtain pre-liver SI we averaged SI value of 8 measurements (2 measurements for each section) on pre-enhanced imaging. The same procedure was repeated on contrast-enhanced imaging to establish liver SI.

The following formulae were used to calculate CER, CEI, LMR and LSR: CER = liver SI/pre-liver SI, CEI = SI_{post}/SI_{pre}, where SI_{post} and SI_{pre} are the liver-to-muscle (LMR) signal intensity ratios in the hepatocyte phase and pre-enhanced images, respectively; LMR = liver SI/muscle SI, LSR = liver SI/spleen SI.

Muscle SI was the mean value of 4 SI measurements (2 measurements for the right erector spinae muscle and 2 for the left) at the hepatobiliary phase. Spleen SI was the average value of 2 SI measurements at the hepatobiliary phase.

**Statistical analysis**

Statistical analysis was performed with Statistica software (version 13.3, StatSoft, Poland). The results are expressed as the mean ± standard deviation (SD). t-Student, U Mann-Whitney and Cochran-Cox tests were used to evaluate statistical differences between study and control groups. Assessment of the equality of variances and normality in groups was performed with Levene and Shapiro-Wilk tests.

The differences between four groups (control group, Child-Pugh A, B and C) were tested using the one-way ANOVA and the Kruskal-Wallis test.
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To indicate exactly which averages are different from each other, Turkey’s and Dunn’s post-hoc tests were performed.

In order to determine the possible relationship between CER and serum liver function tests, multiple regression analysis was performed.

**Results**

The mean and median values of the CEI, CER, LMR and LSR parameters in each group are listed in Table 3.

| Stage of liver function impairment | CEI   | CER   | LMR   | LSR   |
|-----------------------------------|-------|-------|-------|-------|
| Control group                     | 1.46 ±0.292 | 1.63 ±0.178 | 0.97 ±0.225 | 1.30 ±0.408 |
| Mild (Child-Pugh A)               | 1.32 ±0.201 | 1.51 ±0.172 | 0.74 ±0.181 | 1.27 ±0.304 |
| Moderate (Child-Pugh B)           | 1.19 ±0.152 | 1.38 ±0.116 | 0.64 ±0.091 | 1.18 ±0.206 |
| Severe (Child-Pugh C)             | 1.15 ±0.132 | 1.24 ±0.119 | 0.54 ±0.121 | 0.97 ±0.212 |
| Study group (Child-Pugh A + B + C)| 1.27 ±0.198 | 1.45 ±0.181 | 0.69 ±0.172 | 1.22 ±0.289 |

The graphic representation of distribution of CER, CEI, LMR and LSR values in patients with different liver function is shown in Figures 5–9.

Patients from the control group presented a significantly higher CER, CEI and LMR level compared to the study group (Child-Pugh A + B + C) with \( p = 0.0000003 \), \( p = 0.0019 \) and \( p << 0.0001 \), respectively. There was no significant difference in LSR values between the control group and the study group \( (p = 0.303159) \).

The values of all four parameters were significantly lower in patients with moderate or severe liver

**Figure 5.** Distribution of the CER values (mean, mean ± SD, mean ± 1.96 × SD)

**Figure 6.** Distribution of the CEI values (median, 25–75%; non-outlier range)

**Figure 7.** Distribution of the LMR values (median, 25–75%; non-outlier range)

**Figure 8.** Distribution of the LSR values (mean, mean ± SD, mean ± 1.96 × SD)

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function impairment (CP-B and CP-C) than in patients with mild impairment (CP-A) (Figure 9).

In order to determine diagnostic performance of all 4 parameters in predicting advanced liver function impairment, receiver operating characteristic (ROC) analysis was performed. CER and LMR showed higher sensitivity and specificity compared to CEI and LSR (CER: sensitivity 0.812, specificity 0.813, AUROC 0.912; LMR: sensitivity 0.875, specificity 0.813, AUROC 0.911; CEI: sensitivity 0.813, specificity 0.688, AUROC 0.760; LSR: sensitivity 0.875, specificity 0.813, AUROC 0.654) (Figure 10).

