Research Square

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Lipid Accumulation Product Correlates with Metabolic Dysfunction- Associated Steatohepatitis: Implications for Hepatic Steatosis in Patients with Obesity

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Abstract

Objectives

The primary objective of this investigation was to rigorously characterize the relationship between LAP and MASH inpatients with obesity.

Methods

This investigation enrolled 259 adults with obesity who had liver biopsies during laparoscopic sleeve gastrectomy. Based on histological grading of steatosis, ballooning, and inflammation, the cohort was divided into MASH and non-MASH subgroups. We systematically collected and compared clinical, anthropometric, obesity-related, and biochemical data across two groups. LAP levels were compared between MASH and non-MASH groups and across different grades of steatosis, ballooning, and inflammation. Binary logistic regression was used to assess the relationship between LAP and MASH presence.

Results

A study of 259 obese adults undergoing sleeve gastrectomy with liver biopsy found 49.03% MASH prevalence. LAP was higher in MASH, differing by steatosis grade but not ballooning or inflammation. Higher LAP tertiles independently linked to MASH risk (Tertile 2 OR 2.11, Tertile 3 OR 2.49). Per SD increase, LAP raised MASH odds by 76%.

Conclusion

Our findings indicate LAP is a key independent predictor of MASH, especially hepatic steatosis severity, supporting its use as a non-invasive tool for early risk stratification and screening.

Introduction

Driven by shifts in modern lifestyles, nonalcoholic fatty liver disease (NAFLD) has emerged as a pervasive global health challenge, affecting roughly one-quarter of adults worldwide and representing the predominant form of chronic liver disease[1]. NAFLD is a metabolic disorder closely linked to obesity, dyslipidemia, diabetes, hypertension and other metabolic comorbidities, and its precise etiology remains incompletely elucidated[2]. Notably, the complex pathogenesis of NAFLD—underlying its progression to liver fibrosis and hepatocellular carcinoma (HCC)—has been described by the "multi-parallel hit" hypothesis, involving key pathways such as insulin resistance, meta-inflammation, and oxidative stress. Significantly, these pathogenic drivers that promote disease progression are strongly associated with obesity.[3]. Consequently, to better capture the fundamental forces propelling this condition, the

terminology of metabolic dysfunction-associated fatty liver disease (MAFLD) has been introduced in recent years[4].

MAFLD represents a dynamic pathological spectrum that can evolve from simple hepatic steatosis into metabolic dysfunction-associated steatohepatitis (MASH), potentially advancing further to liver fibrosis, cirrhosis, and ultimately HCC[5]. As a progressive manifestation of MAFLD, MASH is characterized by chronic hepatic inflammation. Its histological diagnosis requires the concurrent presence of steatosis affecting at least 5% of hepatocytes, hepatocyte ballooning degeneration, and lobular inflammation, irrespective of fibrotic status[6]. Relative to simple hepatic steatosis, MASH confers a significantly elevated probability of deteriorating into end-stage liver conditions, including cirrhosis and HCC, while also correlating with a heightened incidence of cardiovascular events[7]. The clinical presentation of MASH is often insidious, with the majority of patients remaining asymptomatic or exhibiting only vague complaints such as fatigue or mild abdominal discomfort, leading to frequent under-recognition. Consequently, MASH is frequently termed a 'silent killer'. Given its substantial burden on global health and healthcare systems, early diagnosis of MASH is critical to preventing adverse health outcomes. Liver biopsy is the gold standard for diagnosing MASH. However, its invasive nature limits its utility for population screening and long-term follow-up. Therefore, an urgent need persists for cost-effective, accessible, non-invasive strategies suitable for general population assessment.

To develop such non-invasive tools, it is critical to identify key risk factors underlying MASH progression. Extant study has firmly established visceral adiposity and dyslipidemia as primary determinants in the etiology of MAFLD [8, 9]. In the context of abdominal obesity, adipocytes release a diverse of adipokines and cytokines, including leptin, adiponectin, resistin, visfatin, and chemerin[10]. Elevated resistin and leptin levels, coupled with reduced adiponectin levels, are associated with insulin resistance[11]. These adipokines exert a pivotal influence on MAFLD, regulating key stages from steatosis and MASH to cirrhosis and carcinogenesis[12]. Recent investigations indicate that interventions involving probiotics and omega-3 supplementation can ameliorate hepatic enzyme profiles as well as clinical and metabolic parameters in MAFLD cohorts[11, 13, 14]. Moreover, omega-3 fatty acids have been shown to mitigate hepatic steatosis by lowering triglyceride (TG) concentrations, thereby underscoring the pathogenic significance of hypertriglyceridemia in MAFLD development[15]. Concordantly, the escalating global prevalence of MAFLD parallels the rising incidence of obesity[16]. A recent systematic review and meta-analysis reported that 50.7% of overweight or obese adults have MAFLD[17]. Additionally, numerous studies have documented robust associations between MAFLD and various anthropometric metrics, such as body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WHtR)[18, 19]. Given that WC and serum TG are two central correlates of MAFLD pathogenesis [20, 21], composite indices integrating these two parameters may offer improved predictive value for MASH.

Against the unmet need for non-invasive markers for MASH screening, the Lipid Accumulation Product (LAP)—a composite index calculated from WC and TG concentrations—offers a superior reflection of ectopic lipid burden[22]. Accumulating data indicate that LAP functions as a robust predictor for type 2 diabetes, insulin resistance, metabolic syndrome (MetS), and MAFLD within the general population, while

also correlating with cardiovascular event risk[22–25]. In a cross-sectional analysis, Taverna et al. [26] established the high diagnostic precision of LAP for MetS. Considering the well-documented link between MetS and MAFLD reported in prior literature, this finding holds significant clinical relevance. Ebrahimi et al. identified 16 observational studies involving 96,101 participants that explored the association between LAP and NAFLD[27], supporting the notion that LAP—integrating WC and TG—is significantly associated with NASH, particularly in obese populations. Despite this, conflicting evidence exists, with some studies failing to confirm this association.

