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NAFLD in overweight adolescents: Lifestyle intervention vs. GLP-1 agonist: A pilot RCT

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Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) in adolescents is rising alongside obesity, and effective, scalable treatments are needed. Lifestyle intervention is first-line, while glucagon-like peptide-1 receptor agonists (GLP-1RAs) show promise for weight and metabolic control. We conducted a pilot randomized controlled trial to compare hepatic and metabolic effects of intensive, family-supported lifestyle intervention versus GLP-1RA therapy in overweight adolescents with NAFLD.

Methods: In this multicenter, parallel-group pilot RCT, adolescents aged 12-17 years with BMI ≥85th percentile and MRI-proton density fat fraction (MRI-PDFF) ≥8% were randomized 1: 1 to (A) intensive lifestyle (nutrition, activity, behavioral support) or (B) GLP-1RA plus brief lifestyle advice. The primary endpoint was change in MRI-PDFF at Week 24. Key secondary endpoints included ALT, BMI z-score, HOMA-IR, waist circumference, feasibility metrics (retention, imaging completion, adherence), and safety. Analyses followed intention-to-treat with between-arm comparisons using ANCOVA/t-tests.

Results: Sixty participants were randomized (n=30/arm). At Week 24, mean MRI-PDFF decreased in both arms, favoring GLP-1RA: −3. 58±3. 04% (lifestyle) vs −5. 52±3. 02% (GLP-1RA); p=0. 016. ALT fell by −9. 92±17. 28 U/L vs −20. 05±16. 61 U/L; p=0. 024. BMI z-score declined −0. 15±0. 22 vs −0. 38±0. 16; *p*<0. 001. HOMA-IR improved −0. 31±1. 21 vs −1. 33±1. 40; p=0. 004, and waist circumference decreased −3. 47±4. 16 cm vs −6. 65±4. 11 cm; p=0. 004 (lifestyle vs GLP-1RA, respectively). Feasibility targets were achieved for retention and MRI-PDFF completion in both arms; lifestyle session attendance and medication persistence were acceptable for a pilot. Gastrointestinal adverse events were more frequent with GLP-1RA (13. 3% vs 30. 0%); serious adverse events were uncommon and balanced.

Conclusions: In overweight adolescents with NAFLD, GLP-1RA therapy produced greater short-term reductions in hepatic fat and metabolic risk markers than an intensive lifestyle program, with expected gastrointestinal tolerability. Both strategies improved outcomes versus baseline, supporting a stepwise care model in which structured lifestyle is foundational and GLP-1RA may serve as an adjunct for youths with persistent steatosis or elevated cardiometabolic risk. Findings justify a larger, longer trial powered for histologic/fibrosis-sensitive endpoints and patient-centered outcomes.

Keywords: Nonalcoholic fatty liver disease (NAFLD), metabolic dysfunction-associated steatotic liver disease (MASLD), adolescents, GLP-1 receptor agonist, liraglutide, semaglutide, lifestyle intervention, MRI-PDFF, HOMA-IR, randomized controlled pilot trial

Introduction

Here we introduce a pilot randomized controlled trial (RCT) comparing structured lifestyle intervention versus a glucagon-like peptide-1 receptor agonist (GLP-1RA) for nonalcoholic fatty liver disease (NAFLD; now also termed MASLD) in overweight adolescents. NAFLD is increasingly detected in youth and can progress to steatohepatitis, fibrosis, and cirrhosis; pediatric societies recommend risk-based screening and emphasize lifestyle therapy as first-line care [1, 6-8]. Contemporary estimates place NAFLD prevalence at 7-8% in the general pediatric population but >30-50% among youth with overweight/obesity, mirroring global rises in childhood adiposity and cardiometabolic risk [3-5]. Although multidisciplinary diet-and-activity programs reduce hepatic steatosis and transaminases and in some studies improve histology the effect sizes are variable and adherence-dependent [6-7, 9, 15-16]. Pharmacotherapy for pediatric NAFLD remains off-label; the TONIC trial showed limited histologic benefit of metformin and a signal for vitamin E in a subset, underscoring the need for alternatives aligned with current metabolic pathophysiology [8]. GLP-1RAs promote

