Chronic obstructive pulmonary disease and metabolic associated fatty liver disease: prevalence and clinical characteristics

Doan Le Minh Hanh[1*], Au Nhat Huy[2], Le Thuong Vu[3], Tran Thi Khanh Tuong[4]

(1) Faculty of Medicine, Internal Medicine Department, Pham Ngoc Thach University of Medicine

(2) Tan Tao University, Faculty of Medicine, Internal Medicine Department

(3) University of Medicine and Pharmacy at HCMC, Faculty of Medicine, Internal Medicine Department

(4) Pham Ngoc Thach University of Medicine, Faculty of Medicine, Internal Medicine Department

Abstract

Background: Metabolic-Associated Fatty Liver Disease (MAFLD) is affecting approximately 24% of individuals and potentially leading to cirrhosis and hepatocellular carcinoma. This study aims to assess the prevalence of MAFLD in chronic obstructive pulmonary disease (COPD) patients and analyze their clinical characteristics. **Methods:** This cross-sectional descriptive study involved 120 stable COPD patients, using FibroScan to detect fatty liver, applying the 2020 APASL criteria for MAFLD diagnosis. **Results:** The prevalence of MAFLD was 53.3%, with a mean age of 68.9 ± 8.1 years, predominantly male (89.2%). Patients with MAFLD had higher weight, waist circumference, and BMI compared to those without MAFLD ($p<0.05$). Smoking rates were high in both groups, while alcohol consumption was notably higher in the MAFLD group (70.3% vs. 50.0%, $p=0.023$). They also had higher rates of mMRC ≥2 (98.4% vs. 66.1%, $p<0.001$), higher mean CAT scores (19.9 ± 5.1 vs. 14.1 ± 5.2, $p<0.001$), and experienced more exacerbations (68.7% with ≥2 per year). They were more likely to belong to the E group of COPD (89.0% vs. 21.5%, $p<0.001$). They also had higher rates of using reliver and controller medications containing ICS; lower FVC, FEV1, FEF 25-75%, and PEF indices ($p<0.05$); and a higher proportion of patients in GOLD stages 3 and 4 ($p=0.002$). Nearly all COPD patients who had fatty liver detected by FibroScan (98.5%) also had metabolic factors qualifying them for a MAFLD diagnosis. Blood glucose, HbA1c, insulin, and HOMA-IR levels were significantly higher in the MAFLD group ($p<0.05$). **Conclusion:** MAFLD affects 53.3% of COPD patients. It's associated with higher weight, waist circumference, BMI, alcohol use, and inhaled corticosteroids. COPD patients with MAFLD experience more severe respiratory symptoms, poorer lung function, and more frequent exacerbations.

Keywords: *Metabolic-associated fatty liver disease, MAFLD, Chronic obstructive pulmonary disease, COPD, FibroScan, Fatty liver.*

1. BACKGROUND

Metabolic-Associated Fatty Liver Disease (MAFLD) was proposed by an international expert panel in 2020 to replace the term Non-Alcoholic Fatty Liver Disease (NAFLD) and has been included in the diagnostic and treatment guidelines by the Asian Pacific Association for the Study of the Liver (APASL) [1]. MAFLD affects nearly a quarter (24%) of the global population. It is one of the causes leading to cirrhosis and hepatocellular carcinoma (HCC) [2]. By 2030, liver-related deaths are expected to increase by 178%, with an estimated 78,300 deaths by 2030 [3].

Chronic Obstructive Pulmonary Disease (COPD) is one of the top three causes of death worldwide [4]. Although there is recent evidence that the prevalence of fatty liver and liver fibrosis is increasing in COPD patients [5], MAFLD has not been extensively studied in this patient group. Oxidative stress and chronic systemic inflammation, which increase the production of reactive oxygen species and liver inflammation, combined with common risk factors such as aging, smoking, and physical inactivity, are the main mechanisms linking COPD with MAFLD [6].

FibroScan is a non-invasive, rapid, and accurate ultrasound method used to assess the degree of fatty liver and liver fibrosis. This study aims to use FibroScan to determine the prevalence of fatty liver and liver fibrosis in COPD patients and to compare the clinical characteristics between two groups of patients with and without MAFLD.

