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Relationship of Colorectal Polyps and Fatty Liver Disease Diagnosed by Ultrasonography

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초음파로 진단된 지방간 질환과 대장 용종과의 연관성

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Abstract This study proposes a more comprehensive approach for FLD by analyzing the relationship of colorectal polyps, which are precursors of colorectal cancer. In Chi-Square tests of FLD and colorectal polyps, the prevalence of colorectal polyps was significantly high in cases of FLD. The polyps and correlation of each factor showed a positive relationship with all factors, and the correlation coefficient with FLD was highest (r = 0.39, p <.001). In multiple regression analysis, FLD(OR 3.80 95% CI 1.93.-7.50), FBS (OR 2.51; 95% CI 1.12-5.62), and older age (OR 2.12; 95% CI 1.27-3.54) were independent risk factors for colorectal polyps. FLD was associated with the prevalence of colorectal polyps. These results show a meaningful influenceof FLD by ultrasonography in the occurrence of colorectal polyps, and that positive consideration of colonoscopy is needed for diagnosed FLD.

Key Words : Ultrasonography, Colorectal Polyp, Fatty Liver Disease, Colonoscopy, Colon cancer

요 약 지방간은 초음파검사에 의해 진단되는 임상적으로 흔한 간질환이다. 본 연구에서는 지방간과 대장암의 전구병변인 대장용종과의 연관성을 분석하여 지방간에 대한 보다 포괄적인 접근방법을 제시하고자 한다. 2012년부터 2013년 1년 동안 청주소재 소화기내과전문센터에서 복부초음파와 대장내시경검사를 동시에 시행한 만성간질환이나 대장질환이 없는 성인 348명을 대상으로 하였다. 지방간과 대장용종의 Chi-Square test에서 지방간이 있는 사람이 지방간이 없는 사람보다 유의미하게 용종이 많이 발생하였다(p<.001). 각 요인별 상관관계를 보았을 때 지방간과 대장용종간의 상관관계가 가장 높았다(p<.001). 다중회귀분석에서는 지방간(OR 3.80; 95% CI 1.93.-7.50), 공복 시 혈당(OR 2.51; 95% CI 1.12-5.62), 나이(OR 2.12; 95% CI 1.27-3.54) 이 대장용종의 발생에 유의미하게 작용하였다. 이상의 연구결과에서 초음파검사로 진단된 지방간이 대장용종의 발생에 있어 유의미한 영향력을 나타내어 지방간으로 진단되었을 때에는 대장내시경검사를 좀 더 적극적으로 고려해보는 것이 좋을 것이다.

주제어 : 초음파, 지방간, 대장용종, 대장암, 대장내시경검사

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1. Introduction

The changes of modern society have led to modern diseases such as obesity, insulin resistance syndrome, FLD and colorectal cancer. Medical check up programs at individual and national levels are developing rapidly for preventive medicine.

The usefulness of ultrasound has already made it a popular examination method in health checkup programs. This method is the common for imaging diagnosis of liver disease, particularly FLD. FLD was first diagnosed by ultrasound in most cases, but patients tend to easily overlook the diagnosis because they do not have serious subjective symptoms when they have FLD diagnoses. Colorectal cancer, which is rapidly increasing along with the FLD, is the third most frequently occurring disease among all cancers in South Korea, and it has been increasing by an average of 6.9% annually from 1999 to 2008, overtaking the US and UK, which are current representative risky countries for colorectal cancer [1].

Many epidemiologic studies reported that insulin resistance syndrome is a factor increasing the occurrence of malignant tumors of the colon [2][3]. Currently, the most important method to prevent colorectal cancer is the early detection and removal of colorectal polyps, which are known as precursors of colorectal cancer [4]. The numbers of progressive adenoma and occurring polyps in the whole colon have been increased for the last 10 years, and the rate of patients having colon polypectomies is also increasing [5]. The correlation between adenomatous polyps and non-alcoholic fatty liver disease has been reported recently in South Korea, but there are few cases, and the consistency of the results is inadequate. The purpose of this research is aggressive recognition for fatty liver, and to satisfy the needs of ultrasonography and colonoscopy by analyzing the correlation between diagnosed fatty liver and colorectal polyps by ultrasonography.