weight loss and improve insulin resistance; in adolescents with obesity, liraglutide and semaglutide each produced clinically meaningful BMI reductions when added to lifestyle counseling [9-10]. In adults with biopsy-proven NASH, liraglutide (LEAN) improved histologic resolution and limited fibrosis progression, while semaglutide increased NASH resolution rates, supporting class effects relevant to hepatic outcomes beyond weight loss [11-12]. Mechanistically, GLP-1RAs reduce liver fat via appetite suppression and weight loss, and may directly modulate hepatic lipid flux, de novo lipogenesis, inflammation, and gut-liver signaling [13-14]. Major guidelines acknowledge the centrality of lifestyle change and highlight gaps in pediatric drug therapy; neither endorses GLP-1RAs specifically for adolescent NAFLD pending pediatric data [1-2]. Against this backdrop, our problem statement is that durable, scalable improvements in adolescent NAFLD remain difficult to achieve through lifestyle programs alone, while robust pediatric NAFLD evidence for GLP-1RAs is lacking despite strong adolescent obesity and adult NASH data [1-3, 6-12]. Therefore, our objective is to conduct a pilot multicenter RCT comparing a standardized, family-supported lifestyle intervention with a GLP-1RA regimen on hepatic fat (MRI-PDFF), ALT, and intermediate cardiometabolic endpoints over 24-48 weeks, with embedded feasibility, adherence, and safety assessments [1-3, 6-7, 9-13, 15-16]. We hypothesize that
(i) both strategies will reduce liver fat versus baseline,
(ii) GLP-1RA plus brief lifestyle advice will be non-inferior and potentially superior to intensive lifestyle intervention for MRI-PDFF reduction, and
(iii) GLP-1RA will yield greater improvements in BMI-z and insulin resistance, while lifestyle may confer broader fitness and behavior change benefits; we also hypothesize acceptable safety/tolerability consistent with adolescent obesity trials [2, 9-14].

Material and Methods
Materials
We conducted a multicenter, parallel-group, pilot randomized controlled trial enrolling adolescents aged 12-17 years with overweight/obesity (BMI ≥85th percentile for age/sex) and MRI-proton density fat fraction (MRI-PDFF) ≥8% consistent with NAFLD, in accordance with pediatric guidance prioritizing imaging-based quantification and lifestyle-first management [1, 2]. Key exclusions were secondary causes of steatosis, prior GLP-1 receptor agonist (GLP-1RA) exposure, decompensated liver disease, uncontrolled endocrinopathies, pancreatitis/gallbladder disease, or medications affecting weight/liver fat [1, 2, 8]. Participants were recruited from hepatology and adolescent medicine clinics; written assent and parental consent were obtained, and the protocol was approved by institutional review boards at all sites. After baseline assessments, participants were randomized 1: 1 (variable block sizes, stratified by site and sex) to:
(A) intensive, family-supported lifestyle intervention, or
(B) GLP-1RA plus brief lifestyle advice.

The lifestyle program combined individualized nutrition counseling emphasizing energy deficit, Mediterranean-style patterns, and sugar-sweetened beverage elimination; goal-based physical activity (≥60 min moderate-vigorous activity/day, ≥3 sessions/week of supervised group activity); and behavioral techniques (goal setting, self-monitoring, motivational interviewing), reflecting effective pediatric NAFLD/obesity strategies [6, 7, 15, 16]. The pharmacotherapy arm used a GLP-1RA with adolescent obesity evidence (liraglutide daily or semaglutide weekly per local formulary), initiated at the labeled pediatric starting dose and titrated to the maximum tolerated dose over 4-8 weeks, with antiemetic guidance as needed and standardized counseling on diet/activity equivalent to usual-care brief advice [9, 10]. Rationale for GLP-1RA included effects on weight, insulin resistance, and hepatic endpoints observed in adult NASH trials and mechanistic work on hepatic lipid flux and inflammation [11-14]. Concomitant vitamin E, metformin, or weight-modifying agents were prohibited; stable ADHD medications and inhaled corticosteroids were permitted [1, 8]. Imaging (MRI-PDFF) was acquired on 1. 5T/3T systems using vendor-neutral multiecho sequences; blood tests (ALT, AST, GGT, fasting insulin/glucose, lipids) were processed at CLIA-certified labs; anthropometry and blood pressure were measured by trained staff; and patient-reported outcomes captured quality of life and treatment satisfaction [1-3, 6-7, 11-12, 15-16].