A 2023 meta-analysis encompassing 16 studies demonstrated that although 14 reported a statistically significant association between LAP and NAFLD, the remaining two studies found no such association[28]. Notably, research specifically examining the LAP-MASH association is limited, especially within obese Chinese cohorts—a significant gap given the elevated MAFLD prevalence in this demographic. Consequently, this study aims to investigate the association between LAP and MASH among patients with obesity[6, 29]. The components of metabolic syndrome include overweight or obesity, elevated arterial blood pressure or hypertension, prediabetes or type 2 diabetes, elevated blood triglycerides, and low high-density lipoprotein cholesterol.

Methods

Participants

This cross-sectional study included 301 individuals with obesity who received laparoscopic sleeve gastrectomy and concomitant intraoperative liver biopsy at the Department of General Surgery, Tianjin Medical University General Hospital, conducted between January 2020 and April 2022. All procedures were performed in strict adherence to the 2019 Chinese Clinical Practice Guidelines for the Surgical Management of Obesity and Type 2 diabetes mellitus (T2DM)[30].

Inclusion criteria

Participants were required to be aged 18 to 60 years, deemed suitable candidates for laparoscopic sleeve gastrectomy, and capable of comprehending and executing informed consent documentation covering both the surgical procedure and the concurrent intraoperative liver biopsy.

Exclusion criteria

Participants were excluded based on the following conditions: (1) age under 18 or over 60 years; (2) obesity attributable to endocrine disorders; (3) weekly alcohol intake surpassing 210 g for males and 140 g for females; (4) prior exposure to medications known to cause liver injury; (5) co-existing diagnoses of viral hepatitis, autoimmune hepatic conditions, hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency, or any other liver pathology with a confirmed cause; (6) unsuitability for

anesthesia or surgical intervention; (7) a record of serious psychiatric disorders; (8) significant impairment of critical organs—including the heart, brain, lungs, liver, or kidneys, or the presence of malignant neoplasms; (9) Refusal to accept the potential risks of surgical complications or to comply with postoperative dietary and lifestyle modifications.

Diagnostic Criteria for Comorbidities

T2DM was diagnosed based on WHO criteria or a previously established diagnosis of diabetes. Hypertension was characterized by a systolic blood pressure (SBP) ≥ 140 mmHg, a diastolic blood pressure (DBP) ≥ 90 mmHg, or current engagement in antihypertensive therapy[31]. Hyperlipidemia was established when total cholesterol (TC) reached ≥ 6.2 mmol/L, TG exceeded ≥ 2.3 mmol/L, low density lipoprotein cholesterol (LDL-C) surpassed ≥ 4.1 mmol/L, high density lipoprotein cholesterol (HDL-C) fell below 1.0 mmol/L, or if there was a recorded history of lipid disorders[32].

Study variables

For every participant, we systematically recorded preoperative clinical characteristics, encompassing demographic variables (age and sex), lifestyle factors (tobacco use and alcohol intake), exposure to hepatotoxic medications, and relevant comorbidities, specifically T2DM, systemic hypertension, and hyperlipidemia. Following an overnight fast, venous blood was drawn to quantify a comprehensive panel of biochemical indices: serum TG, TC, HDL-C, LDL-C, FPG, uric acid (UA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyltransferase (γ-GGT), fasting insulin, and glycated hemoglobin (HbA1c).

Anthropometric assessments encompassed body weight, stature, WC, hip circumference (HC), BMI, and the waist-to-hip ratio (WHR). Weight and height were recorded under standardized conditions, with subjects clad in minimal attire and barefoot. WC was determined via a flexible tape measure positioned at the anatomical midpoint between the inferior margin of the costal arch and the superior aspect of the iliac crest. BMI was derived by dividing body mass in kilograms by the square of height in meters. Notably, WHR was computed as the quotient of WC and height, both expressed in centimeters.

LAP was estimated using sex-specific equations: LAP =[WC(cm) − 65)]×TG concentration(mmol/L) for males; LAP =[WC(cm) − 58)]×TG for females[22].

Liver Biopsy and NASH Diagnosis

Intraoperative liver wedge biopsy was performed during laparoscopic sleeve gastrectomy. Potential complications, including bleeding, pain, and organ perforation, were monitored. Following collection, tissue samples underwent fixation in formalin, paraffin embedding, and standard hematoxylin and eosin (H&E) staining. To eliminate observer bias, all histological sections were assessed by pathologists who remained blinded to clinical data. Liver biopsy tissues were evaluated based on three histopathological

criteria: (1) hepatic steatosis, categorized as grade 0 (< 5%), 1 (5%–33%), 2 (34%–66%), or 3 (> 66%); (2) lobular inflammation, determined by counting necroinflammatory foci at 20× magnification and graded as 0 (absent), 1 (< 2 foci), 2 (2–4 foci), or 3 (> 4 foci); and (3) hepatocyte ballooning, classified as grade 0 (absent), 1 (rare), or 2 (frequent). MAFLD was diagnosed when diagnosed, excluded the excessive alcohol consumption and other defined causes of hepatic steatosis, and at least one criterion of metabolic syndrome was met. The components of metabolic syndrome included overweight or obesity, elevated arterial blood pressure or hypertension, prediabetes or T2DM, elevated TG, and low HDL-C. MASH was diagnosed when hepatic steatosis exceeded 5% in conjunction with both hepatocyte ballooning (≥ grade 1) and lobular inflammation (≥ grade 1)[6, 33].

