Heliyon 9 (2023) e22391

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Increased detection rates of advanced colorectal adenoma in women with metabolic dysfunction-associated fatty liver disease

Yan Gong [a,1], Juan Kang [b,1], Xinyan Wang [c,d], Yansong Zheng [a], Ying Sui [e,**], Wenping Lu [f,*]

[a] Department of Health Medicine, The Second Medical Center and National Clinical Research Center for Geriatric Disease, Chinese PLA General Hospital, China
[b] Department of Emergency, The Second Medical Center & National Clinical Research Center for Geriatric Disease, Chinese PLA General Hospital, China
[c] Chinese PLA Medical School, China
[d] China Unit 93658 of the PLA, No. 1, China
[e] The 6th Health Department, Second Medical Center & National Clinical Research Center for Geriatric Diseases, Chinese People's Liberation Army General Hospital, Beijing, China
[f] Faculty of Hepatopancreatobiliary Surgery, First Medical Center, Chinese PLA General Hospital, China

ARTICLE INFO

Keywords:
Adenoma
Advanced adenoma
Neoplasm
Metabolic dysfunction
MAFLD

ABSTRACT

Background: Metabolic dysfunction-associated fatty liver disease (MAFLD) is a new concept with its own diagnostic criteria. There are few studies on its relationship with colorectal adenoma.
Objective: This study aimed to explore the relationship between MAFLD and colorectal adenoma and to compare the predictive value of MAFLD with other risk factors.
Methods: A total of 4436 consecutive physical examination subjects were enrolled. They all underwent colonoscopy and abdominal ultrasound. MAFLD was diagnosed by both fatty liver disease and metabolic dysfunction. The correlation between colorectal adenoma and MAFLD was studied using a logistic regression model. **Results**: The prevalence of MAFLD was 31.72 % (1407/4436). The adenoma detection rate in MAFLD patients was higher than that in controls (13.50 %, 190/1407 vs. 10.70 %, 324/3029, $p < 0.001$). Univariate analysis indicated that MAFLD individuals were 1.303-fold as likely to have colonic adenoma as controls [odds ratio (OR) 1.303 and 95 % confidence interval (CI), 1.076–1.578, $p = 0.007$]. Multivariate analysis showed that age, male sex, BMI and smoking were positively associated with the risk of colorectal adenoma, with OR values of 1.044 (95 % CI, 1.031 to 1.058), 1.720 (95 % CI, 1.221 to 2.424), 1.046 (95 % CI, 1.009 to 1.085) and 1.342 (95 % CI, 1.072 to 1.680), respectively. MAFLD in women, but not in men, had an independent relationship with increased detection of advanced adenoma (OR 3.932, 95 % CI, 1.023–15.1117, $p = 0.046$).
Conclusion: Individuals with MAFLD are more likely to develop colorectal adenoma than those without MAFLD. The influence of MAFLD on advanced colorectal adenoma was especially prominent in females.

* Corresponding author. Faculty of Hepatopancreatobiliary Surgery, First Medical Center, Chinese PLA General Hospital, Beijing, 100853, China.
** Corresponding author.
E-mail addresses: entsyy@163.com (Y. Sui), lvwenping301@126.com (W. Lu).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2023.e22391
Received 27 April 2023; Received in revised form 9 November 2023; Accepted 10 November 2023
Available online 16 November 2023

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) is one of the most prevalent chronic liver diseases. The global prevalence of NAFLD is approximately 25 %. Its prevalence appears to be continually increasing, with an estimated 3.6 million new cases each year [1]. NAFLD is a continuum of liver diseases, starting from simple steatosis (NAFL) and gradually progressing to nonalcoholic steatohepatitis (NASH), which can progress to liver fibrosis, cirrhosis and even hepatocellular carcinoma [2]. As NAFLD is a disease caused by excessive fat accumulation in the liver closely related to metabolic dysfunction, which excludes alcohol and other diseases, a recent consensus among international experts has proposed NAFLD as a change of nomenclature for metabolic dysfunction-associated fatty liver disease (MAFLD) [3,4], reflecting the significant overlap between NAFLD and MAFLD populations. The epidemiological and clinical significance of this important nomenclature change remains to be determined.

Colorectal cancer (CRC) ranks fifth in global cancer incidence, with an estimated 1.88 million new cases in 2020 [5]. The incidence rate varies widely across the world. In recent years, CRC incidence in China has been on the rise due to improved living standards, changes in lifestyle and the growing elderly population [6]. Most CRCs develop from benign polyps (adenoma and serrated polyps) through a series of genetic and epigenetic changes over a period of approximately 10–15 years. Advanced adenoma is a precancerous lesion that includes adenomatous polyps greater than 10 mm in diameter and/or the pathological presence of villous structures and/or highly atypical hyperplasia [7].

Both MAFLD and colorectal neoplasms share inflammation-promoting factors [8]. They are also associated with other extrahepatic diseases, such as obesity, type 2 diabetes mellitus (T2DM) and metabolic syndrome (MS) [8.9]. Therefore, there might be a link between MAFLD and colorectal neoplasms [9]. A network meta-analysis reported that colorectal neoplasms increased with MAFLD progression from simple steatosis to severe MAFLD [10]. However, few studies have investigated the risk of colorectal neoplasms in MAFLD patients by sex. A recent study suggested that NAFLD increases the risk of colorectal polyps in men but not in women [11]. Another study conducted in Korea reported that MAFLD had a strong relationship with colorectal adenoma only in females [12]. The underlying mechanism would be a decrease in estrogen, resulting in the transfer of fat deposits to visceral organs and leading to metabolic complications. Thus, the results on MAFLD and colorectal adenocarcinoma have been inconsistent.

Different lifestyles and living environments can affect adenoma and MAFLD. Although some studies have been performed to evaluate the association between colon adenoma and MAFLD, few related studies in the Chinese Han population have been reported. In the present study, we explored the relationship between MAFLD and colonic adenoma in a Chinese population seen for regular physical examinations. We also compared the relationship of adenoma with MAFLD in both men and women. We aimed to provide real-world evidence for the association between MAFLD and colonic neoplasms in China.