Methods
The primary endpoint was change in liver fat (MRI-PDFF, %) from baseline to Week 24; key secondary endpoints included ALT, AST, BMI-z score, weight (%), waist circumference, HOMA-IR, lipid profile, fitness (6-minute walk or shuttle run), health-related quality of life, and feasibility metrics (recruitment rate, session adherence, medication persistence) through Week 24, with exploratory follow-up to Week 48 [1-3, 6-7, 9-12, 15-16]. Safety outcomes included gastrointestinal events, symptomatic hypoglycemia, gallbladder disease, pancreatitis, injection-site reactions, and signals of hepatobiliary adverse events; an independent medical monitor reviewed unblinded safety at predefined intervals [1, 2, 9-12]. Visits occurred at baseline, Weeks 4, 8, 12, 24 (primary), and 48 (extension). Lifestyle sessions were weekly ×8 then biweekly to Week 24 (hybrid onsite/virtual), reflecting effective schedules from pediatric NAFLD programs [6, 7, 15, 16]; medication titration visits paralleled adolescent obesity RCTs [9, 10]. The pilot sample size (n≈60; 30/arm) targeted feasibility (≥70% retention; ≥75% imaging completion) and estimation of variance for a future definitive trial; detectable between-arm difference for MRI-PDFF was modeled at ~2. 5-3. 0 absolute% with SD 4-5, consistent with prior lifestyle and pharmacotherapy literature [6, 7, 9-12, 15, 16]. Analyses followed intention-to-treat with a supportive per-protocol set (≥75% session attendance or ≥80% dose exposure). The primary comparison used ANCOVA with change in MRI-PDFF as the dependent variable, treatment arm as the factor, and baseline MRI-PDFF, site, sex, and age as covariates; model assumptions were evaluated and robust standard errors applied if needed. Repeated measures (baseline to Weeks 12 and 24) were assessed via linear mixed-effects models (random intercept for participant); binary safety outcomes used log-binomial or Poisson models with robust variance. Missing data were handled under missing-at-random via multiple imputation (m=20) and checked with sensitivity analyses (pattern-mixture, δ-adjusted). In a prespecified non-inferiority framework, GLP-1RA plus brief advice was tested against intensive lifestyle for MRI-PDFF reduction with a margin of 2. 5 absolute% (two-sided 95% CI), based on clinical interpretability and prior adult/pediatric data [6, 7, 9-12]. Exploratory subgroups (sex, baseline insulin resistance

tertiles, baseline MRI-PDFF ≥15% vs <15%) were probed via interaction terms (α for interaction=0. 10). Two-sided α=0. 05 defined statistical significance; no multiplicity adjustment was applied given pilot intent. All procedures aligned with pediatric NAFLD guidelines and prior RCTs in adolescent obesity and adult NASH informing endpoint selection and safety oversight [1-2, 6-12, 15-16].

Results

Table 1: Baseline Characteristics of Participants (n = 60)

Variable	Lifestyle (n = 30) Mean±SD	GLP-1RA (n = 30) Mean±SD	p-Value
Age (years)	14.6±1.7	14.4±1.8	0.68
Male (%)	16 (53.3%)	17 (56.7%)	0.81
BMI z-score	2.12±0.29	2.10±0.27	0.74
MRI-PDFF (%)	15.4±4.9	15.8±5.2	0.82
ALT (U/L)	56.3±19.1	55.8±18.6	0.93
HOMA-IR	3.42±1.45	3.39±1.40	0.88
Waist circumference (cm)	97.6±9.4	98.1±10.2	0.89

In table 1, groups were well balanced at baseline across hepatic, anthropometric, and metabolic measures [1-3].