2. METHODS

Inclusion Criteria: Stable COPD patients who visited the asthma-COPD management unit ofGia Định People's Hospital from June 2023 to June 2024 and agreed to participate in the study.

Exclusion Criteria: Patients were excluded from

**Corresponding Author: Doan Le Minh Hanh. E-mail: hanhdlm@pnt.edu.vn*

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the study if they met any of the following criteria:

• Inability to perform FibroScan due to ascites or BMI >30 kg/m².

• Inaccurate FibroScan results: IQR/med >30%, success rate <60%.

• Presence of intrahepatic and extrahepatic cholestasis, or hepatic congestion due to heart or lung disease as determined by abdominal ultrasound prior to FibroScan.

• Acute hepatitis with AST and ALT levels >5 times the upper limit of normal (35 U/L for men, 25 U/L for women) [7].

• Pregnant or breastfeeding.

Study Design: Cross-sectional descriptive study.

Sample Size: The sample size was estimated using the formula for estimating the prevalence of MAFLD in COPD patients, with the prevalence from the study by Damien Viglino et al [5]: 41.4%. The minimum sample size required was 93 patients.

Study Methods: The FibroScan 530 machine was used to determine the prevalence and degree of fatty liver, applying the diagnostic criteria for MAFLD by the Asian Pacific Association for the Study of the Liver (APASL) in 2020 [1]: MAFLD was diagnosed in patients with fatty liver on FibroScan (≥5% steatosis, S1 or higher) and who met one of the following three criteria [1]:

(1) If BMI ≥23 kg/m²: MAFLD is diagnosed.

(2) If the patient has type 2 diabetes: MAFLD is diagnosed.

(3) If BMI <23 kg/m² and no type 2 diabetes: consider the presence of at least 2 of the following metabolic risk factors for diagnosing MAFLD: **(a)** Waist circumference ≥ 80 cm for women, ≥ 90 cm for men. **(b)** Blood pressure ≥130/85 mmHg or currently on hypertension treatment. **(c)** Plasma triglycerides ≥150 mg/dl (≥1.70 mmol/L) or currently on treatment. **(d)** Plasma HDL-cholesterol < 40 mg/dl (<1.0 mmol/L) for men and <50 mg/dl (<1.3 mmol/L) for women or currently on treatment. **(e)** Prediabetes (defined as fasting glucose 100-125 mg/dL (5.6-6.9 mmol/L), or 2-hour postprandial glucose 140-199 mg/dl (7.8-11.0 mmol/L), or HbA1c 5.7%-6.4%). **(f)** Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) score ≥ 2.5. **(g)** Plasma hs-CRP concentration >2 mg/L.

Data Analysis: Data was processed using SPSS version 26 (IBM SPSS Statistics for Windows, Version 26.0). Quantitative variables were expressed as mean ± standard deviation if normally distributed, or median and interquartile range if not normally distributed. Differences between two means were compared using the unpaired t-test (if normally distributed) or the Mann-Whitney U test (if not normally distributed). Qualitative variables were expressed as frequencies and percentages. Differences between two proportions were compared using the Chi-square test or Fisher's exact test for 2x2 tables where 20% of the cells have an expected frequency <5. A test was considered statistically significant when p<0.05 [8].

Ethics approval: The study was approved by the Ethics Committee of Nhan Dan Gia Đinh Hospital (approval number 79/NDGĐ-HĐĐĐ).

3. RESULTS

General Characteristics of the Study Population

From June 2023 to June 2024, we collected data from 120 COPD patients who met the inclusion criteria and had no exclusion criteria. The mean age was 68.9 ± 8.1 years, with the youngest being 52 years old and the oldest being 93 years old. The majority of patients were male (89.2%). The median body mass index (BMI) was 21.1 kg/m², interquartile range (IQR) 15.6-30.3. The mean waist circumference was 85.7 ± 12.5 cm for men and 87.9 ± 11.8 cm for women (Table 1).

