Patients with non-alcoholic fatty liver disease may be a high-risk group for the development of colorectal polyps: A cross-sectional study

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Abstract. Non-alcoholic fatty liver disease (NAFLD) and colorectal polyps have been shown to have similar pathogenic factors. The understanding of the association between these two pathologies may contribute to the early diagnosis and treatment of colorectal tumors. The present study compared the biological characteristics of colorectal polyps between patients with and without NAFLD. For this purpose, 1,538 patients with colorectal polyps treated from July, 2013 and June, 2020 were included and divided into the NAFLD and control group (non-NAFLD group). The location, number, morphology, size and pathology of the polyps were compared between the 2 groups. For the analysis of the biological characteristics of the polyps, the multiple of number (74.5%), percentages of polyps >1.0 cm in diameter (62%) and polyps with advanced adenomas. For the analysis of the biological characteristics of the polyps, the multiple of number (74.5%), percentages of polyps in diameter of 1.0 to <2.0 cm + ≥2.0 cm (48.4 and 13.6%, respectively) and polyps with advanced adenomas (62.9%) in the NAFLD group exhibited significant differences compared with the control group (69.5, 39.2, 6.3 and 55.3%, respectively; all P<0.05); however, no significant differences were observed in the location and morphology of the colorectal polyps between the patients with NAFLD and the controls (P>0.05). When the patients were stratified by sex, age and body mass index, it was found that the patients in the NAFLD group with a polyp size <1.0 cm and those with advanced adenomas exhibited significant differences compared with the control group (P<0.05, respectively). Further analysis revealed that the classification percentage of advanced adenomas in the NAFLD group only exhibited a statistically significant difference compared with the control group in patients with a lower weight (P<0.05). On the whole, the present study demonstrates that NAFLD is significantly associated with the presence of colorectal polyps, particularly in patients with multiple polyps, those with a large size and with villous features (advanced adenomas). Patients with NAFLD may thus be considered a target group for screening colonoscopy.

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Introduction

Colorectal polyps have been considered precursors of hereditary and sporadic colorectal cancer. Currently, the incidence of colorectal polyps and colorectal cancer has been increasing over the recent decades worldwide. The identification of risk factors for colorectal cancer and performing colonoscopy are considered efficient surveillance programs for the detection of colorectal polyps and for the reduction of malignant progression and mortality among the general population (1).

Non-alcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease. There is currently increasing evidence to indicate that NAFLD is a multisystem disease, affecting extra-hepatic organs. For example, NAFLD increases the risk of developing type 2 diabetes mellitus, cardiovascular (CVD) and cardiac diseases, and chronic kidney disease. Moreover, epidemiological research has found that the occurrence of NAFLD is associated with colorectal adenomas and advanced neoplasms (2). A previous study investigated 2,917 subjects, who had been divided into 2 groups (556 with adenomatous polyps and 2,361 who were polyp-free), and found that NAFLD was an independent risk factor for colorectal adenoma (3). However, that study did not examine the association between the location, number, morphology, size, pathological features and advanced adenomatous polyps and NAFLD.

In the present study, 1,538 cases of patients with colorectal polyps were retrospectively surveyed to compare the biological characteristics of colorectal polyps in patients with and without NAFLD. The association between NAFLD and features of colorectal polyps was also analyzed, so as to provide clinical evidence for the guidance of colorectal polyp screening in patients with NAFLD.

Patients and methods

Study design. The present study is a cross-sectional retrospective study that was performed at the Department of Gastroenterology, Shanghai Ruijin Hospital North from July, 2013 and June, 2020. All the patients signed an informed consent form prior to the procedure. The informed consent forms obtained the consent of the patients to use their clinical data, and they were assured that no identifiable personal information would be disclosed. The present study was approved by the Clinical Trial Ethics Committee of Ruijin Hospital North, Shanghai Jiaotong University School of Medicine (Shanghai, China; approval no. 2017-2-01).

