

Research Article

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Characteristics of Overweight and Obese Patients with Metabolic Associated Fatty Liver Disease and Predictive Factors for Significant Liver Fibrosis

Tran Thi Khanh Tuong¹, Dao Thanh Duy¹, Au Nhat Huy²

¹Department of General Internal Medicine, Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam.

²Faculty of Medicine, Tan Tao University

Abstract

Background: Overweight and obesity are high-risk groups for developing Metabolic Associated Fatty Liver Disease (MAFLD), with an odds ratio (OR) of 5.5. MAFLD is the second most common cause of hepatocellular carcinoma. Furthermore, using transient elastography, up to 6.41% of overweight and obese patients with MAFLD have significant liver fibrosis, and overweight and obesity are strong predictors of advanced fibrosis, with an increase of over 72%. Therefore, we conducted this study to describe the characteristics and risk factors of significant liver fibrosis in overweight and obese patients with MAFLD, contributing to better management of this patient population.

Methods: A cross-sectional descriptive study was conducted on overweight and obese patients aged 18 years and older who attended the outpatient clinic of 115 People's Hospital from March 2024 to June 2024.

Results: A total of 192 overweight and obese patients were included in the study. Among overweight and obese patients with MAFLD, BMI, glucose, total cholesterol, LDL-c, triglycerides, AST, ALT, GGT, as well as the prevalence of metabolic disorders were significantly higher compared to the non-MAFLD group ($p < 0.05$). Multivariate analysis identified only BMI ≥ 25 kg/m² (OR: 4.17) and coexisting MAFLD (OR: 4.74) as risk factors for significant fibrosis.

Conclusions: Among overweight and obese patients with MAFLD, the prevalence of metabolic disorders, liver stiffness values, and hepatic steatosis were higher compared to those without MAFLD. Coexisting MAFLD and BMI ≥ 25 kg/m² were identified as risk factors for significant liver fibrosis in overweight and obese patients with MAFLD.

Keywords: Metabolic associated fatty liver disease, fibrosis, steatosis, overweight, obesity

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Author contact:

Dao Thanh Duy

Email: dtdtuy12345@gmail.com

Phone: 0907391678

1. INTRODUCTION

Overweight and obese individuals are at high risk of developing Metabolic Associated Fatty Liver Disease (MAFLD) with odds ratios (OR) of 5.5[1], and advanced liver fibrosis with an OR of 4.7[2]. MAFLD is the second most common cause of hepatocellular

carcinoma, accounting for approximately 41%[3]. Zysk's study showed a linear correlation between liver fat content and body mass index (BMI) with $r = 0.7$ [4], and Gopalakrishna also indicated a linear correlation between BMI and liver stiffness with $r = 0.3$ [5]. However, these studies were conducted on patients with non-alcoholic liver disease, excluding

comorbid liver conditions that increase liver fat content and fibrosis, thereby contributing to the increased risk of liver-related mortality.

In Vietnam, liver cancer accounted for 11.7% and ranked second among all cancer causes in 2022. Vietnam is a country with high rates of hepatitis B and hepatitis C infections at 8–19% and 1–3.3%[6], respectively, and 40% of people consume alcohol at levels harmful to health[7]. This leads to an increased risk of liver fibrosis, fatty liver disease, and subsequently hepatocellular carcinoma. Therefore, we conducted this study to describe the characteristics and risk factors of significant liver fibrosis in overweight and obese patients with MAFLD, contributing to better management of this patient population.

Research Objectives

1. To compare clinical and subclinical characteristics between overweight and obese patients with and without MAFLD.
2. To identify risk factors for significant liver fibrosis in overweight and obese patients with MAFLD.

2. STUDY SUBJECTS AND METHODS

2.1. Study Subjects

Overweight and obese patients aged 18 years and older visiting the outpatient clinic of Nhan Dan 115 Hospital between March 2024 and June 2024.

2.2. Inclusion Criteria

Patients aged 18 years and older diagnosed with overweight or obesity according to the criteria for the Asian region based on Body Mass Index (BMI)[8] and diagnosed with Metabolic Associated Fatty Liver Disease (MAFLD).

MAFLD is diagnosed when one of three groups of patients — overweight/obese individuals, patients with type 2 diabetes, or patients with normal or low weight according to BMI but with at least two metabolic risk factors — shows evidence of fatty liver by imaging, biochemistry, or liver biopsy. Therefore, in our study, MAFLD was diagnosed when overweight or obese patients had fatty liver confirmed by FibroScan, using a controlled attenuation parameter (CAP) value of ≥ 236 dB/m[9].