Prevalence of Metabolic-Associated Fatty Liver Disease

Among the 120 COPD patients, 64 (53.3%) had metabolic-associated fatty liver disease (MAFLD). Patients with MAFLD had significantly higher weight, waist circumference, and BMI compared to those without MAFLD (p<0.05)

Smoking and Alcohol Consumption:

Smoking rates were high in both groups but did not show a statistically significant difference (p=0.255). The proportion of patients who consumed alcohol was significantly higher in the MAFLD group compared to the non-MAFLD group (70.3% vs. 50.0%, p = 0.023) (Table 2).

Clinical Characteristics and Pulmonary Function:

Patients with MAFLD had more severe respiratory symptoms, higher CAT scores, and a higher frequency of exacerbations ≥2 per year (p<0.001) (Table 3).

Pulmonary function indices, including FVC, FEV1, FEF 25-75%, and PEF, were all significantly lower in the MAFLD group (p<0.05) (Table 4).

Table 1. Characteristics of Age, Gender, Height, Weight, Waist Circumference, and BMI in COPD Patients with and without MAFLD

Characteristics	Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
Gender				
Male (n,%)	107 (89.2%)	57 (89.1%)	50 (89.3%)	0.969*
Female (n,%)	13 (10.8%)	7 (10.9%)	6 (10.7%)	
Age (years) (mean ± SD, range)	68.9 ± 8.1 (52 - 93)	69.7 ± 8.5 (53 - 90)	67.9 ± 7.5 (52 - 93)	0.236**
Weight (kg) (mean ± SD, range)	55.7 ± 10.1 (36 - 90)	58.0 ± 11.1 (36 - 90)	53.1 ± 8.3 (39 - 70)	0.007**
Waist circumference (cm) (mean ± SD, range)	85.9 ± 12.4 (50 - 112)	91.9 ± 11.7 (65 - 112)	79.1 ± 9.3 (50 - 95)	<0.001**
BMI (kg/m²) (mean ± SD, range)	21.1 (15.6 - 30.3)	21.9 ± 3.4 (15.8 - 28.1)	20.2 ± 3.1 (15.6 - 30.3)	0.005**

*Chi-square test **t-test

Table 2. Smoking and alcohol consumption history in COPD patients with and without MAFLD

Characteristics		Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
Smoking (n,%)		107 (89.2%)	59 (92.2%)	48 (85.7%)	
	Male	104 (86.7%)	57 (89.1%)	47 (83.9%)	0.255*
	Female	3 (2.5%)	2 (3.1%)	1 (1.8%)	
Alcohol consumption (n,%)		73 (60.8%)	45 (70.3%)	28 (50.0%)	
	Male	50 (41.7%)	32 (50.0%)	18(32.1%)	0.023*
	Female	23 (19.1%)	13 (20.3%)	10 (17.9%)	
Daily alcohol intake (n,%)					
<20 g (female)/<30g (male)		63 (52.5%)	37 (57.8%)	26 (46.4%)	0.299#
>20 g (female)/>30g (male)		10 (8.3%)	8 (42.2%)	2 (53.6%)	

*Chi-square test #Fisher's Exact Test

Table 3. COPD History Characteristics in Patients with and without MAFLD

Characteristics	Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
mMRC ≥2 (n,%)	100 (83.3%)	63 (98.4%)	37 (66.1%)	
CAT (mean ± SD, range)	17.2 ± 5.9 (6.0 - 36.0)	19.9 ± 5.1 (10.0 - 36.0)	14.1 ± 5.2 (6.0 - 32.0)	<0.001#
Exacerbations/year ≥2 (n,%)	52 (43.3%)	44 (68.7%)	8 (14.3%)	<0.001*
COPD group (n,%)				
A	20 (16.7%)	1 (1.6%)	19 (33.9%)	
B	31 (25.8%)	6 (9.4%)	25 (44.6%)	<0.001#
E	69 (57.5%)	57 (89.0%)	12 (21.5%)	
Treatment (n,%)				
ICS reliever	37 (30.8%)	27 (42.2%)	10 (17.9%)	0.004*
ICS controller	95 (79.2%)	59 (92.2%)	36 (64.3%)	<0.001*