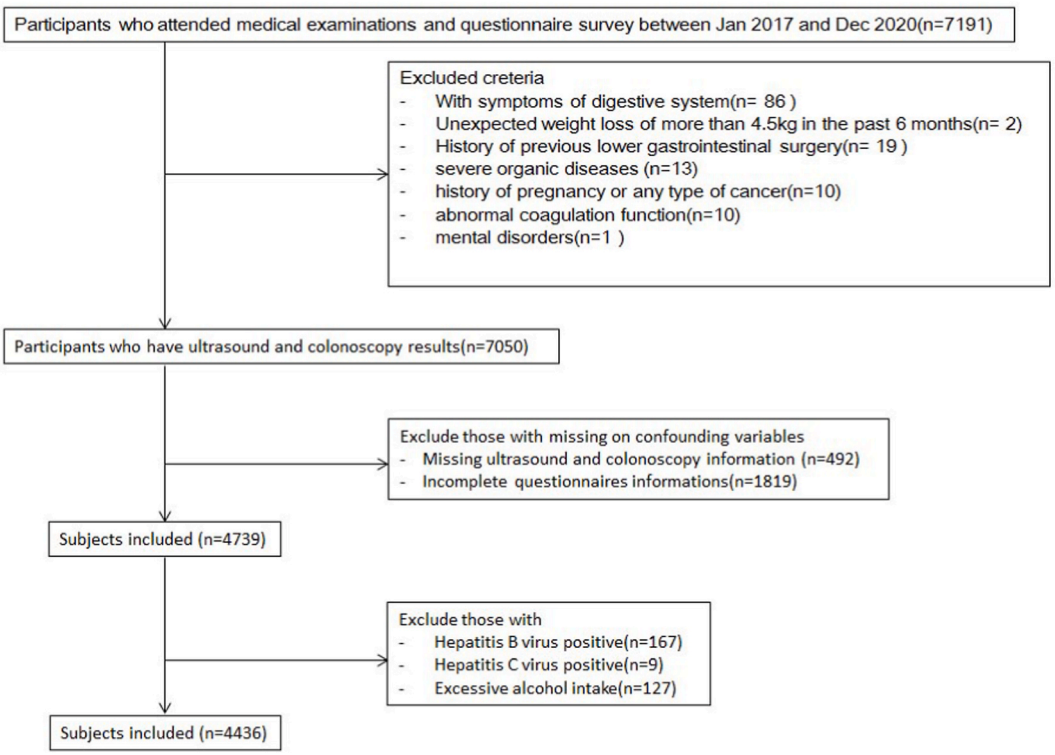

Fig. 1. Flow chart of the study population.

2. Methods

2.1. Study population

This cross-sectional study recruited 7191 individuals (5065 males and 2126 females) aged ≥18 years who underwent health examinations at the Chinese PLA General Hospital, Beijing, China, between January 2017 and December 2020. The questionnaires were sent to each participant before the physical examination and covered lifestyle and medical history. At the outset, subjects with digestive tract symptoms and unexplained weight loss of more than 4.5 kg in the past 6 months were excluded. Other exclusion criteria included a previous history of lower digestive tract surgery; severe organic diseases of the heart, lung, and kidney; and any type of cancer or mental disorders. A total of 7050 participants participated in the study. Among the participants, we excluded 492 participants with missing ultrasound and colonoscopy information and 1819 participants with incomplete questionnaires. Moreover, subjects showing the following possible causes of chronic liver disease were excluded: 167 with hepatitis B virus, 9 with hepatitis C virus, and 127 with excessive alcohol intake (>25 g/day for men and >15 g/day for women). A total of 4436 consecutive participants were included in the final analysis. The mean age was 49.51 years (SD, 7.68 years). The flow chart of the study design is illustrated in Fig. 1. The study protocol was approved by the Ethics Committee of the PLA General Hospital, Beijing, China (No. S2022-720) and was conducted in accordance with the principles of the Helsinki Declaration. Written informed consent was obtained from each enrolled subject.

2.2. Clinical and biochemical Evaluation

The collected data included the results of self-reported health questionnaires, anthropometric measurements and laboratory tests. Briefly, a tape measure was used to wrap around the narrowest part of the waist, and the resulting measurement was the waist circumference (WC). A body composition analyzer was used to measure body weight and height, and the weight was divided by the square of the height to obtain the value of body mass index (BMI). According to the guidelines of the China Obesity Working Groups (WGOC) [13], a BMI of 24.0 kg/m^2 to 27.9 kg/m^2 is considered overweight, and a BMI greater than 28.0 kg/m^2 is considered obese. Smoking was divided into current smoking (consuming ≥10 cigarettes per day for at least 1 year) and noncurrent smoking (continuous cessation of smoking for more than one year). Blood pressure was measured twice with an electronic sphygmomanometer and averaged. Hypertension is defined as three consecutive blood pressure measurements on different days, systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, or taking antihypertensive medications. Diabetes was defined as a fasting blood glucose level of ≥126 mg per deciliter, a glycosylated hemoglobin level (HbA1c) of ≥6.5 %, or a history of taking hypoglycemic medications. Self-reported health questionnaires included diet (such as cereals, meat, fruits and vegetables), physical activity and pressure. Subjects were asked to recall their information for the previous 2 years [14–16].

After fasting for at least 12 h, 5 ml of venous blood was collected, and biochemical parameters were quantitatively determined. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and uric acid (UA) were measured using commercially available reagents (Roche).

2.3. Diagnosis of MAFLD and liver fibrosis

Abdominal ultrasound was performed by experienced radiologists using ultrasound scanners (Siemens, Mountain View, CA, USA). The diagnosis of fatty liver disease was based on the manifestation of increased hepatorenal echo, which contrasts between hepatic and renal parenchyma, deep ultrasound beam attenuation, vascular blurring, and straightness of the hepatic vein lumen [17]. MAFLD was diagnosed on the basis of ultrasonically diagnosed hepatic steatosis and the presence of one of the following three criteria: overweight or obesity, T2DM, or metabolic dysregulation, according to previous criteria [4]. The FIB-4 index was calculated to evaluate liver fibrosis in MAFLD subjects [18]. A FIB-4 index score <1.3 was excluded from hepatic fibrosis [19].

