Elevated Serum Triglyceride Predicates Recurrence of Colorectal Polyps in Patients with Advanced Adenomas

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Research

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Abstract

Background

The recurrence of colorectal polyps is common and impacted by various factors. The aim of this study is to explore the association between lipid profiles and recurrence of colorectal polyps.

Methods

We retrospectively analyzed lipid profiles of 435 patients underwent colonoscopy with removal of colorectal polyps, and observed the recurrence of polyps by follow-up endoscopy within the following 1.5 years. Regression logistic was used to evaluate the association between lipid profiles and polyp recurrence.

Results

During the 1.5-year follow-up, recurrences of colorectal polyps were observed in 135 out of 435 patients (30.34%). Patients with recurrent polyps showed higher levels of total cholesterol (TG) (P = 0.006), lower levels of high-density lipoprotein cholesterol (HDL-C) (P = 0.008) and apoliprotein A1 (ApoA1) (P = 0.033). Regression logistic model suggested that TG was an independent risk factor of polyp recurrence (OR: 1.81; CI: 1.29–2.55; P = 0.039) in patients with advanced adenomas.

Conclusions

The lipid profiles are associated with the recurrence of colorectal polyps. Elevated TG would serve as an independent risk predictor of polyp recurrence in patients with advanced adenomas.

Introduction

Colorectal cancer (CRC) is the third most commonly diagnosed cancer and the fourth most deadly cancer worldwide[1]. It is well-known that CRC develops through the adenoma-carcinoma sequence. Patients with colorectal polyps, especially advanced adenomas are at higher risk of CRC than those without them [2]. Thus, colonoscopy with removal of adenomas is generally applied in clinical practice to destroy this sequence. However, the polyps recurs with a high rate, which poses a hazard threat of progressing into CRC. Therefore, it is important to elucidate the risk factors that predicate the recurrence of colorectal polyps.

Colorectal polyps are lesions that grow on mucosal surface and protrude into the colorectal lumen. There are four types of polyps based on World Health Organization (WHO) classification: adenomatous, inflammatory, hyperplastic, and hamartomic polyps [3]. The occurrence rates of different types of polyps varied largely, ranging from 1–43% [4]. Endoscopic mucosal resection (EMR) is an effective technique for removal of colorectal polyps and prevents the development of CRC [5]. However, the recurrence of polyps happens diversely with a rate of 20–50% within 3 to 5 years after removal[4]. Thus, surveillance colonoscopy is highly recommended in clinical practice. Huang et al. investigated surveillance colonoscopy data in southern Chinese population from 1976 to 2007, and concluded that a 3-year follow-up of patients after polypectomy effectively prevented the recurrence of advanced adenoma in high-risk patients [6]. Another study showed that most local recurrences could be detected in first follow-up colonoscopy, while only a minority were detected after more than one colonoscopy[7].

Identification of risk factors that are predictable for recurrence of colorectal polyps is crucial for protecting at-risk individuals against CRC. Various factors are reported to impact the recurrence rate of polyps, such as gender, age, lifestyle, histology features [8]. Leo et al. reported that metabolic factors accelerated colorectal adenoma recurrence [9]. Previous study suggested that obese patients suffered higher recurrence rates than nonbese patients [10]. Similarly, a large BMI, as well as body size is associated with an increased risk of advanced colorectal polyp recurrence [11, 12]. Multiple studies suggeste dyslipidemia is an independent risk factor for colorectal polyps [13, 14]. Recently, Xie et al. found that increased low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) promoted the formation of colorectal polyps [15]. It is reasonable to speculate that serum lipid profiles may play a role in the

recurrence of colorectal polyps. However, to our knowledge, no study as yet has explored the association between lipid profiles and poly recurrence after endoscopic removal.

In the current study, we compared the lipid profiles as well as other baseline parameters between patients with and without polyp recurrences. The aim of this study is to elucidate the role of serum lipid profiles in the recurrence of colorectal polyp.

