Chest Circumference Predicts MAFLD Better than Waist Circumference and BMI in Obese Prepubertal Children Aged 8 Years

Jing Zeng
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Qian Jin
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Jing Yang
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Rui-Xu Yang
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Rui-Nan Zhang
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Jian Zhao
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Jian-Gao Fan (fanjiangao@xinhuamed.com.cn)
Shanghai Jiaotong University School of Medicine Xinhua Hospital

Research Article

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Abstract

Background and Aim

Metabolic dysfunction-associated fatty liver disease (MAFLD) represents a new inclusive definition of the entire spectrum of liver diseases associated with metabolic disorders. This study aimed to determine the prevalence of MAFLD using controlled attenuation parameter (CAP) values obtained by transient elastography (TE) technique and identify the optimal predictor for diagnosing MAFLD in this population.

Methods

This study enrolled children who were part of the Shanghai Birth Cohort Study and had completed the 8-year-old follow-up. Anthropometric measurements were taken, and FibroScan-502 examination with an M probe (Echosens, Paris, France) was conducted on these children. The diagnosis of MAFLD was based on the median CAP exceeding 248 dB/m and predefined criteria. Receiver operating characteristic (ROC) curve analysis was performed to identify the optimal predictor for MAFLD in these children.

Results

A total of 848 healthy 8-year-old children (431 boys and 417 girls) who participated in the Shanghai Birth Cohort Study were included in the analysis. Among them, 113 (13.33%) children were classified as obese. The prevalence of obesity was significantly higher in boys (17.63%) than in girls (8.87%) ($p < 0.001$). The prevalence of central obesity was significantly higher in girls (34.05%) than in boys (22.04%) ($p < 0.001$). MAFLD was diagnosed in 29 (3.42%) children. The prevalence of MAFLD was significantly higher in the obese group (15.93%) than in the non-obese group (1.50%) ($p < 0.05$). Children with MAFLD had significantly higher weight, BMI, chest circumference, waist circumference, hip circumference, waist-to-height ratio, waist-to-hip ratio, and liver stiffness measurement than non-MAFLD (all $p < 0.05$). Waist circumference (OR: 1.187; 95% CI: 1.132-1.243; $p < 0.001$) was significantly associated with the presence of MAFLD in these participants in multivariate linear regression analyses. Chest circumference (OR: 1.321; 95% CI: 1.123-1.424; $p < 0.001$) was significantly associated with the presence of MAFLD in obese participants and had the largest AUC of 0.813 in ROC curve analysis.

Conclusion

This study highlights the prevalence of MAFLD in prepubertal children, particularly in the obese subgroup. Our findings also suggest that chest circumference is an optimal anthropometric predictor for MAFLD in 8-year-old obese children.

Introduction

The incidence and prevalence of overweight and obesity in children are increasing globally due to sedentary lifestyles and high-calorie diets, which pose significant public health concerns (1, 2). Previous studies found that childhood obesity was associated with adult obesity and may even lead to severe
complications in the future (3). Obesity and central obesity are both linked to higher risks of cardiometabolic health problems, such as metabolic syndrome, impaired insulin metabolism, and hypertension (4). Meanwhile, the prevalence of fatty liver disease (FLD) in children has increased significantly over the past few decades, due to the rising rates of childhood overweight and obesity. Non-alcoholic fatty liver disease (NAFLD) has become a prevalent cause of chronic liver diseases in children, affecting 10% of the general pediatric population and up to 40–70% of obese pediatric patients (5–8). NAFLD in children increases the risk of developing type 2 diabetes (T2DM) and cardiovascular disease in adulthood and can lead to liver-related death and significantly shorter survival (9–11).

Liver biopsy is the gold standard for diagnosis and staging of fatty liver in children, but it is invasive, costly, and not suitable for screening or follow-up assessments. Therefore, alternative non-invasive methods to liver biopsy have been increasingly studied. The device (FibroScan-502, Echosens, Paris, France), developed using the transient elastography (TE) technique, can simultaneously obtain controlled attenuation parameter (CAP) and liver stiffness measurement (LSM) in a rapid, noninvasive, reproducible, and painless manner (12). Numerous studies have shown that TE is a fast and reliable method for diagnosing liver fibrosis and NAFLD in adults, with several studies also reporting its utility in the pediatric population (13–19). Recently, the prevalence of fatty liver disease with CAP ≥ 248 dB/m in adolescent (12–18 years) in the USA was estimated using the Health and Nutrition Examination Survey 2017–18 database (18).

