의학석사 학위논문

대규모 정상 인구에서 자기공명영상을 이용하여 측정한 proton density fat fraction (PDFF)의 분포와 참고 구간

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이 논문을 의학석사학위 논문으로 제출함

2019 년 12 월

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영문요약

Distribution and reference interval of MRI-PDFF in a large normal population

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Background: To define normal reference ranges of MRI-based proton density fat fraction (PDFF) values in a large normal population without any risk factor for hepatic steatosis and metabolic syndrome.

Methods: A retrospective search of the electronic medical records identified a total of 1529 donor candidates for living donor liver transplantation (LDLT) who underwent preoperative liver MRI between January 2015 and May 2018. A 'normal' population was defined as subjects having no history of liver disease and no identifiable risk factors or associated laboratory data abnormalities of hepatic steatosis and metabolic syndrome. PDFF values from a chemical-shift imaging-based MRI (CS MRI) and the high-speed T2-corrected multiecho MR spectroscopy (HISTO MRS) were at two different regions of interest, respectively. The distribution of PDFF values was analyzed. After logarithmic transformation, the reference interval ranging from 0 to 95th percentile of the reference distribution was determined using parametric methods to set the normal cut-off values. In a subgroup of patients who underwent liver biopsy on the same day with MRI, the proportion of grade 0 steatosis (<5% steatosis) on pathology was calculated to assess the correlation between the normal PDFF range and histopathology.

Results: The final study population defined as the 'normal' population consisted of 562 subjects (283 men; mean age, 30.2 years) with available MRI sequences for PDFF analyses. The distributions of CS MRI-PDFF and HISTO MRS-PDFF were positively skewed with ranges of 0.70–11.4% and 0.50–13.4%, respectively. The 95th percentile reference intervals of CS MRI-PDFF and HISTO MRS-PDFF were 0–6.8% and 0–8.6%, respectively. Among 387 subjects with available liver biopsy on the same day with MRI, the proportions of grade 0 steatosis on pathology were 78.9% according to the CS MRI-PDFF criteria and 79.2% according to the HISTO MRS-PDFF criteria.

Conclusions: The 95th percentile reference intervals of CS MRI-PDFF and HISTO MRS-PDFF in a normal population ranged from 0 to 6.8% and 0 to 8.6%, respectively.

Keywords: fatty liver; reference values; magnetic resonance imaging; magnetic resonance spectroscopy

목차

표 및 그림 차례

서론

As the clinical importance of nonalcoholic fatty liver disease (NAFLD) is in the limelight, quantification of liver fat to diagnose and monitor NAFLD becomes an area of active research. The proton density fat fraction (PDFF) calculated from magnetic resonance imaging (MRI) has been emerged as a noninvasive, reliable, accurate, and quantitative biomarker for hepatic fat with excellent inter- and intraobserver agreement (1-4). PDFF can be estimated by either MR spectroscopy (MRS) or a chemical shift imaging-based MRI (CS-MRI). As MRI sequences dedicated for PDFF measurement have been improved, advanced MRI sequences for this purpose are now commercially available which facilitates widespread use of PDFF in clinical practice.

PDFF from MRS or CS-MRI and histologic fat fraction show a strong correlation and both are expressed as percentages (5). However, PDFF values cannot be directly interchangeable with histologic fat fraction, as they are fundamentally different measures: PDFF is calculated from the signal intensity ratio of triglyceride (TG) and water, while the histologic grade is visual and semiquantitative estimation of the area occupied by fat vacuoles in a cross-section of a liver biopsy (6, 7). Clinically recommended limits of hepatic steatosis based on histologic fat fraction > 5% of hepatocytes (8) cannot be directly applied as a cut-off value of PDFF values. Previous studies on the basis of histologic fat fraction suggested 5.1 – 6.4% as threshold PDFF values to diagnose hepatic steatosis (9, 10). Yet, the use of histologic fat fraction as a reference standard may not be legitimate due to sampling variability related to the spatial heterogeneity of hepatic steatosis as well as interobserver variability (11-14). Moreover, a few studies raised a question on the superiority of histologic fat fraction assessed by pathologists over PDFF derived from MRS (2, 7, 15).