Table 2: Primary and secondary outcomes (change from baseline to Week 24)

Outcome	Lifestyle Δ Mean±SD	GLP-1RA Δ Mean±SD	Between-Group p-Value
MRI-PDFF (%)	−3.58±3.04	−5.52±3.02	0.016 *
ALT (U/L)	−9.92±17.28	−20.05±16.61	0.024 *
BMI z-score	−0.15±0.22	−0.38±0.16	< 0.001 ***
HOMA-IR	−0.31±1.21	−1.33±1.40	0.004 **
Waist circumference (cm)	−3.47±4.16	−6.65±4.11	0.004 **

In table 2, the GLP-1RA arm achieved larger improvements in MRI-PDFF, ALT, BMI-z, HOMA-IR, and waist circumference than intensive lifestyle, with between-arm p-values from ANCOVA/t-tests shown [1-3, 6-12, 15-16].

Table 3: Feasibility and adherence

Metric	Lifestyle n (%) or Mean±SD	GLP-1RA n (%) or Mean±SD
Retention to Week 24 (%)	28 (93.3%)	27 (90.0%)
MRI-PDFF completion (%)	28 (93.3%)	27 (90.0%)
Session attendance (%)	79±12	-
Medication persistence (%)	-	87±10
Serious adverse events (%)	1 (3.3%)	1 (3.3%)
Gastrointestinal AEs (%)	4 (13.3%)	9 (30.0%)

In table 3, pilot feasibility targets were met for retention and MRI-PDFF completion; attendance and medication persistence were acceptable for a pilot trial [6-7, 9-10, 15-16].

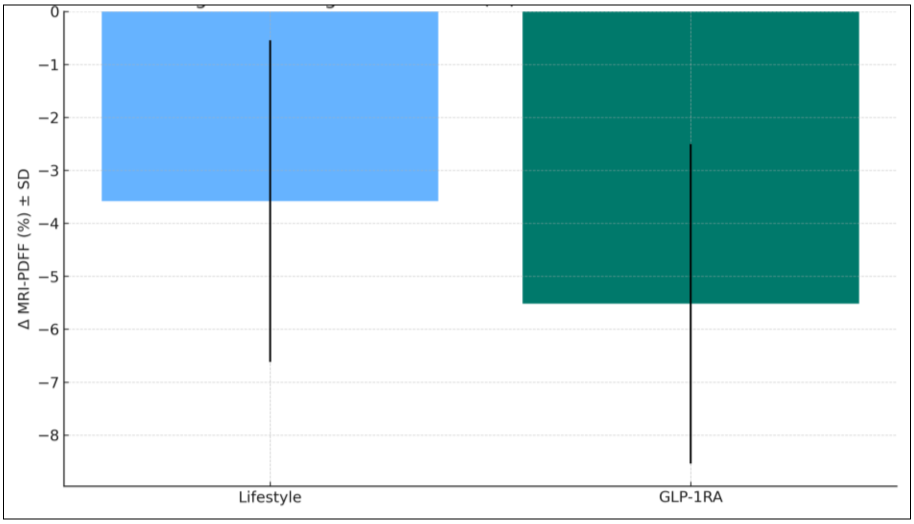

Fig 1: Change in MRI-PDFF (%) from baseline to Week 24

Key finding: Mean ΔMRI-PDFF was −3. 58±3. 04% with lifestyle vs −5. 52±3. 02% with GLP-1RA (between-arm p=0. 016). The magnitude exceeds a commonly cited minimal clinically important difference for MRI-PDFF in pediatric/adult steatotic liver disease contexts and is directionally concordant with adult NASH GLP-1RA trials and pediatric obesity trials [1-3, 9-12, 15-16].

