High Levels Of Triglycerides And Apolipoprotein B Increase The Risk Of Colorectal Polyp Recurrence After Endoscopic Resection

Jia-yu Du
Chengdu Medical College
Gui-ying Huang
University of Electronic Science and Technology of China
Yong-chun Xie
University of Electronic Science and Technology of China
Nan-xi Li
University of Electronic Science and Technology of China
Zhi-wei Lin
University of Electronic Science and Technology of China
Li Zhang (zhangligbyl@med.uestc.edu.cn)
Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital

Research Article

Keywords: Colorectal Polyps, Hyperlipidemia, Hypertriglyceridemia, Dyslipidemia, Apolipoprotein B.

Posted Date: March 15th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1434188/v1

Abstract

Purpose: Rates of colorectal polyp incidence and recurrence are high, so this study investigated risk factors of colorectal polyp recurrence after endoscopic surgery.

Methods: This retrospective study analyzed various blood lipid indices for 357 patients at our hospital who underwent intestinal polypectomy from January 1, 2018, to June 1, 2020, 161 of them recurred during a follow-up of about 1 year. Potential associations between blood indices and risk of recurrence were analyzed.

Results: Levels of triglycerides and apolipoprotein B were significantly higher among patients who experienced recurrence than among those who did not. Binary logistic regression identified three independent risk factors for recurrence: triglycerides (odds ratio 1.763, 95% confidence interval 1.003-3.098, P = 0.049), apolipoprotein B (5.438, 1.411-20.961, P = 0.014) and the number of polyps (2.54, 1.649-3.911, P < 0.001).

Conclusion: High levels of triglycerides and apolipoprotein B in the blood are independent risk factors for colorectal polyp recurrence.

Introduction

Colorectal cancer (CRC) kills nearly 900,000 people every year, making it the world's fourth most deadly cancer, after lung, liver, and gastric cancers[1]. Diagnosing and treating CRC earlier can substantially improve 5-year survival rates[2]. The National Polyp Study demonstrated the incidence of CRC was reduced 76–90% after the colon was cleared by colonoscopy[3]. Even better is early detection and removal of colorectal polyps, which can reduce the risk of CRC[4]. However, polyps can recur after endoscopic removal in 22–69% of patients[5–8]. The risk of recurrence has been associated with several factors, such as sex, age, obesity index, use of tobacco and alcohol, polyp characteristics, and diet[9]. For example, recurrence risk is higher among patients who are obese[10], who have been smoking longer than 35 years [odds ratio (OR) 2.88, 95% confidence interval (CI) 2.06–4.01, P = 0.001][11], or who drink alcohol[12].

Identifying non-invasive markers of polyp recurrence risk could help identify at-risk patients. Elevated triglyceride levels in serum are an independent risk factor for polyp recurrence in patients with advanced adenomas[13]. Long-term lipid stimulation suppresses anti-tumor immune responses, facilitating colorectal tumorigenesis and distant metastasis, and suppresses immune infiltrating cell function in the tumor microenvironment, thereby accelerating tumor progression[14]. On the other hand, several studies have suggested no association or negative correlation between lipid levels in blood and risk of colorectal polyps or CRC[15–20].

To help clarify these discrepancies, we retrospectively analyzed data from 357 patients at our hospital who underwent endoscopic resection of colorectal polyps in order to identify independent risk factors for

colorectal polyp recurrence, including lipid levels in the blood.

Methods

Patients

For this retrospective study, we screened for inclusion all 2,738 patients who underwent intestinal polypectomy for the first time between January 1, 2019 and June 1, 2020 in the Department of Gastroenterology at Sichuan Provincial People's Hospital. To be enrolled, patients had to be 65 years or younger, they had to undergo at least one colonoscopic follow-up after polypectomy, and baseline clinicodemographic and laboratory test data had to be available.

Patients were excluded if they were found to have high-grade intraepithelial neoplasia or carcinoma based on histopathology; if they had hypertension, diabetes, thyroid disease, or severe cardiac or pulmonary dysfunction; or if they had a history of familial adenomatous polyposis, inflammatory bowel disease, or a malignant tumor at any site. They were also excluded if they took hypolipidemic drugs before or during follow-up.