In this sense, PDFF distribution and reference intervals in a large number of normal populations are likely better to set a threshold value for hepatic steatosis. A population-based approach from 345 subjects who had no identifiable risk factors for hepatic steatosis suggested 5.56% as cut-off value of PDFF for hepatic steatosis (16). It has been generally accepted in previous studies (17-20). However, this value was calculated based on a traditional MRS method under free-breathing conditions subject to line broadening and erroneous data acquisition. This method is now replaced by updated MRI techniques using

CS-MRI and high-speed T2-corrected multi-echo (HISTO) MRS obtained within a single breath-hold (21). A recent phantom-based study revealed that measurement of PDFF is not reproducible across sequences, imager vendors, and field strengths (22). Thus, PDFF value based on updated MRI methods may be different from PDFF values using a previous method. In addition, the factors determining the "normal" population in the study were lean body mass index (BMI), absence of type 2 diabetes, normal fasting plasma glucose (FPG), and normal plasma alanine aminotransferase (ALT). These criteria could not adequately exclude patients with alcoholic liver disease or other metabolic risk factors such as dyslipidemia.

Therefore, the aim of this study was to assess the distribution and reference intervals for PDFF measured by currently available PDFF measuring methods in a large population of healthy adults without any identified risk factor for hepatic steatosis and metabolic syndrome.

연구대상 및 연구방법

Study population

This retrospective study was approved by our institutional review board, which waived the requirement for patients' informed consent.

A retrospective search of the electronic medical records of our hospital between January 2015 and May 2018 was performed and a total of 1529 donor candidates for living donor liver transplantation (LDLT) who underwent preoperative liver MRI were identified. Clinical data including demographic information such as sex, age, alcohol history, and the results of laboratory test performed on the date closest to MRI were recorded from the medical records.

A 'normal' population was strictly defined as subjects having no history of liver disease and no identifiable risk factors or associated laboratory data abnormalities of hepatic steatosis. Therefore, the study population was enrolled on the basis of the following criteria: lean (< 25 kg/m2 of BMI), normal FPG (< 100g/dL), normal serum ALT, gamma-glutamyltransferase (r-GT), TG, and high-density lipoprotein-cholesterol (HDL-C) (23-25). Subjects were excluded if they had a history of significant alcohol consumption (≥ 30 g/day in males and ≥ 20 g/day in females) (11), liver disease including hepatitis, or type 2 diabetes mellitus (DM). Of a total of 664 subjects who met these criteria for normal population, 102 subjects were further excluded because of the lack of appropriate MRI sequences for PDFF measurements or measurement error. Figure 1 presents the accrual process for the study population.