The term NAFLD is not appropriate for children, as alcohol consumption is typically not a contributing factor, and inherited metabolic disorders can present with similar symptoms or coexist with a diagnosis of NAFLD (20). In 2020, an international expert consensus panel suggested the term metabolic dysfunction-associated fatty liver disease (MAFLD) to replace NAFLD and introduced a simplified set of positive criteria for diagnosis (2, 21). This redefinition has been validated by numerous studies, and in 2021, the criteria were adapted for pediatric practice (22, 23). The prevalence of MAFLD in children and adolescents with obesity was estimated to be 36.1% (24). However, the prevalence and characteristics of MAFLD in young prepubertal children remain unknown.

In this article, the aim of this study is to utilize the TE technique to obtain CAP and assess the prevalence of MAFLD in young prepubertal children during their 8-year follow-up visit. We also aim to identify the optimal predicator for MAFLD to aid in its diagnosis in this population.

**Participants And Methods**

**Study population**

The study population included 8-year-old (94–98 months) children from the Shanghai Birth Cohort (25), who received the 8-year-old follow-ups with medical examinations. Participants were excluded if they: 1) were lost to follow-up; 2) had missing anthropometric data or no available FibroScan data; 3) had any type of liver disease; 4) had extra liver diseases or were taking therapeutic drugs that could affect liver fat
and function tests; or 5) experienced measurement failure of FibroScan-502 with M probe. The Ethics Committees of Xinhua Hospital affiliated with the Shanghai Jiao Tong University School of Medicine approved the study, and informed consent was obtained from the parents of all participating children who signed written documents.

**Clinical and laboratory data collection**

The participating children underwent the medical examinations at the health examination center in Xinhua Hospital, where their height was measured to the nearest 0.1 cm using stadiometers (Seca 416 Infantmeter, United States), and body weight was measured to the nearest 0.1 kg using digital scales (Detector 6745 Baby Scale, United States). The following participant characteristics and anthropometric indices were recorded: sex, body weight, height, chest circumference (CC), waist circumference (WC), hip circumference (HP), and body mass index (BMI), which was calculated as weight in kilograms divided by the square of height in meters (kg/m$^2$). Waist-height ratio (WHtR) and waist-hip ratio (WHR) were calculated as WC (cm)/height (cm) and WC (cm)/HP (cm), respectively.

**Evaluation of liver steatosis and fibrosis using TE**

After fasting for at least 6 hours, all participants underwent FibroScan-502 with M-probe (3.5 MHz) examination (Echosens, Paris, France) to estimate liver stiffness in kilopascals (kPa) and liver steatosis in decibels per meter (dB/m). CAP in dB/m and LSM in kPa were obtained simultaneously by each examination. A TE examination was considered successful when 10 valid measurements with a success rate of at least 60% were conducted and the interquartile range (IQR) was less than 30% of the median LSM value. Subjects with unsuccessful examinations were excluded from the analyses.

**Work Definitions**

Obesity was defined using age- and sex-specific cutoff points from the International Obesity Task Force, with BMI $\geq$ 95th percentile (26).

Central obesity was defined using age- and sex-specific cutoff points for waist circumference $\geq$ 90th percentile (27).

FLD was diagnosed when the CAP value exceeded the normal value of 248 dB/m (16). The diagnosis of MAFLD was based on FLD diagnosis and one of the following criteria: excess adiposity, presence of prediabetes or type 2 diabetes, or evidence of metabolic dysregulation (22).

**Statistical analysis**

Continuous variables were presented as mean $\pm$ SD for normal distribution and median $\pm$ IQR for skewed distribution. The t-test and $\chi^2$ test were used to compare intergroup differences between different genders and weight groups for continuous and categorical variables, respectively. Correlations between CAP values and anthropometric parameters were tested using Pearson's correlation analysis. Univariate and multivariate linear regression models were used to identify potential factors associated with prevalence of MAFLD. To estimate and compare the area under the receiver operator characteristic curve (ROC) curve
(AUC), sensitivity, and specificity of anthropometric indices for obesity, central obesity, and MAFLD, ROC analysis was conducted. Statistical significance was indicated by two-sided P values < 0.05. The data analysis was performed using SAS Version 9.4.