Patients. Abdominal ultrasonography was performed by professional radiologists to diagnose fatty liver. According to the 4 knowledgeable ultrasound criteria (liver brightness, deep attenuation, hepatorenal echo contrast and vascular blurring), subjects who met the hepatorenal contrast and liver brightness criteria were diagnosed with fatty liver disease. The inclusion and diagnosis of NAFLD were based on the clinical diagnostic criteria or the working definition of NAFLD in the Guidelines for the Diagnosis and Treatment of Non-Alcoholic Fatty Liver Disease (Revised in January, 2010) formulated by the Fatty Liver and Alcoholic Liver Disease Group of the Hepatology Branch of the Chinese Medical Association when fatty liver was present in the absence of the following: i) Viral hepatitis (hepatitis B or hepatitis C); ii) hepatic cirrhosis and liver carcinoma; iii) autoimmune liver disease or other liver disease; and iv) excess alcohol consumption (>140 g/week for males or >70 g/week for females) (4).

All asymptomatic Chinese subjects were received screening colonoscopies at the large Endoscopy Center of Ruijin Hospital North were prospectively recruited in the present study. The inclusion criteria included the following: i) No symptoms of colorectal cancer, including rectal bleeding, anorexia, or changes in bowel habits over the past 4 weeks, or a weight loss of >5 kg over the past 6 months; and ii) not having received any colorectal cancer-related colonoscopy screening tests over the past 5 years. The exclusion criteria were as follows: i) Long-term and heavy alcohol consumption, but with a B ultrasound examination which revealed negative results for fatty liver; ii) any other intestinal diseases; iii) the long-term use of aspirin or any other non-steroidal anti-inflammatory drugs (NSAIDs); iv) a history of any malignant tumors; v) a definite family history of gastrointestinal malignancy or familial adenomatous polyposis. The following factors were examined retrospectively: Age, sex, weight, height and body mass index (BMI). The (BMI) is calculated by dividing the person's weight in kilograms by the square of their height in meters, and is thus given in units of kg/m^2. The definition of obesity was based on a BMI ≥24 kg/m^2 in both sexes of the following China Diabetes Federation metabolic syndrome criteria (5).

The enrolled patients were divided into the NAFLD group and the control group (non-NAFLD group). A total of 1,538 cases of patients were enrolled in the present study, as presented in Table I.

Endoscopic procedure. Routine bowel preparation procedures with a total of 3 liters of polyethylene glycol lavage solution in split dosing were performed. A colonoscopy examination was performed by experienced gastroenterologists at Ruijin Hospital North. The completed colonoscopy examination was defined as cecal intubation with photographic evidence of the cecum using endoscopes (Fujinon VP-4450HD-EG-590WM; Fujifilm) equipped with a Picture Archiving and Communication System (PacsVideo diagnostic work station, Neusoft Group Co., Ltd.). The size, morphology and number of polyps were estimated by gastroenterologists. The gastroenterologists performing the colonoscopies were blinded to the study design. They defined the location of all lesions as distal (for lesions located in the rectum, sigmoid, or descending colon) and proximal (those located in the splenic flexure, transverse colon, hepatic flexure, ascending colon, or rectum). All polyp samples were sent for histological examination in an accredited laboratory. Histological specimens were reviewed by an experienced team of pathologists who were blinded to the colonoscopy reports and the study design throughout the study.

The pathological types of colorectal polyps were classified into adenomatous polyps, hyperplastic polyps, hamartomatous polyps and inflammatory polyps according to the World Health Organization histology reporting criteria (6). The latter three were classified as non-adenomatous polyps in the present study. The adenomatous polyps were divided into non-advanced adenomatous and advanced adenomatous polyps, and were defined as an adenoma sized at ≥10 mm, any lesions with at least 25% villous components and adenomas with high-grade intraepithelial neoplasia. The biological characteristics of the multiple polyps were described by the individual with the largest diameter or the highest pathological grades; if the two were not the same polyp, the individual with the higher pathological grade was used.

Histological evaluation. The biopsy samples were fixed in 4% formalin, embedded in paraffin at room temperature, and were performed on 4-μm-thick sections. The histopathological changes of the specimens were examined by hematoxylin and eosin staining and were observed under a light microscope at x400 magnification (Olympus BX-51; Olympus Corporation). Histological diagnosis was independently performed by 2 experienced pathologists.

Statistical analysis. The SPSS 19.0 (IBM Corp.) statistical package for Windows was used for the statistical analysis. Data concerning age and BMI are expressed as the means ± SD. Differences in age and BMI between the 2 groups were analyzed by the independent samples t-test. The Chi-square test was used to compare categorical variables between the different groups. All of the calculated P-values were two-tailed. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Characteristics of patients with and without NAFLD. A total of 1,538 cases of eligible patients with colorectal polyps, including 550 cases of NAFLD (NAFLD group), 988 cases without NAFLD (control group), were enrolled in the present study. No statistically significant differences were observed in sex and age between the 2 groups ($P>0.05$). The BMI and body

Table I. Characteristics of patients with and without NAFLD.