Statistical analysis

Continuous data exhibiting a normal distribution are summarized as the mean accompanied by the standard deviation (SD), whereas non-normal distributions are characterized by the median alongside the interquartile range (IQR). For categorical parameters, we report absolute counts (n) and corresponding proportions (%). Statistical comparisons for normally distributed continuous variables employed one-way analysis of variance (ANOVA), while the Kruskal-Wallis H test and Dunn's test was utilized for datasets deviating from normality. Differences between categorical groups were assessed via the chi-square test.

To evaluate the association between LAP and MASH, we employed binary logistic regression analyses. Two models were constructed: Model 1 remained unadjusted for any covariates, whereas Model 2 was adjusted for age, gender, BMI, and current smoking. In these models, LAP levels were divided into tertiles, with the lowest tertile serving as the reference category. Additionally, LAP was analyzed as a continuous variable to examine the dose-response relationship, specifically assessing the risk of MASH incidence per SD increment. The strength of these associations was quantified using odds ratios (OR) and 95% confidence intervals (CI).

Statistical calculations and graphing were executed utilizing SPSS Statistics software, version 25.0 (IBM Corp., Armonk, NY, USA)and R software (version 4.2.1, R Foundation). Within this investigation, a two-tailed P-value falling below the 0.05 threshold was designated as the criterion for statistical significance.

Results

Initially, 301 obese individuals scheduled for laparoscopic sleeve gastrectomy accompanied by intraoperative liver biopsy were recruited for this investigation. Following the exclusion of 42 participants, a final cohort of 259 subjects was retained for comprehensive analysis, as delineated in the study flowchart (Fig. 1).

Description of the pathological results from the intraoperative liver biopsy

Figure 2 presents the distribution of MASH and the severity of hepatic steatosis, hepatocyte ballooning, and lobular inflammation. As shown in Fig. 2A, 127 participants were diagnosed with MASH, corresponding to a prevalence of 49.03%. Figure 2B shows the distribution of hepatic steatosis: 47 patients (18.15%) were at grade 0, 67 patients (25.87%) at grade 1, 83 patients (32.04%) at grade 2, and 62 patients (23.94%) at grade 3. Figure 2C shows the distribution of different grades of hepatocyte ballooning with 15 (5.80%), 176 (67.95%), and 68 (26.25%) patients classified as grades 0, 1, and 2, respectively. Figure 2D shows the grading of lobular inflammation, with 119 patients (45.95%) at grade 0, followed by 80 patients (30.89%) at grade 1, 33 patients (12.74%) at grade 2, and 27 patients (10.42%) at grade 3.

Baseline Characteristics of the Study Cohort

Table 1 presents a comprehensive summary of the demographic, anthropometric, clinical, and biochemical profiles of the study population, stratified according to the presence or absence of MASH. Comparative analysis revealed no statistically significant disparities between the NASH and non-MASH cohorts regarding age, gender distribution, or current smoking (all $P > 0.05$). Likewise, key anthropometric parameters, including body weight, BMI, WC and HC, as well as the WHR, remained comparable across both groups (all $P > 0.05$). In terms of obesity-related comorbidities, however, the prevalence of T2DM was markedly elevated in patients with MASH (45.67%) compared to those without the condition (31.06%, $P = 0.016$). Conversely, no significant differences were detected between the two groups concerning the incidence of systemic hypertension or dyslipidemia ($P > 0.05$).

Table 1
Characteristics of the study participants with and without MASH

Clinical characteristics	Total (n = 259)	Non-MASH (n = 132)	MASH group (n = 127)	*P*
Age (years)	31(27–36)	31(26–36)	32(27–36)	0.193
Sex				0.148
Male	71(27.41%)	31(23.48%)	40(31.50%)	
Female	188(72.59%)	101(76.52%)	87(68.50%)	
Current smoking	38(14.67%)	15(11.36%)	23(18.11%)	0.304
Anthropometric indicators				
Body weight (Kg)	114.00(99.50-128.70)	112.90(98.43–124.00)	115.00(101.80–130.00)	0.179
Body mass index (Kg/m^2)	39.38(35.56–44.08)	38.64 (35.51–43.22)	39.68(35.56–44.98)	0.194
Waist circumstance (cm)	119.00(109.00-129.00)	117.50 (108.25–127.00)	121.00 (111.00-131.00)	0.105
Hip circumstance (cm)	126.00(118.00-134.00)	124.00 (116.00-134.00)	127.00(119.00-134.50)	0.146
Waist-hip ratio	0.94(0.90-1.00)	0.93(0.90-1.00)	0.95(0.90-1.00)	0.397
Obesity related comorbidity				
Type 2 diabetes mellitus	99(38.22%)	41(31.06%)	58(45.67%)	**0.016**
Systemic hypertension	82(31.66%)	41(31.06%)	41(32.28%)	0.832
Dyslipidemia	155(59.85%)	73(55.30%)	82(64.57%)	0.128
Biochemistry				
ALT (U/L)	40.00(25.00–75.00)	32.00(19.25–54.75)	53.00(30.00–89.00)	**0.000**

ALB albumin, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *ALKP* alkaline phosphatase, *GGT* gamma-glutamyltransferase, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *LAP* lipid accumulation product

P values < 0.05 are highlighted in bold.