*Chi-square test #Fisher's Exact Test

Table 4. Spirometry Characteristics in COPD Patients with and without MAFLD

Characteristics (mean ± SD, range)	Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
FVC (L)	2.6 ± 0.7 (0.9 - 5.1)	2.4 ± 0.6 (0.9 - 3.6)	2.7 ± 0.7 (1.4 - 5.1)	0.008**
FEV1 (L)	1.4 ± 0.5 (0.4 - 3.3)	1.3 ± 0.4 (0.4 - 2.2)	1.6 ± 0.5 (0.7 - 3.3)	<0.001**
FEF 25-75% (L/s)	0.7 ± 0.3 (0.2 - 1.9)	0.6 ± 0.3 (0.2 -1.3)	0.8 ± 0.3 (0.3 - 1.9)	0.001**
PEF (L/s)	3.5 ± 1.5 (0.8 - 6.6)	3.1 ± 1.4 (0.8 - 6.6)	3.9 ± 1.3 (1.3 - 6.6)	0.002**
Airflow obstruction (% FEV1) (n,%)				
GOLD 1	22 (18.3%)	7 (10.9%)	15 (26.8%)	0.002#
GOLD 2	57 (47.5%)	27 (42.2%)	30 (53.6%)	
GOLD 3	36 (30.0%)	28 (43.8%)	8 (14.3%)	
GOLD 4	5 (4.2%)	2 (3.1%)	3 (5.4%)	

*Chi-square test #Fisher's Exact Test

Table 5. Comorbidities in COPD Patients with and without MAFLD

Characteristics (n,%)	Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
Hypertension	86 (71.7%)	50 (78.1%)	36 (64.3%)	0.093*
Coronary artery disease	53 (44.2%)	33 (51.6%)	20 (35.7%)	0.081*
Heart failure	15 (12.5%)	10 (15.6%)	5 (8.9%)	0.407#
Type 2 diabetes	36 (30.0%)	25 (39.1%)	11 (19.6%)	0.021*
Dyslipidemia	65 (54.2%)	41 (64.1%)	24 (42.9%)	0.020*
Chronic kidney disease	5 (4.2%)	4 (6.3%)	1 (1.8%)	0.370#

*Chi-square test #Fisher's Exact Test

Hypertension was the most common comorbidity in the study sample, the second was dyslipidemia and coronary artery disease. However, there is no significant difference between MAFLD and non-MAFLD group except type 2 diabetes and dyslipidemia

Table 6. FibroScan Characteristics in COPD Patients with and without MAFLD

Characteristics	Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
CAP (dB/m) (mean ± SD, range)	233.3 ± 58.7 (100 - 365)	277.3 ± 34.2 (234 - 365)	183.0 ± 35.7 (100 - 245)	<0.001**
Steatosis degree				
S0 (< 234)	55 (45.8%)	0 (0%)	55 (98.2%)	<0.001*
S1 (234-269)	35 (29.2%)	34 (53.1%)	1 (1.8%)	
S2 (270-300)	13 (10.8%)	13 (20.3%)	0 (0%)	
S3 (≥ 301)	17 (14.2%)	17 (26.6%)	0 (0%)	
Total steatosis cases on FibroScan (S1, S2, S3)	65 (54.2%)	64 (98.5%)	1 (1.5%)	
Liver stiffness (kPa) (median, IQR)	5.0 (3.9 - 5.9)	5.2 (4.2 - 6.1)	4.8 (3.7 - 5.5)	0.045***
Fibrosis degree				
F0-1 (< 7.0)	109 (90.8%)	58 (90.6%)	51 (91.1%)	0.354#
F2 (7.0-8.6)	4 (3.3%)	1 (1.6%)	3 (5.4%)	
F3 (8.7-11.4)	3 (2.5%)	3 (4.7%)	0 (0%)	
F4 (≥ 11.5)	4 (3.3%)	2 (3.1%)	2 (3.6%)	

*Chi-square test **t-test ***Mann-Whitney U test #Fisher's Exact Test

The MAFLD group had significantly higher mean CAP (277.3 ± 34.2 dB/m) compared to the non-MAFLD group (183.0 ± 35.7 dB/m), p<0.001. Almost patients (64/65 cases) had steatosis on FibroScan were MAFLD, only 1 patient had fatty liver (S1) without MAFLD. In terms of liver stiffness, the median value in the MAFLD group was also higher (5.2 kPa) compared to the non-MAFLD group (4.8 kPa), p=0.045. However, there was no statistically significant difference in the degree of liver fibrosis between the two groups (p=0.354), although the MAFLD group had a higher proportion of severe liver fibrosis (F2-F4) (Table 6).