Characteristic	NAFLD n=550 (%)	Control n=988 (%)	P-value
Sex			0.224
Male	337 (61.3)	574 (58.1)	
Female	213 (38.7)	414 (41.9)	
Age (years)	59.9±10.7	60.1±11.6	0.740
Young of age (<60 years)	231 (42.0)	412 (41.7)	0.909
Older age (≥60 years)	319 (58.0)	576 (58.3)	
BMI (kg/m^2)	25.7±2.9	23.3±2.9	0.001
Normal weight (<24 kg/m^2)	165 (30.0)	592 (59.9)	0.001
Obese (≥24 kg/m^2)	385 (70.0)	396 (40.1)	

Table II. Comparison of location, number, morphology, size, pathological features and advanced adenomatous polyps between the NAFLD and control groups.

Parameter	Total	NAFLD group, n (%)	Control, n (%)	P-value
Location				0.618
Right colon	167 (10.9)	56 (10.2)	111 (11.2)	
Left colon+ rectum	933 (60.6)	330 (60.0)	603 (61.1)	
Right colon + left colon + rectum	438 (28.5)	164 (29.8)	274 (27.7)	
Number				0.037
Single	441 (28.7)	40 (25.5)	301 (30.5)	
Multiple	1,097 (71.3)	410 (74.5)	687 (69.5)	
Morphology				0.680
Flat	516 (33.6)	182 (33.1)	334 (33.8)	
Subpedunculated	717 (46.6)	264 (48.0)	453 (45.9)	
Pedunculated	305 (19.8)	104 (18.9)	305 (19.8)	
Size				0.001
<0.5 cm	120 (7.8)	29 (5.3)	91 (9.2)	
0.5 to <1.0 cm	628 (40.8)	180 (32.7)	448 (45.3)	
1.0 to <2.0 cm	653 (42.5)	266 (48.4)	387 (39.2)	
≥ 2.0 cm	137 (8.9)	75 (13.6)	62 (6.3)	
Pathological features				0.001
Non-adenomas	145 (9.4)	23 (4.2)	122 (12.3)	
Non-advanced adenomas	501 (32.6)	181 (32.9)	320 (32.4)	
Advanced adenomas	892 (58.0)	346 (62.9)	546 (55.3)	
Advanced adenomas				0.012
Size ≥1 cm	594 (66.6)	239 (69.1)	355 (65.0)	
>25% Villous components	256 (28.7)	84 (24.3)	172 (31.5)	
High-grade intraepithelial neoplasia	42 (4.7)	23 (6.6)	19 (3.5)	

weights of the patients in the NAFLD group were significantly higher than those of the control group, with the difference being statistically significant (P<0.05; Table I).

Biological characteristics of polyps. No statistically significant differences were observed in the location of polyps between the NAFLD group and control group (P>0.05); however, the number of polyps in patients in the NAFLD group was higher than that in the control group (P<0.05). The morphology of the polyps was mainly that of subpedunculated polyps in the 2 groups (P>0.05). In the NAFLD group, the percentage of the size of polyps ranging from 1.0 to 2.0 cm was 48.4%; moreover, the percentage of the size of polyps ranging from 0.5 to 1.0 cm was 45.3% in the control group, revealing statistically significant differences between the 2 groups (P<0.05; Table II).

The pathological features of the polyps in both groups were mainly those of advanced adenomas;

Table III. Comparison of features of polyps between the NAFLD and control groups according to sex.