2. Method

2.1 Subject

A total of 348 patients were selected as subjects from 380 adults who had colonoscopy and abdomen ultrasonography at the Digestive Internal Medical Center located in Cheongju, Chungbuk,from October 2012 to March 2013, excluding patients with acute and chronic liver disease or colon disease. The sex ratio of the subjects was 59.2%(206) male and 40.8% (142) female, and the average age of subjects was 51.51(±10.95). 55.2%(192) of the subjects were diagnosed for fatty liver disease by ultrasonography and 50.3%(175) subjects were diagnosed with colorectal polyps by colonoscopy.

2.2 Ultrasonography

The instrument used for abdomen ultrasonography was a Prosound SSD-4000(ALOKA, Japan). Subjects were fasted at least 6 hours before examination, and a convex probe of 5.0 MHz was used by three skilled radiologists and sonographers who did not have information on the purpose of the examination and clinical pathological results. Fatty liver is classified into 4 stages from known 4 standards regarding liver brightness, hepatorenal echogenic contrast, deep attenuation, and vascular blurring. The number of subjects diagnosed with fatty liver disease was 55.22%(192), and the average age was 53.06. The distributions were the normal group 44.8%(156), mild fatty liver 24.4%(85), moderate fatty liver 25.3%(88), and severe fatty liver 5.5%(19). This research is only analyzed by the status of fatty liver for irregular distribution of subjects according to the degree of fatty liver.

2.3 Colonoscopy

The colonoscopy instrument used for the examination was a CF-Q260AL(Olympus optical Co., Japan). Following bowel preparation with 4 L of

polyethylene glycol lavage solution, colonoscopy was performed by 3 endoscopy specialists until the last part of the distal colon. A subject was included in the polyp group if at least one polyp was present, regardless of number and size of the polyp. 175 subjects(50.3%) were diagnosed with colorectal polyps, and the average age of the subjects was 53.80(±10.33).

2.4 Measurements and data

The height and weight of each subject were measured by a skilled nurse with subjects only wearing a check up gown from the hospital. Blood was collected 8 hours after fasting, and blood pressure was measured in a sitting position 5 minutes after stabilization by a standard mercury sphygmomanometer. Abdominal obesity was considered for waist circumference over 85 cm for females and over 90 cm for males according to the abdominal obesity standard of the Korean Society for the Study of Obesity.

Cholesterol standards were 240 mg/dL of total cholesterol(TC) and 160 mg/dL of low-density lipoprotein cholesterol(LDL-C) according to the National Cholesterol Education Program Adult Treatment panel Phase III(NCEP-ATP III) modified guideline. Triglyceride(TG) standards were 150 mg/dL, 40 mg/dL for males, and 50 mg/dL for females of high-density lipoprotein cholesterol (HDL-C), 140 mmHgof maximal systolic blood pressure, 90 mmHg of diastolic blood pressure, and 111 mg/dL of blood sugar(glucose) in fasting according to the CNEP-ATP III guideline revised in 2004. The body mass index(BMI, kg/m^2) over 25 kg/m^2 was considered as obesity according to the Korean nutrition survey standard. The standards of liver function rate were AST 12-38 IU/L, ALT 7-41 IU/L, and GGT 9-58 IU/L.

2.5 Data analysis

The statistical analysis was performed with the SPSS program V.12.0 in Windows. The statistical results were presented as the mean ± standard deviation. Statistical analyses included an independent t-test, X2-test, and Pearson's correlation analysis. The relationship of FLD with the presence of colorectal polyps was evaluated by multiple logistic regression analysis after adjustment for independent variables.

The p value under 0.05 was considered as statistically significant, and the significance level was 95%.

3. Results

3.1 Baseline characteristics of the study participants

Among the 348 subjects in this study, 192 subjects(55.2%) were diagnosed with fatty liver disease, and 173 subjects(49.7%) were diagnosed with colorectal polyps. The average age of subjects who have polyps was 53.80(±10.33), and the average age of subjects who did not have polyps was 49.53 (±11.71). The baseline characteristics of the mean values summarized are in [Table 1].

3.2 Basic frequency of study participants with risk factors of polyps

Polyps were found in 112 people(54.3%) of 206 people(59.2%) among male subjects, and 118 people[1)] (57.8%) of 204 people(58.6%) with older age ($p=0.036$)($p<0.001$).

