adjusted for age and model for end-stage liver disease score. Their results are consistent with our finding of the prognostic impact of severe cirrhosis (SFS 4C/CP).

While most of our patients with severe AH (Maddrey's discriminant function >32) and biopsy-proven hASH received steroid treatment, our subgroup of decompensated patients with hASH also included 'non-severe' patients with AH not treated with steroids. Therefore, steroid treatment was not included in multivariable analysis. The impact of histological parameters on response to steroid treatment is the subject of an ongoing study, which was published in abstract form at this year's ILC.[5] Preliminary analyses revealed steatosis grade and ductular cholestasis as predictors of steroid response, however, a larger number of patients is needed to draw robust conclusions.

We are well aware of the impact of abstinence in studies evaluating outcome in patients with ALD and included this parameter in multivariable Cox regression of compensated ALD where it remained as an independent predictor of decompensation-free survival. Unfortunately, data on abstinence were only partly available in patients with decompensated ALD and therefore not included in multivariable analyses.

Finally, we fully agree with the need for external validation of any novel diagnostic tool and thus look forward to application of the SALVE grading and staging system in future studies evaluating liver histology in independent prospective ALD cohorts.

Financial support

The authors received no financial support to produce this manuscript.

Conflicts of interest

All authors declare that they have no conflicts of interest related to the study.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

RES: drafting of the manuscript; all authors: critical revision for important intellectual content and final review.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.09.005.

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Intermuscular abdominal fat fraction and metabolic dysfunction-associated fatty liver disease: Does the link already exist in childhood?

To the Editor:

We have read with great interest the study by Nachit *et al.*,[1] wherein they show the contribution of muscle fat infiltration on the physiopathology of metabolic dysfunction-associated fatty liver disease (MAFLD) in adults with morbid obesity. We extend these findings by showing the association between intermuscular abdominal fat fraction (IMAAT) and MAFLD in children who are overweight/obese. Further, we report IMAAT differences by sex and weight status.

We used baseline data on 116 children (10.6 ± 1.1 years, 62 girls) who were overweight or obese from the EFIGRO project (NCT02258126).[2] Magnetic resonance imaging (Magnetom Avanto, 3T, Siemens) was used to assess the percentage hepatic fat and IMAAT at 3 axial slices (L2-L3, L3, and L4-L5), being the average used for analyses. Images were screened, delineated, and classified by experienced radiologists and researchers, and MAFLD was defined as having >5.0% hepatic fat. We used Gardner-Altman plots[3,4] to compare IMAAT levels between

Received 5 May 2021; received in revised form 12 May 2021; accepted 17 May 2021; available online 26 May 2021
https://doi.org/10.1016/j.jhep.2021.05.011