Materials And Methods

Study Subjects

This is a retrospective study. The study subjects were selected from patients in the Endoscopic Center of the Gastroenterology Department at Meizhou People's Hospital to undergo a complete colonoscopy and first-time removal of colorectal polyps at Jan. 2018 to June 2019. Patient was qualified for analysis if meeting the criteria: (1) histologically diagnosed as colorectal polyps; (2) at least one follow-up colonoscopy was performed six months after polyp removal; (3) has sufficient baseline clinical and laboratory data. Patients were excluded if they had present/previous gastrointestinal tumors, cardiac or pulmonary disease. The study was approved by the Ethics Committee of Meizhou People's Hospital Affiliated to Sun Yat-Sen University.

A total of 3,980 patients took initial colonoscopy and underwent removal of colorectal polyps during this period. 3,207 patients were excluded for absent of follow-up colonoscopy and left 773 patients chosen in our study. Participants were further filtered for lacking pathology reports (n = 80), and/or lipid data (n = 50), or follow-up colonoscopy performed less than 6 months after removal (n = 30). Finally, there were 435 patients going into analysis (**Figure 1**).

Polyp classification and definition of polyp recurrence

Pathology characteristics of colorectal polyps were obtained from pathology reports. Polyps were classified into hyperplastic polyp, inflammatory polyp, tubular adenoma, tubulovillous adenoma. Advanced polyp was defined if one or more following conditions were met: a tubular adenoma with 10 mm or larger in diameter, tubulovillous adenoma, or the presence of high-grade dysplasia[16]. The location of polyps was divided into proximal (cecum, ascending colon, hepatic flexure, transverse colon, and splenic flexure) and distal (descending colon, sigmoid colon, and rectum). In patients with multiple polyps, histologic type, size and location counted on the largest and/or most advanced adenoma.

Polyp recurrence was defined if any polyp was found in the follow-up colonoscopy performed at least 6 months after initial removal, including both at the same location and other locations.

Data collection

Clinical characteristics and laboratory results were obtained from medical records when patients underwent polyp removal. Patients were de-identify before analysis to protect privacy. Baseline characteristics including gender, age, body mass index (BMI), drinking history, smoking history, hypertension, diabetes mellitus (DM) were collected. Lipid profiles were serum total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), apoliprotein A1 (ApoA1) and apoliprotein B(ApoB).

Drinking was defined as positive when consuming alcohol more than 30g/day. Hypertension was defined as blood pressure ≥ 130/85 mmHg and/or current use of anti-hypertensive medication. DM was diagnosed if the patient had either fasting blood glucose of ≥126 mg/dl, a random glucose level of ≥200 mg/dl were taking antidiabetic medication[17]. Dyslipidemia was defined as TC ≥5.17 mmol/L, or TG ≥ 1.7 mmol/L, or HDL-C < 1.04 mmol/L, or LDL-C ≥4.14 mmol/L, or taking anti-dyslipidemic medication.

Statistical analysis

Statistical analyses were performed using SPSS software version 22.0 (SPSS Inc., Armonk, NY). Continuous variables were expressed as mean ± SD. Categorical variables were expressed as proportions. The normality of the distribution of continuous

variables was tested using the Kolmogorov-Smirnov test. Continuous variables were tested by Student's t test, whereas categorical variables were analyzed by Chi-square (χ^2) test or Fisher's exact tests. Univariate and multivariate regression was used to estimate odd ratios (ORs) with 95% CIs. All tests were 2-sided, *P* value < 0.05 was considered statistically significant.

Results

Baseline characteristics of patients

A total of 435 patients went into analysis in the present study. Each patient completed a follow-up of at least 1.5 years, unless found to be presence of recurrent polyps by colonoscopy. The baseline characteristics of the 435 patients are presented in **Table 1**. The average age of total patients was 56.55 years (SD 10.65). Male patients (56.32%) slightly outnumbered female patients. Only a minority of patients were drinking (2.76%) or smoking (11.03%). The proportion of patients with hypertension, DM and dyslipidemia were 19.08%, 6.90% and 26.90%, respectively.