2.4. Colonoscopy examination

All colonoscopies were performed by 10 experienced digestive endoscopists who had performed at least 1000 colonoscopies. Polyethylene glycol lavage solution was used for bowel preparation according to the instructions for use. During colonoscopy, the anesthesiologist may choose to sedate piperidine in combination with midazolam or propofol alone depending on the patient's condition. A complete examination was defined as a colonoscopy that reached the cecum, where a photo of the ileocecal valve was taken. For all colorectal lesions found, their location and size (measured with 7 mm open biopsy forceps) were recorded. The withdrawal time should not be less than 6 min to avoid missing lesions. Only complete examinations were included in the analysis. Usually, the left colon includes the splenic flexure, descending colon, sigmoid colon, and rectum, while the right colon includes the cecum, ascending colon, and transverse colon. All abnormalities found during the colonoscopy were biopsied and confirmed by pathological examinations that followed up-to-date clinical guidelines (WHO Classification of Digestive Tumors: Fifth Edition) [20]. Advanced colorectal adenoma was an adenoma larger than 1 cm in diameter or had a highly atypical hyperplasia or villous structure.

The quality of colonoscopy was evaluated using the Boston Bowel Preparation Scale. It was divided into 4 levels (0–3 points) according to the grade from worst to clean. The total score is 0–9 points, and ≥6 points indicates that the intestinal preparation is qualified [21].

2.5. Statistical analyses

The basic characteristics are presented as the mean ± standard deviation (SD) for normally distributed variables and as the frequency (percentage) for categorical variables. We analyzed continuous variables using Student's *t*-test and ANOVA and compared categorical variables using the chi-squared test. The association between MAFLD and colorectal adenoma was assessed by univariate and multivariate logistic regression analyses. Based on the results of univariate analysis, multivariate regression analysis was

Table 1
Comparison of subjects' baseline characteristics according to MAFLD status.

Feature	MAFLD (N = 1407)	No MAFLD (N = 3029)	*p Value*
Age (years)	49.5 ± 7.6	49.5 ± 7.7	0.909
Sex (male , n (%))	1214 (86.3)	1870 (61.7)	<0.001*
Relative CRC, n (%)	39 (2.8)	71 (2.3)	0.394
BMI (SD), kg/m^2	27.6 ± 3.0	24.2 ± 2.8	<0.001*
Male	27.8 ± 2.9	25.0 ± 2.6	<0.001*
Female	26.7 ± 3.1	22.9 ± 2.7	<0.001*
Waistline, cm	95.1 ± 10.8	81.9 ± 19.4	<0.001*
Male	96.1 ± 10.4	85.7 ± 19.7	<0.001*
Female	88.2 ± 10.6	75.6 ± 17.1	<0.001*
Fasting glucose (SD), mmol/l	5.9 ± 1.2	5.3 ± 0.9	<0.001*
CHO(mg/dL)	4.8 ± 0.9	4.7 ± 0.9	<0.001*
HDL-C (mg/dL)	1.1 ± 0.3	1.3 ± 0.4	<0.001*
LDL –C (mg/dL)	3.2 ± 0.9	3.2 ± 0.9	0.047*
TG(mg/dL)	2.5 ± 1.7	1.6 ± 1.3	<0.001*
ALT (SD),IU/L	32.6 ± 21.6	20.4 ± 17.5	<0.001*
AST (SD),IU/L	22.5 ± 12.5	18.3 ± 10.0	<0.001*
Diabetes, n (%)	90 (6.4)	79 (2.6)	<0.001*
Hypertension, n (%)	429 (30.5)	408 (13.5)	<0.001*
DBP (mmHg)	85.6 ± 11.5	79.1 ± 12.0	<0.001*
SBP (mmHg)	127.3 ± 17.6	117.4 ± 18.7	<0.001*
Cereal intake (g/d)			0.009*
<50	45 (3.2)	114 (3.8)	
50–200	646 (45.9)	1538 (50.8)	
200–500	640 (45.5)	1236 (40.8)	
>500	76 (5.4)	141 (4.6)	
Meat intake (g/d)			<0.001*
0	30 (2.1)	154 (5.1)	
<50	268 (19.1)	904 (29.8)	
50–150	874 (62.1)	1679 (55.5)	
>150	235 (16.7)	292 (9.6)	
Vegetable and fruit intake (g/d)			0.003*
0	26 (1.8)	64 (2.1)	
<50	56 (4.0)	148 (4.9)	
50–200	593 (42.1)	1088 (35.9)	
201–500	643 (45.7)	1512 (49.9)	
>500	89 (6.3)	217 (7.2)	
Taste			<0.001*
very mild	46 (3.3)	194 (6.4)	
slightly mild	350 (24.9)	1036 (34.2)	
medium	373 (26.5)	789 (26.0)	
slightly salty	591 (42.0)	942 (31.1)	
very salty	47 (3.3)	68 (2.2)	
Smoking			<0.001*
No-smoking	742 (52.7)	1948 (64.30)	
Current smoking	505 (35.9)	812 (26.8)	
Past smoking	160 (11.4)	269 (8.9)	
Alcohol consumption			<0.001*
No-drinking	332 (23.6)	1141 (37.7)	
Past drinking	145 (10.3)	359 (11.9)	
Drinking	930 (37.8)	1529 (50.5)	
Pressure			<0.001*
No pressure	213 (15.1)	547 (18.1)	
less pressure	280 (19.9)	601 (19.8)	
average	328 (23.3)	855 (28.2)	
more pressure	522 (37.1)	924 (30.5)	
a lot of pressure	64 (4.5)	102 (3.4)	
Adenoma	190 (13.5)	324 (10.7)	0.007*

Data are shown as the mean ± SD. MAFLD, metabolic dysfunction-associated fatty liver disease; BMI, body mass index; CHO, cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; ALT, alanine aminotransferase; AST, aspartate aminotransferase; DBP, diastolic blood pressure; SBP, systolic blood pressure. The level of significance in each factor was set at $p\ value < 0.05$ (*).

conducted on variables with a p value less than 0.05 with clinical importance. All statistical analyses were performed using SPSS 22.0 software (SPSS Inc., Chicago, Illinois, USA).