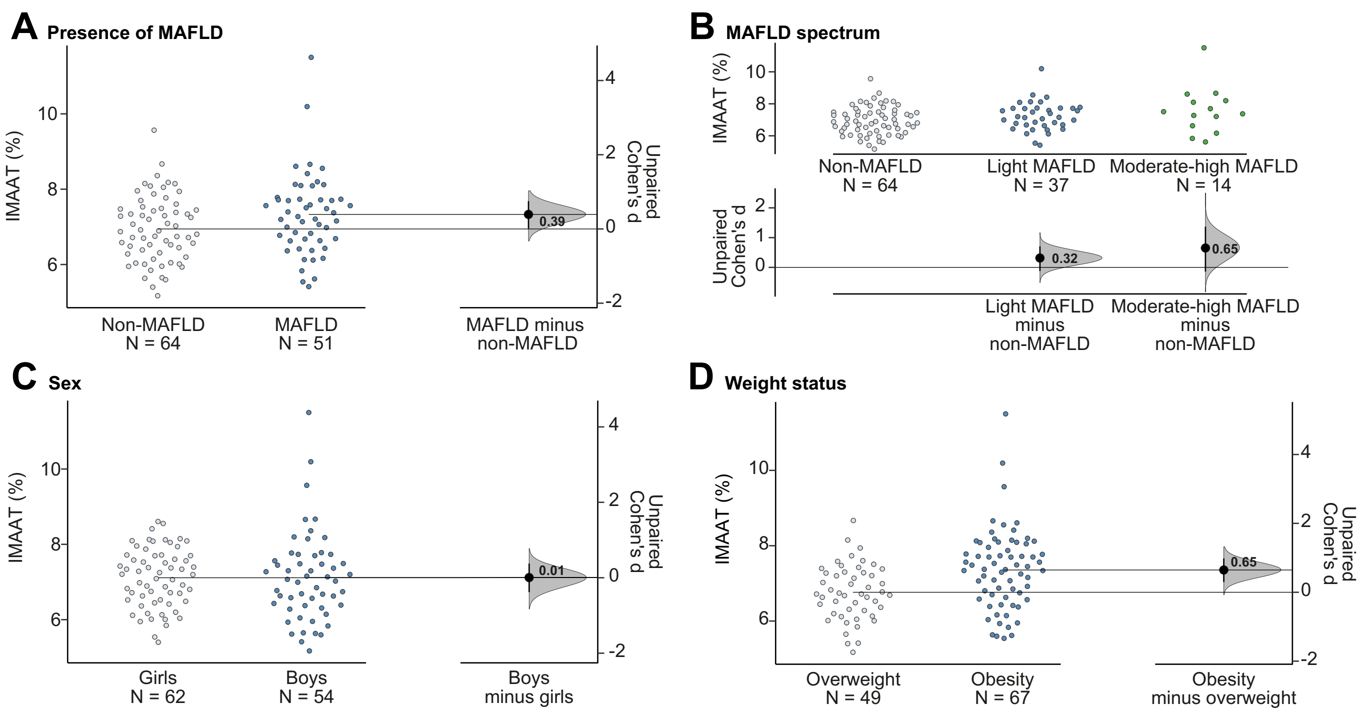

Fig. 1. IMAAT levels based on the presence MAFLD, steatosis severity, sex and weight status. (A) Children with and without MAFLD. (B) MAFLD spectrum (*i.e.*, Non-MAFLD: hepatic fat <5%, light MAFLD: hepatic fat between 5% and 8%, moderate to high MAFLD: hepatic fat ≥9%). (C) MAFLD in girls and boys. (D) MAFLD in children who are overweight and those who are obese. All data are based on Gardner-Altman plots[3,4] which show a representation of observed values by the 2-group comparison and its effect size (black circle), and 95% CIs. The curve indicates the resampled distribution of the effect size given the observed data. IMAAT, intermuscular abdominal fat fraction; MAFLD, metabolic dysfunction-associated fatty liver disease.

children with and without MAFLD, as well as across the MAFLD spectrum, by sex and weight status.

IMAAT was higher in children with MAFLD (44.3%) (Fig. 1A, ES: 0.39), and in those with light (Fig.1B, ES: 0.32) and moderate-high MAFLD (Fig. 1B, ES: 0.65) than in those without. IMAAT was similar in boys and girls (Fig. 1C, ES: 0.01), while children with obesity presented higher IMAAT than those who were overweight (Fig. 1D, ES: 0.63).

Our results in children concur with those reported by Nachit *et al.*[1] in adults with morbid obesity, and suggest that fatty infiltration of muscle mass could contribute to the physiopathology of MAFLD from childhood. Nachit *et al.*[1] also observed that non-alcoholic steatohepatitis improved in those patients who significantly decreased muscle fat content, suggesting that the reduction of fat infiltration in the muscle may be a relevant therapeutic target for patients with MAFLD. Muscle fat content is sensitive to exercise-based interventions,[5] and could therefore be a strategy to improve MAFLD. Further studies should test this hypothesis, particularly in children where the prevalence of MAFLD is alarming.[6]

In conclusion, our data extend previous observations reported in adults with morbid obesity[1] to children who are overweight/obese, and support the screening of muscle fat as a potential marker of the presence and progression of MAFLD that might unravel new relevant therapeutic targets. Further studies are needed to confirm our findings.