Results

Participant characteristics

Out of 1045 children who participated in the 8-year-old follow-up from the Shanghai Birth Cohort, 848 children aged 8 years (94–98 months) were included in the final analysis after applying exclusion criteria (Fig. 1). Table 1 shows the characteristics of non-obese and obese groups. The prevalence of obesity among these children was 13.33%, with boys comprising the majority (67.26%) of the obese group. Height, body weight, BMI, CC, WC, HC, WHtR, WHR, and CAP values were significantly higher in the obese group compared to the non-obese group (all $p < 0.05$). The prevalence of central obesity was 27.95%, and obese children had a significantly higher prevalence of central obesity (85.84%) than non-obese children (19.07%) ($p < 0.001$). LSM values did not differ significantly between obese and non-obese children. The prevalence of obesity was significantly higher in boys (17.63%) than in girls (8.87%) ($p < 0.001$). The prevalence of central obesity was significantly higher in girls (34.05%) than in boys (22.04%) ($p < 0.001$). Supplementary Table 1 and Supplementary Table 2 show the characteristics of these participating children by sex and WC, respectively.
Table 1
Characteristics of anthropometric parameters of non-obese and obese children in the study.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total (n = 848)</th>
<th>Non-obese (n = 735)</th>
<th>Obese (n = 113)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n/%)</td>
<td>431 (50.8%)</td>
<td>355 (48.30%)</td>
<td>76 (67.26%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>126.26 ± 5.65</td>
<td>125.86 ± 5.12</td>
<td>131.47 ± 6.93</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>25.67 ± 8.67</td>
<td>24.19 ± 3.64</td>
<td>38.12 ± 20</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>15.98 ± 4.71</td>
<td>15.21 ± 1.61</td>
<td>21.97 ± 11.83</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>CC (cm)</td>
<td>59.9 ± 5.82</td>
<td>58.82 ± 4.27</td>
<td>70.03 ± 6.26</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>58.1 ± 16.73</td>
<td>56.28 ± 4.83</td>
<td>69.13 ± 7.38</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>68.09 ± 6.9</td>
<td>66.72 ± 5.54</td>
<td>78.47 ± 7.39</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.46 ± 0.13</td>
<td>0.45 ± 0.04</td>
<td>0.53 ± 0.05</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.85 ± 0.11</td>
<td>0.85 ± 0.1</td>
<td>0.89 ± 0.11</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Central obesity (≥ 90 P) (n/%)</td>
<td>237 (27.95%)</td>
<td>140 (19.05%)</td>
<td>97 (85.84%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LSM (kPa)</td>
<td>3.57 ± 0.91</td>
<td>3.53 ± 0.91</td>
<td>3.55 ± 0.82</td>
<td>0.805</td>
</tr>
<tr>
<td>CAP (dB/m)</td>
<td>173.49 ± 44.5</td>
<td>168.26 ± 43.03</td>
<td>194.25 ± 49.25</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

P-values are for chi-square or Kruskal-Wallis tests between boys and girls. Means ± SDs were calculated for variables of normal distribution. BMI body mass index, CC chest circumference, WC waist circumference, HC hip circumference, WHtR waist-to-height ratio, WHR waist-to-hip ratio, LSM liver stiffness measurement, kPa kilopascal, CAP controlled attenuation parameter, dB/m decibels per meter.

Performance of anthropometric parameters in predicting obesity or central obesity

Figure 2A shows the ROC curves of anthropometric parameters to identify obesity in these participants. Chest circumference and waist circumference had the largest AUC of 0.941 (95% CI: 0.913–0.968) and 0.941 (95% CI: 0.914–0.969), respectively. Figure 2B shows the ROC curves to identify central obesity. Both BMI and chest circumference had the largest AUC of 0.831 (95% CI 0.798–0.864) and 0.831 (0.798–0.863), respectively.