Table 1: Diagnosis of Overweight and Obesity by BMI

| Category | BMI |
|------------|------------------------------------|
| Overweight | BMI: 23.0–24.9 kg/m ² |
| Obesity | BMI: ≥ 25.0 kg/m ² |

2.3. Exclusion Criteria

- Patients who do not agree to participate in the study.
- ALT > 120 U/L, cholestasis, heart failure.
- Ascites, fasting <3 hours, currently taking beta blockers, pregnancy.
- FibroScan result with a success rate <60%, IQR >30%, or skin-to-liver capsule distance >25 mm[10].

2.4. Research Methods

2.4.1. Study Design:

Cross-sectional descriptive study.

2.4.2. Sample Size:

Objective 1

Sample size was calculated using the following formula[11]:

$$n = Z_{1-\alpha/2}^2 \frac{p(1-p)}{d^2} . \text{ Where}$$

n: minimum required sample size

$Z_{(1- \alpha/2)}^2 = 1,96^2$, $\alpha = 0,05$ (Confidence Interval: 95%)

p: prevalence of MAFLD in the overweight and obese adult population.

Given:

$p=0,317$ [12], $d=7,5\% \Rightarrow n \geq 147,8$

Objective 2

According to the study by Zhao et al[13], the authors found 8 risk factors associated with liver fibrosis in patients with type 2 diabetes \Rightarrow sample size for objective 2 is $8 \times 8 = 64$ patients.

Thus, at least 148 overweight and obese adult patients are required.

2.5. Definition of Variables

Hepatitis B Virus (HBV): when the patient has a positive HbsAg[14] or is currently receiving treatment for HBV.

Hepatitis C Virus (HCV): when the patient has a positive anti-HCV and HCV-RNA[15] or is currently receiving treatment for HCV.

Alcoholic Liver Disease: when a patient regularly consumes alcohol $>20\text{g/day}$ for females and $>30\text{g/day}$ for males over 2 years or has a history of alcoholic liver disease[16]

Comorbid MAFLD: when the study patient concurrently has HBV, HCV, or alcoholic liver disease, meeting the above-mentioned criteria[8]

Significant Fibrosis: defined as liver stiffness measurement (LSM) by FibroScan ≥ 7 kPa[17].

Central Obesity: waist circumference ≥ 90 cm for men and ≥ 80 cm for women[8].

Metabolic Syndrome: according to AHA[18], dyslipidemia according to ATP

III[19], type 2 diabetes and impaired fasting glucose according to ADA[20], and hypertension according to ISH[21].

2.6. Data Analysis and Processing

The study was drafted using Microsoft Word. The collected data were managed and processed using SPSS and Microsoft Excel. Quantitative variables were presented as mean and standard deviation for normally distributed data, or median and interquartile range for non-normally distributed data. Qualitative variables were presented as frequencies and percentages. For normally distributed data, quantitative variables were compared using the t-test, and for non-normally distributed data, the Mann-Whitney test was used. Qualitative variables were compared using the Chi-square test.

For Objective 1, the correlation between liver fat content based on CAP values and liver fibrosis degree based on LSM values with BMI was analyzed using linear regression.

For Objective 2, the risk factors for significant liver fibrosis in overweight and obese patients with MAFLD were determined using univariate and multivariate logistic regression analysis.

2.7. Ethical Considerations

The study was approved by the Ethics Committee of Pham Ngoc Thach University of Medicine in November 2023. Patients were only included in the study after giving full voluntary consent and signing the informed consent form.

3. RESULTS

3.1. Comparison of Clinical and Subclinical Characteristics between Overweight and Obese Patients with and without MAFLD

Table 2: Comparison of symptoms between overweight and obese patients with and without MAFLD (n=192)

| Symptom | MAFLD (n=140) | Non-MAFLD (n=52) | p-value* |
|---------------------------------|---------------|------------------|----------|
| Bloating, indigestion, n (%) | 26 (18.6%) | 5 (9.6%) | 0.134 |
| Fatigue, n (%) | 21 (15.0%) | 4 (7.7%) | 0.181 |
| Asymptomatic, n (%) | 86 (61.4%) | 40 (76.9%) | 0.045 |
| Right hypochondrium pain, n (%) | 7 (5.0%) | 1 (1.9%) | 0.685 |
| Other symptoms, n (%) | 16 (11.4%) | 6 (11.5%) | 0.983 |

* Chi-square test.

