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Relationship between abdominal fat stores and liver fat, pancreatic fat, and metabolic comorbidities in a pediatric population with non-alcoholic fatty liver disease

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Abstract

Purpose To define the relationship between compartmental abdominal fat stores, liver and pancreatic fat fractions, and type 2 diabetes mellitus (T2DM) in children with non-alcoholic fatty liver disease (NAFLD).

Methods This was a retrospective study of patients with NAFLD who underwent abdominal MRI between August 2015 and July 2017. Using an axial multi-echo Dixon-based sequence, liver fat fraction (LFF) and pancreatic fat fraction (PFF) were measured. The fat image was used to quantify abdominal fat depots (thickness, cross-sectional area) at the L2 vertebral level. Multivariable models with stepwise selection were created for prediction of LFF, PFF, and T2DM status based upon variables of clinical interest.

Results 86 patients (70% male, 25% Hispanic, 58% Caucasian, 11% African American) with a mean age of 14.2 ± 3.2 years were included. 19 (22%) patients were pre-diabetic or diabetic. Only ethnicity was a predictor of LFF ($P = 0.0023$) with Hispanic ethnicity associated with the highest LFF. Depending on the model, either total abdominal fat area ($P = 0.0003$) or patient weight ($P = 0.008$) were the only predictors of PFF. No patient variable predicted T2DM status.

Conclusions In our population, there was an association between ethnicity and LFF, with the highest LFF in Hispanics. The presence or severity of hepatic steatosis could not be predicted based on patient size or the distribution of abdominal fat in our cohort. Neither LFF nor PFF were predictive of T2DM.

Keywords NAFLD · Steatosis · Pancreas · Diabetes · MRI · PDFF

Introduction

Obesity is a significant and growing public health problem [1]. Among the multitude of health problems associated with obesity, non-alcoholic fatty liver disease (NAFLD) is increasing in prevalence [2]. NAFLD has become a dominant cause of chronic liver disease in children and young adults [3]. Factors predictive of the severity of fatty liver disease remain elusive. Body habitus measurements are confounded measures and are variably predictive of the severity of liver disease [4, 5]. Further understanding of the interrelationship between such measures and liver fat deposition is needed.

The reference standard for diagnosis of NAFLD and for assessment of liver disease severity is biopsy, which is invasive. As such, imaging, particularly magnetic resonance imaging (MRI), is being increasingly used as an adjunct to serologic biomarkers of liver disease severity.

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MRI facilitates the assessment of the natural history of fatty liver disease, can serve as a tool that further informs decisions regarding the need for liver biopsy and can be used to monitor the impact of treatment [6–9].

There are data, largely in the adult literature, that suggest the distribution of abdominal adipose tissue is predictive of disease states associated with obesity [e.g., type 2 diabetes mellitus (T2DM), metabolic syndrome] [10, 11]. MRI provides a non-ionizing, non-invasive means of measuring body fat stores. In prior work by Mantatzis et al., intraperitoneal and retroperitoneal fat volumes were shown to be greater in adult patients with T2DM and metabolic syndrome than in body mass index (BMI)-matched controls without these comorbidities [12]. Similarly, there are data that suggest a relationship between pancreatic fat content and the presence of diabetes, but predictors of pancreatic fat and the relationship between pancreatic fat and liver fat remain incompletely defined [13–15].

The relationship between abdominal fat stores and fat deposition in the liver and pancreas has been inadequately assessed in the pediatric population. Understanding these relationships may further our understanding of the pathophysiology of conditions associated with excess adiposity, and might suggest strategies to predict disease or guide interventions aimed at optimizing weight loss in obese patients at risk for NAFLD. The primary purpose of this study was to define the relationship between compartmental abdominal fat stores, liver and pancreatic fat fractions, and associated measures of liver disease severity (e.g., stiffness) in a pediatric population. We also sought to define any predictors of pre-diabetes/diabetes and metabolic disease in the same patient population.

Methods

This was an Institutional Review Board approved, retrospective study performed in a single institution. Existing clinical data, extracted from the electronic medical record, and MR images were reviewed for patients with presumed (hepatic steatosis on imaging and/or elevated aminotransferases in the context of a negative work up for other liver diseases) or histologically confirmed fatty liver disease, who had undergone an abbreviated MRI examination for clinical indications between August 2015 and July 2017.