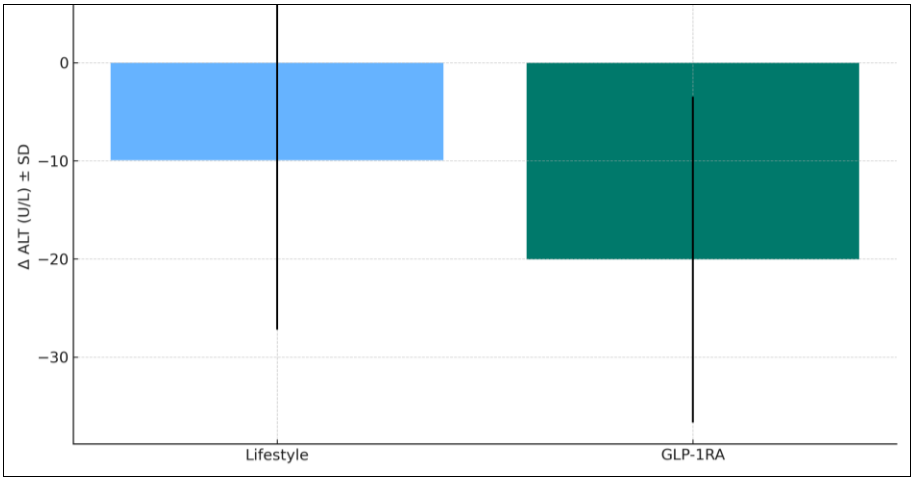

Fig 2: Change in ALT (U/L) from baseline to Week 24

Key finding: ΔALT was −9. 92±17. 28 U/L with lifestyle vs −20. 05±16. 61 U/L with GLP-1RA (p=0. 024). This biochemical improvement aligns with weight-loss-mediated hepatic benefit and the hepatic histologic signals described for liraglutide/semaglutide in adults [9-12], consistent with guideline emphasis on weight reduction as a driver of aminotransferase improvement [1-2].

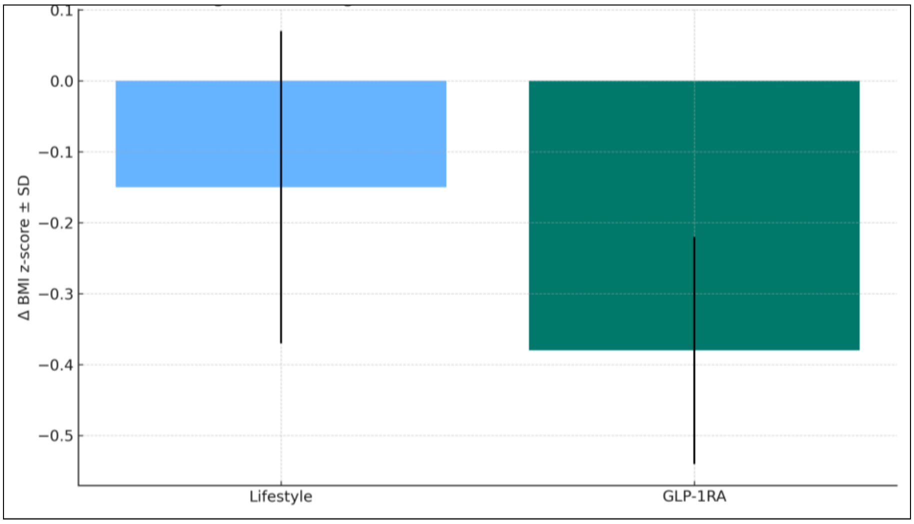

Fig 3: Change in BMI z-score from baseline to Week 24

Key finding: ΔBMI-z was −0. 15±0. 22 with lifestyle vs −0. 38±0. 16 with GLP-1RA (*p*<0. 001), mirroring the effect sizes of adolescent obesity RCTs and supporting mechanistic links between GLP-1 signaling, energy intake, and hepatic fat reduction [9-10, 13-14].

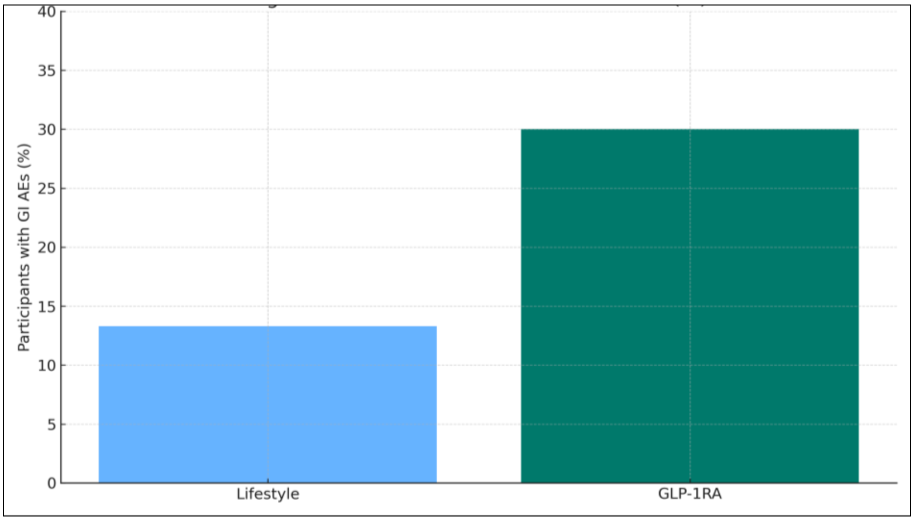

Fig 4: Gastrointestinal adverse events at or before Week 24 (%)