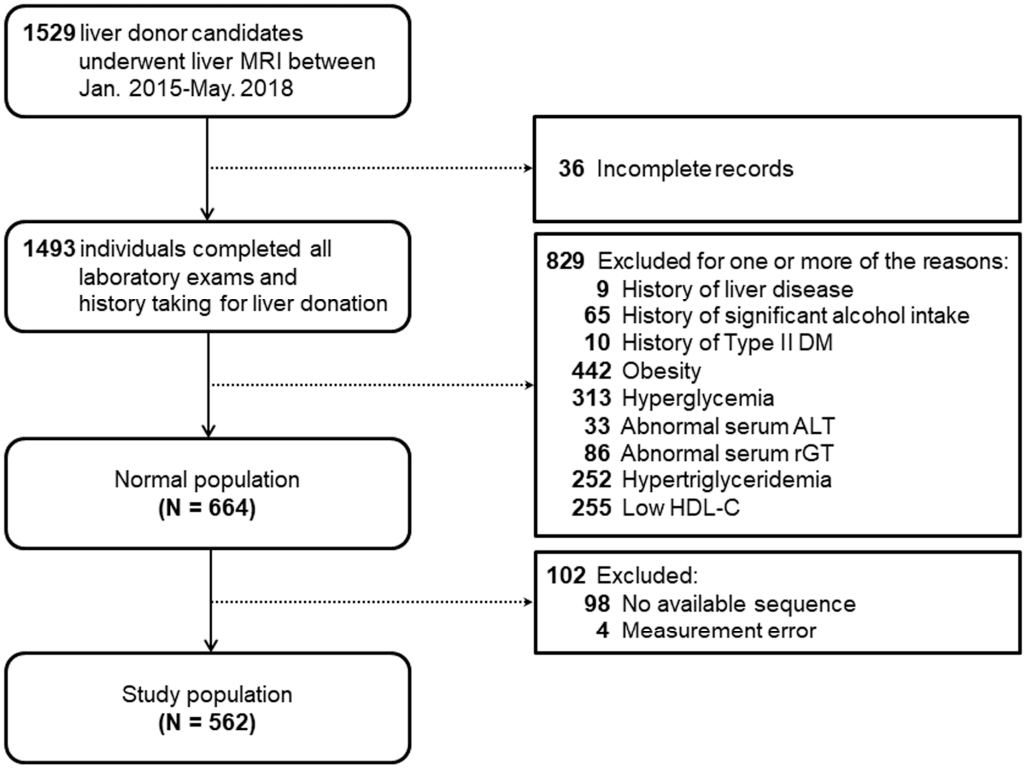


Figure 1. Flowchart of the patient inclusion process. Abbreviations: ALT, alanine aminotransferase; DM, diabetes mellitus; rGT, gamma-glutamyltransferase; HDL-C, high-density lipoprotein-cholesterol; MRI, magnetic resonance imaging

MRI acquisition techniques and PDFF measurement

All patients were imaged using a 3T MRI system (Magnetom Skyra, Siemens, Germany) with a 32-channel body matrix coil. As one of the routine liver MRI pulse sequences for living liver donor work-up, MRI techniques for hepatic fat quantification were performed before the intravenous administration of contrast media.

In CS MRI, a whole-liver volume was acquired within a single breath hold (scan time of 16–20 s), using a multi-echo 3D spoiled gradient-echo acquisition which is an investigational variant of "hybrid multi-step adaptive fitting approach with multi-echo volume interpolated breath-hold examination (VIBE) acquisition", which in consequence, generates a hepatic PDFF map (26-28). The parameters were as follows: repetition time (TR), 9.0 msec; echo time (TE), 1.09, 2.49, 3.69, 4.92, 6.15, 7.38 msec; flip angle, 4; slice thickness, 3.5mm; receiver bandwidth, 1080 Hz/pixel; field of view 380 x 380 mm; and parallel imaging factor, 2 x 2. The images were processed using a commercially available software (syngo MR D13, Siemens, Germany) to create water/fat images, water/fat R2* maps, an effective R2* map, and water/fat percentage maps (26, 28). One radiologist (J.H.K with 5 years of clinical experience in MRI) who was blinded to clinical profiles and histologic results interpreted MRI. PDFF values from the CS-MRI (CS MRI-PDFF) were measured at two different 30 mm x 30 mm regions of interest (ROIs) which were manually placed in the similar region where MRS measurements.

The HISTO MRS was performed by using a modified stimulated-echo acquisition sequence (STEAM) at TEs of 12, 24, 36, 48, and 72 msec. Each acquisition was completed during one breath hold (approximately 15 seconds). The parameters were as follows: TR, 3000 msec; mixing time, 10 msec; flip angle 90°; receiver bandwidth 1200 Hz/pixel. Experienced radiologic technicians manually placed two different ROIs (30 × 30 × 30 mm3) per a subject in 3-plane localizing images in the right hepatic lobe away from large vessels, large bile ducts, and focal hepatic lesions. HISTO MRS data was automatically post-processed using a software (syngo MR D13, Siemens, Germany). Each of the T2 values of water and fat was calculated separately, and T2 correction was applied for both the water and fat peaks to obtain an accurate hepatic fat fraction. Then T2-corrected fat fractions by using the equation: [M0lipid/(M0lipid + M0water)] x 100 %, M0 is the equilibrium magnetization

(21). The measurements were displayed as a percentage and the average of the two measurements was used as the representative PDFF value for each subject.

Histopathologic analysis

Among the 562 subjects in study population, an ultrasound-guided percutaneous liver biopsy was performed in 387 subjects on the same day with MRI for preoperative donor work-up. Biopsy samples approximately 1.5 cm in length were obtained from two different sites in the right hepatic lobe by using an 18-gauge needle (Stericut 18G coaxial; TSK Laboratory, Tochigi, Japan) with the patients under local anesthesia. All specimens were reviewed by pathologists with more than 5 years of experience. Histologic fat fraction determined as the fraction of hepatocytes that contained macrovesicular and/or microvesicular fat droplets on hematoxylin-eosin-stained specimens was collected from the pathologic reports. Hepatic steatosis is categorized based on the percentage of fat within the hepatocytes: grade 0 (healthy, <5%), grade 1 (mild, 5%-33%), grade 2 (moderate, 34%-66%), and grade 3 (severe, >66%) (29).