	Male			Female		
Parameter	NAFLD (n=337)	Control (n=574)	P-value	NAFLD (n=213)	Control (n=414)	P-value
Location			0.642			0.381
Right colon	22 (6.5)	47 (8.2)		34 (15.9)	64 (15.4)	
Left colon + rectum	205 (60.8)	339 (59.0)		125 (58.7)	264 (63.8)	
Right colon + left colon + rectum	110 (32.7)	188 (32.8)		54 (25.4)	86 (20.8)	
Number			0.085			0.338
Single	65 (19.3)	139 (24.2)		75 (35.2)	162 (39.1)	
Multiple	272 (80.7)	435 (75.8)		138 (64.8)	252 (60.9)	
Morphology			0.356			0.382
Flat	92 (27.3)	180 (31.3)		90 (42.3)	154 (37.2)	
Subpedunculated	173 (51.3)	269 (46.9)		91 (42.7)	184 (44.4)	
Pedunculated	72 (21.4)	125 (21.8)		32 (15.0)	76 (18.4)	
Size			0.000			0.001
<0.5 cm	18 (5.4)	51 (8.9)		11 (5.2)	40 (9.7)	
0.5-<1.0 cm	111 (32.9)	236 (41.1)		69 (32.4)	212 (51.2)	
1.0-<2.0 cm	156 (46.3)	249 (43.4)		110 (51.6)	138 (33.3)	
≥2.0 cm	52 (15.4)	38 (6.6)		23 (10.8)	24 (5.8)	
Pathological features			0.006			0.001
Non-adenomas	16 (4.8)	63 (11.0)		7 (3.3)	59 (14.3)	
Non-advanced adenomas	112 (33.2)	178 (31.0)		69 (32.4)	142 (34.3)	
Advanced adenoma	209 (62.0)	333 (58.0)		137 (64.3)	213 (51.4)	
Advanced adenomas			0.126			0.082
Size ≥1 cm	147 (70.4)	225 (67.6)		92 (67.2)	130 (61.0)	
>25% Villous components	49 (23.4)	97 (29.1)		35 (25.5)	75 (35.2)	
High-grade intraepithelial neoplasia	13 (6.2)	11 (3.3)		10 (7.3)	8 (3.8)	

however, the proportion of advanced adenomas in the NAFLD group (62.9%) was significantly higher than that in the control group (55.3%); the proportion of non-adenomatous polyps (4.2%) in the NAFLD group was lower than that in the control group (12.3%), revealing a statistically significantly difference between the 2 groups (P<0.05; Table II). According to the advanced adenoma definitions, in the 2 groups of patients, the sizes of the polyps were mainly ≥1 cm; however, the percentage of high-grade intraepithelial neoplasia (6.6%) in the NAFLD group was higher than that in the control group (3.5%), revealing statistically significant differences (P<0.05; Table II).

Stratification analysis of subgroups according to sex, age and BMI

Sex stratification. In male and female patients, the polyp distribution area, number or morphology exhibited no statistically significant differences between the NAFLD group and control group (P>0.05, respectively); however, a polyp size of 1.0-<2.0 cm and ≥2.0 cm or the percentage of advanced adenomas were significantly higher in the NAFLD group compared with the control group (P<0.05). Further statistical analysis revealed that the classification percentage of advanced adenomas did not exhibit any statistically significant differences between the NAFLD and the control group in the male and female patients (P>0.05, respectively; Table III).

Age stratification. In the stratification of young and elderly patients, the location, number and morphology of polyps exhibited no statistically significant differences between the NAFLD group and the control group (P>0.05, respectively); however, in the stratification of the young and elderly patients, the polyp size of 1.0-<2.0 cm and ≥2.0 cm and the number of advanced adenomatous polyps were significantly higher in the NAFLD group compared with the control group (P<0.05, respectively). Further analysis revealed that the classification percentage of advanced adenomas did not exhibit a statistically significant difference between the NAFLD group and the control groups in the young and elderly patients (P>0.05; Table IV).

BMI stratification. In the stratification of patients with normal weight and those who were obese (overweight), the location, number and morphology of the polyps exhibited no statistically significant differences between the NAFLD group and the controls (P>0.05, respectively); however, in this stratification of body weight, a polyp size of 1.0-<2.0 cm and ≥2.0 cm and the number of advanced adenomatous polyps were significantly higher in the NAFLD group compared with the control group (P<0.05, respectively). Further analysis

Table IV. Comparison of features of polyps between the NAFLD and control groups according to age.