3. Results

3.1. Baseline characteristics of the study population

A total of 4436 subjects, including 1407 subjects with MAFLD and 3029 control subjects, were enrolled in the final analysis (mean age 49.51 ± 7.68 years). The proportion of males was 69.52 % (n = 3084). The prevalence of MAFLD was 31.72 % (1407/4436). Baseline characteristics in the MAFLD and non-MALFD groups are given in Table 1. MAFLD was more common in males and smokers than in non-MAFLD subjects, and MAFLD subjects had a significantly increased risk of diabetes and hypertension. WC, BMI, and levels of AST, ALT, TG, and UA were significantly elevated in MAFLD subjects compared with non-MAFLD subjects ($p < 0.001$). The prevalence of MAFLD was significantly higher in subjects with high meat consumption, salt consumption, and stress. Colorectal adenoma was more common in subjects with MAFLD than in subjects without MAFLD (13.5 %, 190/1407 vs. 10.7 %, 324/3029, $p < 0.001$).

3.2. Detection rates of colorectal neoplasms in MAFLD subjects

Overall, the detection rates of colorectal polyps, adenoma and advanced adenoma were 17.40 % (772/4436), 11.59 % (514/4436) and 1.19 % (49/4436), respectively. MAFLD patients had a higher detection rate of colorectal polyps (21 %, 295/1407 vs. 15.7 %, 477/3029, $p < 0.001$), hyperplastic polyps (6.3 %, 89/1407 vs. 4.5 %, 136/3029, $p = 0.01$) and adenoma (13.5 %, 190/1407 vs. 10.7 %, 324/3029, $p = 0.007$) than non-MAFLD subjects, as illustrated in Table 2. The detection rates of colorectal adenoma in male MAFLD and female MAFLD patients were 14 % (170/1214) and 10.36 % (20/193), respectively. Female MAFLD subjects had a higher detection rate of advanced neoplasms than male subjects (3.63 %, 7/193 vs. 0.58 %, 7/1214, $p < 0.05$). After stratification by age and sex, the detection rate of colorectal adenoma in female MAFLD subjects aged ≥50 years was higher than that in non-MAFLD females aged ≥50, but the differences were too small to be statistically significant. The advanced adenoma detection rate was significantly increased in female MAFLD individuals ≥50 years of age compared with the control group ($p < 0.05$) (Fig. 2).

Patients with MAFLD are more likely to develop left colonic adenomas. Among 190 MAFLD patients with adenomatous polyps detected, 113 (57.36 %) had left colonic lesions, 84 (42.64 %) had right colonic lesions, and 7 (3.55 %) had whole colonic lesions. In contrast, among the 339 non-MAFLD patients with adenomatous polyps, there were 175 (51.62 %) left colonic lesions, 164 (48.38 %) right colonic lesions, and 15 (4.42 %) whole colonic lesions. Among 14 MAFLD patients with advanced colorectal adenomas, left and right colonic lesions were found in 8 (5.1 %) and 6 (4.1 %) cases, respectively. In contrast, in the group of 35 non-MAFLD patients with advanced adenomas, there were 17 left-sided colonic lesions and 19 right-sided colonic lesions. **(Table 2)**.

3.3. Risk analysis between colon adenoma and MAFLD

We first analyzed the relationship between colorectal adenomas and MAFLD. Univariate analysis showed that individuals with MAFLD were 1.303 times more likely to develop colorectal adenomas than non-MAFLD individuals (odds ratio [OR] 1.303, 95 % confidence interval [CI], 1.076–1.578, $p = 0.007$). However, after adjusting for age, sex, BMI, WC, TC, HDL-C, DM, hypertension, and smoking, the strong association between colorectal adenomas and MAFLD disappeared, with an OR of 1.275 (95 % CI, 0.743–2.190, $p = 0.378$). Age, male sex, BMI and smoking were positively associated with the risk of colorectal adenoma, with OR values of 1.044 (95 % CI, 1.031 to 1.058), 1.720 (95 % CI, 1.221 to 2.424), 1.046 (95 % CI, 1.009 to 1.085) and 1.342 (95 % CI, 1.072 to 1.680), respectively (Table 3). When we performed the analysis stratified by sex, no significant association was found between MAFLD and colorectal adenomas in men or women, while smoking increased the risk of colorectal adenomas in men by 33.6 % (OR 1.336, 95 % CI

Table 2
Types and detection rates of colorectal lesions in MAFLD and control subjects.

Colorectal lesions, n (%)	MAFLD (N = 1407)	No MAFLD (N = 3029)	p Value
Endoscopic polyps	295 (21.0)	477 (15.7)	<0.001*
Hyperplastic polyps	89 (6.3)	136 (4.5)	0.01*
Adenomatous polyps	190 (13.5)	324 (10.7)	0.007*
Left sided colon	113 (72.4)	175 (72.6)	
Right sided colon	84 (56.8)	164 (64.1)	
Advanced adenomas	14 (1.0)	35 (1.2)	0.643
Left sided colon	8 (5.1)	17 (7.1)	
Right sided colon	6 (4.1)	19 (7.4)	
Serrated adenomas	9 (0.6)	9 (0.3)	0.095
Colorectal cancers	1 (0.1)	3 (0.1)	1.000

Advanced adenoma was defined as the presence of adenomatous polyps larger than 10 mm in diameter and/or the pathological presence of villous structures and/or highly atypical hyperplasia. The level of significance of patients with MAFLD versus controls was set at p *value* < 0.05 (*). MAFLD, metabolic dysfunction-associated fatty liver disease.

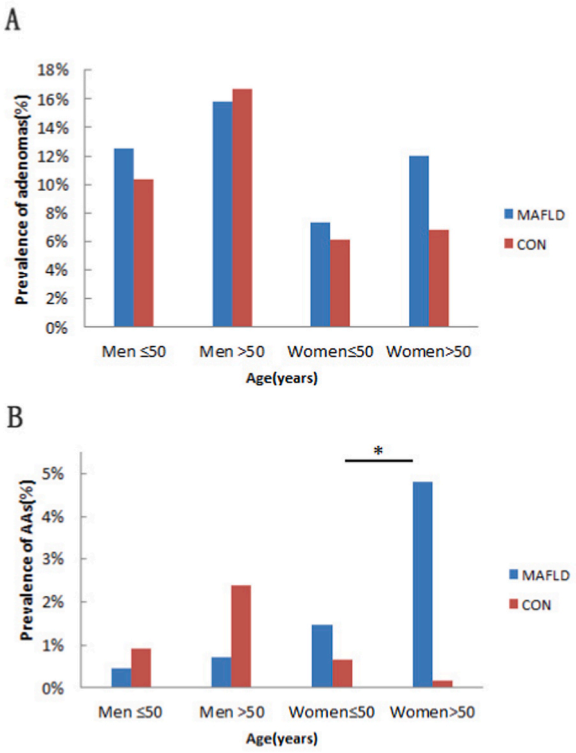

Fig. 2. Detection rates of colorectal adenoma and advanced adenoma by age and sex in metabolic dysfunction-associated fatty liver disease (MAFLD) and control subjects: (A) colorectal adenoma, (B) advanced adenoma vs. the controls (*$p < 0.05$).