Statistical analysis

In order to assess reference distribution, histograms of CS MRI-PDFF and HISTO MRS-PDFF were plotted and compared to a normal distribution. Then, the normality of the PDFF in the reference population was tested by using the Shapiro-Wilk test and the histograms. Possible outliers were identified using Dixen/Reed method. When the data distribution does not fit a Gaussian distribution, logarithmic transformation was considered to be applied. Right-sided reference limits of 95^{th} percentiles and their confidence intervals (CI) were calculated by a parametric method which was regarded as an upper limit of normality of PDFF values, i.e. a cut-off value to diagnose hepatic steatosis (30). Agreement between these PDFF values and histopathology was investigated using the 95% Bland-Altman limit of agreement (LOA). In the reference population based on the cut-off values of CS MRI-PDFF and HISTO MRS-PDFF, the proportion of subjects with grade 0 steatosis (< 5% steatosis) based on the NASH Clinical Research Network criteria (31) was calculated. The repeatability of PDFF value on MRI was calculated using intraclass correlation

coefficients (ICC) for CS MRI-PDFF and HISTO MRS-PDFF. Agreement between CS MRI-PDFF and HISTO MRS-PDFF was evaluated. ICC values less than 0.5, between 0.5 and 0.75, between 0.75 and 0.9, and greater than 0.90 were considered poor, moderate, good, and excellent, respectively (32). The correlation of the PDFF values measured on CS MRI and HISTO MRS was evaluated using ICC and the 95% Bland-Altman LOA. All statistical analyses were performed using MedCalc statistical software (MedCalc software, version 18.2.1; Ostend, Belgium).

연구결과

Study subjects

The final study population of 562 subjects (mean age, 30.2 ± 8.4 years; range, 17–71 years) consisted of 283 men (mean age, 28.1 ± 7.3 years) and 279 women (mean age, 32.4 ± 8.8 years) with the mean BMI of 21.9 ± 2.0 kg/m^2 (median, 22.0; range, 12.2–24.9). Their laboratory data revealed mean FPG of 89 ± 7 mg/dL (median, 89; range, 54–99), mean ALT of 15 ± 8 IU/mL (median, 13; range, 5–56), mean r-GT of 16 ± 9 IU/mL (median, 13; range, 4–60), mean TG of 74 ± 29 mg/dL (median, 70; range, 28–149), and mean HDL-C of 63 ± 13 mg/dL (median, 60; range, 40–111). Median interval between laboratory exam and MRI was 34 days. Baseline characteristics of the total population are summarized in Table 1.

Table 1. Clinical and biochemical characteristics in a normal population (n=562)

Characteristics	
Age, years	30.2 ± 8.4
Sex, male, %	50.4 (283/562)
BMI, kg/m^2	21.9 ± 2.0
FPG, mg/dL	89 ± 7
ALT, IU/mL	15 ± 8
r-GT, IU/mL	16 ± 9
TG, mg/dL	74 ± 29
HDL-C, mg/dL	63 ± 13
No. of patient having received liver biopsy	387
Histologic fat fraction, %	3.4 ± 7.2

Note – Data are presented as mean ± standard deviation, unless indicated otherwise

BMI = body mass index; FPG = fasting plasma glucose; ALT = alanine aminotransferase; r-GT = Gamma-glutamyltransferase; TG = triglycerides; HDL-C = High-density lipoprotein cholesterol

Distribution and reference interval of PDFF

The distributions of both CS MRI-PDFF and HISTO MRS-PDFF were non-Gaussian ($P < 0.0001$, both) and positively skewed with a tail extending to higher values (coefficient of skewness = 2.9 and 2.8 for CS MRI-PDFF and HISTO MRS-PDFF, respectively) as shown in Figure 2. CS MRI-PDFF ranges from 0.70% to 11.4% and the median was 2.0%. HISTO MRS-PDFF ranges from 0.50% to 13.4% and the median was 2.0%. Log transformation gave the shape of normal distribution without identified outlier for both CS MRI-PDFF and HISTO MRS-PDFF. Back-transformed means were 2.1% for both CS MRI-PDFF and HISTO MRS-PDFF, respectively. Parametric 95th percentiles of MRI-PDFF which came to be the upper limits of the reference intervals were 6.8% (95% CI, 5.8–8.8) which included 535 subjects. Parametric 95th percentiles of HISTO MRS-PDFF were 8.6% (95% CI, 6.8–10.3) which included 534 subjects. Thus, estimated right-sided reference intervals determined by 95th percentiles of CS MRI-PDFF and HISTO MRS-PDFF were 0 – 6.8% and 0 – 8.6%, respectively.