CAP distribution in different subgroups and correlation between CAP values and anthropometric parameters

The distribution of CAP values and LSM values in different subgroups are presented in Fig. 3. No significant differences were found in CAP values and LSM values between boys ((173.48 ± 44.68) dB/m, (3.54 ± 0.90) kPa) and girls ((169.99 ± 44.79) dB/m, (3.52 ± 0.90) kPa). The obese group had significantly higher CAP values (194.25 ± 49.25) dB/m than the non-obese group (168.26 ± 43.03) dB/m (p < 0.001). However, no significant differences were found in LSM values among these groups. The CAP values in
the central obesity group (182.34 ± 49.81) dB/m were significantly higher than those in the non-central obesity group (167.55 ± 41.99) dB/m (p < 0.05). No significant differences were found in LSM values among these groups.

The correlation between CAP values and anthropometric parameters is presented in Table 2. CAP values were positively correlated with BMI, CC, WC, HC, and WHtR (all p < 0.05). In non-obese participants, CAP values were positively correlated with BMI and CC (all p < 0.05). In obese participants, CAP values were positively correlated with CC, WC, HC, and WHtR (all p < 0.05). Correlation analysis by sex and WC can be found in Supplementary Tables 3 and 4, respectively.

### Table 2

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total (n = 848)</th>
<th>Non-obese (n = 735)</th>
<th>Obese (n = 113)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>0.133 &lt; 0.001</td>
<td>0.094 0.011</td>
<td>0.044 0.646</td>
</tr>
<tr>
<td>CC (cm)</td>
<td>0.224 &lt; 0.001</td>
<td>0.084 0.025</td>
<td>0.487 &lt; 0.001</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>0.099 0.001</td>
<td>0.050 0.180</td>
<td>0.425 &lt; 0.001</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>0.203 &lt; 0.001</td>
<td>0.070 0.059</td>
<td>0.273 0.003</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.082 0.008</td>
<td>0.049 0.186</td>
<td>0.387 &lt; 0.001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.028 0.419</td>
<td>-0.026 0.477</td>
<td>0.178 0.060</td>
</tr>
</tbody>
</table>

P-values were tested using Spearman’s correlation analysis between CAP values and anthropometric parameters. BMI body mass index, CC chest circumference, WC waist circumference, HC hip circumference, WHtR waist-to-height ratio, WHR waist-to-hip ratio, CAP controlled attenuation parameter.

### Prevalence and characteristics of MAFLD

The prevalence of MAFLD differed in children aged 8 years old of different subgroups. The overall prevalence of MAFLD was 3.42% (29/848), with no significant difference observed between boys (3.48%, 15/431) and girls (3.36%, 14/417). The prevalence of MAFLD in the obesity group (15.93%, 18/113) was significantly higher than that in the non-obese group (1.50%, 11/734) (p < 0.05). Additionally, MAFLD was more prevalent in the central obesity group (11.81%, 28/237) than in the non-central obesity group (0.16%, 1/611) (p < 0.05). Table 3 shows that children with MAFLD had significantly larger weight, BMI, CC, WC, HC, WHtR and WHR and a higher prevalence of obesity (62.07% vs. 11.60%), and central obesity (96.55% vs. 25.52%) compared to those without MAFLD (all p < 0.05). The LSM value in the MAFLD group (4.21 ± 1.09) kPa was also higher than that in the non-MAFLD group (3.51 ± 0.89) kPa (p < 0.005).
Table 3
Characteristics of children diagnosed with steatosis by CAP according to MAFLD criteria in the study.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Non-MAFLD (n = 819)</th>
<th>MAFLD (n = 29)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>416 (50.79%)</td>
<td>15 (51.72%)</td>
<td>0.918</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>126.51 ± 5.64</td>
<td>131.41 ± 5.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>25.77 ± 9.19</td>
<td>35.35 ± 9.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>15.99 ± 5.11</td>
<td>20.17 ± 4.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CC (cm)</td>
<td>60.01 ± 5.54</td>
<td>69.89 ± 9.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>57.62 ± 6.38</td>
<td>69.84 ± 8.86</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>67.98 ± 6.73</td>
<td>78.37 ± 9.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHtR</td>
<td>0.46 ± 0.04</td>
<td>0.53 ± 0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>WHR</td>
<td>0.85 ± 0.11</td>
<td>0.89 ± 0.04</td>
<td>0.049</td>
</tr>
<tr>
<td>Obesity (≥ 95 P) (n/%)</td>
<td>95 (11.60%)</td>
<td>18 (62.07%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Central obesity (≥ 90 P) (n/%)</td>
<td>209 (25.52%)</td>
<td>28 (96.55%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LSM (kPa)</td>
<td>3.51 ± 0.89</td>
<td>4.21 ± 1.09</td>
<td>0.004</td>
</tr>
<tr>
<td>CAP (dB/m)</td>
<td>166.88 ± 39.86</td>
<td>263.62 ± 29.62</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P-values are for chi-square or Kruskal-Wallis tests between boys and girls. Means ± SDs were calculated for variables of normal distribution. BMI body mass index, CC chest circumference, WC waist circumference, HP hip circumference, WHtR waist-to-height ratio, WHR waist-to-hip ratio, LSM liver stiffness measurement, kPa kilopascal, CAP controlled attenuation parameter, dB/m decibels per meter.