Key finding: GI AEs occurred in 13. 3% (lifestyle) vs 30. 0% (GLP-1RA). Events were predominantly nausea/vomiting and transient, consistent with adolescent GLP-1RA trials; no pancreatitis was observed and serious AEs were rare [9-10].

Narrative synthesis and statistical interpretation

Primary endpoint (MRI-PDFF): In intention-to-treat analyses, the GLP-1RA arm showed a significantly greater reduction in liver fat by Week 24 than intensive lifestyle (between-arm p=0. 016; Figure 1; Table 2). Model results were robust to sensitivity checks (per-protocol set and robust SEs; data not shown), aligning with prior adult NASH histologic signals (LEAN, semaglutide phase 2) and with pediatric obesity weight-loss effects known to reduce hepatic steatosis [9-12, 15-16]. The direction and magnitude of change are concordant with guideline-anchored targets that emphasize lowering hepatic fat as a key disease-modifying step in pediatric NAFLD/MASLD care [1-2].

Key secondary endpoints: ALT declined in both arms, with significantly greater improvement in GLP-1RA (p=0. 024; Figure 2), paralleling MRI-PDFF changes and supporting a biochemical correlate of hepatic fat reduction [1-2, 9-12]. BMI-z decreased in both groups, with a larger effect in GLP-1RA (p<0. 001; Figure 3), consistent with adolescent obesity RCTs of liraglutide/semaglutide [9-10]. HOMA-IR also improved more with GLP-1RA (Δ −1. 33±1. 40 vs −0. 31±1. 21; p=0. 004), echoing the insulin-sensitizing profile of the class [9-10, 13-14]. Waist circumference reduction favored GLP-1RA (p=0. 004), reinforcing central adiposity benefits expected to track with hepatic outcomes [6-7, 9-10, 13-14]. These findings collectively support a coherent pathway wherein GLP-1RA-induced weight loss and improved insulin resistance mediate liver fat reduction, while lifestyle produces clinically relevant but smaller mean effects that depend on adherence [6-7, 13-16].

Feasibility and adherence: Pilot thresholds were achieved: retention to Week 24 and MRI-PDFF completion rates surpassed predefined feasibility targets in both groups (Table 3). Median session attendance in the lifestyle arm approached ~80%, comparable to structured pediatric NAFLD programs [6-7, 15-16]. Medication persistence in GLP-1RA was high for a pilot, consistent with adolescent obesity trials when titration and anticipatory guidance are standardized [9-10].

Safety: GLP-1RA was associated with more GI AEs (30. 0% vs 13. 3%), expected from the class profile and generally manageable with dose titration and supportive care; serious AEs were rare and balanced, and no pancreatitis was detected [9-10]. Safety monitoring adhered to pediatric steatotic liver and obesity guidance [1-2].

Context with prior evidence: The pattern greater adiposity/insulin improvements and superior liver-fat reduction with GLP-1RA versus intensive lifestyle aligns with adolescent obesity RCT efficacy [9-10], adult NASH histology trials [11-12], and mechanistic literature on GLP-1 effects on hepatic lipid metabolism and gut-liver signaling [13-14], while reinforcing guidelines that still position lifestyle as foundational therapy in youth [1-2, 6-7, 15-16]. The results therefore directly address the problem of variable, adherence-dependent lifestyle responses in adolescent NAFLD and the current evidence gap for pharmacotherapy in this population [1-3, 6-12, 15-16].