MRI examinations had been performed at 1.5 Tesla (Philips Ingenia, Philips Healthcare; Best, the Netherlands) utilizing a 16-channel anterior body phase array and 12 channel posterior element coil. Exams included a commercially available axial multi-echo Dixon-based sequence designed for quantification of liver proton density fat fraction (PDFF) (mDixon Quant®, Philips Healthcare; Best, the Netherlands). This sequence generates water and fat images as well as fat fraction and T2* parametric maps. Additionally, the examinations included MR elastography (MRE) performed with either a two-dimensional (2D) gradient-recalled echo-based sequence or a 2D spin-echo echoplanar imaging-based sequence at 60 Hz as well as an axial T2 weighted fast spin-echo sequence.

As part of the routine clinical exam, liver stiffness, liver fat fraction, and liver volume had been generated by a group of dedicated post-processing technologists. MRE had been post-processed as previously described with generation of a weighted mean liver stiffness value based on the mean stiffness value measured on each of four images [16]. Liver fat fraction had been measured on the fat fraction parametric maps by placing as large of an ovoid region of interest in the right hepatic lobe while avoiding major vessels with the mean proton density fat fraction (%) reported. Both liver stiffness and fat fraction measurements were performed in Intellispace Portal (Philips Healthcare; Best, the Netherlands). Liver volume had been measured based on manual segmentation of the axial T2 weighted images (Vitrea, Vital Images, Inc.; Minnetonka, MN).

Pancreatic fat fractions were measured on the fat fraction parametric maps by a single reviewer (DEH) who placed ovoid regions of interest in the head/uncinate process of the pancreas and in the pancreatic tail on a single image each. Mean fat fraction was reported for the pancreas based on the average of the two measurements.

Measurement of abdominal fat stores

Abdominal fat stores were measured on the fat image generated from the mDixon sequence. All measurements were performed on a single axial image at the level of the midportion of the L2 vertebral body. The following measurements were performed (Fig. 1):

- Subcutaneous fat thickness (cm)—linear measurement at midline from skin surface to the anterior surface of the rectus muscle
- Midline abdominal fat thickness (cm)—linear measurement at midline from in the inner surface of the rectus muscle to the anterior edge of the L2 vertebral body
- Total fat area (mm^2)—included abdominal wall and intra-abdominal fat
- Abdominal fat area (mm^2)—limited to fat bounded by the abdominal wall muscles
- Retroperitoneal fat area (mm^2)—limited to abdominal fat, bounded anteriorly by a line transecting the ascending and descending colon

Based on these measures, subcutaneous and intraperitoneal fat areas (mm^2) were calculated:

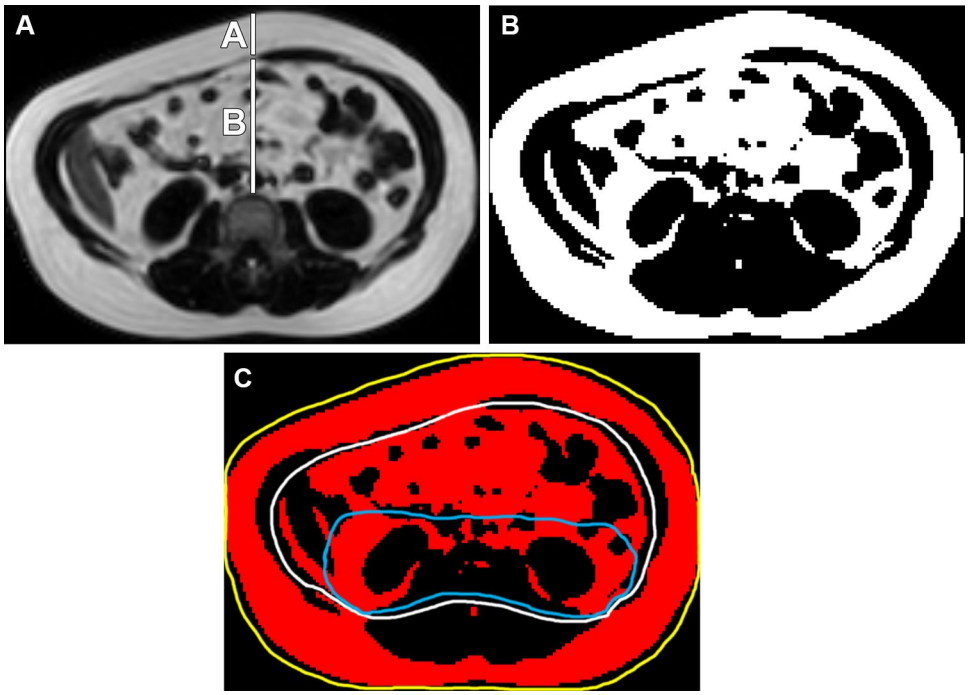

Fig. 1 Measurement of abdominal fat stores on axial MR images obtained of an 11-year-old Caucasian boy with fatty liver disease. All measurements were performed at the L2 vertebral level. **a** Fat image from mDixon sequence showing measurement of subcutaneous fat thickness "A" and midline abdominal fat thickness "B". **b** Fat image after iterative thresholding. **c** Representation of regions of interest (ROI) drawn to calculate cross-sectional fat area. The yellow ROI demarcates "total fat area". The white ROI demarcates "abdominal fat area". The blue ROI demarcates "retroperitoneal fat area". Based on these measurements, "subcutaneous fat area" and "intraperitoneal fat area" were calculated

- Subcutaneous fat area = total fat area minus abdominal fat area
- Intraperitoneal fat area = abdominal fat area minus retroperitoneal fat area

Linear measurements were performed by a single reviewer (DEH) utilizing Intellispace Portal. Fat area measurements were performed by a separate reviewer (ATT) utilizing ImageJ (v1.48k 2013, National Institutes of Health, Bethesda, MD). In ImageJ, iterative thresholding was applied to the fat image using the isodata algorithm which essentially separates the image into two elements (in this case, fat and not fat) [17]. The cross-sectional area of fat pixels for the single slice was then measured using the freehand ROI tool.

Chart review

Electronic medical records (EPIC, Verona, WI) were reviewed for patient height, weight, BMI (and BMI z-score), and age at the time of the MR exam. Records were also reviewed for self-reported ethnicity, for T2DM status categorized as an ordinal variable: diabetic, insulin resistant, or non-diabetic, and for use of metformin in diabetic patients. Hemoglobin A1c measurements closest to the MRI examination were used to define T2DM status with ≥ 5.7%–6.4 considered pre-diabetes and ≥ 6.5% considered diabetes [18]. For the purpose of analysis, pre-diabetes and diabetes were combined due to the low frequency of diabetes in the population.

Statistical analysis

For the purpose of assessment of predictive variables, abdominal fat areas were considered in terms of absolute area, as well as in terms of distribution, expressed as a percentage of total abdominal fat area. Proportional odds logistic modeling was used for assessment of univariate associations between continuous variables and diabetes status (categorical variable). Fisher's exact test was used for assessment of univariate associations between categorical variables. Analysis of variance (ANOVA) was used for assessment of univariate associations between continuous variables and patient ethnicity with Tukey's test used for comparison of differences between specific paired ethnicities. Multivariable models with stepwise selection were created based upon variables of clinical interest and relevance. All analyses were performed using SAS version 9.4 (SAS Institute Inc.; Cary, NC). *P* values less than 0.05 were considered statistically significant.

Results

A total of 86 patients ($n = 60$, 69.8% male), with a mean age of 14.2 ± 3.2 years, were included in this study. The majority of the patients ($n = 50$, 58.1%) were Caucasian, 24.4% ($n = 21$) were Hispanic, 10.5% ($n = 9$) were African American, and the remainder were non-Hispanic, not otherwise specified. The mean BMI z-score of the study cohort was 2.46 ± 0.39. Based on hemoglobin A1c, two patients (2.3%

of 86) had T2DM, one of whom was on metformin, and 17 (19.8%) were pre-T2DM. Mean liver fat fraction for the population was 19.01 ± 10.54% and 8 patients (9.3% of 86) had pancreatic steatosis based on an adult definition of pancreatic fat fraction > 10.4% [19].

There were significant associations between ethnicity and multiple variables (Table 1). Specifically, when compared to Hispanic patients, African American patients were older (mean difference: 5.0 years, $P < 0.001$), heavier (mean difference: 55.1 kg, $P < 0.001$), taller (mean difference: 21.7 cm, $P < 0.001$), and had a higher BMI (mean difference: 11.7 kg/m^2, $P < 0.001$ [BMI z-score was not significantly different]). Despite these differences, liver fat was, on average 12% lower in African American patients ($P = 0.015$). Similarly, when compared to Hispanic patients, Caucasian patients were older (mean difference: 3.0 years, $P = 0.001$), heavier (mean difference 33.7 kg, $P < 0.001$), taller (mean difference: 18.9 cm, $P < 0.001$), and had a higher BMI (mean difference: 6.2 kg/m^2, $P = 0.006$ [BMI z-score was not significantly different]). Further, liver volume was on average 528 mL higher in Caucasian patients. Despite these differences, liver fat was, on average, 7% lower in Caucasian patients ($P = 0.025$). There were no significant differences between African American and Caucasian patients with respect to the individual variables in Table 1.