1.065 to 1.676) (Table 4).

3.4. Risk analysis between advanced colon adenoma and MAFLD

Next, we analyzed the association between advanced colorectal adenomas and MAFLD. Multivariate analysis showed a strong association between MAFLD and advanced adenomas with an OR value of 6.021 (95 % CI, 1.772–20.454, $p = 0.004$). In addition, age

Table 3
Factors associated with colorectal adenomas in 4436 subjects.

Factors	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P	OR (95%CI)	*P*
MAFLD	1.303 (1.076–1.578)	0.007*	1.275(0.743–2.190)	0.378
Age (years)	1.040(1.026–1.578)	<0.001*	1.044(1.031–1.058)	<0.001*
Male sex	2.080(1.649–2.625)	<0.001*	1.720(1.221–2.424)	0.002*
BMI	1.067(1.038–1.096)	<0.001	1.046(1.009–1.085)	0.015*
Waistline	1.003(0.998–1.009)	0.241	0.994(0.989–0.999)	0.019*
CHO	1.086(0.981–1.201)	0.112	1.098(0.978–1.232)	0.115
HDL-C	0.598(0.450–0.794)	<0.001*	0.859(0.591–1.251)	0.429
TG	1.075(1.022–1.131)	0.005*	1.010(0.943–1.081)	0.781
Diabetes	1.025(0.637–1.650)	0.918	0.803(0.495–1.303)	0.374
Hypertension	1.311(1.050–1.636)	0.017*	1.105(0.876–1.394)	0.399
Drinking		<0.001*		0.287
No-drinking	1		1	
Past drinking	1.134(0.807–1.594)	0.468	0.900(0.627–1.290)	0.565
Drinking	1.562(1.263–1.932)	<0.001*	1.140(0.879–1.480)	0.323
Smoking		<0.001*		0.036*
No-smoking	1		1	
Current smoking	1.651(1.354–2.013)	<0.001*	1.342(1.072–1.680)	0.010*
Past smoking	1.467(1.082–1.991)	0.014*	1.103(0.799–1.523)	0.551
MAFLD&gender	1.362(1.119–1.659)	0.002*	0.765(0.435–1.347)	0.353

MAFLD, metabolic dysfunction-associated fatty liver disease, BMI, body mass index; CHO, cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride, OR, odds ratio; CI, confidence interval; MAFLD: adjusted for age, sex, BMI, waist circumference, CHO, HDL-C, TGs, diabetes, hypertension, drinking and smoking. *$p < 0.05$.

Table 4
Multivariate analyses of the risk for colorectal adenomas according to sex.

	Men		Women	
Factors	Multivariate analysis		Multivariate analysis	
	OR (95 % CI)	p Value	OR (95 % CI)	*p Value*
MAFLD	1.022 (0.805–1.299)	0.856	1.182 (0.643–2.174)	0.590
Age	1.049 (1.034–1.065)	<0.001*	1.021 (0.991–1.052)	0.180
BMI	1.048 (1.007–1.091)	0.022 *	1.060 (0.982–1.144)	0.135
Waistline	0.993 (0.988–0.999)	0.019*	0.997 (0.985–1.008)	0.586
Hypertension	1.024 (0.793–1.322)	0.857	1.675 (0.974–2.880)	0.062
Alcohol consumption		0.105		0.426
No-drinking	1	–	1	–
Past drinking	0.943 (0.616–1.445)	0.789	0.862 (0.414–1.792)	0.690
Drinking	1.271 (0.939–1.720)	0.121	0.648 (0.336–1.252)	0.197
Smoking		0.032 *		0.068
No-smoking	1	–	1	–
Current smoking	1.336 (1.065–1.676)	0.012*	1.572 (0.452–5.467)	0.477
Past smoking	1.028 (0.741–1.427)	0.869	7.374 (1.288–42.204)	0.025*

MAFLD, metabolic dysfunction-associated fatty liver disease. OR, odds ratio; CI, confidence interval; MAFLD: adjusted for age, BMI, waistline, hypertension, drinking and smoking. *$p < 0.05$.

(OR 1.054, 95 % CI, 1.011–1.099, $p = 0.013$) was an independent risk factor for advanced adenomas (Table 5). When further stratified by sex, the results indicated that female MAFLD subjects were 3.932-fold more likely to develop advanced adenomas than controls (OR 3.932, 95 % CI, 1.023–15.117, $p = 0.046$). There was a significant association between CHO and advanced adenomas in women (OR 2.141, 95 % CI, 1.257–3.647, $p = 0.005$) (Table 6).

3.5. Subgroup analysis of subjects with MAFLD

Finally, we investigated whether there was a correlation between fibrosis of the liver and adenomas in MAFLD subjects. MAFLD individuals were divided into groups with and without fibrosis according to the FIB-4 index score. The results showed that although patients with a high FIB-4 index score had a higher incidence of colorectal adenomas than those with a low FIB-4 index score, the difference was not statistically significant due to the small number of patients in this subgroup (Supplemental Table 1).

4. Discussion

In this retrospective cohort study, we found significantly higher detection rates of adenoma on colonoscopy in patients with MAFLD than in controls. MAFLD in female patients was independently associated with increased detection rates in subjects with advanced

Table 5
Factors associated with advanced adenomas in 4436 subjects.