	Young (<60 years old)			Elderly (≥60 years old)		
Parameter	NAFLD (n=231)	Control (n=412)	P-value	NAFLD (n=319)	Control (n=576)	P-value
Location			0.099			0.316
Right colon	17 (7.4)	53 (12.9)		39 (12.2)	58 (10.1)	
Left colon + rectum	161 (69.7)	269 (65.3)		169 (53.0)	334 (58.0)	
Right colon + left colon + rectum	53 (22.9)	90 (21.8)		111 (34.8)	184 (31.9)	
Number of polyps			0.294			0.062
Single	67 (29.0)	136 (33.0)		73 (22.9)	165 (28.6)	
Multiple	164 (71.0)	276 (67.0)		246 (77.1)	411 (71.4)	
Morphology			0.581			0.671
Flat	66 (28.6)	133 (32.3)		116 (36.4)	201 (34.9)	
Subpedunculated	118 (51.1)	195 (47.3)		146 (45.7)	258 (44.8)	
Pedunculated	47 (20.3)	84 (20.4)		57 (17.9)	117 (20.3)	
Size			0.000			0.001
<0.5 cm	9 (3.9)	39 (9.5)		20 (6.2)	52 (9.0)	
0.5-<1.0 cm	76 (32.9)	193 (46.8)		104 (32.6)	255 (44.3)	
1.0-<2.0 cm	112 (48.5)	151 (36.7)		154 (48.3)	236 (41.0)	
≥2.0 cm	34 (14.7)	29 (7.0)		41 (12.9)	33 (5.7)	
Pathological features			0.000			0.014
Non-adenomas	7 (3.0)	60 (14.6)		16 (5.0)	62 (10.8)	
Non-advanced adenomas	77 (33.3)	140 (34.0)		104 (32.6)	180 (31.3)	
Advanced adenoma	147 (63.7)	212 (51.4)		199 (62.4)	334 (58.0)	
Advanced adenomas			0.173			0.059
Size ≥1 cm	108 (73.5)	150 (70.8)		131 (65.8)	205 (61.4)	
>25% Villous components	32 (21.8)	58 (27.4)		52 (26.1)	114 (34.1)	
High-grade intraepithelial neoplasia	7 (4.7)	4 (1.9)		16 (8.0)	15 (4.5)	

revealed that the percentage of patients of normal weight with high-grade intraepithelial neoplasia was significantly higher in the NAFLD group (10.4%) compared with the control group (2.5%; P>0.05), however, no statistically significant differences were observed in the obese patients between the NAFLD group and the controls as regards the percentage of advanced adenomas (P>0.05; Table V).

Discussion

Colorectal cancer is a common malignancy, ranking fourth among the causes of cancer-related mortality in China. Its incidence has increased in recent decades, and now more than one million Colorectal cancer patients are diagnosed and thousands succumb to the disease annually (7). The 5-year survival rate varies according to the stage at diagnosis, which is approximately 90% in the early stages of disease, and <10% in advanced disease (8).

Colorectal polyps, particularly adenomatous polyps (including serrated adenomas), have been shown to be associated with the development of colorectal cancer. In addition to genetic factors, it has been found that colorectal cancer is closely associated with individual lifestyle and dietary habits, including physical activity, being overweight, cardiac obesity, a high-fat diet and smoking (9), which are also risk factors for the onset of NAFLD (10). In recent years, some studies have proposed a significantly association between NAFLD and the risk of developing colorectal adenoma (11-14).

It was previously demonstrated in a related study population that colorectal cancer patients with NAFLD had higher BMI and ALT values than colorectal cancer patients without NAFLD (11). Additionally, colorectal cancer patients with NAFLD were diagnosed earlier than colorectal cancer patients without NAFLD. However, no significant differences were observed between the 2 groups as regards the location and differentiation of tumors. The cumulative 1-, 3- and 5-year survival rates in colorectal cancer patients with NAFLD were 98.3, 89.8 and 86.4%, respectively, which were higher, but statistically not significant than those of the CRC patients without NAFLD (90.4, 79.6 and 74.8%, respectively). During the follow-up, freedom from recurrence was similarly observed in colorectal cancer patients with and without NAFLD. The results of that study suggest that the presence of NAFLD does not influence the prognosis of colorectal cancer patients; however, NAFLD is a risk factor for colorectal cancer and may be related with the development of colorectal polyps (11). Moreover, another retrospective study included data from 5,517 females, 15.1% of whom were diagnosed with NAFLD (12). During the follow-up,

Table V. Comparison of features of polyps between the NAFLD and control groups according to BMI.