Liver fat fraction

Based on univariate analysis, the only variables that were significantly associated with liver fat fraction were liver volume ($r = 0.38$, $P = 0.0004$) and liver stiffness ($r = -0.24$, $P = 0.0249$) (Table 2). There was no significant relationship between liver fat fraction and patient size (height, weight), sex or quantity or distribution of abdominal fat.

Table 1 Association between self-reported ethnicity and patient specific variables

Variable	Caucasian ($n = 50$) mean ± SD	Hispanic ($n = 21$) mean ± SD	African American ($n = 9$) mean ± SD	Non-Hispanic, NOS ($n = 6$) mean ± SD	*P* value
Age	14.82 ± 2.72	11.81 ± 3.3	16.78 ± 3.07	13.33 ± 3.14	**0.0001**
Sex (male)	76% ($n = 38$)	52% ($n = 11$)	67% ($n = 6$)	83% ($n = 5$)	0.2211
Weight (kg)	106.4 ± 27.3	72.7 ± 28.9	127.8 ± 32.1	89.8 ± 39.5	**< .0001**
Height (cm)	168.6 ± 10.4	149.7 ± 17.1	171.3 ± 12.0	164.7 ± 19.2	**< .0001**
BMI (kg/m^2)	37.4 ± 7.0	31.3 ± 6.6	42.9 ± 6.1	31.2 ± 9.5	**0.0001**
BMI z-score	2.5 ± 0.4	2.3 ± 0.4	2.7 ± 0.4	2.3 ± 0.4	0.0586
Diabetes status	Pre/Yes: 16% ($n = 8$)	Pre/Yes: 28.6% ($n = 6$)	Pre/Yes: 22.2% ($n = 2$)	Pre: 50% ($n = 3$)	0.1955
Liver stiffness (kPa)	2.61 ± 1.01	2.20 ± 0.48	2.02 ± 0.23	2.88 ± 0.80	0.0709
Liver volume (mL)	2359 ± 628	1831 ± 629	2061 ± 758	1957 ± 642	**0.0157**
Pancreatic fat fraction (%)	6 ± 4	5 ± 5	5 ± 4	6 ± 3	0.5748
Liver fat fraction (%)	18 ± 10	26 ± 9	13 ± 10	12 ± 12	**0.0023**
Total fat area (mm^2)	52,276 ± 15,053	38,687 ± 15,796	58,947 ± 13,962	40,292 ± 19,251	**0.0020**
Intra-abdominal fat area (mm^2)	14,589 ± 5849	9311 ± 4868	13,424 ± 7701	9128 ± 4282	**0.0042**
Retroperitoneal fat area (mm^2)	5932 ± 2546	3811 ± 1728	5144 ± 3844	3429 ± 2226	**0.0074**
Intraperitoneal fat area (mm^2)	8657 ± 3985	5500 ± 3723	8280 ± 4599	5699 ± 2325	**0.0172**
Subcutaneous fat area (mm^2)	37,686 ± 11,657	29,376 ± 12,993	45,523 ± 12,602	31,164 ± 16,656	**0.0098**
Percent intraperitoneal fat	16 ± 6	14 ± 8	14 ± 9	17 ± 9	0.6102
Percent retroperitoneal fat	11 ± 4	10 ± 4	9 ± 5	10 ± 6	0.3117
Percent subcutaneous fat	72 ± 8	75 ± 10	77 ± 13	73 ± 14	0.4266
Subcutaneous fat thickness (cm)	4.1 ± 1.1	3.9 ± 1.1	4.8 ± 1.4	3.8 ± 1.7	0.1974
Midline abdominal fat thickness (cm)	9.1 ± 2.0	8.0 ± 2.0	8.5 ± 2.8	7.7 ± 2.4	0.1610

ANOVA was used for continuous variables and Fisher Exact test was used for categorical variables. Significant differences largely reflect differences between Hispanic patients and Caucasian patients and between Hispanic patients and African American patients (see "Results" section)