During 1.5-year follow-up, polyp recurrences were found in 132 patients (30.34%). Patients with recurrent polyps were older than those nonrecurrent (*P* < 0.008), and had higher rate of male patients (*P* < 0.001). Patients with recurrent polyps had higher level of TG (*P* = 0.006), and lower level of HDL-C (*P* = 0.008), ApoA1 (*P* = 0.033). The ratio of TG to HDL (TG/HDL) was significantly elevated in patients with recurrent polyps (*P* = 0.006).

Comparison of polyp characteristics between patients with and without recurrence

The characteristics of removed polyps are presented in **Table 2**. Most polyps (74.94%) had a diameter of smaller than 10 mm. In patients with recurrent polyps, large polyps (≥ 20 mm) were more frequent than that in nonrecurrent patients (16.67% *vs.* 8.25%). The polyp number of recurrent and nonrecurrent patients was significant different (*P* < 0.001). The recurrent patients had higher proportion of multiple polyps (≥3) than the nonrecurrent patients(66.67% *vs.* 34.98%). The histology of polyps was different between recurrent and nonrecurrent patients (*P* = 0.028), with higher rate of tubulovillous adenoma in recurrent (21.97% *vs.* 11.55%). The poly location distribution and adenoma classification was not significantly different between recurrent and nonrecurrent patients.

Comparison of serum lipid profiles between patients with and without polyp recurrence

We further analyzed the serum lipid levels in patients with different colorectal polyps. In patients with hyperplastic polyps, recurrent patients presented elevated values of TG and TG/HDL (*P* < 0.05). In patients with tubulovillous adenomas, recurrent patients had higher values of TG and TG/HDL (*P* < 0.05), as well as lower levels of HDL and ApoA1 (*P* < 0.05). Although in patients with inflammatory polyp or tubular adenoma, recurrent patients showed higher values of TG and TG/HDL, the difference didn't reach statistical significance. There was an increased trend of LDL-C values in all patient groups, but the differences were not significant in the four polyp groups (**Table 3**).

Elevated TG associated with the recurrence of colorectal polyps

Regression analysis was used to determine the risk factors associated with polyp recurrence. As shown in **Table 4**, male (OR: 2.26; CI: 1.46 - 3.48), polyp number (OR: 3.66; CI: 2.38 - 5.64), polyp size (OR: 2.22; CI: 1.20 - 4.11), TG (OR: 1.30; CI: 1.07 -1.58) and BMI(OR: 1.10; CI: 1.03 - 1.17) significantly increased the risk of polyp recurrence, while HDL-C (OR: 0.45; CI: 0.25 - 0.82) and ApoA1 (OR: 0.53; CI: 0.29 - 0.95) decreased the risk of poly recurrence. By adjusting for other confounding factors, only male, BMI and polyp number remained the significant predictors for polyp recurrence.

Next, we analyzed the risk factors of polyp recurrence in patients with advanced adenomas. As shown in **Table 5**, polyp number (OR: 3.85; CI: 1.89 -7.89), polyp size (OR: 2.54; CI: 1.22 - 5.36) and TG (OR: 1.81; CI: 1.29-2.55) increased the risk of polyp recurrence, while

HDL (OR: 0.22; CI: 0.08 - 0.62) and ApoA1 (OR: 0.19; CI: 0.06 - 0.61) decreased the risk of polyp recurrence in patients with advanced adenomas. After adjusted for other factors, TG, polyp number polyp size remained as significant predictors for polyp recurrence.

