



European Association for the Study of the Liver

# Nonalcoholic steatohepatitis is associated with a higher risk of advanced colorectal neoplasm

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#### INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is known to increase the risk of adenomatous colonic polyps.

However, the role of screening colonoscopy in patients with biopsy-proven NAFLD in detecting advanced colorectal neoplasm is not clearly evidence-based.

### AIM

We investigated whether the histological severity of NAFLD is associated with advanced colorectal neoplasm.

### METHOD

This study included patients >18 years old who underwent routine colonoscopy between 2013 and 2018 within a biopsyevaluated prospective NAFLD cohort.

Advanced colorectal neoplasm was defined as an adenomatous polyp greater than 10 mm in diameter and/or with villous histology and/or with high-grade dysplasia or adenocarcinoma.

#### RESULTS

Among the 476 subjects with biopsyproven NAFLD (n = 379) and healthy controls without any evidence of NAFLD (n = 97) who underwent colonoscopy, the prevalence of advanced colorectal neoplasm was 11.1% (n = 53).

Patients with advanced colorectal neoplasm had higher grade of steatosis (P = 0.004) and higher stage of hepatic fibrosis (P = 0.044) than those with normal colonoscopic findings or low-grade adenomatous polyp.

Multivariable logistic regression analysis revealed that the presence of nonalcoholic steatohepatitis (NASH) was an independent risk factor for both colorectal polyp (odds ratio [OR], 2.08; 95% confidential interval [CI], 1.12 - 3.86; P = 0.020) and advanced colorectal neoplasm (OR, 2.81; 95% CI, 1.01-7.87; P = 0.049).

	No colorectal adenoma (n = 329)	Low-grade tubular adenoma (n = 95)	Advanced colorectal neoplasm (n = 48)	Total (n = 472)	P-value	
Histological spec	ctrum of NAFLD				.076	
No NAFLD	63 (19.1%)	14 (14.7%)	5 (10.4%)	82 (17.4%)		
NAFL	122 (37.1%)	50 (52.6%)	22 (45.8%)	194 (41.1%)		
NASH	132 (40.1%)	30 (31.6%)	21 (43.8%)	183 (38.8%)		
NAS	3.2 ± 1.9	$3.0 \pm 1.7$	3.4 ± 1.5	3.2 ± 1.8	.524	
Steatosis grade,	Steatosis grade, n (%)					
0 (<5%)	74 (22.5%)	15 (15.8%)	5 (10.4%)	94 (19.9%)		
1 (5-33%)	80 (24.3%)	40 (42.1%)	20 (41.7%)	140 (29.7%)		
2 (34–66%)	87 (26.4%)	24 (25.3%)	12 (25%)	123 (26.1%)		
3 (≥67%)	88 (26.7%)	16 (16.8%)	11 (22.9%)	115 (24.4%)		
Lobular inflamm	ation, n (%)				.159	
0	87 (26.4%)	20 (21.1%)	6 (12.5%)	113 (23.9%)		
1	196 (59.6%)	59 (62.1%)	33 (68.8%)	288 (61.0%)		
2	45 (13.7%)	14 (14.7%)	9 (18.8%)	68 (14.4%)		
3	1 (0.3%)	2 (2.1%)	0 (0%)	3 (0.6%)		
Portal inflamma	tion, n (%)				.557	
Absent	131 (39.8%)	34 (35.8%)	18 (37.5%)	181 (38.3%)		
Minimal	105 (31.9%)	31 (32.6%)	17 (35.4%)	153 (32.4%)		
Mild	58 (17.6%)	16 (16.8%)	7 (14.6%)	81 (17.2%)		
Moderate	22 (6.7%)	13 (13.7%)	4 (8.3%)	39 (8.3%)		
Severe	7 (2.1%)	1 (1.1%)	2 (4.2%)	10 (2.1%)		
Ballooning, n (%	)				.493	
0	140 (42.6%)	46 (48.4%)	16 (33.3%)	202 (42.8%)		
1	46 (14.0%)	44 (46.3%)	30 (62.5%)	247 (52.3%)		
2	16 (4.9%)	5 (5.3%)	2 (4.2%)	23 (4.9%)		
Fibrosis, n (%)					.029	
F0	101 (30.7%)	37 (38.9%)	8 (16.7%)	146 (30.9%)		
F1	127 (38.6%)	28 (29.5%)	23 (47.9%)	178 (37.7%)		
F2	57 (17.3%)	16 (16.8%)	7 (14.6%)	80 (16.9%)		
F3	17 (5.2%)	8 (8.4%)	1 (2.1%)	26 (5.5%)		
F4	27 (8.2%)	6 (6.3%)	9 (18.8%)	42 (8.9%)		
NAS, NAFLD act nonalcoholic	ivity score; NAFLD,	nonalcoholic fatty	liver disease; NAF	L, nonalcoholic fat	ty liver; NASH,	

Table 1. Histological characteristics according to the presence of low-grade tubular adenoma or advanced colorectal neoplasm

	U	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value	
Age (year)	1.03	1.01-1.06	.001	1.03	1.004-1.06	.024	
Sex	1.06	0.72-1.58	.759	0.74	0.41-1.33	.307	
BMI (kg/m2)	1.02	0.96-1.08	.491	1.004	0.92-1.10	.938	
Waist circumference (cm)	1.00	0.98-1.03	.915				
Diabetes mellitus	1.27	0.78-2.06	.339				
Hypertension	2.37	1.46-3.86	<.0001	1.64	0.90-2.98	.106	
Smoking	1.14	0.70-1.86	.591				
hsCRP (mg/dL)	1.47	0.87-2.50	.154				
HOMA-IR	0.98	0.92-1.04	.447				
Metabolic syndrome	2.24	1.36-3.66	.001	1.64	0.79-2.66	.229	
Lobular inflammation							
0	1		a .054				
1	1.41	0.85-2.34	.187				
2	1.53	0.78-3.00	.211				
3	6.00	0.52-68.9	.150				
Ballooning							
0	1		a .780				
1	0.90	0.60-1.36	.626				
2	0.92	0.36-2.36	.870				
Steatosis grade							
0	1			1			
1-3	8.20	3.04-22.1	<.0001	3.89	1.41-10.7	009	
Advanced fibrosis							
F0-F2	1						
F3-F4	1.50	0.79-2.83	.209				

OR, odds ratio; 95% CI, 95% confidential interval; BMI, body mass index; hsCRP, high sensitivity C-reactive protein; HOMA-IR, homeostasis model assessment of insulin resistance; NAFLD, nonalcoholic fatty liver disease; NAFL nonalcoholic fatty liver; NASH, nonalcoholic steatohepatitis. <sup>a</sup> P-value for the test of trend of odds.

Table 2. Univariate and multivariate analyses for development of adenomatous colorectal polyp

## CONCLUSIONS

The presence of biopsy-proven NASH was significantly associated with an increased risk of advanced colorectal neoplasm among patients with NAFLD.

This finding may alert physicians to conduct screening colonoscopy in patients with NASH to detect advanced colorectal neoplasm early.

# CONTACT INFORMATION

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