Clinical characteristics	Total (n = 259)	Non-MASH (n = 132)	MASH group (n = 127)	*P*
AST (U/L)	24.00(17.00–41.00)	19.50(15.25–30.75)	33.00(20.00–50.00)	**0.000**
GGT (U/L)	38.00(25.00–55.00)	32.00(21.25–52.75)	44.00(29.00–65.00)	**0.001**
TC (mmol/L)	4.94(4.44–5.45)	4.91(4.36–5.45)	5.00(4.49–5.58)	0.218
TG (mmol/L)	1.87(1.43–2.58)	1.71 (1.36–2.41)	2.06(1.57–2.90)	**0.004**
HDL-C (mmol/L)	1.08(0.96–1.20)	1.10(0.95–1.25)	1.06(0.96–1.13)	**0.039**
LDL-C (mmol/L)	3.27 ± 0.72	3.23 ± 0.74	3.32 ± 0.70	0.275
Uric acid (mmol/L)	434.00 (363.00-505.00)	444.00(367.00-487.0)	420.00(361.25–515.00)	0.631
Fasting plasma glucose (mmol/L)	5.49(4.94–7.04)	5.30(4.82–6.44)	5.80(5.12–7.51)	**0.002**
Fasting blood insulin (uIU/ml)	22.00(16.60–31.10)	20.55(15.33–29.28)	23.60(17.80–34.10)	**0.025**
HbA1c (%)	6.20(5.70-7.00)	5.90(5.60–6.70)	6.40(5.90–7.30)	**0.001**
LAP	113.85(83.52–161.20)	105.51(75.38-143.35)	127.12(96.80-182.28)	**0.001**

ALB albumin, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *ALKP* alkaline phosphatase, *GGT* gamma-glutamyltransferase, *TC* total cholesterol, *TG* triglycerides, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *LAP* lipid accumulation product

P values < 0.05 are highlighted in bold.

Regarding biochemical parameters, participants with NASH demonstrated significantly elevated serum levels of ALT, AST, GGT, TG, FPG, fasting blood insulin,and HbA1c(all $P < 0.05$). Conversely, the NASH cohort presented with significantly diminished HDL-C levels ($P = 0.039$). However, no statistically discernible variations were observed between the two groups concerning TC, LDL-C, or UA concentrations (all $P > 0.05$).

Comparisons of LAP levels between the MASH and nonMASH groups

As shown in Fig. 3A, LAP was markedly elevated in patients with NASH compared to non-MASH group (median [IQR]: 127.12 [96.80-182.28] vs. 105.51 [75.38-143.35], $P = 0.001$). Figure 3B illustrates that the prevalence of MASH increased significantly across the LAP tertiles, rising from 34.5% in the first tertile

to 53.5% in the second, and further to 59.3% in the third tertile (P = 0.003). In contrast, the proportion of participants without MASH showed a corresponding decrease.

Comparison of LAP levels between different grades of hepatic steatosis, ballooning, and intralobular inflammation

As shown in Fig. 4, LAP levels were compared across different grades of hepatic steatosis, hepatocyte ballooning, and lobular inflammation. As shown in Fig. 4A, LAP levels of steatosis Grade 0, 1, 2, and 3 were 82.56 (61.38-114.89), 117.26 (89.45–159.7), 112.88 (92.125–171.89), and 136.5 (102.23-183.56) respectively, showing a statistically significant difference (P = 0.000). As shown in Fig. 4B, LAP levels of hepatocyte ballooning Grade 0, 1, and 2 were 115.6 (81.31-135.04), 112.69 (83.42-162.31), and 119.51 (87.81-164.45) respectively, with no statistically significant difference (P = 0.560). As shown in Fig. 4C, LAP levels of lobular inflammation Grade 0, 1, 2, and 3 were 110.33 (79.48–145.1), 111.36 (95.01-179.95), 129.22 (87.5-180.4), and 124.52 (86.17-165.69) respectively, with no statistically significant difference (P = 0.240).

Associations of LAP levels with the risk of NASH

To rigorously examine the association between LAP and the risk of MASH, we categorized subjects into three groups based on LAP tertiles. Figure 5 presents the resulting ORs alongside their corresponding 95% CIs, which quantify the strength of the association between LAP and MASH risk.

In the crude analysis (Model 1), relative to subjects in the lowest LAP tertile, those in the second and third tertiles exhibited unadjusted ORs for MASH of 2.19 (95% CI: 1.18–4.03) and 2.77 (95% CI: 1.49–5.13), respectively, with a statistically significant trend (P = 0.003). Furthermore, a per-SD increase in LAP was associated with an elevated MASH risk, yielding an OR of 1.89 (95% CI: 1.26–2.83; P = 0.002).

Following adjustment for key confounders, including age, sex, BMI, and current smoking (Model 2), the observed association retained its statistical significance. Relative to individuals in the lowest LAP tertile (Tertile 1), the adjusted ORs for MASH in Model 2 were 2.11 (1.13–3.96) for Tertile 2 and 2.49 (1.31–4.75) for Tertile 3 (P = 0.013). Furthermore, a per-SD increase in LAP corresponded to an OR of 1.76 (95% CI: 1.17–2.64; P = 0.007) for MASH risk.