Also, polyps were found in 50 people(76.9%) of 65 people(18.7%) with a higher fasting glucose, 129 people(67.2%) of 192 people(55.2%) with FLD, 68 people(52.3%) of 103 people(29.6%) with higher triglycerides, and 44 people(66.7%) of 66 people(19.0%) with higher GGT. 63 people(36.3%) had no polyps with fatty liver and 44 people(25.4%) had no fatty liver with polyps.

<Table 1> Comparison of baseline characteristic of the study participants

	variables	without polyp n=175(50.3%)	polyp n=173(49.7%)
NL n=156 (44.8%)	Age	48.8±11.4	52.9±11.7
	SBP(mmHg)	119.3±12.4	121.4±12.8
	DBP(mmHg)	77.0±9.5	76.7±8.8
	TC(mg/dL)	187.7±37.3	190.2±27.0
	AST(mg/dL)	24.3±9.5	23.1±9.0
	ALT(mg/dL)	24.2±11.7	20.9±8.2
	rGT(mg/dL)	29.9±21.1	28.3±13.2
	WC(cm)	79.6±7.3	79.3±8.0
	BMI(kg/㎡)	22.4±2.3	22.6±2.4
	TG(mg/dL)	97.6±55.0	106.5±48.3
	HDL(mg/dL)	55.9±17.6	54±13.2
FLD n=192 (55.2%)	LDL(mg/dL)	110.5±34.3	111.2±22.1
	Age(years)	50.9±12.2	54.1±9.9
	SBP(mmHg)	127.2±18.2	127.5±13.8
	DBP(mmHg)	82.6±11.1	82.5±9.2
	TC	206.7±37.3	207.6±37.6
	AST	26.0±9.4	32.9±15.8
	ALT	32.3±18.2	38.6±24.2
	rGT	48.3±35.9	55.4±47.0
	WC(cm)	87.9±8.0	90.7±7.8
	BMI(kg/㎡)	25.8±2.7	26.0±2.8
	TG	153.9±104.6	165.7±96.5
	HDL	52.3±16.0	50.8±15.6
	LDL	124.6±37.5	116.9±36.9

NL;normal liver FLD;fatty liver disease
WC;.waist circumference
SBP;Systolic blood pressure DBP;Diastolic blood pressure

Compared with normal subjects, the polyp group subjects were more likely to be men, and to have FLD, older age, higher BMI, WC, fasting glucose, TG, GGT, AST, and ALT <Table 2>

<Table 2> baseline characteristic of the study participant with polyps

Variable		n(%)	normal	polyp: n(%)	p*
Gender	M	206(59.2)	94(45.6)	112(54.4)	
	F	142(40.8)	81(57.0)	61(43.0)	0.036
Age	<50	144(41.4)	89(61.8)	55(38.1)	
	≥50	204(58.6)	86(42.1)	118(57.8)	<0.001
High BMI	Yes	140(40.2)	54(38.6)	86(61.4)	
	No	208(59.8)	121(58.1)	87(41.8)	0.001
FLD	Yes	192(55.2)	63(32.8)	129(67.1)	
	No	156(44.8)	112(71.8)	44(28.2)	<0.001
Raised WC	Yes	200(57.5)	79(39.6)	121(60.5)	
	No	148(42.5)	96(64.9)	52(35.1)	<0.001
Raised glucose	Yes	65(18.7)	15(23.0)	50(77.0)	
	No	282(81.0)	160(56.7)	122(43.2)	<0.001
Elevate SBP	Yes	53(15.2)	22(12.6)	32(17.9)	
	No	295(84.8)	153(87.4)	142(82.1)	0.196
Elevate DBP	Yes	74(21.3)	34(19.4)	40(23.1)	
	No	274(78.7)	141(80.6)	133(76.9)	0.467
Raised TG	Yes	103(29.6)	35(20)	68(39.3)	
	No	245(70.4)	140(80)	105(60.7)	<0.001
Raised TC	Yes	47(13.5)	23(13.1)	24(13.9)	
	No	301(86.5)	152(86.9)	149(86.1)	0.843
Raised GGT	Yes	66(19.0)	22(12.6)	44(25.4)	
	No	282(81.0)	153(87.4)	129(74.6)	0.003
Raised ALT	Yes	68(19.5)	24(13.7)	44(25.4)	
	No	280(80.5)	151(86.3)	129(74.6)	0.007
Raised AST	Yes	54(15.5)	19(10.9)	35(20.2)	
	No	294(84.5)	156(89.1)	138(79.8)	0.019
Low HDL	Yes	129(37.1)	100(57.1)	119(68.8)	
	No	219(62.9)	75(42.9)	54(31.2)	0.055
Raised LDL	Yes	309(88.8)	24(13.7)	15(8.7)	
	No	39(11.2)	151(86.3)	158(91.3)	0.221