Statistically significant *P* values are indicated in bold

ANOVA analysis of variance, *NOS* not otherwise specified, *Pre* pre-diabetes, *kPa* kilopascals, *SD* standard deviation

Table 2 Univariate relationships (Pearson's *r*) between predictor variables and liver fat fraction, liver stiffness, and pancreatic fat fraction

Variable	Liver fat fraction	Liver stiffness	Pancreatic fat fraction
Age	−0.107 (*P* = 0.3303)	0.111 (*P* = 0.3103)	0.218 (*P* = 0.0511)
Sex[a]	(*P* = 0.134)	(*P* = 0.874)	(*P* = 0.331)
Height	−0.119 (*P* = 0.2820)	0.0834 (*P* = 0.4481)	0.20299 (*P* = 0.0709)
Weight	−0.0888 (*P* = 0.4190)	0.133 (*P* = 0.2239)	**0.293 (*P* = 0.0080)**
BMI z-score	0.0384 (*P* = 0.7301)	0.0763 (*P* = 0.4906)	**0.2303 (*P* = 0.0411)**
Liver volume	**0.379 (*P* = 0.0004)**	0.148 (*P* = 0.1775)	**0.235 (*P* = 0.0362)**
Liver fat fraction		**−0.243 (*P* = 0.0249)**	−0.00828 (*P* = 0.9419)
Liver stiffness	**−0.243 (*P* = 0.0249)**		−0.0611 (*P* = 0.5877)
Pancreatic fat fraction	−0.00828 (*P* = 0.9419)	−0.06114 (*P* = 0.5877)	
Total fat area	−0.0513 (*P* = 0.6471)	0.146 (*P* = 0.1876)	**0.395 (*P* = 0.0003)**
Abdominal fat area	0.0739 (*P* = 0.5093)	0.173 (*P* = 0.1183)	**0.407 (*P* = 0.0002)**
Intraperitoneal fat area	0.0448 (*P* = 0.6896)	0.163 (*P* = 0.1417)	**0.387 (*P* = 0.0004)**
Retroperitoneal fat area	0.102 (*P* = 0.3626)	0.148 (*P* = 0.1811)	**0.347 (*P* = 0.0017)**
Subcutaneous fat area	−0.100 (*P* = 0.3705)	0.104 (*P* = 0.3480)	**0.304 (*P* = 0.0064)**
% intraperitoneal fat	0.0593 (*P* = 0.5970)	0.0730 (*P* = 0.5120)	0.141 (*P* = 0.2159)
% retroperitoneal fat	0.107 (*P* = 0.3372)	0.0860 (*P* = 0.4395)	0.110 (*P* = 0.3365)
% subcutaneous fat	−0.0895 (*P* = 0.4241)	−0.0910 (*P* = 0.4150)	−0.150 (*P* = 0.1857)
Subcutaneous fat thickness	−0.0890 (*P* = 0.4179)	−0.0796 (*P* = 0.4665)	0.170 (*P* = 0.1282)
Abdominal fat thickness	0.186 (*P* = 0.0888)	**0.298 (*P* = 0.0053)**	**0.311 (*P* = 0.0047)**

Statistically significant associations are indicated in bold

[a]Two sample *t* test used for comparison of means

In a multivariable model to predict liver fat percentage based on age, height, weight, ethnicity, diabetes status, and percent fat in each abdominal depot (intraperitoneal, retroperitoneal, subcutaneous), only ethnicity was a significant predictor of liver fat ($P = 0.0023$) with Hispanic ethnicity associated with the highest liver fat fraction.

Liver stiffness

In addition to its correlation with liver fat fraction, the only other variable with which liver stiffness was significantly associated on univariate analysis was midline abdominal fat thickness ($r = 0.3$, $P = 0.0053$). This was despite lack of correlation with absolute area of abdominal fat stores or with relative distribution of abdominal fat (Table 2).

Pancreatic fat fraction

Based on univariate analysis, pancreatic fat was significantly associated with patient weight ($r = 0.29$, $P = 0.008$), BMI z-score ($r = 0.23$, $P = 0.0411$), absolute fat area in each location of abdominal fat stores ($r = 0.30$–0.40 depending on location; Table 2), and with midline abdominal fat thickness ($r = 0.31$, $P = 0.0047$). There was no significant association between pancreatic fat and abdominal fat stores when expressed in terms of distribution (percent fat in each depot: intraperitoneal, retroperitoneal, subcutaneous).