Discussion

The purpose of our study was to establish whether there is a relationship between hepatocyte-specific contrast-enhanced MR imaging and liver function impairment classified by the Child-Pugh scoring system. We revealed a significant correlation for following enhancement ratios: CER, LMR and CEI, whereas a poor correlation was found for LSR. These findings are in concordance with some previous papers assessing the role of Gd-EOB-DTPA in liver cirrhosis [17, 18, 22, 24, 25]. However those studies focused on staging of liver fibrosis in correlation with histopathology results, whereas our study focused on the relationship between enhancement ratios and clinical assessment of liver impairment. Two of four analyzed CE ratios (CER and LMR) were the most strongly correlated with liver function impairment based on the Child-Pugh scoring system (Table 4); furthermore amongst all analyzed parameters CER and LMR predicted advanced liver dysfunction (≥ CP-B) with highest sensitivity (0.81 and 0.88, respectively) and specificity (0.81), with AUROCs of 0.91.

So far, the most commonly used parameter in Gd-EOB-DTPA-enhanced MRI for evaluating liver function [20] and staging of liver fibrosis was CEI. Li et al. [20] assumed that this parameter enables the most objective evaluation of the liver fibrosis as it is utilizing SI values from paraspinal muscle parenchyma as a reference values. On the other hand, our study revealed that the role of CEI in detecting liver function impairment in patients with fibrosis is inferior to other MRI-biomarkers such as CER and LMR, still we cannot exclude that it could be due to different methodology and reference standard we adopted.

We noted significant overlaps in CE values among patients in different Child-Pugh subgroups, however comparison between patients with mild (CP-A) and moderate + severe liver dysfunction (CP-B + CP-C) revealed significant differences for all four parameters. Therefore we presume that MRI CE ratios may be feasible in assessment of patients with advanced liver dysfunction.
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Gadolinium-ethoxybenzyl-diethylenetriamine (Gd-EOB-DTPA) is a hydrophilic, paramagnetic and liver-specific contrast medium, uptaken by hepatocytes with about 50% of the administered dose secreted by the hepatobiliary pathway [31]. The hepatocyte phase, defined as peak enhancement, is usually reached within 20 min after the contrast injection in patients with normal hepatic function and lasts for at least 60 min [32]. Nevertheless, there is a diversity in the methodology and parameters used for hepatocellular contrast-enhanced MRI regarding both acquisition and analysis of images. Chen et al. [33] achieved the best differentiation between no fibrosis and any fibrosis at 10 min post Gd-EOB-DTPA administration, however most authors support liver assessment at 20 min post injection.

The number of ROIs and their location for SI measurements also differ in various studies. In most studies 1 to 4 ROIs were used to calculate CEI, and no authors relied on the SI measurements only in the left lobe as its lateral segments may be affected by the motion artifacts from the heartbeat, resulting in poor reproducibility of measurements [34]. To decrease this effect we proposed mean value of 8 SI measurements, 2 in each liver section, including both liver lobes.

Changes of liver SI at the hepatobiliary phase are mainly related to the number of functioning hepatocytes, and to some extent to the functional reserve of the liver. Using the Child-Pugh scoring system for clinical assessment of liver function, we performed a correlation with the enhancement ratios of CER, LMR, LSR and CEI.