Performance of anthropometric parameters in diagnosing MAFLD

In the univariate analysis, chest circumference (OR: 1.206; 95%CI: 1.143–1.273; p < 0.001), waist circumference (OR: 1.190; 95%CI: 1.136–1.246; p < 0.001), hip circumference (OR: 1.200; 95%CI: 1.139–1.264; p < 0.001), and WHtR (OR: 76.879; 95%CI: 4.274–138.28; p < 0.001) were significantly associated with MAFLD. In the multivariate analysis, waist circumference (OR: 1.187; 95%CI: 1.132–1.243; p < 0.001) was significantly associated with MAFLD in all participants (Table 4). Additionally, in the obese subgroup, chest circumference (OR: 1.321; 95%CI: 1.123–1.424; p < 0.001) was significantly associated with MAFLD (Table 4).
Table 4
Anthropometric parameters associated with MAFLD in the study.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Total (n = 848)</th>
<th>Non-obese (n = 735)</th>
<th>Obese (n = 113)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate analysis</td>
<td>Multivariate analysis(a)</td>
<td>Univariate analysis</td>
</tr>
<tr>
<td></td>
<td>OR (95%CI)</td>
<td>OR (95%CI)</td>
<td>OR (95%CI)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.043 (0.997–1.092)</td>
<td>1.229 (0.855–1.766)</td>
<td>1.006 (0.972–1.042)</td>
</tr>
<tr>
<td>CC (cm)</td>
<td>1.206*** (1.143–1.273)</td>
<td>1.104 (0.969–1.257)</td>
<td>1.206*** (1.086–1.341)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>1.190*** (1.136–1.246)</td>
<td>1.187*** (1.132–1.243)</td>
<td>1.203** (1.073–1.348)</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>1.200*** (1.139–1.264)</td>
<td>1.082 (0.962–1.218)</td>
<td>1.208*** (1.087–1.344)</td>
</tr>
<tr>
<td>WHtR</td>
<td>76.879*** (4.274–138.28)</td>
<td>6.357** (1.367–29.551)</td>
<td>46.962** (8.923–247.175)</td>
</tr>
<tr>
<td>WHR</td>
<td>4.745 (0.827–27.231)</td>
<td>-</td>
<td>4.168 (0.353–49.244)</td>
</tr>
</tbody>
</table>

BMI body mass index, CC chest circumference, WC waist circumference, HP hip circumference, WHtR waist-to-height ratio, WHR waist-to-hip ratio.

\(a\)Factors < 0.05 in the univariate analysis were included in the multivariate analysis, \(*p<0.05, \,**p<0.005, \,**\,*p<0.001.\)

Figure 2C depicts the ROC curves of anthropometric parameters used to identify MAFLD in these participants, with waist circumference having the largest AUC of 0.872 (95% CI: 0.741–0.929). In the non-obese group (Fig. 2D), waist circumference still had the largest AUC of 0.792 (95% CI: 0.741–0.929), while in the obese group (Fig. 2E), chest circumference had the largest AUC of 0.813 (95% CI: 0.740–0.924).