Discussion

This cross-sectional investigation was designed to elucidate the relationship between the LAP and MASH in patients with obesity. Our data reveal that LAP indices are markedly higher in individuals diagnosed with MASH and exhibit a robust correlation with the extent of hepatic steatosis. These observations are discussed regarding their relevance to MASH pathophysiology and the clinical significance of lipid-driven hepatocellular damage.[34]

Given the widespread global incidence of MAFLD, timely detection and therapeutic intervention are imperative to alleviate its associated disease burden. Nevertheless, the precise etiological factors governing MAFLD development and progression remain incompletely understood. Studies have demonstrated that obesity, particularly abdominal obesity, independently increases the risk of MAFLD[35]. In subjects exhibiting abdominal obesity, accelerated oxidation of glucose and lipids triggers an overproduction of free fatty acids (FFAs). Once FFA levels exceed the buffering capacity of peripheral adipose tissue, hepatic fat accumulation ensues, accelerating the development of insulin resistance (IR) and MAFLD[36]. IR subsequently augments the secretion of very low-density lipoprotein (VLDL) and TG while suppressing HDL-C levels[37, 38]. Furthermore, IR exacerbates MAFLD pathogenesis by stimulating TG hydrolysis within adipose tissue and upregulating de novo lipogenesis in the liver[34]. Visceral adipocytes also generate pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-α, which facilitate macrophage recruitment and sustain chronic, low-grade inflammation[39].Adipocytes concurrently secrete adipokines and chemokines that modulate carbohydrate and lipid metabolism[40]. Sustained inflammation disrupts signaling pathways in immune cells, including T cells (e.g., invariant natural killer T cells), eosinophils, B-regulatory cells (Bregs), and macrophages, thereby promoting IR, hepatic steatosis, and MAFLD progression[15]. Collectively, these findings underscore abdominal obesity and hypertriglyceridemia as central drivers of MAFLD pathogenesis.

Our results revealed that patients with MASH presented a markedly increased incidence of T2DM, accompanied by elevated liver enzymes, triglycerides, and insulin resistance markers such as HOMA-IR. Notably, traditional obesity-related indices, including BMI and WC, showed no significant differences between the MASH and non-MASH groups, highlighting the inadequate ability of conventional metabolic markers to assess metabolic risk.

LAP, derived from WC and TG levels and initially proposed by the National Nutrition Survey[41],provides a more comprehensive assessment of excess lipid accumulation compared with traditional obesity indices. Evidence indicates that LAP surpasses BMI in forecasting diabetes susceptibility[42] while serving as a robust proxy for insulin resistance. Moreover, comparative analyses reveal that LAP exhibits heightened diagnostic precision for MetS relative to BMI, WC, and the WHtR[24, 43].

Collectively, these metabolic disturbances, in conjunction with our LAP data, underscore the pivotal contribution of adipose tissue malfunction and insulin resistance to the pathogenesis of MASH. The strong correlation between LAP and these metabolic parameters further supports its utility as an integrated measure of both lipid accumulation and insulin resistance, offering a more comprehensive assessment of metabolic risk than traditional markers like BMI or WC alone. Driven by these observations, we sought to determine whether LAP could function as a reliable biomarker for the identification of MAFLD.

In recent years, extensive investigations have elucidated the correlation between LAP and MAFLD. Nevertheless, research specifically addressing the link between LAP and MASH, a progressive subtype

of MAFLD, remains limited. Our observation showed that both the prevalence of MASH and the grade of hepatic steatosis increased progressively across LAP tertiles, which aligns with and extends previous studies that have identified LAP as a potent surrogate indicator for visceral adiposity and cardiometabolic vulnerability.

Aligning with our findings, multiple investigations have established the LAP as the most robust predictor for obesity-associated MAFLD, characterized by the highest ORs[18, 44]. Within a Chinese cohort, LAP emerged as a pragmatic metric for both screening and quantifying NAFLD, exhibiting a notably stronger correlation among female subjects[45]. A meta-analysis by Ebrahimi et al. evaluated the diagnostic

efficacy of LAP for NAFLD, reporting a sensitivity of 94% and specificity of 85%[27].

Correspondingly, Wang et al. examined data from the 2017–2020 National Health and Nutrition Examination Survey (NHANES), encompassing 2,878 adults; they observed that every 10-unit elevation in LAP corresponded to a 15% increment in NAFLD risk (OR = 1.15, 95% confidence interval [CI]: 1.11–1.20). Furthermore, LAP displayed superior predictive capability, with an area under the curve (AUC) of 0.794 (95% CI: 0.778–0.810) [46]. A cross-sectional study involving 40,459 participants from southern China also demonstrated a strong association between LAP and NAFLD diagnosis and severity, which is consistent with our findings in a northern Chinese population[47]. Collectively, these previous studies, alongside our current data, substantiate that LAP provides a more feasible and economical approach for clinical assessment of MAFLD and MASH.

However, the relationship between LAP and key histopathological features of MASH-hepatic steatosis, ballooning degeneration, and intra-lobular inflammation remains unclear. In our study, hepatic steatosis grade increased progressively across LAP tertiles. Contrary to our expectations, LAP was not associated with hepatocyte ballooning or lobular inflammation. This critical finding suggests that while LAP is closely linked to the initial stage of hepatic steatosis, it may not reflect the progression to the inflammatory and fibrotic phases of MASH.

In parallel, a single-center cross-sectional investigation involving 178 participants demonstrated a robust positive correlation between LAP indices and the severity of hepatic steatosis (r = 0.61). While multivariate regression models confirmed a significant link between elevated LAP and the occurrence of fatty liver, no such association was detected regarding fibrotic progression[48].Furthermore, a large-scale retrospective cohort comprising more than 2,000 subjects revealed that MetS substantially elevates disease risk; specifically, it increases the probability of hepatosteatosis by up to 36% and hepatic fibrosis by up to 47%, irrespective of the diagnostic criteria applied. Among individual components, central adiposity and hypertriglyceridemia emerged as the most potent independent predictors[49].

This finding aligns with the established understanding that while hepatic steatosis is primarily driven by adipose tissue-derived lipid overflow, the subsequent progression to inflammation and hepatocellular injury involves more complex, multifactorial pathways—including oxidative stress, gut dysbiosis, and

genetic predispositions[36], which are not fully captured by LAP alone. This distinction is clinically relevant, as it suggests that LAP may be particularly valuable for screening the earliest, most prevalent stage of MAFLD, whereas additional biomarkers will be necessary to detect the more advanced, progressive forms of MASH.