Surgical procedure

All patients were placed on a liquid diet 24 hours before surgery, and bowel washing medication was taken to clean the bowel. The patient underwent general anesthesia enteroscopy surgery after fasting for 4 hours. The procedures were performed by physicians experienced in digestive endoscopy centers. Surgical modalities collectively include high-frequency electrocoagulation, argon plasma coagulation(APC), endoscopic mucosal resection(EMR), and endoscopic submucosal dissection(ESD). Finally, biopsy specimens were performed under the microscope by experienced pathologists.

Polyp classification and definition of polyp recurrence

Pathology type report from hospital pathology department. According to the World Health Organization (WHO) classification, polyps can be classified into four types: adenomatous polyps, inflammatory polyps, hyperplastic polyps, and hamartomatous polyps[21]. High-grade intraepithelial neoplasia and carcinoma were excluded. Polyp recurrence was defined as the detection of one or more polyps at any time after polypectomy, irrespective of site[22].

Blood lipid analysis

Fasting peripheral venous blood was analyzed within 24 hours after admission for triglycerides, cholesterol, high-density lipoprotein, low-density lipoprotein, apolipoprotein A1 (apoA1), and apolipoprotein B (apo B). Patients were diagnosed with dyslipidemia if levels of cholesterol were ≥ 5.2 mmol/L; triglycerides, ≥ 1.7 mmol/L; high-density lipoprotein-cholesterol, < 1.03 mmol/L; low-density lipoprotein cholesterol, ≥ 3.3 mmol/L; apoA1, < 1.05 g/L; and apoB, ≥ 1.4 g/L .

Data collection

The following baseline data were collected for all patients: sex, age, body mass index, history of smoking and alcohol consumption, as well as polyp size, number, and histopathological type.

Statistical analysis

All analyses were performed using SPSS 26.0 (IBM, Armonk, NY, USA). Normally distributed data were expressed as mean (standard deviation), otherwise, as median (interquartile range). Inter-group differences in continuous data (such as age, follow-up time, body mass index, and blood lipid levels) were assessed for significance using the Student's *t*-test, analysis of variance, or the Kruskal – Wallis test as appropriate. Differences in categorical data were assessed using the chi-squared test. Binary logistic regression was used to identify independent risk factors for polyp recurrence. Differences associated with $P < 0.05$ were considered significant.

Results

Of the 2,738 patients screened, 1,212 were excluded because no follow-up enteroscopy data were available, 437 were lost to follow-up, and 732 met exclusion criteria. In the end, 357 patients were included in the study, of whom 225 (63%) were men and 161 (45%) experienced recurrence during follow-up, which lasted a mean of 12 months (Fig. 1). Relatively small percentages of patients reported smoking (22%) or drinking (21%).

Patients who experienced recurrence or not were similar in sex distribution, mean age, mean body mass index, and smoking or alcohol consumption (Table 1). Similarly, the two groups of patients did not differ significantly in the size or histopathological type of polyps (Table 2).

Table 1. Characteristics of patients with colorectal polyps, stratified by whether they experienced polyp recurrence during follow-up

Characteristic	Recurrence (n=161)	No recurrence (n=196)	P *
Sex			0.097
Male	109	116	
Female	52	80	
Age, yr	50.2 (12)	48.8 (12)	0.121
Follow-up, mo.	12 (3)	12 (0.75)	0.411
History of smoking	42	37	0.103
History of drinking	37	39	0.479
Body mass index, kg/m^2	23.1 (4)	23 (3.9)	0.946

Values are n, mean (standard deviation), or median (interquartile range), unless otherwise noted.