Factors	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P	OR (95%CI)	*P*
MAFLD	0.860(0.461–1.603)	0.634	6.021(1.772–20.454)	0.004*
Age (years)	1.052(1.012–1.094)	0.011*	1.054(1.011–1.099)	0.013*
Male sex	1.356(0.705–2.609)	0.362	1.838(0.568–5.943)	0.310
BMI	1.049(0.966–1.140)	0.254	1.054(0.943–1.178)	0.351
Waistline	0.995(0.981–1.008)	0.424	0.991(0.979–1.004)	0.169
CHO	1.218(0.902–1.645)	0.199	1.334(0.944–1.883)	0.102
HDL-C	0.470(0.189–1.165)	0.103	0.313(0.090–1.092)	0.068
TG	1.054(0.912–1.218)	0.474	0.950(0.764–1.182)	0.644
Diabetes	1.075(0.259–4.464)	0.920	0.808(0.189–3.454)	0.774
Hypertension	0.837(0.391–1.793)	0.648	0.731(0.332–1.607)	0.435
Drinking		0.314		0.241
No-drinking	1		1	
Past drinking	0.624(0.179–2.180)	0.460	0.576(0.156–2.124)	0.407
Drinking	1.374(0.731–2.584)	0.324	1.498(0.672–3.340)	0.323
Smoking		0.062		0.149
No-smoking	1		1	
Current smoking	1.516(0.807–2.848)	0.196	1.421(0.671–3.009)	0.358
Past smoking	2.485(1.142–5.407)	0.022*	2.388(0.996–5.723)	0.051
MAFLD&gender	0.439(0.197–0.980)	0.045*	0.052(0.013–0.219)	<0.001*

MAFLD, metabolic dysfunction-associated fatty liver disease, BMI, body mass index; CHO, cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglyceride, OR, odds ratio; CI, confidence interval; MAFLD: adjusted for age, sex, BMI, waist circumference, CHO, HDL-C, TGs, diabetes, hypertension, drinking and smoking. *$p < 0.05$.

Table 6
Multivariate analyses of the risk for advanced adenomas according to sex.

Factors	Men		Women	
	Multivariate analysis		Multivariate analysis	
	OR (95 % CI)	p Value	OR (95 % CI)	*p Value*
MAFLD	0.350 (0.144–0.850)	0.020 *	3.932 (1.023–15.117)	0.046 *
Age	1.051 (1.005–1.100)	0.029*	1.008 (0.920–1.104)	0.864
BMI	1.018 (0.901–1.149)	0.775	1.162 (0.971–1.391)	0.101
CHO	0.963 (0.665–1.394)	0.841	2.141 (1.257–3.647)	0.005*

MAFLD, metabolic dysfunction-associated fatty liver disease; OR, odds ratio; CI, confidence interval; MAFLD: adjusted for age, BMI, and CHO. *$p < 0.05$.

adenoma but not in males. Smoking was a factor strongly linking MAFLD and colorectal adenoma in males. Additionally, age, male sex and BMI had strong associations with the risk of colorectal adenoma.

In our study, the adenoma detection rate (ADR) was 11.59 %, which is inferior to the adenoma detection rate in Western populations but close to the results reported in Chinese studies. For instance, in a study from Germany in 2003–2012, the ADRs of 4,407,971 opportunistic screening colonoscopies were 31.3 % and 20.1 % for men and women in 2012, respectively. The overall ADR was only 11.49 % in a screening cohort with 25,593 Chinese individuals [22]. In another study, the adenoma detection rate in 41,010 screened patients from Southwest China was 17.6 % [23]. Therefore, the low ADR in our study might be explained by the relatively low prevalence of colorectal neoplasms in China compared with other European and North American countries. Another reason for this difference may be that the cohort was a healthy screening population and thus had a low prevalence of colorectal neoplasms.

A study from Korea was the first to demonstrate that NAFLD subjects diagnosed by ultrasound had an increased risk of colorectal adenomas by 28 % over non-NAFLD subjects [24]. In 2020, a study from the United States showed that the adenoma detection rate in the histologically confirmed NAFLD group was significantly higher than that in the control group, and NAFLD remained an independent risk factor for adenoma in multivariate analyses, including hyperlipidemia, diabetes, and obesity [25]. Researchers from Taipei have found that NAFLD was an independent risk factor for adenoma formation after colonoscopy was negative, and patients with NAFLD with other diseases, such as metabolic syndrome, hypertension, or smoking, had an elevated colorectal adenoma risk [26]. In our study, MAFLD individuals had a higher occurrence rate of colorectal polyps (21 % vs. 15.7 %) and adenoma (13.5 % vs. 10.7 %) than the control group. The univariate model showed that MAFLD increased the risk of colorectal adenoma (OR 1.303), which was consistent with the report linking NAFLD and the ultrasound diagnosis of colorectal adenomatous polyps described above. However, MAFLD is not an independent risk factor for colorectal adenomatous polyps.

Previous studies have suggested that MAFLD patients of different sexes have different clinical epidemiology and clinic pathological features, including extrahepatic diseases associated with fatty liver disease [27]. We therefore evaluated the association between MAFLD and colorectal adenoma by sex, and the data suggest that female MAFLD individuals, but not male MAFLD individuals, are at significantly increased risk of advanced adenomas. This is consistent with a report from South Korea [12]. However, a study from China reported that NAFLD was an important risk factor for colorectal adenoma in men but not in women [28], and a meta-analysis similarly found that NAFLD was significantly associated with a higher risk of colorectal polyps only in men [11]. The reasons for these inconsistent results are uncertain, but one possible explanation is that MAFLD is not just the new name for NAFLD, and there are differences between them. Another possibility is that MAFLD comorbidities, including diabetes mellitus and hypertension, differ between the sexes and are involved in colorectal adenomas.

Our study shows that colorectal adenoma is associated with sex specificity in MAFLD, which should be because MAFLD itself is sexually dimorphic. Compared with women, men are more likely to develop visceral fat deposits and leptin resistance due to smoking, drinking and other poor lifestyle habits and tend to synthesize fatty acids for fat storage in the absence of estrogen receptors. It seems that liver fibrosis is more severe in male patients and that their incidence of liver cancer is higher. Although men have a higher risk of developing NAFLD than women, once NAFLD occurs, liver fibrosis progresses faster in women, and the level of hepatocyte injury and inflammation is higher, especially after the age of 50 [29]. In this study, compared with men of the same age, women aged 50 years or older with MAFLD had a higher occurrence rate of advanced neoplasms than male patients (3.63 %, 7/193 vs. 0.58 %, 7/1214, $p < 0.05$), which supports this explanation.