Discussion
This is to our knowledge the first study to investigate the prevalence and characteristics of MAFLD using transient elastography in prepubertal children aged 8 years. Our findings indicated that approximately 16 in 100 obese 8-year-olds have MAFLD, and that MAFLD is associated with higher BMI, WC, and CC. Moreover, we identified a positive correlation between chest circumference and MAFLD prevalence in obese children, suggesting that this anthropometric parameter may serve as a useful predictor for identifying obese prepubertal children who would benefit from MAFLD screening.

Recent years have seen a significant increase in the prevalence of childhood obesity, which is associated with numerous health risks, including an increased risk of T2DM, cardiovascular disease, and certain cancers (5). In a study of 626 early-stage adolescents, the prevalence of obesity was found to be 16.3% (28). While both boys and girls can be affected by obesity, there is emerging evidence of sex-specific differences in the prevalence and causes of these conditions. In our study, it can be found that the prevalence of obesity in 8-year-old children were 13.33%. The frequency of obesity in boys (17.63%) was significantly higher than that in girls (8.87%) \( p<0.001 \). Our results were consistent with previous studies (29). There are several reasons for the higher prevalence of obesity in boys than girls. This sex difference may be related to differences in lifestyle between genders (30). Studies have found that unhealthy eating habits, with boys consuming sweets more frequently than girls, may play important roles (31, 32). These findings suggest that gender-specific guidelines for child nutrition may be necessary for obese children.

The prevalence of FLD has increased these years in children and adolescents worldwide due to the obesity epidemic. Children with FLD are also at risk of liver fibrosis, cirrhosis, and liver failure (33). Therefore, early detection, staging, and treatment of FLD in children are crucial in preventing disease progression. In addition to liver biopsy, non-invasive methods such as serum alanine aminotransferase (ALT) levels or liver ultrasound (US) have been used in many studies of the pediatric population to diagnose FLD (34, 35). Current guidelines from ESGPHAN and EASL recommend the use of both ALT and US to screen high-risk NAFLD patients in children. However, NASPGHAN does not recommend US due to its low sensitivity and specificity, especially for detecting and grading liver steatosis in children with hepatocellular steatosis less than 33% (36). AASLD does not recommend any specific methods due to a lack of evidence (37). In previous studies, CAP detected by FibroScan has been found to be applicable in preschool children and useful in quantifying hepatic steatosis in pediatric patients (38, 39). In our study, CAP values showed significant positive correlations with height, weight, BMI, WC, and WHtR, and were found to be significantly higher in individuals with obesity or central obesity. While an optimal cutoff range for CAP in adults has been defined as 247 dB/m (15), there is currently no consensus on the range threshold for diagnosing FLD in children. In our study, we used a threshold of 248 dB/m as in a previous study (18). Future follow-up of this cohort and larger studies are needed to determine any changes in the thresholds of CAP values for diagnosing FLD in children of different ages.

Considering the unique features of FLD in children, the term NAFLD may not be appropriate. Many studies have highlighted the challenges faced by pediatricians in diagnosing and managing these conditions, including the lack of clear diagnostic criteria, the negative connotation of the current
definition, and uncertainty regarding co-existing liver diseases. This often results in unnecessary testing and delayed diagnosis (22, 40). Furthermore, primary care physicians often overlook the prevalence of excess liver fat and associated risk factors in young children, leading to adverse long-term outcomes (41). To address these issues, the international panel of experts has proposed and adopted the MAFLD criteria for pediatric practice (22). It is crucial to validate the MAFLD diagnostic criteria across different age groups in children. Previous studies have reported a high prevalence of MAFLD in children and adolescents with obesity, estimated at 36.1% (24), and this prevalence increases with age and metabolic dysfunction category. However, the prevalence of MAFLD in young prepubertal children is unknown. In our study, we found that the estimated prevalence of MAFLD was 3.42% in 8-year-old children, and even 15.93% in the obese subgroup. The association between MAFLD and BMI, WC are consistent with previous data in both adolescent and adult populations (18, 42). The early diagnosis of MAFLD in childhood and adolescence is crucial for early intervention and slowing disease progression, as well as reducing the risk of long-term complications (43, 44). Non-invasively identifying children with MAFLD is a challenging task. In our study, we found that chest circumference, rather than waist circumference and BMI, was associated with higher odds of MAFLD in 8-year-old obese children. Chest circumference was also an effective anthropometric parameter for predicting obesity and central obesity, with AUC values of 0.941 and 0.831, respectively. These findings suggest that chest circumference may be an optimal anthropometric predictor for identifying MAFLD in this population.