Table 1
Baseline characteristics of the study participants

Parameter	Total (n = 435)	Recurrent (n = 132)	Nonrecurrent (n = 303)	*P*-value
Age (years)	56.55 ± 10.65	58.59 ± 9.73	55.66 ± 10.93	0.008
Male (n, %)	245(56.32%)	92(69.70%)	153(50.50%)	< 0.001
Follow-up (month)	10.80 ± 4.47	11.72 ± 5.00	10.36 ± 4.16	0.003
BMI (kg/m^2)	23.23±3.30	22.91 ± 3.15	23.95 ± 3.54	0.003
Drink (n, %)	12(2.76%)	8(6.06%)	4(1.32%)	0.009
Smoke (n, %)	48(11.03%)	18(13.64%)	30(9.90%)	0.249
Hypertension (n, %)	83(19.08%)	29(21.97%)	54(17.2%)	0.353
Diabetes Mellitus (n, %)	30(6.90%)	9(6.82%)	21(6.93%)	1.00
Dyslipidemia (n, %)	117(26.90%)	42(31.82%)	75(24.75%)	0.127
TC (mmol/L)	5.49 ± 1.22	5.44 ± 1.23	5.40 ± 1.14	0.727
TG (mmol/L)	1.72 ± 1.15	1.74 ± 1.24	1.44 ± 0.92	0.006
HDL-C (mmol/L)	1.35 ± 0.33	1.32 ± 0.33	1.42 ± 0.38	0.008
LDL-C (mmol/L)	3.21 ± 0.85	3.12 ± 0.85	3.08 ± 0.83	0.646
ApoA1(g/L)	1.29 ± 0.33	1.28 ± 0.33	1.37 ± 0.40	0.033
ApoB(g/L)	1.02 ± 0.28	0.97 ± 0.28	0.96 ± 0.28	0.653
TG/HDL	1.47 ± 1.24	1.48 ± 1.37	1.16 ± 1.00	0.006

BMI: body mass index; TC: total cholesterol; TG: triglycerides; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; ApoA1: apoliprotein A1; ApoB: apoliprotein B.

P-value: Comparison between recurrent and nonrecurrent performed by Student's t test or Chi-square (χ^2) test.

Table 2
Comparison of polyps between patients with and without polyp recurrence

Parameter	Total (n = 435)	Recurrent (n = 132)	Nonrecurrent (n = 303)	*P*-value
Polyp size (mm)				0.019
≤10	326 (74.94%)	96(72.73%)	230(75.91%)	
10 - 19	62 (14.25%)	14(10.61%)	48(15.84%)	
≥20	47 (10.80%)	22(16.67%)	25(8.25%)	
Polyp number, n (%)				< 0.001
1	139(31.95%)	20(15.15%)	119(39.27%)	
2	101(23.22%)	24(18.18%)	77(25.41%)	
≥ 3	194(44.60%)	88(66.67%)	106(34.98%)	
Polyp classification, n (%)				0.028
Hyperplastic	53(12.18%)	17(12.88%)	36(11.88%)	
Inflammatory	33(7.59%)	7(5.30%)	26(8.58%)	
Tubular adenoma	285(62.52%)	79(59.85%)	206(67.99%)	
Tubulovillous adenoma	64(14.71%)	29(21.97%)	35(11.55%)	
Polyp location, n (%)				0.149
Proximal	137(31.50%)	48(36.36%)	89(29.37%)	
Dismal	298(68.50%)	84(63.64%)	214(70.63%)	
Adenoma, n (%)				0.116
Advanced	150(42.86%)	53(49.07%)	97(40.08%)	
Nonadvanced	200(57.14%)	55(50.93%)	145(59.92%)	

P-value: Comparison between recurrent and nonrecurrent performed by Chi-square χ^2 test.