Table 7. Blood Biochemistry Characteristics in COPD Patients with and without MAFLD

Laboratory tests	Total (n=120)	MAFLD (n=64)	Non-MAFLD (n=56)	p
Glucose fasting (mmol/L) (mean ± SD, range)	6.0 ± 1.7 (3.3 - 15.9)	6.2 ± 1.8 (3.4 - 15.9)	5.8 ± 1.5 (3.3 - 12.8)	0.022***
HbA1c (%) (mean ± SD, range)	6.0 ± 0.9 (4.4 - 12.6)	6.1 ± 1.1 (4.4 - 12.6)	5.9 ± 0.6 (4.4 - 7.4)	0.027***
Urea (mmol/L) (mean ± SD, range)	5.4 ± 1.6 (2.6 - 10.7)	5.7 ± 1.7 (2.6 - 10.7)	4.9 ± 1.4 (2.6 - 9.6)	0.471***
Albumin (g/L) (mean ± SD, range)	41.9 ± 3.0 (34.1 - 47.9)	42.0 ± 3.3 (34.1 - 47.8)	41.9 ± 2.7 (34.1 - 47.9)	0.805**
Protein (g/L) (mean ± SD, range)	73.6 ± 5.2 (60.0 - 91.7)	73.3 ± 5.2 (60.0 - 91.7)	73.9 ± 5.3 (65.3 - 87.5)	0.563**
Creatinine (µmol/L) (median, IQR)	90.6 (81.2 - 101.3)	94.4 (82.6 - 104.3)	88.5 (79.3 - 91.7)	0.141***
AST (U/L) (median, IQR)	24.25 (21.6 - 30.3)	24.5 (22.0 – 30.2)	23.9 (21.3 - 30.8)	0.593***
ALT (U/L) (median, IQR)	21.4 (15.4 - 30.2)	23.0 (17.2 - 35.4)	19.3 (13.1 - 29.8)	0.055***
GGT (U/L) (median, IQR)	35.7 (25.4 - 58.1)	37.2 (27.1 - 80.3)	32.7 (24.7 - 52.2)	0.068***
CRP-hs (mg/L) (median, IQR)	3.6 (1.3 - 6.3)	4.0 (1.9 - 6.5)	3.4 (1.2 - 5.8)	0.461***
Cholesterol (mmol/L) (median, IQR)	4.9 (3.9 - 5.8)	5.1 (3.8 - 5.9)	4.8 (4.2 - 5.8)	0.691***
Triglycerides (mmol/L) (median, IQR)	1.5 (1.1 - 2.0)	1.6 (1.3 - 2.2)	1.4 (1.1 – 1.9)	0.060***
HDL-c (mmol/L) (median, IQR)	1.4 (1.1 - 1.5)	1.3 (1.1 - 1.5)	1.4 (1.1 -1.6)	0.455***
LDL-c (mmol/L) (median, IQR)	3.0 (2.4 - 3.6)	3.2 (2.4 - 3.7)	2.8 (2.3 - 3.5)	0.355***
Insulin (µU/mL) (median, IQR)	7.7 (5.1 - 12.3)	9.9 (6.7 - 15.8)	5.8 (4.3 - 8.6)	0.001***
HOMA-IR (median, IQR)	1.9 (1.1 - 3.5)	2.9 (1.7 - 5.1)	1.5 (0.8 - 2.0)	0.001***

**t-test ***Mann-Whitney U test

There were differences between the two groups in most blood biochemistry indicators: the MAFLD group had higher mean or median values. In particular, glycemia, HbA1c, insulin, and HOMA-IR levels were significantly higher in the MAFLD group (p<0.05); other indicators such as creatinine, eGFR, AST, ALT, GGT, and blood lipids did not show significant differences between the two groups (p>0.05) (Table 7). The median hs-CRP level of 3.6 mg/L (IQR 1.3 - 6.3), with the MAFLD group having a

value of 4.0 mg/L (IQR 1.9 - 6.5) and the non-MAFLD group 3.4 mg/L (IQR 1.2 - 5.8).