In a multivariable model to predict pancreatic fat percentage based on age, height, weight, ethnicity, liver fat percentage, and total fat area, only total fat area was a significant predictor of pancreatic fat percentage ($P = 0.0003$). Specifically, each 1000 mm^2 increase in total fat area was associated with a 0.11% increase in pancreatic fat fraction.

In a second multivariable model to predict pancreatic fat percentage based on age, height, weight, ethnicity, liver fat percentage, and fat distribution (percent in each depot: intraperitoneal, retroperitoneal, subcutaneous), only weight was a significant predictor of pancreatic fat percentage ($P = 0.008$). Specifically, each 10 kg increase in weight was associated with a 0.39% increase in pancreatic fat.

Diabetes status

Based on univariate logistic regression, no single variable was statistically significantly predictive of diabetes status (Table 3). Midline abdominal fat thickness approached significance ($P = 0.0603$) but the confidence interval for the odds spanned 1. Attempts at multivariable modeling with stepwise selection failed to result in generation of a model to predict diabetes status.

Table 3 Association between diabetes status (diabetes vs. pre-diabetes or no diabetes) and predictor variables based on univariate logistic regression

Variable	Odds ratio [95% CI]	*P* value
Age	1.06 [0.91–1.25]	0.45
Ethnicity (African American)	0.29 [0.03–2.69]	0.27
Ethnicity (Caucasian)	0.19 [0.03–1.12]	
Ethnicity (Hispanic)	0.4 [0.06–2.57]	
Sex	1.98 [0.69–5.71]	0.21
Height (cm)	1.01 [0.98–1.04]	0.6
Weight (kg)	1.00 [0.99–1.02]	0.68
BMI (kg/m^2)	1.01 [0.95–1.08]	0.74
BMI z-score	0.66 [0.18–2.44]	0.53
Liver volume (mL)	1.00 [1]	0.67
Liver fat (%)	1.03 [0.98–1.08]	0.23
Liver stiffness (kPa)	1.32 [0.78–2.23]	0.3
Average pancreatic fat (%)	1.02 [0.91–1.14]	0.79
Total fat area (mm^2)	1.00 [1]	0.38
Intra-abdominal fat area (mm^2)	1.00 [1]	0.99
Retroperitoneal fat area (mm^2)	1.00 [1]	0.77
Intraperitoneal fat area (mm^2)	1.00 [1]	0.83
Subcutaneous fat area (mm^2)	1.00 [1]	0.26
% intraperitoneal fat	0.96 [0.89–1.04]	0.32
% retroperitoneal fat	0.97 [0.85–1.11]	0.66
% subcutaneous fat	1.03 [0.97–1.09]	0.35
Subcutaneous fat thickness (cm)	1.47 [0.93–2.3]	0.096
Midline abdominal fat thickness (cm)	0.78 [0.6–1.01]	0.060

CI confidence interval

Discussion

In this study we have sought to define patient specific factors (including body habitus, characterized in terms of the distribution of abdominal fat) that are predictive of liver fat fraction, pancreatic fat fraction, and T2DM status in a pediatric population. There were no clear patient specific morphometric predictors of liver fat fraction. That is to say, neither patient height nor weight nor BMI (or BMI z-score) were predictive. The distribution and quantity of abdominal fat also failed to predict liver fat fraction. As such, it is not clear that the presence or severity of fatty liver disease can be predicted based on external measures of patient size or based on the particular distribution of fat for a given pediatric patient. This result conflicts with prior adult studies which have shown associations between liver fat content and both waist circumference and the quantity of intra-abdominal fat [4, 20, 21]. Further study is needed to clarify these conflicting findings.

Of note, in our population, there was a clear and strong association between self-reported ethnicity and liver fat fraction. Hispanic patients as a group had higher liver fat fraction that either Caucasian or African American patients. This was despite Hispanic patients being younger and despite Caucasian and African American patients having higher BMI values (and BMI z-scores that trended towards statistically significant differences) in our population. Toledo-Corral et al. similarly showed higher liver fat fraction in Hispanic adolescent patients compared with African American patients [22]. Results in adults, however, have been conflicting with Browning et al. showing a higher average liver fat among Hispanics in a study of more than 2000 adults but Nazare et al. reporting no ethnic differences in liver fat fraction despite differences in the distribution in abdominal adiposity among more than 4000 adults [23, 24].