Strengths and limitations

This investigation is the first to explore the link between LAP and biopsy-confirmed MASH and grade of steatosis, inflammation, ballooning. However, limitations include its cross-sectional design, modest sample size, and focus on obese individuals. Despite this, it provides critical preliminary evidence for non-invasive MASH diagnostics.

Conclusions

In conclusion, our findings establish the LAP as a robust, independent predictor of both MASH and hepatic steatosis within the obese population scheduled for bariatric intervention. Given its non-invasive characteristics and substantial association with liver fat content, LAP emerges as a valuable instrument for risk stratification and initial screening. Subsequent longitudinal investigations are warranted to elucidate the capacity of LAP in forecasting the evolution of MAFLD toward advanced MASH or fibrosis, while also assessing its viability as a therapeutic target aimed at mitigating hepatic lipid deposition.

Declarations

Data availability Statement

The data supporting the conclusions of this study are available from the corresponding author upon reasonable request.

Authors’contributions

J.X., C.Z., and L.C. designed research, collected clinical data, and wrote the manuscript. B.Y.was involved in clinical data collection and revision of the paper. X.L., and J.Q. designed the study, revised and edited the manuscript paper. Q.H. be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors contributed to the article and approved the submitted version.

Ethics approval and consent to participate

The study was approved by the Tianjin Medical University General Hospital Institutional Review Board (approval number IRB2020 -YX-029-01) with wavier of individual patient consent and performed in

accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Conflict of Interest

The authors declared no conflict of interest.