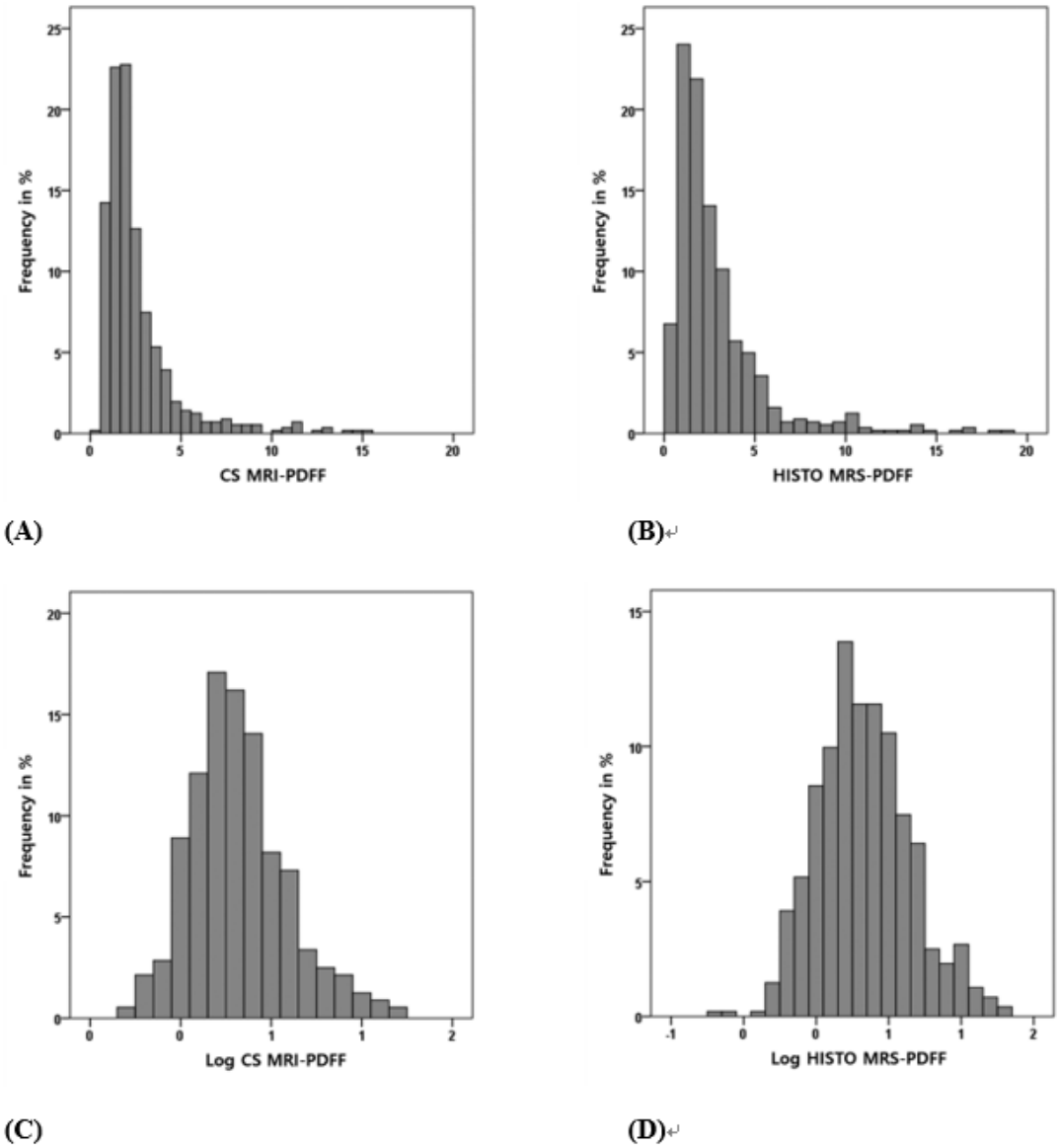


Figure 2. Histograms representing the distributions of MR-PDFF in a normal population before and after logarithmic transformation. The distributions of both CS MRI-PDFF (A) and HISTO MRS-PDFF (B) of 562 subjects defined as a normal population were positively skewed and median values were 2.0% (range, 0.70% - 11.4%) and 2.0% (range, 0.50% - 13.4%) for CS MRI-PDFF and HISTO MRS-PDFF, respectively.