Table 3
Comparison of serum lipid and lipoproteins between patients with and without polyp recurrence

	Hyperplastic polyp		Inflammatory polyp		Tubular adenoma		Tubulovillous adenoma	
	Recurrent	Nonrecurrent	Recurrent	Nonrecurrent	Recurrent	Nonrecurrent	Recurrent	Nonrecurrent
TG (mmol/L)	2.04±1.48	1.29±0.71*	1.98±1.84	1.44±0.85	1.60±1.04	1.50±0.97	1.91±1.44	1.24±0.82*
CHO (mmol/L)	5.64±1.19	5.52±1.53	5.23±0.81	4.85±1.26	5.31±1.18	5.39±1.05	5.73±1.44	5.72±0.98
HDL-C (mmol/L)	1.28±0.35	1.45±0.34	1.30±0.34	1.42±0.42	1.36±0.33	1.40±0.36	1.26±0.32	1.50±0.48*
LDL-C (mmol/L)	3.20±0.89	3.10±1.02	3.00±0.61	2.66±0.87	3.06±0.81	3.10±0.79	3.29±0.98	3.26±0.72
ApoA1 (g/L)	1.24±0.47	1.41±0.39	1.33±0.42	1.32±0.29	1.31±0.29	1.35±0.41	1.23±0.32	1.45±0.36*
ApoB (g/L)	1.00±0.31	0.96±0.31	1.00±0.28	0.80±0.25	0.93±0.24	0.97±0.27	1.05±0.34	0.97±0.25
TG/HDL	1.74±1.64	0.96±0.74*	1.75±1.90	1.16±0.93	1.36±1.19	1.23±1.07	1.60±1.55	0.93±0.81*

*: $P < 0.05$, comparison between recurrent and nonrecurrent performed by Student's t test.

Table 4
Univariate and multivariate analysis of risk factors associated with polyp recurrence

Parameter	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age (years)	1.03(1.01-1.05)	0.009	1.02(1.00-1.04)	0.063
Male	2.26(1.46-3.48)	< 0.001	1.75(1.06-2.89)	0.029
BMI (kg/m^2)	1.10(1.03-1.17)	0.003	1.11(1.02-1.19)	0.012
Number (≥ 3)	3.66(2.38-5.64)	< 0.001	3.42(2.15-5.45)	< 0.001
Size (≥ 20 mm)	2.22(1.20-4.11)	0.011	1.72(0.87-3.40)	0.117
TG (mmol/L)	1.30(1.07-1.58)	0.007	1.15(0.90-1.48)	0.257
HDL-C (mmol/L)	0.45(0.25-0.82)	0.009	1.47(0.50-4.31)	0.481
ApoA1 (g/L)	0.53(0.29-0.95)	0.034	0.62(0.25-1.58)	0.318

OR: odd ratio; CI: confidence interval; BMI: body mass index; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol, ApoA1: apoliprotein A1; ApoB: apoliprotein B.

Table 5
Univariate and multivariate analysis of risk factors associated with advanced adenoma recurrence

Parameter	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age (years)	1.04(1.01-1.08)	0.017	1.02(0.99-1.06)	0.231
Male	1.39(0.69-2.79)	0.357	0.94(0.41-2.16)	0.891
BMI (kg/m^2)	0.93(0.83-1.04)	0.200,	0.96(0.84-1.09)	0.501
Number (≥3)	3.85(1.89-7.89)	< 0.001	3.28(1.44-7.47)	0.005
Size (≥20 mm)	2.54(1.22-5.36)	0.013	2.86(1.24-6.61)	0.014
TG (mmol/L)	1.81(1.29-2.55)	0.001	1.55(1.02-2.35)	0.039
HDL-C (mmol/L)	0.22(0.08-0.62)	0.004	0.73(0.11-4.70)	0.737
ApoA1 (g/L)	0.19(0.06-0.61)	0.005	0.364(0.06-2.40)	0.294

OR: odd ratio; CI: confidence interval; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol; ApoA1: apoliprotein A1.

Discussion

Recurrence of colorectal polyps is common and remains as a crucial problem to prevent against CRC. Though many factors have been revealed to impact the recurrent rate, few studies focused on the role of lipid profiles. In the present study, we analyzed the baseline serum lipid levels in patients with colorectal polyps and observed the recurrence of polyps with a short follow-up. Our data showed that TG level was significant higher, and HDL-C and ApoA1 levels were significantly lower in patients with recurrent polyps in comparison with those without it. We found that elevated TG levels, as well as polyp number and polyp size, served as significant predictors for polyp recurrence in patients with advanced adenomas.