Despite the lack of observed association between liver fat fraction and morphometric measures, we did find that pancreatic fat fraction relates to the degree of patient obesity. Specifically, univariate analysis suggests that pancreatic fat fraction is predicted more by the absolute quantity of abdominal fat than the distribution of fat. Positive associations were observed between pancreatic fat and patient weight and fat area in each abdominal depot but without particular association with one depot. Notably, weight and total abdominal fat area remained the only significant predictors of pancreatic fat fraction on multivariable analysis. Our results are concordant with an adult study of 685 adult Chinese volunteers. In that study, pancreatic steatosis (defined as > 10.4%) was observed in 16% of patients and was associated with central obesity (waist circumference). In their study, Le et al. also showed an association between abdominal fat and pancreatic fat fraction but showed that association to be limited to visceral adiposity, not subcutaneous adiposity [19]. While not entirely concordant, these findings suggest that there is at least some association between the severity of abdominal obesity and pancreatic fat fraction.

Our study failed to show associations between liver fat fraction and pancreatic fat fraction and T2DM status. In our population, no patient factor was statistically significantly associated with diabetes status (normal vs. pre-diabetic + diabetic). As such, our study fails to confirm prior data showing relationships between distribution of abdominal fat, liver fat fraction, pancreatic fat fraction, and diabetes status. Such relationships have largely been demonstrated in adults but have also been shown in pediatric studies [21, 22, 25–28]. Pacifico et al. showed that in 158 adolescents, liver fat fraction was predictive of pre-diabetes, and Toledo-Corral et al. showed relationships between liver fat fraction or pancreatic fat fraction and diabetes in obese adolescents [22, 27]. Other studies, however, have shown relationships between pancreatic fat fraction and metabolic syndrome, but not frank glucose intolerance [29, 30]. It is possible that the discordance between our study and prior studies reflects the low prevalence of frank diabetes in our population.

While this study was focused on identifying predictors of hepatic and pancreatic fat fraction as well as diabetes status, we have confirmed our prior findings that liver fat, liver volume and liver stiffness are interrelated [31]. Specifically, liver fat appears to have a softening effect (an inverse relationship with liver stiffness) and is associated with an increase in liver volume. Of note, some of the patients in the current cohort were included in our prior study. As such, the strength of this confirmation should not be over-interpreted. Newly identified in this study, however, is a fair positive correlation between liver stiffness and midline abdominal fat thickness. To our knowledge, such a relationship has not been previously identified and its significance is uncertain. One could interpret this to suggest that increased abdominal adiposity is associated with increased stiffness but the lack of demonstrable relationship between measured fat areas and distribution and liver stiffness argues against this.

While our study has some unique findings, it has important limitations. First, this was a retrospective study with image sequences not optimized for, or targeted at, quantification of fat distribution. Most studies in the literature favor performing these measures at L3/L4. Due to anatomic coverage for clinical indications, we were forced to perform these measurements at L2. The significance of this difference is uncertain but we do note that one study has shown abdominal fat areas at L2/L3 to best correlate with volumetric assessments of abdominal adiposity [32]. Second, we have not defined the reproducibility of the fat depot measurements performed in this study. Third, measurements in this study were of cross-sectional fat area. Recently, there has been increased attention paid to volumetric measures of abdominal and total adiposity which were not used in this study. That said, at least one study suggests that cross-sectional measures strongly correlate with volumetric measures of abdominal adiposity [32]. Last, the frequency of diabetes in our population was low (2% diabetes, 20% pre-diabetes) which may influence the observed significance, or lack thereof, of some findings.

In conclusion, in our population of children and young adults with known or suspected fatty liver disease, there was a clear association between self-reported ethnicity and liver fat fraction, with the highest fat fractions in Hispanic patients. It is not clear that the presence or severity of fatty liver disease can be predicted based on patient size measures or the distribution of abdominal fat among measured depots. There was some suggestion that pancreatic fat fraction does relate to the degree of obesity but only to overall fat quantity, not the distribution of fat. Neither liver fat fraction nor pancreatic fat fraction was predictive of diabetes status in our population.

Compliance with ethical standards

Conflict of interest None relevant to this article. Dr. Trout receives unrelated grant support from Siemens Medical Solutions and Canon Medical Systems for ultrasound research. Dr. Trout also receives royalties for authorship from Reed Elsevier and Wolters Kluwer. Dr. Dillman receives unrelated grant support from Siemens Medical Solutions and Bracco.

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