After logarithmic transformation, the distributions of both CS MRI-PDFF (C) and HISTO MRS-PDFF (D) gave the shape of normal distribution and back-transformed means were 2.1% for both CS MRI-PDFF and HISTO MRS-PDFF.

Repeatability and agreement of CS MRI-PDFF and HISTO MRS-PDFF

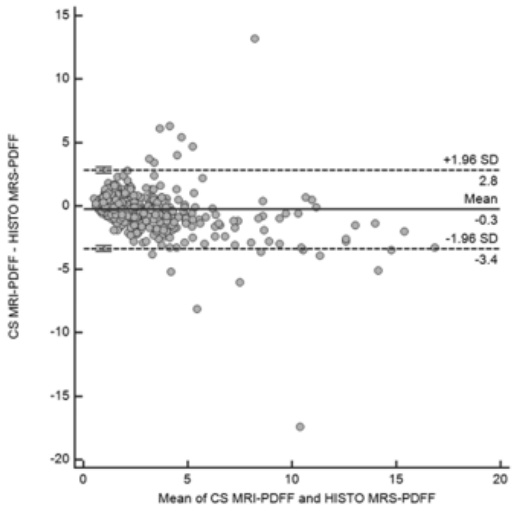
Repeatability between the first and second measurement of PDFF values were both excellent in CS MRI (ICC, 0.997; 95% CI, 0.997–0.998) and HISTO MRS (ICC, 0.915; 95% CI, 0.900–0.928), which provided the basis of performing further analysis with using the mean value of two measurements as a representative value in each of CS MRI-PDFF and HISTO MRS-PDFF.

Correlation between CS MRI-PDFF and HISTO MRS-PDFF within the same subjects were good (ICC, 0.883; 95% CI, 0.862–0.901). The Bland-Altman 95% LOA showed significant bias (mean bias ± 1.96·SD, -0.26 ± 3.09; $P < 0.001$).

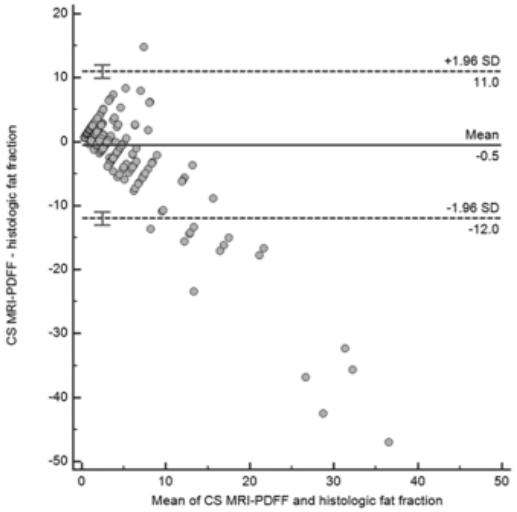
Relationship between PDFF and histology

In total 387 subjects who underwent liver biopsy on the same day with MRI, histologic fat fraction of ranged from 0 to 60 % and the median value was 1 %. The majority of patients were in grade 0 steatosis (74.9% [290/387]), followed by grade 1 steatosis (23.8% [92/387]), and grade 2 steatosis (1.3% [5/387]). The Bland-Altman 95% LOAs between PDFF and histologic fat fraction revealed a smaller bias in the HISTO MRS-PDFF (mean bias ± 1.96·SD, -0.26 ± 10.60; $P = 0.352$) than in the CS MRI-PDFF (mean bias ± 1.96·SD, -0.52 ± 11.50; $P = 0.082$) (Figure 3).

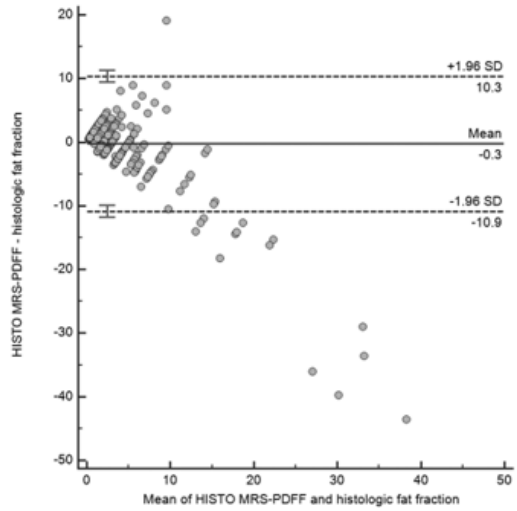
In 361 subjects whose CS MRI-PDFF values were within the reference range based on the 95th percentile criteria, median pathologic fat fraction was 1% and the proportion of pathologic grade 0 steatosis was 78.9% (285/361). In 361 subjects whose HISTO MRS-PDFF values were within the reference range, median pathologic fat fraction was 1% and the proportion of grade 0 steatosis on pathology was 79.2% (286/361). The median pathologic fat fractions of the other subjects whose PDFFs were above the 95th percentile criteria were both 15% (range, 0 – 60%).