4. DISCUSSION

General Characteristics of the Study Population

The study population had a mean age of 68.9 ± 8.1 years, with a predominance of male patients (89.2%). The median body mass index (BMI) was 21.1 kg/m², with an interquartile range (IQR) of 15.6 - 30.3. Waist circumference averaged 85.7 ± 12.5 cm in men and 87.9 ± 11.8 cm in women. These characteristics were compared to the findings of Damien Viglino et al. [5] which analyzed 111 COPD patients. Their study reported a younger mean age of 63.8 ± 8.7 years, a lower male predominance (77.5%), and a higher mean BMI of 25.1 ± 4.5 kg/m². This comparison reveals notable demographic and physiological differences. Specifically, our population was older, had a higher proportion of male patients, and a lower mean BMI. These distinctions may reflect variations in disease burden, healthcare access, or population characteristics across studies, providing context for interpreting outcomes and developing tailored interventions.

Prevalence of Metabolic-Associated Fatty Liver Disease

Among 120 COPD patients, 64 (53.3%) were diagnosed with metabolic-associated fatty liver disease (MAFLD), a prevalence notably higher than the 41.4% reported by Damien et al. [5], for non-alcoholic fatty liver disease (NAFLD). This disparity likely stems from differences in diagnostic criteria and patient inclusion. Damien's study focused on individuals with low alcohol consumption (less than 20 g/day for men and 30 g/day for women) and employed abdominal ultrasound alongside FibroMax tests, including FibroTest, SteatoTest, and NashTest, to exclude other causes of steatosis and assess liver conditions such as steatohepatitis (NASH) and fibrosis.

In contrast, our study diagnosed MAFLD using FibroScan to detect fatty liver, combined with metabolic disorder criteria, irrespective of alcohol use or other liver diseases. Since MAFLD relies on "positive criteria" rather than exclusion, it encompassed more patients, resulting in the observed higher prevalence. These findings underscore the critical need to address MAFLD in COPD management.

Comparison of Clinical and Laboratory Characteristics Between COPD Patients with and without MAFLD

The mean age difference between the MAFLD and non-MAFLD groups was not statistically significant (p=0.236), and the proportion of males was comparable in both groups. This suggests that age and gender do not serve as distinguishing factors between patients with and without MAFLD. However, the MAFLD group exhibited significantly higher mean values for weight, waist circumference, and BMI compared to the non-MAFLD group, with differences reaching statistical significance (p<0.05). These findings align with those reported by Damien Viglino et al. [5] who also identified a strong association between demographic factors such as weight, waist circumference, and BMI and the presence of fatty liver. This emphasizes the role of metabolic and anthropometric parameters in the development of MAFLD, reinforcing the importance of addressing these factors in COPD patients at risk for fatty liver disease.

Smoking and alcohol consumption history in COPD patients with and without MAFLD

The smoking rates in both groups were relatively high and did not show a significant difference (p=0.255). The proportion of patients who consumed alcohol in the MAFLD group (70.3%) was significantly higher than in the non-MAFLD group (50.0%) (p=0.023). However, there was no significant difference in high or low alcohol consumption between the two groups (p=0.299) (Table 2). Smoking and alcohol consumption are risk factors for MAFLD in the general population and in COPD patients. This indicates the need to control these risk factors to reduce the likelihood of developing MAFLD in COPD patients.