The proportion of MAFLD patients exhibiting symptoms was higher than that of non-MAFLD patients; however, the difference was not statistically significant ($p > 0.05$).

Table 3: Comparison of clinical and subclinical characteristics between overweight and obese patients with and without MAFLD (n=192)

| Variable | MAFLD (n=140) | Non-MAFLD (n=52) | p-value* |
|---------------------------------|---------------|------------------|----------|
| Age (years) | 53.2 (14.1) | 49.5 (11.7) | 0.099 |
| Male, n (%) | 70 (50.0%) | 31 (59.6%) | 0.236 |
| BMI (kg/m ²) | 25.1 (2.1) | 24.2 (1.3) | <0.001 |
| CAP (dB/m) | 287.2 (36.9) | 190.6 (31.8) | <0.001 |
| LSM (kPa) | 5.6 (2.9) | 4.3 (1.4) | <0.001 |
| Type 2 diabetes, n (%) | 42 (30.0%) | 4 (7.7%) | 0.001 |
| Dyslipidemia, n (%) | 90 (64.3%) | 15 (28.9%) | <0.001 |
| Hypertension, n (%) | 68 (48.6%) | 13 (25.0%) | 0.003 |
| Metabolic syndrome, n (%) | 79 (56.4%) | 7 (13.5%) | <0.001 |
| Central obesity, n (%) | 90 (64.3%) | 21 (40.4%) | 0.003 |
| Impaired fasting glucose, n (%) | 90 (64.3%) | 8 (15.4%) | <0.001 |
| Hypercholesterolemia, n (%) | 26 (18.6%) | 5 (9.6%) | 0.134 |
| Low HDL-c, n (%) | 32 (22.9%) | 10 (19.2%) | 0.589 |
| High LDL-c, n (%) | 58 (41.4%) | 3 (5.8%) | <0.001 |

| | | | |
|------------------------------------|------------|------------|--------|
| High triglycerides, n (%) | 65 (46.4%) | 6 (11.5%) | <0.001 |
| ALT/AST ratio >1, n (%) | 54 (38.6%) | 21 (40.4%) | 0.819 |
| BMI ≥ 25 kg/m ² , n (%) | 72 (51.4%) | 11 (21.2%) | <0.001 |
| HBV infection, n (%) | 32 (22.9%) | 7 (13.5%) | 0.150 |
| HCV infection, n (%) | 7 (5.0%) | 2 (3.9%) | 0.541 |
| Alcoholic liver disease, n (%) | 14 (10.0%) | 3 (5.8%) | 0.272 |

* t-test was used for normally distributed variables and Mann-Whitney test for non-normally distributed variables.

Summary: Overweight and obese patients with MAFLD had higher rates of metabolic-related conditions such as type 2 diabetes, dyslipidemia, hypertension, metabolic syndrome, central obesity, impaired fasting glucose, elevated LDL-c, elevated triglycerides, and BMI ≥25 kg/m² compared to non-MAFLD patients (p < 0.05).

3.2. Risk Factors for Significant Liver Fibrosis in Patients with MAFLD

Table 5: Risk factors for significant liver fibrosis in MAFLD patients in univariate and multivariate analyses (n=140)

| | Univariate Analysis | | Multivariate Analysis | |
|----------------------------|---------------------|----------|-----------------------|----------|
| | OR (95% CI) | p-value* | OR (95% CI) | p-value* |
| Age | 1.1 (0.9–1.1) | 0.215 | | |
| Sex | 0.6 (0.3–1.3) | 0.207 | | |
| BMI ≥ 25 kg/m ² | 7.9 (3.3–18.9) | <0.001 | 4.2 (1.3–13.1) | 0.014 |
| Central obesity | 4.5 (1.8–11.1) | 0.001 | | |
| Hypertension | 4.7 (2.16–10.3) | <0.001 | | |
| Type 2 diabetes | 4.9 (2.2–10.7) | <0.001 | | |
| | OR (95% CI) | p-value* | OR (95% CI) | p-value* |
| Dyslipidemia | 4.5 (1.8–11.1) | 0.001 | | |
| Metabolic syndrome | 7.2 (2.9–17.6) | <0.001 | | |
| Low HDL-c | 1.4 (0.6–3.1) | 0.461 | | |
| High LDL-c | 2.4 (1.1–4.8) | 0.021 | | |
| High triglycerides | 2.9 (1.4–6.2) | 0.004 | | |
| ALT/AST ratio >1 | 1.3 (0.6–2.6) | 0.542 | | |
| Comorbid MAFLD | 5.4 (2.5–11.5) | <0.001 | 4.7 (1.8–12.3) | 0.001 |

* Logistic regression analysis: univariate and multivariate

Summary: In multivariate analysis, only BMI ≥25 kg/m² and comorbid MAFLD were identified as risk factors for significant liver fibrosis with p < 0.001.