Colorectal polyps are precursors of CRC, and removal of polyps effectively reduces the risk of developing CRC. Endoscopic resection is now widely used to excise colorectal polyps and thus reduces deaths caused by CRC [18]. However, the high recurrence rate after piecemeal resection poses serious clinical problems. Clinical trial showed that 20–50% of patients with colorectal adenomas suffered recurrence in a 3- to 5-year period [19]. In our study, through a short term follow-up, we observed polyp recurrence in 132 out of 435 patients (30.34%). Elucidation of the causative factors of polyp recurrence would practically reduce or delay the recurrence rate of polyps.

A series of factors have been reported to associate with polyp recurrence, e.g. age, gender, lifestype, genetic background, characteristics of polyps, procedural factors [8, 20–23]. This study compared the baseline clinical characteristics of patients, as well as of colorectal polyps. In accordance with previous studies, significant difference were observed in age, gender, polyp size, polyp number between patients with and without polyp recurrence. Obese population has sharply increased and obesity causes or aggravates diseases. Epidemiologic studies suggested that obesity serve as a risk factor for colorectal adenomas[24] and CRC mortality[25]. Several studies have determined that obese individuals (or with higher BMI) had higher chance of recurrence than nonbese subjects. The supposed mechanism underlying is that obesity increases insulin and insulin-like growth factor-1, pushing non-advanced colorectal polyps into advanced stage and causing recurrence [26–28]. However, other study showed that weight loss or gain over 4 years did not affect adenoma recurrence [29]. In this study, we observed that patients with recurrent polyps had larger BMI than patients without it. Our data supports BMI as an independent risk factor of polyp recurrence.

Several studies have investigated the influence of lipid profiles on the development of colorectal polyps. In some studies, TG level seemed to significantly elevate in patients with advanced adenoma and served as a risk factor of neoplasia, while in other studies, this link was negative[30, 31]. Liu et al. reported that dyslipidemia was an independent risk factor for colorectal adenoma [14]. Other study showed that high levels of TG, as well as low levels of HDL-C was potential markers for advanced adenoma [32, 33]. Our study

found that patients with recurrent polyps had a significant higher level of TG, and lower levels of HDL-C and ApoA1. The dyslipidemia rate between recurrent and nonrecurrent patients was similar. To be noted, multivariate regression analysis showed that elevated TG was an independent risk factor for polyp recurrence in patients with advanced adenoma rather than in those with colorectal polyps. In other lipid parameters, no significant association was observed.

There are some limitations of this study. The first is that the 1.5-year follow-up may be not long enough to observe more recurrence. The second is that many patients lack of follow-up colonoscopy examination and were excluded from our analysis, which made the sample size was quite small.

Conclusions

In summary, our study investigated the role of lipid profiles in the recurrence of colorectal polyps. We found that elevated TG level, as well as polyp size and poly number, were independent risk factors of the recurrence of colorectal polyps in patients with advanced adenomas. Since serum TG level is easily detected in clinical practice, our finding may contribute to defining high-risk groups of polyp recurrence.

Abbreviations

CRC
colorectal cancer; WHO:World Health Organization; EMR:endoscopic mucosal resection; TC:total cholesterol; TG:triglycerides; HDL-C:high-density lipoprotein cholesterol; LDL-C:low-density lipoprotein cholesterol; ApoA1:apoliprotein A1; ApoB:apoliprotein B; BMI:body mass index; DM:diabetes mellitus; OR:odd ratio; CI:confidence index.

Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Meizhou People's Hospital Affiliated to Sun Yat-Sen University (Ethical Approval Number: MPH-HEC 2017-A-28).