	Normal weight (BMI<24 kg/m^2)			Obese (overweight) (BMI≥24 kg/m^2)		
Parameter	NAFLD (n=165)	Control (n=592)	P-value	NAFLD (n=385)	Control (n=396)	P-value
Location			0.422			0.719
Right colon	16 (9.7)	69 (11.7)		40 (10.4)	42 (10.6)	
Left colon + rectum	112 (67.9)	369 (62.3)		218 (56.6)	234 (59.1)	
Colorectal	37 (22.4)	154 (26.0)		127 (33.0)	120 (30.3)	
Number of polyps			0.920			0.082
Single	52 (31.5)	189 (31.9)		88 (22.9)	112 (28.3)	
Multiple	113 (68.5)	403 (68.1)		297 (77.1)	284 (71.7)	
Morphology			0.423			0.653
Flat	67 (40.6)	210 (35.5)		115 (29.9)	124 (31.3)	
Subpedunculated	64 (38.8)	260 (43.9)		200 (51.9)	193 (48.7)	
Pedunculated	34 (20.6)	122 (20.6)		70 (18.2)	79 (20.0)	
Size			0.000			0.001
<0.5 cm	9 (5.5)	59 (10.0)		20 (5.2)	32 (8.1)	
0.5-<1.0 cm	45 (27.3)	279 (47.1)		135 (35.1)	169 (42.7)	
1.0-<2.0 cm	90 (54.5)	218 (36.8)		176 (45.7)	169 (42.7)	
≥2.0 cm	21 (12.7)	36 (6.1)		54 (14.0)	26 (6.5)	
Pathological features			0.001			0.001
Non-adenomas	8 (4.8)	76 (12.8)		15 (3.9)	46 (11.6)	
Non-advanced adenoma	42 (25.5)	189 (31.9)		139 (36.1)	131 (33.1)	
Advanced adenomas	115 (69.7)	327 (55.2)		231 (60.0)	219 (55.3)	
Advanced adenomas			0.001			0.661
Size ≥1 cm	77 (67.0)	210 (64.2)		162 (70.1)	145 (66.2)	
>25% Villous components	26 (22.6)	109 (33.3)		58 (25.1)	63 (28.8)	
High-grade intraepithelial neoplasia	12 (10.4)	8 (2.5)		11 (4.8)	11 (5.0)	

the findings demonstrated a significant association between NAFLD and colorectal neoplasms. Among the various manifestations of metabolic syndrome, NAFLD may predict the development of colorectal neoplasms in women (12). Therefore, the study of the association between NAFLD and colorectal adenoma was conducive to the early screening and treatment of colorectal tumors.

In the present study, the personal and family tumor histories and other chronic intestinal diseases which affected the development of colorectal polyps were excluded; the revealed no statistically significant differences between the NAFLD group and the control group as regards the location and morphology of the polyps. However, the polyps in the patients with NAFLD tended to be multiple (74.5%) compared with those in the non-NAFLD patients. Previous meta-analyses demonstrated that NAFLD was significantly associated with the number of colorectal adenomas (13,14). Secondly, in the present study, the polyps in the patients with NAFLD were relatively larger in size, with >60% of patients having polyps ≥1.0 cm in size, of which a polyp size of ≥2.0 cm accounted for 13.6% of the patients with NAFLD; however, in the control group, a polyp size of ≥2.0 cm only accounted for 6.3% of the patients. Therefore, endoscopists should pay attention to the characteristics of such patients. It is recommended that the patient's bowel preparation should be more adequate and attention should be paid to the parts that are easily missed during the examination, such as the back of the fold, the lengthy sigmoid colon, etc. Moreover, multiple and large polyps increase the difficulty of endoscopic treatment, and also require endoscopists to be vigilant to avoid surgical complications. As regards histopathology, the present study demonstrated that the percentage of advanced adenomas in the NAFLD group was higher than that of the control group (62.9 vs. 55.3%). The study by Wong *et al* (15) demonstrated that in patients with NAFLD and colorectal tumors, the percentage of advanced adenomas was significantly higher than that of the non-NAFLD group. In addition, the study by Stadlmayr *et al* (16) demonstrated that the percentage of tubular adenomas was increased, although the percentage of advanced adenomas did not differ between the NAFLD group compared with the non-NAFLD group. Although the results of these studies slightly differ, the data of these studies indicate that the incidence of colorectal adenomas was significantly higher in NAFLD patients than in the general population. Therefore, attention should be paid to the characteristics of this class of patients with a high polyp histopathology, and early detection and timely treatment are of particular importance for these patients. As advanced adenomas become cancerous, patients will have to endure an increasing number of severe

consequences, such as surgery and chemotherapy. At the same time, post-operative follow-up needs to emphasize the interval and number of examinations in order to avoid missed diagnosis and the recurrence of advanced adenoma. In terms of etiology, it may be related to the chronic inflammatory state and the abnormal hormone levels of NAFLD.