3.3 The association of FLD and polyps by the X^2-test

According to the conditions of FLD, there are differences in the presence of colorectal polyps (p <.001). 129 subjects(74.6%) had FLD among the 173 subjects who had polyps, and 44 subjects(25.4%) had polyps among the 156 subjects who did not have FLD (p<.001), <Table3>.

<Table 3> The association of FLD and colorectal polyps

	colorectal polyp			X^2
	polyp n(%)	normal n(%)	total n(%)	
FLD	129 (74.6)	63 (36.3)	192 (55.2)	52.32 (p< 0.001)
NL	44 (25.4)	112 (64)	156 (44.8)	
total	173 (49.7)	175 (50.3)	348 (100.0)	

*By the chi-square test at α=0.05
NL;normal liver FLD;fatty liver disease

3.4 Correlation degree of the risk factors of polyps

Correlation analysis was used with the variables which were significant in the univariate analysis of the prevalence of polyps. Correlation coefficients were the

highest in FLD(r = 0.39, p <.001), followed by FBC(r = 0.26, p <.001), WC(r =0.25, p <.001), TG(r = 0.21, p <.001), age(r = 0.19, p <.001), GGT(r = 0.16, p = .002), ALT(r = 0.15, p = .006), AST(r =0.13, p = .016), <Table4>.

<Table 4> Correlation of risk factors for polyps

	Age	WC	BMI	FBS	FL	TG	AST	ALT	GGT	P
Age	1									
WC	0.10	1								
BMI	0.01	0.50	1							
FBS	0.17	0.2	0.23	1						
FL	0.09	0.49	0.49	0.27	1					
TG	0.10	0.19	0.24	0.25	0.31	1				
AST	0.19	0.11	0.05	0.06	0.15	0.11	1			
ALT	0.10	0.20	0.26	0.14	0.28	0.25	0.47	1		
GGT	0.03	0.22	0.26	0.16	0.32	0.3	0.28	0.40	1	
P	0.19**	0.25**	0.19**	0.26**	0.39**	0.21**	0.13*	0.15**	0.16**	1

*Statistically significant difference by Pearson's correlation coefficient

3.4 Relationship with the risk factors for polyps by the multiple logistic regression analysis

Multiple regression analysis was conducted with each variable that has effective meanings in the occurrences of colorectal polyps in univariate analysis. Multivariate analysis results showed the following odds ratios for FLD(OR 3.80; 95% CI 1.93.-7.50) , FBS(OR 2.51; 95% CI 1.12-5.62), and older age(OR 2.12; 95% CI 1.27-3.54), which were significantly effective to the occurrence of colorectal polyps.

<Table 5> Risk for colorectal polyps by multiple logistic regression analysis Digital

Variable	OR	95% CI		P*
		Lower	Upper	
FG(mg/dL)				0.025
< 111	1			
≥111	2.51	1.12	5.62	
FLD				<0.001
Absence	1			
Presence	3.80	1.93	7.50	
Age				0.004
< 50	1			
≥50	2.12	1.27	3.54	

Adjusted for age, gender OR;odds ratio
CI;confidence interval FG;fasting glucose
FLD;fatty liver disease

4. Conclusions and Discussion

The most reliable diagnosis method for fatty liver is liver biopsy, but this is not a common medical method. Ultrasonography is very sensitive for the recognition of fatty degeneration of liver tissue. Because ultrasound has excellent sensitivity and is less expensive compared with CT, it has become a common health screening method. Also, there is no radiation risk. The incidence of FLD is likely to rise further compared to the past, and colorectal cancer is a typical westernized cancer with a rapid tendency of increasing with obesity.

For the adenoma-carcinoma sequence theory in which adenomatous polyps proceed to cancer, much research has been performed since it was first reported in 1951[6].

