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ACCURACY OF ULTRASONOGRAPHY IN THE DIAGNOSIS OF HEPATIC STEATOSIS AND ABDOMINAL FAT IN ADOLESCENTS: A SYSTEMATIC REVIEW

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ABSTRACT

INTRODUCTION: With the growing number of overweight adolescents, there was an increase in the prevalence of non-alcoholic fatty liver disease.
MATERIAL AND METHOD: We performed a systematic review of the literature to identify and synthesize the available evidence on the ultrasonography accuracy in the diagnosis of hepatic steatosis and measurement of abdominal fat compared to computed tomography or magnetic resonance imaging in obese adolescents. Seven databases (MEDLINE, Cochrane Database of Systematic Reviews, SCOPUS, WEB of SCIENCE, EMBASE, LILACS and ADOLEC) were reviewed.
RESULTS: three studies were included in a qualitative synthesis.
CONCLUSIONS: Ultrasonography does not have the accuracy needed to classify the degree of steatosis. Magnetic resonance imaging would be considered a more useful and objective method than ultrasonography to discriminate differences in liver fat content and for monitoring of young patients with hepatic steatosis.

INTRODUCTION

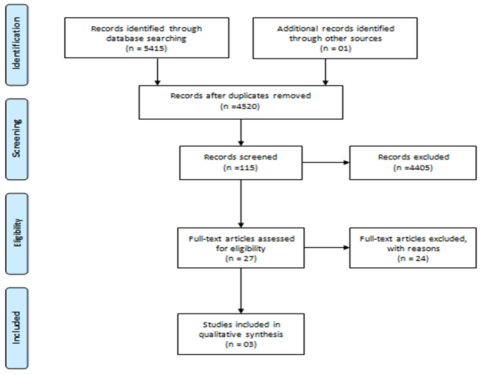
Non-alcoholic fatty liver disease (NAFLD) is considered the most common cause of chronic liver disease in adolescents in industrialized countries1. In a systematic review based on studies in childhood obesity, Anderson et al found prevalence of NAFLD that varied from 7.6% to 34.2%2. The clinical spectrum of NAFLD ranges from simple steatosis to nonalcoholic steatohepatitis, fibrosis, and cirrhosis3. Studies demonstrated that visceral adiposity is a risk factor for NAFLD4,5. In the last decades, with the increasing prevalence of childhood obesity, studies involving hepatic steatosis, abdominal fat and imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (US) were developed in this age group. We intend to analyze the available literature on the accuracy of the US compared with CT or MRI to detect hepatic steatosis and abdominal fat measurement in adolescents.

MATERIALS AND METHODS

The process and manuscript development are consistent with the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses6. Diagnostic accuracy studies involving US in the diagnosis of hepatic steatosis and measurement of abdominal fat thickness in adolescents were systematically searched in the scientific literature in seven databases (MEDLINE/Pubmed, Cochrane Database of Systematic Reviews, SCOPUS, WEB of SCIENCE, EMBASE, LILACS and ADOLEC) without language restriction and publication year was limited to after January 2000. The search strategy used was: "(((intraabdominal fat OR abdominal visceral fat OR visceral adiposity OR visceral adipose tissue OR visceral fat thickness OR abdominal obesity) OR (subcutaneous fat OR abdominal subcutaneous adipose tissue OR abdominal subcutaneous fat)) AND (nonalcoholic fatty liver disease OR fatty liver OR steatosis OR hepatic steatosis OR fat liver disease)))".

The full texts of potentially relevant papers were reviewed for inclusion by the same reviewers independently. Inclusion criteria were: (a) obese adolescents (10-19 years); (b) hepatic steatosis and/or abdominal fat measurement evaluated with US, CT and/or MRI; (c) data on diagnostic accuracy reported. Exclusion criteria were: (a) other causes of hepatic steatosis that were not obesity; (b) duplicate publication; (c) conference, abstracts, letters, editorials, review articles, animal studies, theses and dissertations. Papers were not blinded with regard to authors' names, affiliations or journal. The reviewers resolved all disagreements by consensus. We also supplemented by manual searches of reference lists. Data extraction was completed independently by two researchers. Relevant data on study design and variables were summarized. The flowchart of the various stages of the review is shown in Figure 1.

FIGURE 1 - Flowchart for the data collection and selection process.



RESULTS

No studies involving US accuracy have been identified as to the thickness of subcutaneous and visceral abdominal fat in obese adolescents, compared to CT or MRI. Three prospective cross-sectional studies compared the US accuracy with MRI in the

diagnosis of hepatic steatosis were included7,8,9. Two studies were Italian and also included children and adolescents7,8. The overall prevalence of hepatic steatosis in obese patients found in the studies varied from 23.3% to 83%. The main characteristics of the studies are outlined in Table 1.