Table 4. Spearman’s rank correlation coefficients for enhancement ratios with liver function based on the Child-Pugh scoring system. A strong indirect relationship was found for CER and LMR.

| MR parameter | Correlation coefficient | P-value | interpretation of Spearman ρ |
|--------------|------------------------|---------|-----------------------------|
| CER          | −0.57                  | 0.000   | Strong indirect relationship|
| LMR          | −0.58                  | 0.000   | Strong indirect relationship|
| CEI          | −0.38                  | 0.000   | Moderate indirect relationship|
| LSR          | −0.22                  | 0.014   | Weak indirect relationship |

Figure 10. The ROC curves for the diagnostic performance of CER (A), LMR (B), LSR (C) and CEI (D) in predicting moderate or greater (≥ CP-B vs. control group) liver function impairment.
Table 5. Results of multiple regression analysis performed in order to assess the impact of blood biochemical parameters on Contrast Enhancement Ratio (CER). Amongst all blood biochemical parameters, only serum bilirubin and albumin were statistically significant, with $p = 0.047$ and 0.037, respectively.

| Blood biochemical parameter | $P$-value |
|-----------------------------|-----------|
| Serum bilirubin             | 0.047     |
| Serum albumin               | 0.037     |
| ALT                         | 0.476     |
| AST                         | 0.524     |
| GGT                         | 0.053     |
| ALP                         | 0.093     |
| Hemoglobin                  | 0.504     |
| Thrombocytes                | 0.343     |
| Creatinine                  | 0.766     |

Table 6. Percentage share and size of classes in the study group – biopsy, elastography

| Parameter          | Number | %  |
|--------------------|--------|----|
| Biopsy:            |        |    |
| No                 | 89     | 95 |
| F6                 | 4      | 4  |
| PBC stage 4        | 1      | 1  |
| Total              | 94     | 100|
| Elastography:      |        |    |
| No                 | 53     | 56 |
| F4                 | 40     | 43 |
| Total              | 94     | 100|

patients using Gd-EOB-DTPA MR imaging and clinical assessment. CER and LMR showed the best relationship with the Child-Pugh scoring system amongst all enhancement ratios.

Conflict of interest
The authors declare no conflict of interest.

References
1. Zhou WC, Zhang QB, Qiao L. Pathogenesis of liver cirrhosis. World J Gastroenterol 2014; 20: 7312-7324.
2. Tschochatzis EA, Bosch J, Burroughs AK. Liver cirrhosis. Lancet 2014; 383: 1749-1761.
3. Pinheiro D, Dias I, Ribeiro Silva K, Stumbo AC, Thole A, Cortez E, de Carvalho L, Weiskirchen R, Carvalho S. Mechanisms underlying cell therapy in liver fibrosis: an overview. Cells 2019; 8: 1339.
4. Lai M, Afdhal NH. Liver fibrosis determination. Gastroenterol Clin North Am 2019; 48: 281-289.
5. Castera L, Friedrieh-Rust M, Loomba R. Noninvasive assessment of liver disease in patients with nonalcoholic fatty liver disease. Gastroenterology 2019; 156: 1264-1281.e4.
6. Sharma S, Khalili K, Nguyen GC. Non-invasive diagnosis of advanced fibrosis and cirrhosis. World J Gastroenterol 2014; 20: 16820-16830.
7. Lambrecht J, Verhulst S, Mannuerts I, Reynaert H, van Grunsven LA. Prospects in non-invasive assessment of liver fibrosis: liquid biopsy as the future gold standard? Biochim Biophys Acta Mol Basis Dis 2018; 1864: 1024-1036.
8. Potretzke TA, Saling LJ, Middleton WD, Robinson KA. Bleeding complications after percutaneous liver biopsy: do subcapsular lesions pose a higher risk? AJR Am J Roentgenol 2018; 211: 204-210.
9. Lurie Y, Webb M, Cytters-Kuin R, Shteingart S, Lederkremer GZ. Non-invasive diagnosis of liver fibrosis and cirrhosis. World J Gastroenterol 2015; 21: 11567-11583.
10. Sebastiani G, Gkouvatsos K, Pantopoulos K. Chronic hepatitis C and liver fibrosis. World J Gastroenterol 2014; 20: 11033-11053.
11. Bakan AA, Inci E, Baskan S, Goturk S, Cimilli T. Utility of diffusion-weighted imaging in the evaluation of liver fibrosis. Eur Radiol 2012; 22: e682-687.
12. Nishie A, Asayama Y, Ishigami K, Tajima T, Kakkihara D, Nakayama T, Takayama Y, Okamoto D, Taketomi A, Shira k P, Fujita N, Obara M, Yoshimitsu K, Honda H. MR prediction of liver fibrosis using a liver-specific contrast agent: superparamagnetic iron oxide versus Gd-EOB-DTPA. J Magn Reson Imaging 2012; 36: 664-671.
13. Xiao G, Zhu S, Xiao X, Yan L, Yang J, Wu G. Comparison of laboratory tests, ultrasound, or magnetic resonance elastography to detect fibrosis in patients with nonalcoholic fatty liver disease: a meta-analysis. Hepatology 2017; 66: 1486-1501.
14. Lewin M, Poujol-Robert A, Boelle PY, Wendum D, Lassnier E, Viallon M, Guéchot J, Hoefcell C, Arvéil L, Tubiana JM, Poupon R. Diffusion-weighted magnetic resonance imaging for the assessment of fibrosis in chronic hepatitis C. Hepatology 2007; 46: 658-665.
15. Taouli B, Tolia AJ, Losada M, Babb JS, Chan ES, Bannan MA, Tobias H. Diffusion-weighted MRI for quantifi-
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15. Goshima S, Kanematsu M, Watanabe H, Kondo H, Kawada H, Moriyama N, Baek KT. Gd-EOB-DTPA-enhanced MR imaging: prediction of hepatic fibrosis stages using liver contrast enhancement index and liver-to-spleen volumetric ratio. J Magn Reson Imaging 2012; 36: 1148-1153.