The time for malignant transformation from adenoma to cancer is about 5 to 15 years, and over 95% of colorectal cancer is a result of adenomatous polyps. According to the results of comparison between diameter and pathological expression for endoscopic treatment performed for cancer, a small lesion with size less than 5 mm showed 80.8% adenoma, 18.6% hyperplastic polyp, and 0.6% malignant polyp [7]. Hyperplastic polyps turning into colorectal cancer, unlike adenomatous polyps, are controversial. However, the clinical importance of hyperplastic polyps cannot be ignored for histological malignant tumors found in hyperplastic polyps. In addition, risk factors of hyperplastic polyps and adenomatous polyps had no difference, and smoking particularly showed a higher prevalence rate in the analysis of colorectal polyps and life habits.

Colorectal cancer has high relation with metabolic syndromes such as obesity, hyperlipidemia, and glucose in the process of carcinogenesis. After association between obesity and colorectal cancer was established, there has been much research on the relations between colorectal polyps and obesity [8-11]. BMI is used as an

obesity index, but consistent data in the prevalence rate of polyps is not found [12][13]. In the other words, BMI alone cannot be a predictive factor for polyps. This would be an issue for the suitability of BMI in the degree of obesity. Meanwhile, all correlations in the number and size of polyps and BMI were consistent, which means the number and size of polyps simultaneously increased as the BMI increased. In this study, BMI in the prevalence of polyps showed a significant relationship with the onset. The hepatic steatosis index of non-alcoholic fatty liver also considered obesity as an important factor [14]. According to a research report on NAFLD of non-obesity patients, higher weight compared to the past caused a higher rate of fatty liver and many abnormal factors of metabolic syndrome, even with a normal obesity index[15][16]. FLD is associated with risk factors of metabolic syndrome and has higher positive predictive values than body mass index(BMI) and waist circumference [17]. NAFLD could be an early clue to forecast the metabolic disorders in adults who are not obese. NAFLD itself increases the atherosclerosis occurrence risks by 55% in the absence of other risk factors [18]. FLD had the highest impact on the occurrence of polyps in the present report. Fasting glucose, triglycerides, and obesity appeared as risk factors for polyps, which were similar to the results of other studies. Colorectal cancer is highly associated with obesity, hyperlipidemia, and metabolic syndrome in the process of carcinogenesis.

In the present report, drinking and the components of polyps were not considered. Similar results were obtained from other studies regarding the prevalence of polyps. The reason is estimated to be the similar involvement of the metabolic syndrome in FLD and NAFLD, and the highest distribution of adenomatous colorectal polyps[19].

In one study associated with the metabolic syndrome that occupied 69.9% of mild FLD, FLD was not mentioned as a significant factor for metabolic syndrome[20]. Additionally, in another study, NAFLD was mentioned not to have a relationship with the prevalence of colorectal adenomas, showing different opinions from existing study results [21]. Analysis in degrees of FLD was not considered in those studies. The analysis of FLD according to the degrees was not considered in the present report as well. In the cases of highly occupied mild fatty liver, the relation between fatty liver and colorectal polyps could have differences in the results of this study. Therefore, more thorough research for the relation of fatty liver degree by colorectal polyps and ultrasonography is needed in the future. In addition, more complex and broad research analysis with various environmental factors is needed.

The World Health Organization(WHO) said that 1/3 of cancer cases are preventable, and 1/3 are curable when diagnosed early. Colorectal cancer treatment is limited in terms of time, and diagnosis of the earliest colorectal cancer is diagnosable by colonoscopy [22][23].

Colorectal polyps in other research showed frequency increases in males and with age. Glucose, smoking, and hyperlipidemia were risk factors among subjects with no subjective symptoms[24]. This research found polyps in 54.4% of males and 57.8% in those with age over 50. Often, colorectal polyps have no significant associative correlation with subjective symptoms.

The divergence between incidence and mortality rates would suggest that possible explanations may lie in improved accessibility to endoscopy increased early detection with a corresponding shift to an earlier disease stage[25][26]. This trend is having important consequences in regard to disease prevalence and burden of care.

Colonoscopy should actively be encouraged for earlier-stage diagnosis of colorectal cancer, and ultrasonography will also continuously increase and expand for its usability. Since clinically common fatty liver increases the incidence of colorectal polyps, a

more positive attitude is needed for colonoscopy when diagnosing fatty liver by ultrasound.

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