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Sudong Liu conceived the design and wrote the draft; Boying Liu reviewed pathology reports and medical records, chose eligible patients; Pinwu Wen collected clinical data;

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Figures

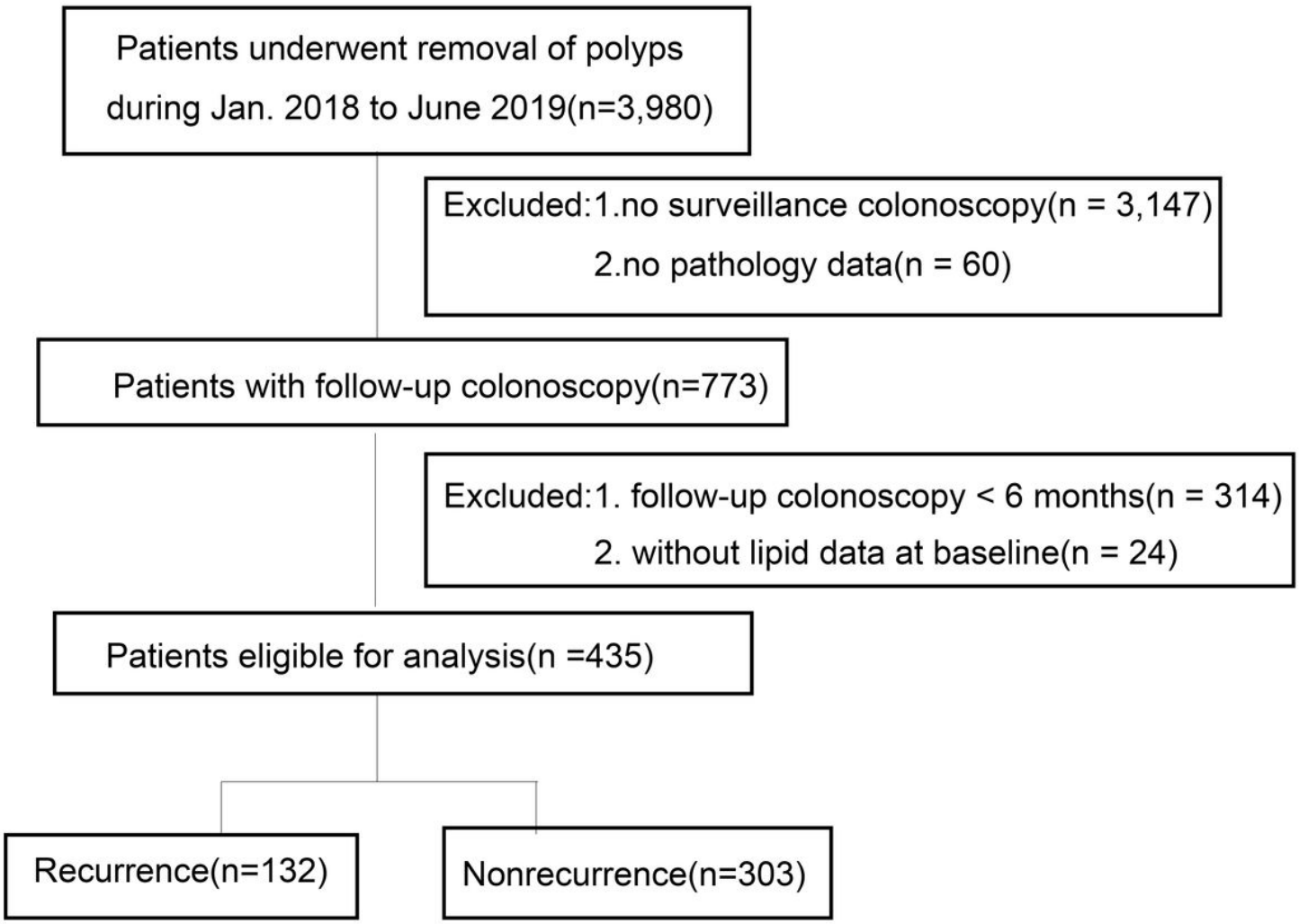

Figure 1

Inclusion and exclusion criteria of the study participants.