16. Watanabe H, Kanematsu M, Goshima S, Kondo H, Onozuka M, Moriyama N, Baek KT. Staging hepatic fibrosis: comparison of gadoxetate disodium-enhanced and diffusion-weighted MR imaging: preliminary observations. Radiology 2011; 259: 142-150.

17. Lee S, Choi D, Jeong WK. Hepatic enhancement of Gd-EOB-DTPA-enhanced 3 Tesla MR imaging: assessing severity of liver cirrhosis. J Magn Reson Imaging 2016; 44: 1339-1345.

18. Li X, Liu H, Wang R, Yang J, Zhang Y, Li C. Gadoxetate-disodium-enhanced magnetic resonance imaging for liver fibrosis staging: a systematic review and meta-analysis. Clin Radiol 2020; 75: e111-e119.

19. Nishie A, Asayama Y, Ishigami K, Tajima T, Kakihara D, Nakayama T, Takayama Y, Okaminoto D, Taketomi A, Shibara K, Fujita N, Ohara M, Yoshimizu K, Honda H. MR prediction of liver fibrosis using a liver-specific contrast agent: superparamagnetic iron oxide versus Gd-EOB-DTPA. J Magn Reson Imaging 2012; 36: 664-671.

20. Harada TL, Saito K, Araki Y, Matsubayashi J, Nagao T, Sugimoto K, Tokuuye K. Prediction of high-stage liver fibrosis: comparison of gadoxetate disodium-enhanced and diffusion-weighted MR imaging: preliminary observations. AJR Am J Roentgenol 2010; 195: 13-28.

21. Chen BB, Hsu CY, Yu CW, Wei SY, Kao JH, Lee HS, Shih TT. Clinical and histologic implications of delayed hepatobiliary enhancement on magnetic resonance imaging with gadolinium ethoxybenzyl diethylenetriaminepentaacetic acid. Invest Radiol 2012; 47: 649-655.

22. Kwee TC, Takahara T, Niwa T, Ivancevic MK, Herigault G, Van Cauteren M, Luijten PR. Influence of cardiac motion on diffusion-weighted magnetic resonance imaging of the liver. MAGMA 2009; 22: 319-325.

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