NAFLD is a type of acquired metabolic stress liver injury. Various changes in dietary intake which have occurred in recent years, characterized by an increase in energy intake due to enhancements in the consumption of flour, cereal products, added sugars and fats, and/or in total fat and fruit intake, are changes that have undoubtedly played a role in the increase in the prevalence of NAFLD in association with the increase in obesity. Consequently, the high prevalence of a high energy diet and obesity are closely associated with the incidence of colorectal tumors (17).

Some researchers have found that the serum levels of pro-inflammatory cytokines, such as including tumor necrosis factor (TNF)-α, interleukin (IL)-6 and IL-8 in patients with NAFLD are significantly higher than those in the normal population (18), which have been found to be significantly associated with the risk of developing colorectal cancer (19). These pro-inflammatory cytokines can stimulate cell growth, and induce the malignant transformation of cells by regulating the body's immunity. Therefore, these pro-inflammatory cytokines also regulate the progression of colorectal adenomas to colorectal cancerous. Similarly, the long-term use of drugs, such as aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) may reduce the risk of colorectal cancer by inhibiting inflammatory responses (20). However, patients with NAFLD also exhibit an increase in hepatic oxidative stress and pro-lipogenic states. These are very important aspects as the decrease in the activity of the transcription factor, peroxisome proliferator-activated receptor (PPAR)-α, allows for an increase in the pro-lipogenic and pro-inflammatory state in patients with NAFLD by the lower synthesis and/or deposits of n-3 polyunsaturated fatty acids (PUFAs). These are directly related to alterations in the regulation of cell reproduction to promote growth of colon polyps (21).

The levels of hormones are another important factor for the development of colorectal tumors in patients with NAFLD. For example, insulin resistance, as a risk factor for NAFLD, is closely related to colorectal adenoma and colorectal cancer (22). Increased levels of insulin regulate the number of liver growth hormone receptors to reduce insulin-like growth factor binding protein, upregulating insulin-like growth factor 1 (IGF-1), and subsequently inhibiting cell apoptosis through the IGF-1 signaling pathway, and thus promoting the malignant proliferation of cells (23). Adiponectin has been shown to be negatively associated with insulin resistance, and to play an anticancer role by inducing tumor cell apoptosis and inhibiting tumor angiogenesis (24). On the contrary, leptin play a promoting role in cancer, which is positively associated with insulin resistance, and promotes the proliferation, migration and invasion of tumor cells through various signaling pathways (25). Moreover, compared with the healthy population, the levels of adiponectin are decreased and the levels of leptin are increased in patients with NAFLD (26), both of which play important roles in the fat metabolic axis. Some studies (27,28) have confirmed that adiponectin and leptin are involved into the occurrence of colorectal tumors.

The analysis of other data in the present study revealed that sex, age and being overweight only affected individual data as regards the association between NAFLD and colorectal polyps; however, a larger polyp size and the incidence of advanced adenomas in patients with NAFLD was more common compared with that in the control group. It should be noted that the proportion of high-grade intraepithelial neoplasia in patients with NAFLD with a normal weight was higher than that in the control group, the results of which will be further analyzed and discussed in future studies.

In conclusion, NAFLD has an impact on the development of colorectal polyps, which are characterized by a larger size, multiple polyps or the increasing incidence of advanced adenomas in affected patients. Therefore, clinical attention should be paid to the colonoscopy screening of patients with NAFLD. For patients with NAFLD with normal colonoscopy results, a change in their lifestyle and diet should be suggested, so as to prevent the occurrence of colorectal polyps.

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Availability of data and materials

The datasets used during the present study are available from the corresponding author upon reasonable request.

Authors' contributions

XYu, LX and PC conceived and designed the study. YZ collected and assembled the data. XYuan and YW performed the data analysis and interpretation. All the authors contributed to the writing and final approval of the manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics approval and consent to participate

All the patients signed an informed consent form prior to the procedure. The informed consent forms obtained the consent of patients to use their clinical data, and they were assured that no identifiable personal information would be disclosed. The present study was approved by Ruijin Hospital North, Shanghai Jiaotong University School of Medicine (Shanghai, China) (approval no. 2017-2-01).

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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