In our study, smoking was closely associated with adenoma, with an OR of 1.336 for males. The mechanism by which smoking increases the risk of colorectal adenoma remains unclear, but smoking may accelerate abnormal promoter hypermethylation of DNA, resulting in high microsatellite instability and the CpG island methylator phenotype in tumors. Furthermore, cigarette smoke contains several carcinogens, such as polycyclic aromatic hydrocarbons, that can be directly absorbed into the colon mucosa, which also increases the risk of colorectal adenoma[31 , 32].

The study has several limitations. First, it was a single-center study, the included subjects were not representative of the general population in China, and selection bias cannot be ruled out. Second, MAFLD was only evaluated by ultrasound in this study. Due to the limitations of ultrasound and individual differences in the population, there is a possibility of inaccurate diagnosis in patients with low liver fat content. It is true that in clinical practice, asymptomatic individual screening is usually performed using imaging techniques such as ultrasound or magnetic resonance imaging to diagnose MAFLD. Third, as this study group comes from the physical examination population, they usually care more about their own health status, so they are not representative of the general population in this regard.

5. Conclusion

The association between MAFLD and the risk of colon adenoma in a Chinese Han population was explored in this study. Our results suggest that the detection rate of colorectal neoplasms is higher in MAFLD individuals than in controls. MAFLD subjects may have an elevated risk of advanced colonic adenoma in women. Older age and past smoking were independent risk factors for advanced colorectal adenoma. The underlying mechanisms for this increased risk should be further explored. Future studies should confirm whether this population will benefit from earlier screening for the detection and prevention of colorectal cancer in MAFLD subjects.

Data availability statement

Data will be made available on request.

Funding

This work was supported by the Natural Science Foundation of Beijing (grant number: J200011).

Ethics approval

The study protocol was approved by the Chinese People's Liberation Army General Hospital ethics committee (No. S2022-720) and were conducted in accordance with the principles of the Declaration of Helsinki and its contemporary amendments.

CRediT authorship contribution statement

Yan Gong: Writing – original draft, Conceptualization. **Juan Kang:** Software, Data curation. **Xinyan Wang:** Visualization, Validation. **Yansong Zheng:** Supervision, Methodology, Formal analysis. **Ying Sui:** Visualization, Validation, Data curation. **Wenping Lu:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We express our gratitude to all of the participants in the study, including the patients and their families, as well as the researchers.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e22391.

References

[1] T.G. Cotter, M. Rinella, Nonalcoholic fatty liver disease 2020: the state of the disease, Gastroenterology 158 (2020) 1851–1864, https://doi.org/10.1053/j.gastro.2020.01.052.
[2] M.F. Abdelmalek, Nonalcoholic fatty liver disease: another leap forward, Nat. Rev. Gastroenterol. Hepatol. 18 (2021) 85–86, https://doi.org/10.1038/s41575-020-00406-0.
[3] S.H. Kang, Y. Cho, S.W. Jeong, S.U. Kim, J.W. Lee, From nonalcoholic fatty liver disease to metabolic-associated fatty liver disease: Big wave or ripple? Clin. Mol. Hepatol. 27 (2021) 257–269, https://doi.org/10.3350/cmh.2021.0067.
[4] M. Eslam, P.N. Newsome, S.K. Sarin, Q.M. Anstee, G. Targher, M.R. Gomez, S.Z. Sagi, V.W. Wong, J. Dufour, J.M. Schattenberg, T. Kawaguchi, M. Arrese, L. Valenti, G. Shiha, C. Tiribelli, H. Järvinen, J.G. Fan, H. Grønbæk, Y. Yilmaz, H.C. Pinto, C.P. Oliveira, P. Bedossa, L.A. Adams, M.H. Zheng, Y. Fouad, W. K. Chan, N.M. Sanchez, S.H. Ahn, L. Castera, E. Bugianesi, V.R. George, A new definition for metabolic dysfunction-associated fatty liver disease: an international expert consensus statement, J Hepatol. 73 202 (2020) 209, https://doi.org/10.1016/j.jhep.2020.03.039.
[5] H. Sung, J. Ferlay, R.L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries, Ca-Cancer J. Clin. 71 (2021) 209–249, https://doi.org/10.3322/caac.21660.
[6] W. Cao, H.D. Chen, Y.W. Yu, N. Li, W.Q. Chen, Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020, Chin Med J (Engl) . 134 (2021) 783–791, https://doi.org/10.1097/cm9.0000000000001474.
[7] H. Brenner, M. Hoffmeister, C. Stegmaier, G. Brenner, L. Altenhofen, H.U. Ulrike, Risk of progression of advanced adenomas to colorectal cancer by age and sex: estimates based on 840,149 screening colonoscopies, Gut 56 (2007) 1585–1589, https://doi.org/10.1136/gut.2007.122739.
[8] L.A. Adams, Q.M. Anstee, H. Tilg, T.G.T. argher, Nonalcoholic fatty liver disease and its relationship with cardiovascular disease and other extrahepatic disease, Gut 66 (2017) 1138–1153, https://doi.org/10.1136/gutjnl-2017-313884.
[9] S. Fukunaga, D. Nakano, T. Kawaguchi, M. Eslam, A. Ouchi, T. Nagata, H. Kuroki, H. Kawata, H. Abe, R. Nouno, K. Kawaguchi, J. George, K. Mitsuyama, T. Torimura, Non-obese MAFLD is associated with colorectal adenoma in health check examinees: a multicenter retrospective study, Int. J. Mol. Sci. 22 (2021) 5462, https://doi.org/10.3390/ijms22115462.