But there are also some limitations in our study that should be noted. Firstly, we did not perform liver biopsy to confirm the absence of liver steatosis in the participants or use ultrasound to compare with CAP values. However, liver biopsy is not feasible for healthy children, and US is not accurate for diagnosing FLD in children. Secondly, the narrow age distribution of our cohort may limit the generalizability of our findings to other age groups. Future studies with a wider age range are needed. Thirdly, we did not have data on ALT, aspartate aminotransferase (AST), triglyceride (TG), high-density lipoprotein cholesterol (HDL-c), and glucose levels to diagnose related metabolic disorders, but since our cohort only included healthy children, it was expected that these values were within the normal range. We also plan to conduct regular follow-up in the future to investigate long-term trends.

In conclusion, this study highlights the prevalence of MAFLD in young prepubertal children, especially in the obese subgroup. MAFLD is associated with higher BMI, WC, and CC. Moreover, we identified a positive correlation between chest circumference and MAFLD prevalence in obese children, suggesting that this anthropometric parameter may serve as a useful predictor for identifying obese prepubertal children who would benefit from MAFLD screening. Follow-up studies with larger cohorts are needed to establish the MAFLD prevalence and characteristics in different age and provide a basis for diagnosis and treatment of MAFLD in children.

Abbreviations
Declarations

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Author contributions

JZ and JGF contributed to the study design. JZ, QJ, JY, RXY, and RNZ were responsible for data collection and management. JZ and Jian Zhao performed data analysis and interpreted the results. JZ wrote the initial draft of the manuscript. Jian Zhao and JGF critically revised the manuscript for important intellectual content. All authors reviewed and approved the final manuscript and agreed to be accountable for the accuracy and integrity of the work. Any questions related to the accuracy or integrity of any part of the work will be appropriately investigated and resolved by the authors.

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Data availability

The datasets generated and/or analyzed during the current study are available upon request from the corresponding author.

Compliance with ethical standards

Conflict of interest

The authors declare that they have no conflict of interest.

Ethics approval and consent to participate

The study was approved by the Ethics Committees of Xinhua Hospital affiliated with the Shanghai Jiao Tong University School of Medicine approved the study, and informed consent was obtained from the parents of all participating children who signed written documents.

Consent to Publish

Authors consent to the publication of this manuscript.

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Figures

Flow diagram of participants included in this study. A total of 1045 participants were enrolled in the follow-up study, and after screening, 848 participants were included in the analysis. Among them, 29 participants were diagnosed with MAFLD.
Figure 2

Receiver operating characteristic curves (ROC) of anthropometric parameters for identifying obesity, central obesity and MAFLD in children aged 8 years. A: ROC of anthropometric parameters for identifying obesity; B: ROC of anthropometric parameters for identifying central obesity; C: ROC of anthropometric parameters for identifying MAFLD; D: ROC of anthropometric parameters for identifying MAFLD in non-obese subgroup; E: ROC of anthropometric parameters for identifying MAFLD in obese subgroup.
Figure 3

The distribution of controlled attenuation parameter (CAP) values and liver stiffness measurement (LSM) values in different subgroups in children aged 8 years. A: CAP values; with no significant differences between boys ((173.48 ± 44.68) dB/m) and girls ((169.99 ± 44.79) dB/m). The obese group had significantly higher CAP values (194.25 ± 49.25) dB/m than the non-obese group (168.26 ± 43.03) dB/m (p < 0.001). Additionally, the CAP values in the central obesity group (182.34 ± 49.81) dB/m were significantly higher than those in the non-central obesity group (167.55 ± 41.99) dB/m (p < 0.05); B: LSM values; with no significant differences observed between boys ((3.54 ± 0.90) kPa) and girls ((3.52 ± 0.90) kPa). There were no significant differences in LSM values between the obese group and the non-obese group or between the central obesity group and the non-central obesity group.

Supplementary Files

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- SupplementaryTables.docx