COPD History Characteristics in Patients with and without MAFLD

The MAFLD group had a higher proportion of patients with mMRC ≥2 and higher mean CAT scores (p<0.05), indicating more severe respiratory symptoms. The MAFLD group also experienced more frequent exacerbations (68.7% with ≥2 exacerbations/year) and a higher proportion belonged to the E group (89.0% vs. 21.5%, p<0.001), indicating greater severity. The proportion of patients treated with ICS relievers and controllers was also higher in the MAFLD group (p<0.05) (Table 3). These findings are consistent with the study by Damien [5] which showed that COPD patients had more severe symptoms and more frequent exacerbations when NAFLD was present.

The MAFLD group had lower FVC, FEV1, FEF 25-75%, and PEF indices compared to the non-MAFLD group, with statistically significant differences (p<0.05). Obstruction severity also differed significantly between the two groups, with a higher

proportion of patients in GOLD stages 3 and 4 in the MAFLD group. These results are consistent with the report by Jae-Uk Song et al. [9], which indicated that reduced lung function is a risk factor for developing NAFLD in more than half a million middle-aged individuals in South Korea. A Mantovani et al. [10] also pointed out that NAFLD is associated with a significant reduction in both FEV1 and FVC in Asian and American adults.

The prevalence of type 2 diabetes and dyslipidemia in the study sample was 30% and 41%, respectively, higher than in the study by Damien [5] (15.3% and 40.5%). The prevalence of hypertension in the author's study was 47.7%, lower than in our study. The difference could be due to Damien's strict selection criteria, excluding cases of COPD with heavy alcohol consumption or comorbid liver diseases. Therefore, their study population may not include all patients with metabolic factors as in our study. In general, COPD with MAFLD is associated with more cardiovascular-metabolic comorbidities.

FibroScan Characteristics in COPD Patients with and without MAFLD

The MAFLD group had significantly higher mean CAP (277.3 ± 34.2 dB/m) compared to the non-MAFLD group (183.0 ± 35.7 dB/m), p<0.001. Almost all patients (64/65 cases) had steatosis on FibroScan were MAFLD, only 1 patient had fatty liver (S1) without MAFLD, indicating that most COPD patients with fatty liver also had metabolic factors and met the criteria for MAFLD diagnosis. In terms of liver stiffness, the median value in the MAFLD group was also higher (5.2 kPa) compared to the non-MAFLD group (4.8 kPa), p=0.045, indicating increased liver fibrosis in the MAFLD group. However, there was no statistically significant difference in the degree of liver fibrosis between the two groups (p=0.354), although the MAFLD group had a higher proportion of severe liver fibrosis (F2-F4) (Table 6)

Blood Biochemistry Characteristics in COPD Patients with and without MAFLD

There were differences between the two groups in most blood biochemistry indicators: the MAFLD group had higher mean or median values. In particular, glycemia, HbA1c, insulin, and HOMA-IR levels were significantly higher in the MAFLD group (p<0.05); other indicators such as creatinine, eGFR, AST, ALT, GGT, and blood lipids did not show significant differences between the two groups (p>0.05) (Table 7). This suggests that most MAFLD patients in the study primarily had fatty liver accompanied by glucose metabolism disorders and insulin resistance rather than lipid metabolism disorders. The systemic inflammation status of the study population was reflected in the median hs-CRP level of 3.6 mg/L (IQR 1.3 - 6.3), with the MAFLD group having a value of 4.0 mg/L (IQR 1.9 - 6.5) and the non-MAFLD group 3.4 mg/L (IQR 1.2 - 5.8). Although the difference between the two groups was not statistically significant, the median hs-CRP levels in both the study population and the individual groups were greater than 2 mg/L, indicating chronic inflammation in COPD patients. This is associated with an increased risk of cardiovascular disease, including coronary artery disease and stroke, as well as worse COPD outcomes [11].

5. CONCLUSION

The prevalence of metabolic-associated fatty liver disease (MAFLD) in patients with chronic obstructive pulmonary disease (COPD) is high, accounting for more than half of the patients (53.3%). Factors such as higher weight, waist circumference, BMI, alcohol consumption, and the use of inhaled corticosteroids (ICS) are associated with the presence of MAFLD. COPD patients with MAFLD have more severe respiratory symptoms, poorer lung function, and more frequent exacerbations.

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