[10] Y.Q. Zeng, R.Y. Cao, Z.W. Tao, Y.J. Gao, Association between the severity of metabolic dysfunction-associated fatty liver disease and the risk of colorectal neoplasm: a systematic review and meta-analysis, Lipids in Health and Disease21 (2022) 52, https://doi.org/10.1186/s12944-022-01659-1.
[11] W.X. Chen, M.Q. Wang, X.B. Jing, C.F. Wu, Y.C. Zeng, J.W. Peng, X.B. Cai, High risk of colorectal polyps in men with nonalcoholic fatty liver disease: a systematic review and meta-analysis, J. Gastroenterol. Hepatol. 35 (2020) 2051–2065, https://doi.org/10.1111/jgh.15158.
[12] J.Y. Seo, J.H. Bae, M.S. Kwak, J.I. Yang, S.J. Chung, J.Y. Yim, S.H. Lim, G.E. Chung, The risk of colorectal adenoma in nonalcoholic or metabolic-associated fatty liver disease, Biomedicines9 (2021) 1401, https://doi.org/10.3390/biomedicines9101401.
[13] C. Chen, F.C. Lu, The guidelines for prevention and control of overweight and obesity in Chinese adults, Biomedical and environmental sciences 17 (Suppl) (2004) 1–36.
[14] K. Ge, Dietary pattern and physical development in China– based on the 1992 national nutrition survey, Asia Pac. J. Clin. Nutr. 4 (Suppl 1) (1995) 19–23.
[15] Q. Zeng, F. Li, T. Xiang, W.M. Wang, C. Ma, C. Yang, H.X. Chen, H. Xiang, Influence of food groups on plasma total homocysteine for specific MTHFR C677T genotypes in Chinese population, Mol. Nutr. Food Res. 61 (2017), 1600351, https://doi.org/10.1002/mnfr.201600351.
[16] C. Bonifacj, M. Gerber, J. Scali, J.P. Daures, Comparison of dietary assessment methods in a southern French population: use of weighed records, estimated-diet records and a food-frequency questionnaire, Eur. J. Clin. Nutr. 51 (1997) 217–231, https://doi.org/10.1038/sj.ejcn.1600387.
[17] S. Saadeh, Z.M. Younossi, E.M. Remer, T. Gramlich, J.P. Ong, M. Hurley, K.D. Mullen, J.N. Cooper, M.J. Sheridan, The utility of radiological imaging in nonalcoholic fatty liver disease, Gastroenterology 123 (2002) 745.
[18] P. Angulo, J.M. Hui, G. Marchesini, E. Bugianesi, J. George, G.C. Farrell, F. Enders, S. Saksena, A.D. Burt, J.P. Bida, K. Lindor, S.O. Sanderson, M. Lenzi, L. A. Adams, J. Kench, T.M. Therneau, C.P. Day, The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD, Hepatology 45 (2007) 846–854, https://doi.org/10.1002/hep.21496.
[19] S. McPherson, T. Hardy, J.F. Dufour, S. Petta, Gomez M. Romero, M. Allison, C.P. Oliveira, S. Francque, L.V. Gaal, J.M. Schattenberg, D. Tiniakos, A. Burt, E. Bugianesi, V. Ratziu, C.P. Day, Q.M. Anstee, Age as a confounding factor for the accurate noninvasive diagnosis of advanced NAFLD Fibrosis, Am. J. Gastroenterol. 112 (2017) 740–751, https://doi.org/10.1038/ajg.2016.453.
[20] I.D. Nagtegaal, R.D. Odze, D. Klimstra, V. Paradis, M. Rugge, P. Schirmacher, K.M. Washington, F. Carneiro, I.A. Cree, WHO Classification of Tumors Editorial Board, the 2019 WHO classification of tumors of the digestive system, Histopathology 76 (2020) 182–188, https://doi.org/10.1111/his.13975.
[21] R. Parmar, M. Martel, A. Rostom, A.N. Barkun, Validated scales for colon cleansing: a systematic review, Am. J. Gastroenterol. 111 (2016) 197–204, https://doi.org/10.1038/ajg.2015.417.
[22] H.D. Chen, N. Li, J.S. Ren, X.S. Feng, Z.Y. Lyu, L.P. Wei, X. Li, L.W. Guo, Zhaoxu Zheng, S.M. Zou, Y.M. Zhang, J. Li, K. Zhang, W.Q. Chen, M. Dai, J. He, Group of Cancer Screening Program in Urban China (CanSPUC), Participation and yield of a population-based colorectal cancer screening programme in China, Gut 68 (2019) 1450–1457, https://doi.org/10.1136/gutjnl-2018-317124.
[23] J.G. Zhang, H.F. Xu, L.Y. Zheng, J. Yu, Q. Chen, X.Q. Cao, S.Z. Liu, M.J. Gonzalez, L.W. Guo, X.B. Sun, S.K. Zhang, Y.L. Qiao, Determinants of participation and occurrence rate of colorectal cancer from a population-based screening program in China, Front. Oncol. 10 (2020) 1173, https://doi.org/10.3389/fonc.2020.01173.
[24] S.T. Hwang, Y.K. Cho, J.H. Park, H.J. Kim, D.I. Park, C.I. Sohn, W.K. Jeon, B.I. Kim, K.H. Won, W. Jin, Relationship of nonalcoholic fatty liver disease to colorectal adenomatous polyps, J. Gastroenterol. Hepatol. 25 (2010) 562.
[25] J.W. Blackett, E.C. Verna, B. Lebwoh, Increased detection rates of colorectal adenomas in patients with nonalcoholic fatty liver disease: a cross-sectional study, Dig. Dis. 38 (2020) 222–230, https://doi.org/10.1159/000502684.
[26] K.W. Huang, H.B. Leu, Y.J. Wang, J.C. Luo, H.C. Lin, F.Y. Lee, W.L. Chan, J.K. Lin, F. Chang, Patients with nonalcoholic fatty liver disease have higher risk of colorectal adenoma after negative baseline colonoscopy, Colorectal Dis. 15 (2013) 830–835, https://doi.org/10.1111/codi.12172.
[27] X.Y. Chen, C. Wang, C, Y.Z. Huang, L.L. Zhang, Nonalcoholic fatty liver disease shows significant sex dimorphism, World J Clin Cases 10 (2022) 1457–1472, https://doi.org/10.12998/wjcc.v10.i5.1457.
[28] Q.F. Chen, X.D. Zhou, Y.J. Sun, D.H. Fang, Q. Zhao, J.H. Huang, Y. Jin, J.S. Wu, Sex-influenced association of nonalcoholic fatty liver disease with colorectal adenomatous and hyperplastic polyps, World J. Gastroenterol. 23 (2017) 5206–5215, https://doi.org/10.3748/wjg.v23.i28.5206.
[29] M. Balakrishnan, P. Patel, V.S. Dunn, C. Dao, V. Khan, H. Ali, L.E. Serag, R. Hernaez, A. Sisson, A.P. Thrift, Y. Liu, H.B. El-Serag, F. Kanwal, Women have a lower risk of nonalcoholic fatty liver disease but a higher risk of progression vs. Men: a systematic review and meta-analysis, Clin. Gastroenterol. Hepatol. 19 (2021) 61–71, https://doi.org/10.1016/j.cgh.2020.04.067.