CS MRI-PDFF - HISTO MRS-PDFF
Mean of CS MRI-PDFF and HISTO MRS-PDFF
+1.96 SD
2.8
Mean
-0.3
-1.96 SD
-3.4

(A)


CS MRI-PDFF - histologic fat fraction
Mean of CS MRI-PDFF and histologic fat fraction
+1.96 SD
11.0
Mean
-0.5
-1.96 SD
-12.0

(B)


HISTO MRS-PDFF - histologic fat fraction
Mean of HISTO MRS-PDFF and histologic fat fraction
+1.96 SD
10.3
Mean
-0.3
-1.96 SD
-10.9

(C)

Figure 3. Bland-Altman plots showing the relationships between CS-MRI PDFF and HISTO MRS-PDFF and between histologic fat fraction and PDFF. (A)–(C) Graphs show differences between fat fraction measured with different methods. X-axes represent mean and Y-axes represent differences between fat fractions measured by two methods. (A) CS MRI-PDFF and HISTO MRS-PDFF, (B) CS MRI-PDFF and histologic fat fraction, (C) HISTO MRS-PDFF and histologic fat fraction,

고찰

Our study suggested the reference intervals of CS MRI-PDFF and HISTO MRS-PDFF derived from 562 healthy adults without any identified risk factors for hepatic steatosis and metabolic syndrome. The 95th percentile reference intervals of CS MRI-PDFF and HISTO MRS-PDFF were 0–6.8% and 0–8.6%, respectively. In the reference population based on CS MRI-PDFF and HISTO MRS-PDFF, the proportions of histologically-determined grade 0 steatosis were 78.9% (285/361) and 79.2% (286/361). Both CS MRI-PDFF and HISTO MRS-PDFF showed high measurement repeatability (CS MRI-PDFF, ICC = 0.997; HISTO MRS-PDFF, ICC = 0.915) as well as good agreement between two methods (ICC = 0.883).

The estimated 95th percentile of PDFF values in our study were inconsistent with the cut-off values calculated in the prior studies (9, 10, 16). Based on histologic reference standards, the cut-off values to discriminate patients with steatosis grade 0 from those with grade 1 or greater were 6.4% (9) in CS MRI-based PDFF and 4.5–5.1% (10) in MRS–based PDFF. In addition, cut-off value of HISTO MRS-based PDFF in a normal population analyzed by Szczepanial et al. (16) was 5.56% which was lower than the value of our study, 8.6%. Possible explanation of this inconsistency is that out study and prior studies used different sequences, imager vendors and field strengths, which can affect the PDFF measurements (22). Therefore, these factors should be considered when the cut-off value of the PDFF is presented and we used the data obtained from the most recently used MRI and MRS techniques. MRI techniques used in our study are currently available techniques. Thus, we surmise that cut-off values from our study are time-relevant ones.

Regarding correlation with histopathology, although previous study demonstrated good correlation between PDFF and liver biopsy results (r = 0.820 – 0.849) (10, 33), proportions of grade 0 steatosis on pathology according to both CS MRI-PDFF and HISTO MRS-PDFF criteria were below 80%, suggesting insufficient positive predictive value when histopathology is considered as a ground truth. Possible explanation of this discrepancy is different study population. Whereas previous studies included people who received a diagnosis of NALFD or liver disease, our study recruited people who were expected to have normal range of hepatic fat. In addition, histologic fat fraction has an inherent limitation

driven from its subjective nature and sampling bias (11-14). Moreover, a few previous studies suggested that histopathology may not be absolutely superior to the PDFF (2, 7, 15). Therefore, using the data investigated in a large clinical cohort considered as a normal population may be the preferred method to define normal reference ranges.