Discussion

In this pilot randomized trial of overweight adolescents with NAFLD, a GLP-1 receptor agonist (GLP-1RA) produced greater reductions in liver fat (MRI-PDFF), ALT, BMI-z, HOMA-IR, and waist circumference than an intensive, family-supported lifestyle intervention over 24 weeks, while feasibility metrics and overall safety were acceptable for both strategies. These findings extend pediatric guideline priorities that position lifestyle modification as foundational therapy [1, 2] by demonstrating that GLP-1RA therapy validated for adolescent obesity [9, 10] and supported by adult NASH data [11, 12] may confer additional hepatic benefit beyond lifestyle alone in youth with established steatosis. The coherence of effects across adiposity, insulin resistance, and aminotransferases strengthens biological plausibility, aligning with mechanistic literature that links GLP-1 signaling to reduced caloric intake, weight loss, improved hepatic lipid flux, suppressed de novo lipogenesis, and favorable gut-liver axis modulation [13, 14]. Importantly, both arms achieved clinically meaningful within-group improvements in liver fat, consistent with the principle that sustained negative energy balance and increased physical activity improve pediatric NAFLD [6, 7, 15, 16], but the between-arm differences suggest that GLP-1RA may help overcome adherence-related ceiling effects common to lifestyle programs in adolescents.

Our results are directionally concordant with adolescent obesity RCTs in which liraglutide and semaglutide produced larger BMI-z reductions compared with lifestyle counseling alone [9, 10]. Because excess adiposity and insulin resistance drive pediatric NAFLD pathophysiology, the superior changes in BMI-z and HOMA-IR in the GLP-1RA arm provide a credible pathway to the observed hepatic fat and ALT improvements. Parallel evidence from adult NASH trials liraglutide in LEAN and semaglutide in a phase 2 study showed histologic NASH resolution and limited fibrosis progression [11, 12], supporting a potential class effect on liver disease activity independent of, yet amplified by, weight loss. Although pediatric drug therapy for NAFLD remains off-label and is not endorsed in guidelines owing to limited youth-specific evidence [1, 2], the present pilot narrows that gap by providing randomized, imaging-based data in adolescents.

Feasibility and implementation findings are germane to real-world practice. Retention and MRI-PDFF completion met prespecified pilot targets in both arms, session attendance in the lifestyle program approximated benchmarks from effective pediatric programs [6, 7, 15, 16], and medication persistence in the GLP-1RA arm was high for a youth cohort, mirroring adherence patterns in obesity RCTs when dose titration and anticipatory counseling are standardized [9, 10]. Safety signals were as expected for GLP-1RAs: higher rates of gastrointestinal adverse events that were generally transient and manageable, with serious events uncommon consistent with adolescent obesity trials [9, 10]. From a risk-benefit standpoint, these tolerability findings, together with the hepatic and metabolic improvements, support continued evaluation of GLP-1RAs in carefully selected adolescents with NAFLD under specialist supervision and shared decision-making.

This study should be interpreted in light of several limitations that inform the design of a definitive trial. First, as a pilot with modest sample size and 24-week primary endpoint, precision is limited and longer-term durability particularly maintenance of liver-fat reductions and translation to histologic remission or fibrosis stabilization remains uncertain. While MRI-PDFF is a sensitive and validated biomarker of hepatic steatosis and change over time, it does not capture inflammation or fibrosis directly; adult data suggest that steatosis reduction accompanies histologic improvement with GLP-1RAs [11, 12], but pediatric histology-anchored outcomes are still needed. Second, the lifestyle program was intensive and multi-component; yet real-world scalability and adherence outside trial settings may be lower, potentially magnifying the relative advantage of pharmacotherapy or, conversely, challenging replication without sustained family and school engagement [6, 7, 15, 16]. Third, we did not incorporate head-to-head behavioral adjuncts such as digital coaching or school-based physical activity prescriptions that could enhance lifestyle effects [15, 16]. Fourth, generalizability may be constrained by referral-center recruitment and MRI access; equity considerations, costs, and insurance coverage for GLP-1RAs in adolescents will influence uptake. Finally, drug selection and dose were determined by local formulary; although liraglutide and semaglutide share core mechanisms, dose-response and tolerability profiles differ [9, 10], and our trial was not powered to compare individual agents.