TABLE 1: Main characteristics of pediatric studies

Study/Country	Population	Obese patients, N	Age range, y	Sex, M/F	Prevalence of hepatic steatosis,%
Pacifico, 2007 (Italy)	Children and adolescents with BMI > 95th ; hepatomegaly and/or elevated aminotransferases	50	5-16	34/16	40
Pozzato, 2008 (Italy)	Obese children and adolescents with white parents	60	6-14	29/31	23.3
Nascimento, 2015 (Brazil)	Obese adolescents from nutrition clinic and eutrophic (26 volunteers) from a state school	24	11-17	25/25	83

The ultrasonographic criteria for hepatic steatosis diagnosis differed between the studies. Two studies used the criteria for subjective visual steatosis evaluation according the degree of echogenicity7,8. The Brazilian study assessed hepatic steatosis by means of hepatorenal gradient analysis9. Diagnostic of hepatic steatosis by MRI was considered when hepatic fat fraction (HFF) was equal to or greater than 9%, but MRI protocols used differed between them, specifically the echo time and the angle of inclination.

Nascimento et al, in addition to the calculation of the diagnostic performance measures, it was followed by a later generation of receiver operating characteristics (ROC) curve and calculation of the area under the established curve, to determine the best cut-off point for the hepatorenal gradient to predict steatosis's degrees. The ROC curve with a cut-off point of 13 presented sensitivity of 100% and specificity of 100%. The US accuracy was 100% in obese subjects. The prevalence of NAFLD in this Brazilian study was 83% 9.

Pacifico et al and Pozatto et al compared the accuracy of US with dual-echo chemical-shift MRI in severely obese adolescent populations and reported prevalence of hepatic steatosis of 40% and 23.3%, respectively7,8. From the reported data, the majority of patients in Italian studies (67% and 72%, respectively) with mild US steatosis were negative by MRI. Based on extraction of 2x2 accuracy data, US summary estimates compared to MRI are demonstrated in Table 2.

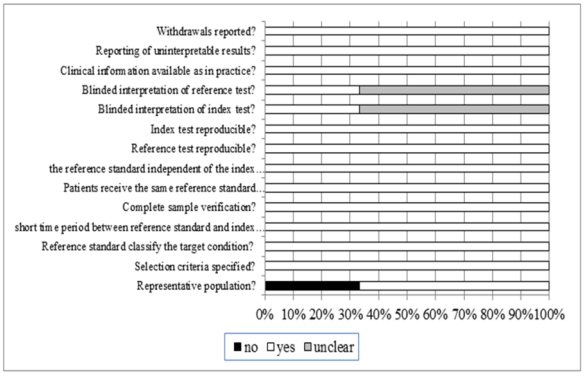
TABLE 2- US summary estimates compared to MRI

Study	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	LR^+
Pacifico et al.	95 (*)	52 (*)	59 (*)	94 (*)	1.97(*)
Pozzato et al.	92	69	48 (*)	97(*)	3.0(*)
Nascimento et al.	100	100	100	100	-

PPV -positive predictive value; NPV- negative predictive value; LR^+ - positive likelihood ratio
(*) – index of diagnostic performance calculated

Metodological quality was assessed based on QUADAS tool (Quality Assessment of Studies of Diagnostic Accuracy)10. Spectrum bias was observed in 33.3% of the studies; one study included eutrophic patients who did not represent the spectrum intended for the test in clinical practice. The set of quality items - gold standard interpreted without result of index test; test index interpreted without the knowledge of gold standard results - was not clear in two of the studies, signaling to a possible inspection bias, which may lead to increased diagnostic accuracy measurements; other quality items obtained positive responses in all studies. An overview of the results is given in Figure 2.

FIGURE 2- Quality assessment of articles (QUADAS)



DISCUSSION

This systematic review had some limitations that must be considered. The exclusion of gray literature, conference summaries, letters, editorials, or the tendency of studies with null or negative results to be unpublished (risk of publication bias) may not have guaranteed the recovery of all evidence of US accuracy in hepatic steatosis and in the measurement of abdominal fat compared to CT or MRI. Another limitation of our study was the sample size of our population. However, due to the complexity of the methodology used, the peculiarity of the studied population and the evaluation of hepatic steatosis by both US and CT or MRI, made it more difficult to find studies that met the eligibility criteria of our review and then, only three studies were selected.

Thus, two studies would indicate that hepatic US does not have the accuracy needed to classify the degree of steatosis7,8; it is only useful in cases of greater severity of hepatic steatosis and MRI would be considered a more useful and objective method than the US to discriminate differences in liver fat content and for monitoring of pediatric patients with hepatic steatosis, despite its high cost and low availability. However, it is important to note that, of the three studies included in this review, only Nascimento et al had the accuracy values well above the others and might have influenced the summary result9.

CONCLUSION

The evidence base is extremely limited and too small to estimate accuracy diagnostic. We recommend additional systematic review and meta-analysis after further studies are performed.

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