4. DISCUSSION

MAFLD is a chronic liver disease, and most MAFLD patients are asymptomatic. If symptoms are present, they are often nonspecific, such as fatigue, bloating, and sometimes right upper quadrant pain[22]. In our study, the majority of patients were asymptomatic, accounting for approximately 61.4%. Following were nonspecific symptoms: fatigue at 15.0%, bloating and indigestion at 18.6%, and right upper quadrant pain at the lowest rate of 5.0%. Our study results are consistent with those of Trần Thị Khánh Tường, who found that most patients were asymptomatic[23]. Therefore, the Asia-Pacific Association for the Study of the Liver (APASL) recommends screening for MAFLD in overweight and obese individuals. Kaya et al. reported a positive correlation between BMI and the controlled attenuation parameter (CAP) measured by FibroScan to assess liver steatosis[24]. Our study also found that MAFLD patients had higher BMIs compared to non-MAFLD patients, consistent with the findings of Yuan et al[25].

Our study recorded that the prevalence of type 2 diabetes in MAFLD patients was 30.0%, higher than in the non-MAFLD group, with a statistically significant difference. These results are consistent with the findings of Limin et al., who reported a 28.1% prevalence. However, our findings are slightly higher than those of Luu Xuân Phát, who reported a prevalence of 25.1%[26]. This discrepancy could be due to differences in the patient selection criteria; Luu Xuân Phát's study diagnosed fatty liver by ultrasound, a method that may introduce operator-dependent variability.

In our study, multivariate analysis identified BMI ≥ 25 kg/m² and comorbid MAFLD (with other liver diseases such as HBV, HCV, and alcoholic liver disease) as risk factors for significant liver fibrosis. Sachar et al., in their study on non-invasive methods for assessing liver fibrosis in MAFLD, found six risk factors for advanced fibrosis: elevated BMI ≥ 25 kg/m² (OR = 5.9, $p < 0.01$), central obesity (OR = 3.5, $p < 0.01$), impaired fasting glucose (OR = 2.5, $p < 0.01$), high triglycerides (OR = 1.9, $p = 0.03$), HCV infection (OR = 14.9, $p = 0.02$), and elevated ferritin (OR = 1.6, $p = 0.05$); ALT > AST ratio (OR = 1.5, $p = 0.04$)[27]. Compared to Sachar's results, our study found only two significant risk factors, which could be explained by our patient population already receiving treatment for hypertension, diabetes, dyslipidemia, and other liver conditions, possibly masking other risk factors. Haifeng et al. studied metabolic risk factors associated with liver fibrosis in MAFLD patients with HBV infection and found that HBV infection increased the risk of advanced fibrosis (OR = 3.1, $p = 0.003$). This result is consistent with our finding that comorbid liver diseases are risk factors for significant liver fibrosis. Huang et al. reported that diabetes was a risk factor for advanced fibrosis in MAFLD when using the FIB-4 score and nonalcoholic fatty liver disease fibrosis score. However, in our study, diabetes was not found to be a risk factor, possibly due to differences in the methods used to assess fibrosis. In Huang et al.'s study, diabetes was found to be a risk factor for liver fibrosis, but it was not identified in our study. This could be explained by differences in the fibrosis assessment methods: their study used the FIB-4 score, which has lower accuracy

compared to our study that used transient elastography (FibroScan)[27, 28]. Additionally, there were differences in study populations; their study included non-obese patients with metabolic disorders and diabetes, while our study only included overweight and obese patients

5. CONCLUSION

In the group of overweight and obese patients with MAFLD, the prevalence of metabolic disorders, liver stiffness, and liver fat content was higher compared to those without MAFLD. Comorbid MAFLD and BMI ≥ 25 kg/m² were identified as risk factors for significant liver fibrosis in overweight and obese patients with MAFLD.

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