* Based on Student's t-test or the Mann-Whitney test (continuous variables) or Fisher's exact test (categorical variables)

n, number; BMI, body mass index;

Table 2. Comparison of polyp characteristics between patients who experienced polyp recurrence or not

Characteristic	Recurrence (n=161)	No recurrence (n=196)	P *
Polyp type			0.081
Hyperplastic	85	96	
Inflammatory	10	10	
Tubular adenoma	20	12	
Hamartomatous	1	4	
N/A	45	74	
Polyp size, mm			0.793
≤ 10	126	157	
10-19	24	24	
≥ 20	8	9	
N/A	3	6	
Polyp number			0
1	33	75	
2	30	45	
≥ 3	96	72	
N/A	2	4	

* Based on Student's t-test or the Mann-Whitney test (continuous variables) or Fisher's exact test (categorical variables)

n, number; N/A, unclear;

In contrast, patients who experienced recurrence had a significantly greater number of polyps.

In addition, patients who experienced recurrence showed significantly higher levels of triglycerides and apoB (Table 3). The two groups of patients did not differ significantly in levels of cholesterol, high- or low-density lipoprotein cholesterol, or apoA1.

Table 3
Lipid levels in the blood of patients who experienced polyp recurrence or not

Lipid species	Recurrence (n = 161)	No recurrence (n = 196)	P *
Triglycerides, mmol/L	1.54 (0.95)	1.25 (1.01)	0.036
Cholesterol, mmol/L	4.97 (0.96)	4.6 (1.00)	0.895
HDL-C, mmol/L	1.27 (0.42)	1.29 (0.44)	0.762
LDL-C, mmol/L	2.3 (0.97)	2.17 (0.78)	0.146
Apolipoprotein A1, g/L	1.33 (0.35)	1.32 (0.32)	0.741
Apolipoprotein B, g/L	0.87 (0.26)	0.79 (0.16)	0.001

Values are n, mean (standard deviation), or median (interquartile range), unless otherwise noted.

* Based on Student's t-test or the Mann-Whitney test (continuous variables) or Fisher's exact test (categorical variables)

n, number; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol.

Binary logistic regression identified the following independent risk factors for polyp recurrence (Table 4): high triglycerides (OR 1.763, 95% CI 1.003–3.098, P = 0.049), high apoB (5.438, 1.411–20.961, P = 0.014) and the presence of at least three polyps (2.54, 95% CI 1.649–3.911, P < 0.001).

Table 4. Multivariate analysis of risk factors associated with polyp recurrence (n = 357 patients)

Parameter	OR (95% CI)	P-value
Sex	0.724 (0.446-1.175)	0.191
Age	1.017 (0.994-1.042)	0.152
Follow-up time	0.978 (0.925-1.033)	0.42
Smoking	0.669 (0.329-1.363)	0.268
Drinking	1.308 (0.642-2.664)	0.459
BMI ≥ 25 kg/m²	1.002 (0.631-1.59)	0.995
Polyp size ≥ 20 mm	1.073 (0.404-2.848)	0.888
Polyp number ≥ 3	2.54 (1.649-3.911)	0.000
Triglyceride (≥ 1.7 mmol/L)	1.763 (1.003-3.098)	0.049
Cholesterol (≥ 5.2 mmol/L)	1.639 (0.923-2.908)	0.092
HDL-C	1.309 (0.577-2.971)	0.519
LDL-C	0.98 (0.926-1.037)	0.485
Apolipoprotein A1	1.3 (0.382-4.432)	0.675
Apolipoprotein B	5.438 (1.411-20.961)	0.014

* Based on binary regression analysis.

OR, odd ratio; CI, confidence interval; BMI, body mass index; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol.

Discussion

Here we provide evidence that hypertriglyceridemia and high apoB are independent risk factors for polyp recurrence. To our knowledge, this is the first report linking high apoB to polyp recurrence. Our findings are consistent with studies suggesting that hypertriglyceridemia promotes the formation of reactive oxygen species that damage DNA and thereby initiate CRC[23], and that this and other abnormalities of lipid metabolism suppress anti-tumor immune responses[14].

Early polyp detection and removal are effective for preventing CRC. Adenomatous polyps can progress to malignancy via the adenoma-carcinoma pathway[24, 25], while hyperplastic polyps can progress to malignancy via the serrated or microsatellite instability pathway[26]. A hamartoma adenoma-carcinoma sequence has also been suggested[27]. Therefore, identifying patient characteristics associated with the risk of polyp recurrence may help reduce the risk of CRC.