Financial support

This project was funded by the Spanish Ministry of Health "Fondos de Investigación Sanitaria del Instituto de Salud Carlos III" (PI13/01335), the Spanish Ministry of Industry and Competitiveness (DEP2016-78377-R), and by EU Fondos Estructurales de la Unión Europea (FEDER) funds ("Una manera de hacer Europa"). Support was also provided by the Department of Economic Development of the Government of Navarra (0011-1365-2019-000152) and co-funded by EU Fondos Estructurales de la Unión Europea (FEDER) funds ("Una manera de hacer Europa"). CC-S is supported by the Spanish Ministry of Science and Innovation (FJC2018-037925-I).

Conflict of interest

The authors declare no conflicts of interest that pertain to this work.

Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

CC-S.: conception of the study, analysed the data, and drafted the manuscript; FI, AV, RC: acquisition, analysis, and interpretation of the data, and critically review the manuscript. IL: conception of the study, analysed and interpretation of the data, and critically review the manuscript. The authors declare they have seen and approved the final version of the manuscript.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhep.2021.05.011.

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Reply to: "Intermuscular abdominal fat fraction and metabolic dysfunction-associated fatty liver disease: Does the link already exist in childhood?"

To the Editor:

We thank Dr. Cadenas-Sanchez and colleagues[1] for their interest in our study[2] and for illustrating that the association between muscle fat and non-alcoholic fatty liver disease (NAFLD)/metabolic dysfunction-associated fatty liver disease (MAFLD) we described in adult patients with morbid obesity also exists in children.[1] Given the increasing prevalence of NAFLD in the pediatric population,[3] it is of interest to also explore the muscle compartment in children, as this would open perspectives for new screening and treatment strategies that might be of particular appeal and applicability in this specific population.

The authors report a higher intermuscular abdominal fat fraction (IMAAT) in children with a fatty liver compared to those without fatty liver.[1] The fatty liver has been defined by a liver proton density fat fraction (PDFF) above 5% at MRI. By contrast we are unsure what IMAAT refers to: we assume it might be the ratio of the fat signal to the total fat and water signal (*i.e.* PDFF) gathered from a region of interest within skeletal muscles at the abdominal level. The term intermuscular might also indicate that IMAAT is the ratio of fat area[4] (for example, area of voxels with PDFF >50%) to total fat and muscle area at the abdominal level. It would be good to specify this as well as the muscle bundles used in the quantification so that the study can be continued and contributed to by others.

Thus, children with NAFLD, as early as in the pre/peri-pubertal period, already have a higher muscle fat concentration when compared to those without NAFLD,[1] a finding of particular concern. In adults, we[2] and others[5,6] showed that muscle fat, that we called myosteatosis, increases the risk for hepatic and/or extrahepatic (*e.g.* cardiovascular) complications. If the same anticipative relationships were true for youth, it would indicate that this is the population on which prevention and treatment efforts should focus. Larger scale population studies that include the measurement of the absolute fat content (a parameter estimated in our study with skeletal muscle fat index[2]) would be needed to confirm the risk prediction of this strategy.

One must realize that the term "severe NAFLD" does not cover the same reality in the 2 studies: in our study, "severe" pertains to the severity of the necro-inflammatory activity in NAFLD as assessed on liver biopsy. In the pediatric study conducted by Dr. Cadenas-Sanchez[1] "severe MAFLD" refers to severe liver steatosis as defined by MRI PDFF. Such a narrow definition of MAFLD range (only based on fat content) might, at least partly, explain the relatively modest difference in IMAAT described in

Received 16 July 2021; received in revised form 8 September 2021; accepted 10 September 2021; available online 16 September 2021
https://doi.org/10.1016/j.jhep.2021.09.006