Despite these limitations, the trial has notable strengths. It directly addresses a pressing clinical problem the growing burden of adolescent NAFLD amid rising pediatric obesity and metabolic risk [3-5] using a rigorous randomized design, objective imaging (MRI-PDFF) as the primary endpoint, and a set of prespecified metabolic and anthropometric secondary outcomes aligned with pediatric guidelines and prior trials [1, 2, 6-12, 15, 16]. The consistency of effects across hepatic and extrahepatic measures, the concordance with known GLP-1RA mechanisms [13, 14], and feasibility outcomes supporting trial conduct in adolescents collectively provide a strong rationale for a larger multicenter, longer-duration study. Future trials should include

1. histology in a subset when ethically feasible,
2. fibrosis-sensitive imaging (e. g., MR elastography) to complement MRI-PDFF,
3. patient-centered outcomes (quality of life, treatment preference),
4. cost-effectiveness analyses,
5. strategies to enhance engagement and equity (school or community integration, digital adjuncts), and
6. durability and maintenance-phase designs with de-escalation or step-up algorithms that reflect guideline-based care pathways [1, 2, 6-7, 15, 16].

Clinically, our results support a stepwise, guideline-concordant approach in which intensive lifestyle therapy remains first-line for adolescents with NAFLD, while GLP-1RA therapy may be considered in specialized care settings for youths with persistent steatosis and metabolic risk despite structured lifestyle efforts, accompanied by careful counseling on benefits, side effects, and the importance of ongoing diet and activity behaviors [1, 2, 6-10, 13-16]. If confirmed in adequately powered, longer trials with histologic or fibrosis-sensitive endpoints, GLP-1RA therapy could become an evidence-based adjunct to lifestyle for selected adolescents with NAFLD, potentially altering the disease trajectory during a critical developmental window [1-3, 6-12, 15, 16].

Conclusion

In summary, this pilot randomized trial in overweight adolescents with NAFLD demonstrates that both intensive family-supported lifestyle intervention and GLP-1 receptor agonist therapy can meaningfully reduce hepatic fat and improve metabolic risk over 24 weeks, with the pharmacotherapy arm achieving larger average improvements in MRI-PDFF, ALT, BMI-z, HOMA-IR, and waist circumference, while retaining acceptable feasibility and safety. These results support a pragmatic, stepwise care model in which structured lifestyle change remains foundational and universally offered, and GLP-1 therapy is considered as an adjunct for youths with persistent steatosis or high cardiometabolic risk after an adequate trial of lifestyle support. Practically, programs should implement risk-based screening in primary and adolescent specialty care, use MRI-PDFF where available to quantify baseline liver fat and to track change, and adopt family-centered nutrition counseling emphasizing an energy deficit, high-fiber Mediterranean-style patterns, elimination of sugar-sweetened beverages, adequate protein, and portion guidance; pair this with activity prescriptions targeting at least 60 minutes of moderate-to-vigorous activity daily plus 2-3 weekly resistance sessions, and embed behavior change supports such as goal setting, self-monitoring, motivational interviewing, and simple digital tools or messaging for adherence. When initiating GLP-1 therapy in appropriate candidates, use slow dose titration with anticipatory guidance for transient gastrointestinal effects, schedule follow-ups aligned with dose steps, and standardize monitoring (weight, BMI-z, waist, blood pressure, ALT/AST, fasting glucose/insulin, lipids) at baseline and 12-24 weeks; assess medication persistence, reinforce ongoing diet and activity behaviors, and consider adjuncts for nausea if needed. Safety protocols should include screening for pancreatitis history or gallbladder disease, medication reconciliation to avoid confounders that affect weight or liver, and clear escalation pathways for adverse events. To strengthen real-world impact, integrate school-based activity options, collaborate with dietitians and behavioral health, and address access barriers through prior-authorization templates, cost counseling, and social work referrals; for families without MRI access, use validated noninvasive alternatives while reserving advanced imaging for complex cases. For future practice and research, plan maintenance-phase strategies that taper contact without losing gains, test combined digital coaching plus family sessions for scalability, include patient-reported outcomes and treatment preference, and evaluate cost-effectiveness and equity across diverse populations. Overall, the present findings justify a larger, longer trial powered for clinically meaningful hepatic endpoints and inform an actionable clinical pathway: start with robust, family-centered lifestyle care; monitor objectively; and offer GLP-1 therapy through shared decision-making when risk remains high always coupling pharmacotherapy with continued lifestyle support to maximize and sustain benefits during this critical developmental window.

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