Original Investigation

^{1}H MRS Assessment of Hepatic Fat Content:

Comparison Between Normal- and Excess-weight Children and Adolescents

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Abbreviations and Acronyms

BMI
body mass index
CT
computed tomography
LFC
liver fat concentration
LFSF
liver fat signal fraction
MRS
magnetic resonance spectroscopy
MR
magnetic resonance
NAFLD
nonalcoholic fatty liver disease
PRESS
point resolved spectroscopy
SD
standard deviation
SDS
standard deviation score
TE
echo time
TR
repetition time
TSE
turbo spin echo
VOI
volume of interest

Rationale and Objectives: The purpose of the present study was to obtain a cutoff value of liver fat content for the diagnosis of hepatic steatosis by comparing magnetic resonance (MR) spectroscopy results in children and adolescents with normal and excess weight.

Materials and Methods: The study included 420 children and adolescents (91 normal-weight, 99 overweight, and 230 obese) 8–18 years of age. Proton magnetic resonance spectroscopy was performed with a 3T MR system using point resolved spectroscopy sequence with series echo times.

Results: The mean absolute mass concentration of liver fat was obtained: 0.5 ± 0.04% in normal-weight boys; 0.5 ± 0.03% in normal-weight girls; 0.9 ± 0.16% in boys with overweight; 1.1 ± 0.24% in girls with overweight; 1.7 ± 0.24% in boys with obesity; and 1.4 ± 0.21% in girls with obesity.

The cutoff value of absolute mass concentration of liver fat for hepatic steatosis was found to be 1.5%. Based on this cutoff value, hepatic steatosis was diagnosed in 16% of boys with overweight, 11% of girls with overweight, 32% of boys with obesity, and 27% of girls with obesity.

Conclusions: Proton magnetic resonance spectroscopy was successfully applied to obtain the cutoff value of absolute mass concentration of liver fat for the diagnosis of hepatic steatosis in children and adolescents. Children and adolescents with obesity have higher risk of hepatic steatosis than their peers with overweight.

Key Words: Adolescents; children; magnetic resonance; obesity; spectroscopy; steatosis.

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INTRODUCTION

Obesity has become a growing health challenge all over the world, beginning at early age in children and progressing into adulthood (1,2). One of the major complications caused and worsened by obesity is nonalcoholic fatty liver disease (NAFLD). NAFLD ranges from simple steatosis through steatohepatitis and fibrosis to end-stage liver disease (cirrhosis) and is defined as triglyceride accumulation in hepatocytes exceeding 5% of the liver weight (3,4). Liver biopsy is the gold standard of diagnosis and severity assessment of NAFLD (5,6). However, it is an invasive procedure associated with serious risks (7).

Proton magnetic resonance spectroscopy (^{1}H MRS) has in recent years been recognized as an alternative noninvasive technique for the measurement of fat content in the liver (8–12). A number of studies have been devoted to the assessment of hepatic steatosis, but there is a disagreement in the literature regarding the cutoff values ranging from 1.8% to 5.6% (10,11,13,14). The cutoff values are dependent on acquisition parameters and on fat fraction calculations. Only few publications mention a cutoff value for absolute mass concentration of liver fat (LFC) measured by ^{1}H MRS in children and adolescents (12,13,15). We found no published studies that have compared LFC assessed in children with obesity to LFC assessed in a large group of normal-weight, healthy children.

The purpose of the present study was to obtain a cutoff value of the liver fat content for the diagnosis of hepatic steatosis by comparing MRS results in normal- and excess-weight children and adolescents.

MATERIALS AND METHODS

Study Population

A total of 420 children and adolescents 8–18 years of age participated in the study (Table 1). The overweight and obese groups were enrolled from The Children's Obesity Clinic (16–18), and the normal-weight group was recruited from schools in the same geographical region. The relative weight status of the three groups was defined according to age- and sex-adjusted body mass index (BMI) charts (19,20): the normal-weight group with a BMI standard deviation score (SDS) below 1.28; the overweight group with a BMI SDS between 1.28 and 2.33; and the obese group with a BMI SDS over 2.33.

Informed assent was provided by all study participants. Written informed consent was obtained from all study participants older than 18 years of age and from parents of children younger than 18 years. The study was approved by the Ethics Committee of Region Zealand, Denmark (ID-no.: SJ-104 and SJ-98), by the Data Protection Agency (ID: REG-06-2014), and is registered at ClinicalTrials.gov (ID: NCT00928473).

TABLE 1. Study Population

	Normal-weight Girls (n = 51)		Normal-weight Boys (n = 40)	
	Age, y	BMI SDS	Age, y	BMI SDS
Mean	13.6	0.02	12.6	0.12
Standard deviation	2.8	0.87	2.3	0.74
Minimum	8.1	−1.72	9.0	−1.70
Maximum	17.8	1.27	17.3	1.18
	Girls With Overweight (n = 62)		**Boys With Overweight (n = 37)**	
	Age, y	BMI SDS	Age, y	BMI SDS
Mean	13.2	1.94	13.0	1.96
Standard deviation	2.6	0.28	2.4	0.30
Minimum	7.3	1.32	9.7	1.31
Maximum	17.8	2.32	17.9	2.32
	Girls With Obesity (n = 122)		**Boys With Obesity (n = 108)**	
	Age, y	BMI SDS	Age, y	BMI SDS
Mean	13.6	2.82	13.0	3.00
Standard deviation	2.2	0.36	1.9	0.40
Minimum	8.8	2.34	8.6	2.33
Maximum	17.9	4.18	17.3	4.11

Magnetic Resonance Examination

MR measurements were performed on a 3T Achieva MR imaging system (Philips Medical Systems, Best, the Netherlands) using SENSE Cardiac coil. T2-weighted turbo spin echo (TSE) coronal and axial slices through the upper abdomen were acquired for positioning the spectroscopy volume of interest (VOI). Parameters for the TSE sequence were as follows: TSE factor = 93, repetition time (TR) = 2182 ms, slice thickness = 7 mm, and echo time (TE) = 80 ms. Spectroscopy VOI (11 mm × 11 mm × 11 mm) was positioned in the right lobe of the liver, avoiding major blood vessels and intrahepatic bile ducts according to TSE images. A single voxel spectrum without water saturation was recorded using a point resolved spectroscopy (PRESS) sequence with the following parameters: TR = 4000 ms, spectral bandwidth = 2000 Hz, 1024 points, and 32 averages. A series of TE (45, 60, 75, 90 and 105 ms) was applied in every patient to compensate the result for T2 relaxation.

The PRESS sequence was used instead of the stimulated echo acquisition mode, because it compensates for extra dephasing due to local magnetic inhomogeneities and therefore allows for the measurement of T2 rather than T2* values. In general, both stimulated echo acquisition mode and PRESS sequences are influenced by J-coupling effects, resulting in an additional signal modulation for CH2 groups with first out-of-phase interference at approximately 60–80 ms (21,22). The series TE from 45 to 105 ms in the present study were chosen to cover both in-phase and out-of-phase interferences and thus to average the influence of J-coupling on T2 values (22).

Measurement of Liver Fat Content

The water peak (4.7 ppm) and the fat peak (the sum of visible lipid peaks at 0.9 ppm, 1.3 ppm, and 1.6 ppm) of the acquired