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Figures

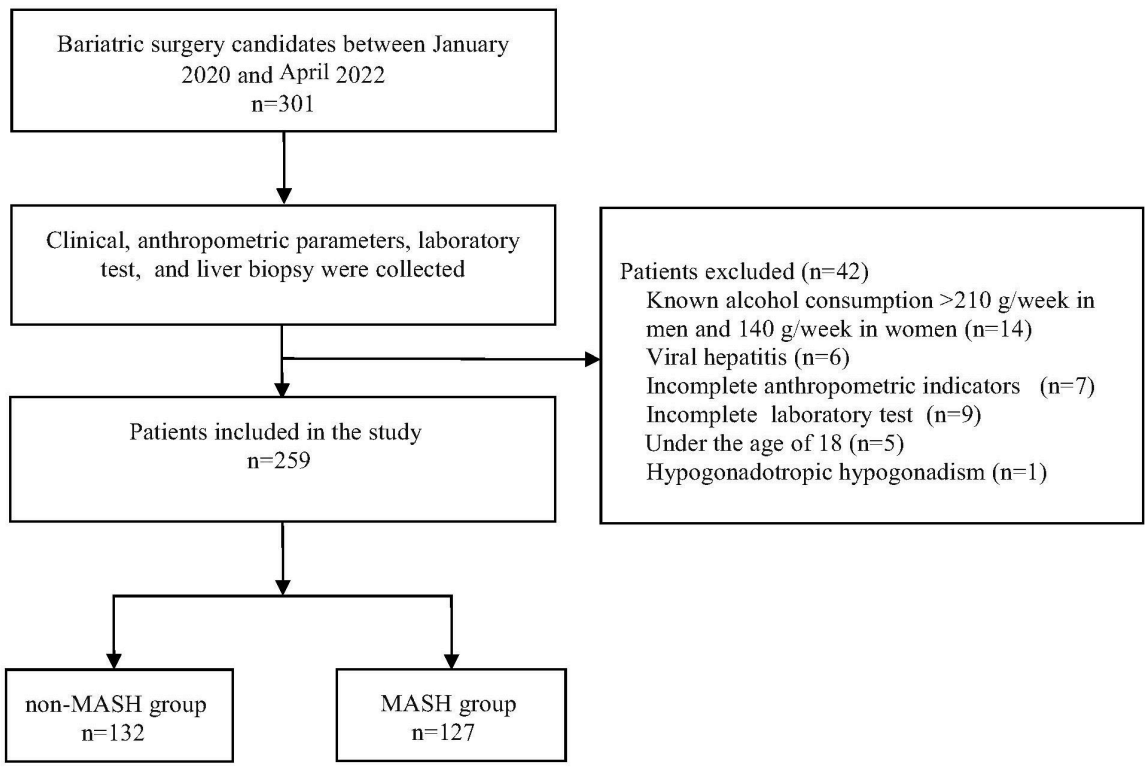


Figure 1

Flowchart of eligible and available patients in the study

MASH, Metabolic Dysfunction-Associated Steatohepatitis

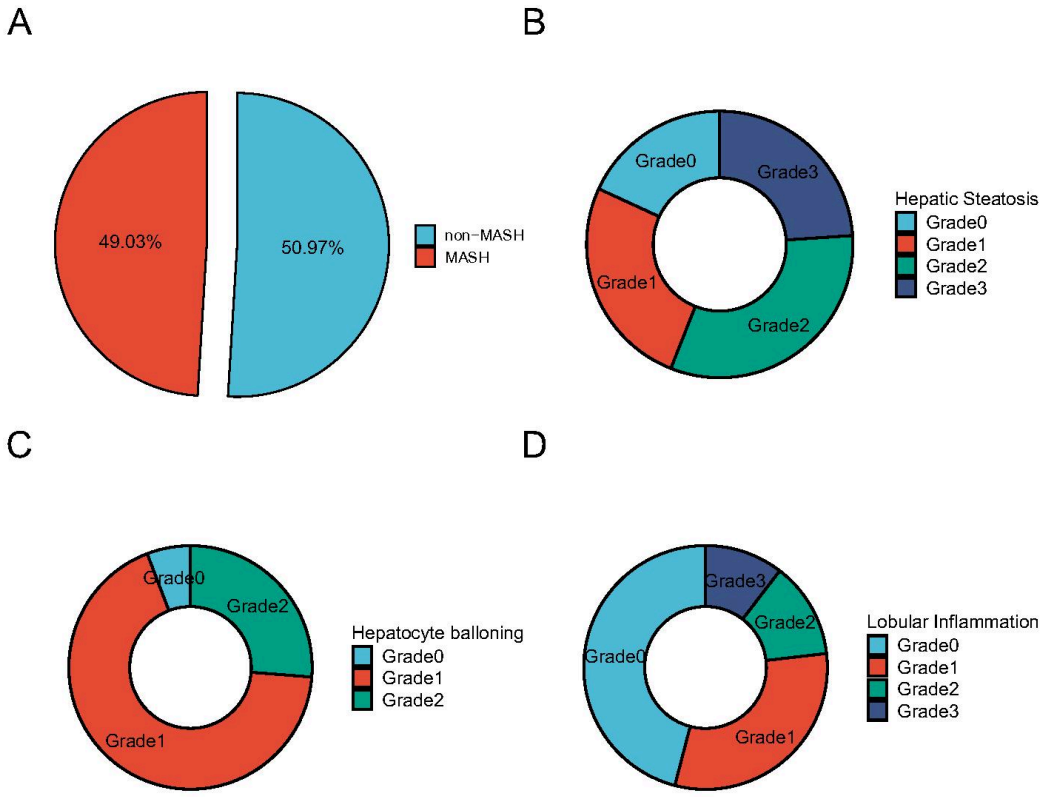


Figure 2

Prevalence of MASH (A) and distribution of hepatocellular steatosis (B), ballooning degeneration (C), and lobular inflammation (D) grading

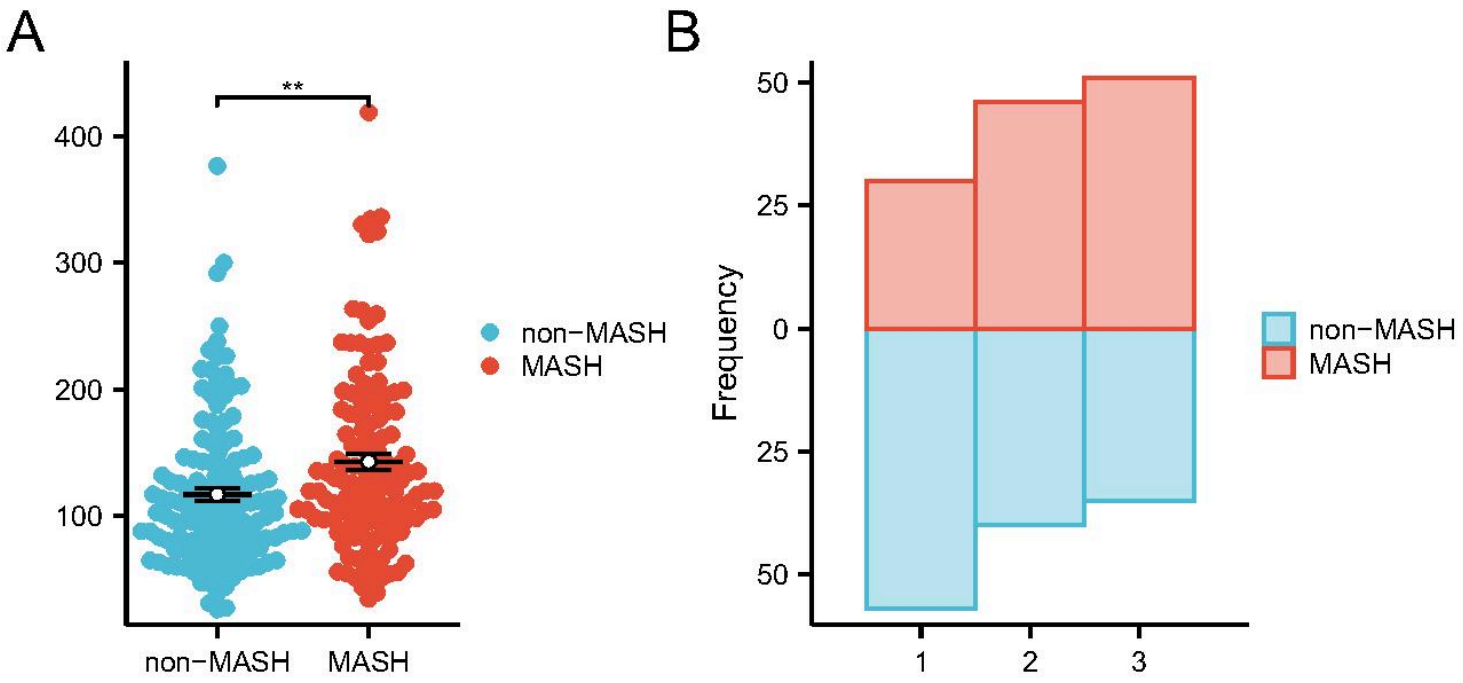


Figure 3

Comparison of LAP Levels in MASH (A) versus non-MASH Groups and MASH Distribution Across LAP Tertiles (B)