Our study showed both CS MRI-PDFF and HISTO MRS-PDFF were highly repeatable in two times of measurements, which is in line with high intra-examination repeatability (ICC, 0.924 – 0.999) shown in previous studies (34-36). In addition, CS MRI-PDFF and HISTO MRS-PDFF achieved good agreement (ICC, 0.883), which is consistent with a result in a recent meta-analysis (4). Although their median values and also back-transformed means of their log-transformed data were same, parametric 95th percentile of HISTO MRS-PDFF were larger than that of CS MRI-PDFF (8.6% vs. 6.8%). In Jang et al's study (22), when the PDFFs acquired from the vendor and field strength which are same with our study were compared, there was a larger bias than our results between CS MRI-PDFF and HISTO MRS-PDFF (3.69% vs. -0.26%). This difference of biases can be explained by different ranges of PDFF values: our study tried to include healthy subjects expected to have a normal hepatic fat and Jang et al's study obtained PDFFs from phantoms of varying fat proportions. This is also supported by that HISTO MRS-PDFF showed a higher linear regression slope than that of CS MRI-PDFF (0.99 vs. 0.84), compared with reference PDFFs in Jang et al's study, suggesting that the difference between two values is relatively small within the range of lower PDFF values and larger the PDFF values, the greater the difference between the two values. The superiority between two when their discrepancy is significant should be investigated in future studies.

Our study has several limitations. First, as this is a retrospective study, several known risk factors for hepatic steatosis and metabolic syndrome such as waist circumference and insulin resistance, were not able to evaluate. However, we conjectured that the majority of significant risk factors for hepatic steatosis and metabolic syndrome were excluded based on clinical profiles and laboratory data abnormalities. Second, the number of the study population was somewhat limited and ethnic diversity was not considered. Although this is the largest study with normal population to estimate the PDFF range, a further study with larger diverse population should be warranted. Third, we only obtained MRI from one

vendor with one field strength and it remains uncertain whether the cut-off values could be applied in general. Detailed and precise cut-off values of each image vendor and each field strength should be corrected in the next studies.

결론

In conclusion, we estimated the 95th percentile reference intervals of CS MRI-PDFF and HISTO MRS-PDFF with currently used imaging protocols in a large normal population, which ranged from 0 to 6.8% and 0 to 8.6%, respectively.

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국문요약

연구제목: 대규모 정상 인구에서 자기공명영상을 이용하여 측정한 proton density fat fraction (PDFF)의 분포와 참고 구간

연구배경: 현재 사용되고 있는 방법의 자기공명영상을 이용하여 측정한 PDFF의 지방간 진단의 경계 값을 정하기 위해, 대규모 정상 인구에서의 PDFF의 분포와 참고 구간을 구해 보고자 한다.

연구방법: 2015년 1월부터 2018년 5월까지 생체 간이식의 기증을 목적으로 간 자기공명영상을 시행한 1529명 중 알려진 지방간과 대사증후군의 위험인자가 없는 사람들을 '정상'인구로 정의하였다. Chemical-shift imaging-based MRI (CS MRI)와 high-speed T2-corrected multiecho MR spectroscopy (HISTO MRS)에서 PDFF를 각각 두번씩 측정하여 PDFF의 분포를 분석하였다. PDFF 값을 로그 변환하여 분포를 구한 후에 모수적 방법으로 95 백분위 값을 계산해 정상의 경계 값으로 정하였고, 이를 바탕으로 참고 범위를 설정하였다. 같은 날 초음파 유도하 간생검을 시행 받았던 일부 사람에서 조직학적 지방 분율과의 연관성을 알아보기 위해, 0등급 지방간 (지방 분율 5% 미만)인 환자들의 비율을 계산하였다.

연구결과: '정상'인구로 정의된 최종 연구 집단은 562명이 포함되었고, 이 인구에서 CS MRI-PDFF와 HISTO MRS-PDFF는 모두 양의 방향으로 치우친 분포를 보였으며 각각 범위는 0.70 – 11.4%, 0.50 – 13.4%였다. 95 백분위의 참고 구간은 각각 0 – 6.8%, 0 – 8.6%로 확인되었다. 같은 날 간 조직검사를 시행한 사람들은 387명이었고, 이 중 PDFF 참고 구간에 포함되는 사람들에서 0등급 지방간은 각각 78.9%, 79.2%였다.

연구결론: 정상 인구에서 구한 CS MRI-PDFF와 HISTO MRS-PDFF의 95 백분위 참고 구간은 각각 0 – 6.8%, 0 – 8.6%였다.