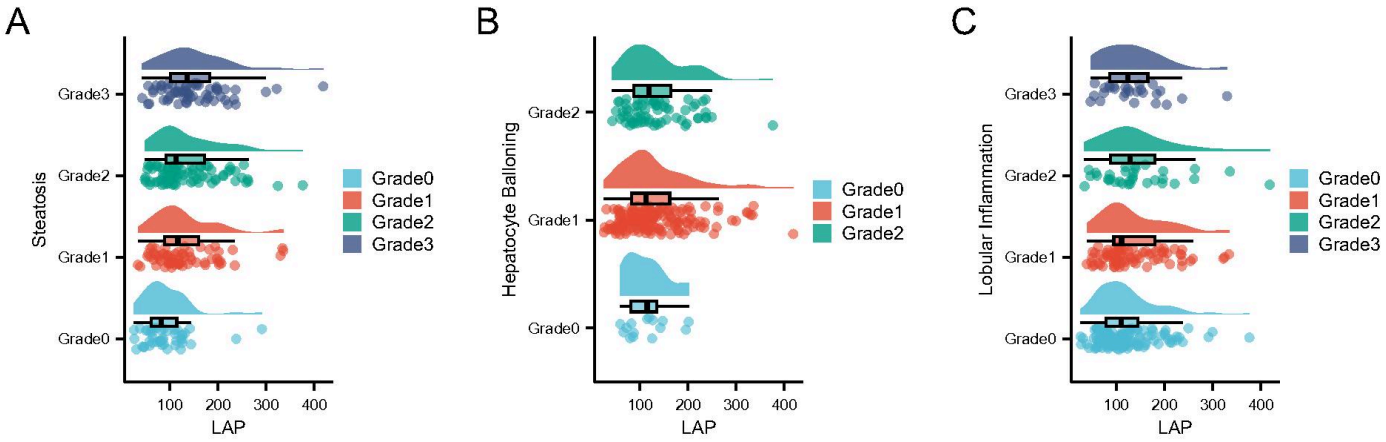


Figure 4

Comparison of LAP Level Among Different Grades of Hepatocellular Steatosis, Ballooning Degeneration, and Intralobular Inflammation

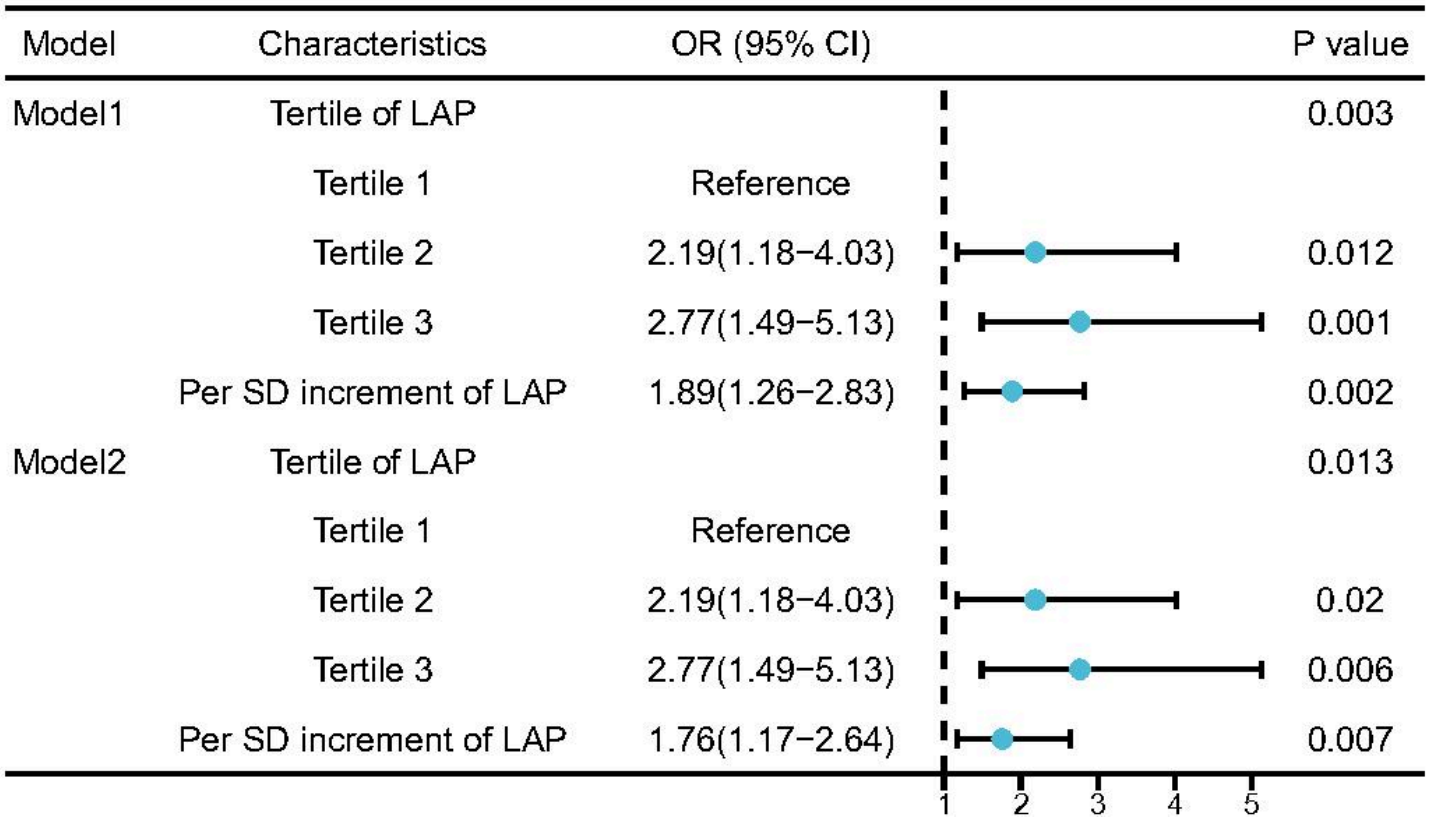


Figure 5

Forest plot of analyses of the association of LAP levels with the risk of MASH

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