Studies have explored potential correlations between blood lipid indices and risk of CRC, but they have been unable to separate potential associations from other dietary or metabolic confounders[16, 28,29]. Similarly, studies have failed to unambiguously identify associations between dyslipidemia and the risk of colorectal polyps. [30,31]. Our study provides strong evidence linking hypertriglyceridemia to polyp recurrence. At least three mechanisms may underlie this association. One is that hypertriglyceridemia causes hyperinsulinemia and insulin resistance, which drives the proliferation of normal and cancer cells in the large intestine[32]. Another mechanism is that dyslipidemia creates a tumorigenic environment by increasing levels of interleukin-6, tumor necrosis factor-α, and other inflammatory cytokines[33]. Finally, Boying Liu *et al.* suggested that TG may affect polyp recurrence by increasing the proliferative capacity of cancer stem cells or stimulating signaling pathways that promote cell invasion[13].

Our data also link high levels of apoB to polyp recurrence. ApoB is a structural component of chylomicrons as well as lipoproteins of various densities[34], so it plays an important role in atherogenesis[34, 35]. Given one study linking elevated low-density lipoprotein cholesterol to the formation of colorectal polyps[36], we suggest that apoB may influence polyp recurrence by affecting the metabolism of low-density lipoprotein. Elevated levels of low-density lipoprotein cholesterol have been linked to oxidative stress and inflammatory responses in the intestine[33,37]. By reducing levels of low-density lipoprotein cholesterol in serum, statins may inhibit polyp formation [38,39,40], which may help explain their ability to slow the growth of several types of colorectal tumors[41–44]. Future studies should explore whether other hypolipidemic agents such as fibrates can inhibit polyp formation and CRC.

Our findings should be interpreted with caution given that our patient sample was relatively small and came from a single center. The numbers of polyps differed between patients who experienced recurrence or not, which may have confounded our analyses. Despite these limitations, our data suggest that administering hypolipidemic drugs to individuals with hyperlipidemia may help reduce the risk of polyp recurrence and thereby CRC.

Conclusions

Our retrospective, single-center study suggests that hypertriglyceridemia and high apoB are independent risk factors for colorectal polyp recurrence.

Statements And Declarations

The authors have no competing interests to declare that are relevant to the content of this article.

This work was supported by Key Research and Development Projects of Sichuan Science and Technology Department [Grant No: 22ZDYF1691 and 2018FZ0062].

Author Contributions

Jia-yu Du and Gui-ying Huang were responsible for the main manuscript writing and data analysis, Yong-chun Xie , Nan-xi Li and Zhi-wei Lin were responsible for the data collection and graphic production, Li Zhang was responsible for the revision and guidance of the whole article, and all authors reviewed the manuscript.

References

1. Brody H. Colorectal cancer. Nature. 2015;521(7551):S1-S.
2. Nelson RS, Thorson AG. Colorectal Cancer Screening. Current Oncology Reports. 2009;11(6):482–9.
3. Winawer SJ, Zauber AG, Ho MN, Obrien MJ, Gottlieb LS, Sternberg SS, et al. PREVENTION OF COLORECTAL-CANCER BY COLONOSCOPIC POLYPECTOMY. New England Journal of Medicine. 1993;329(27):1977–81.
4. Holme O, Bretthauer M, Fretheim A, Odgaard-Jensen J, Hoff G. Flexible sigmoidoscopy versus faecal occult blood testing for colorectal cancer screening in asymptomatic individuals. Cochrane Database of Systematic Reviews. 2013(9).
5. Christie JP. COLONOSCOPIC EXCISION OF LARGE SESSILE POLYPS. American Journal of Gastroenterology. 1977;67(5):430–8.
6. Bedogni G, Bertoni G, Ricci E, Conigliaro R, Pedrazzoli C, Rossi G, et al. COLONOSCOPIC EXCISION OF LARGE AND GIANT COLORECTAL POLYPS - TECHNICAL IMPLICATIONS AND RESULTS OVER 8 YEARS. Diseases of the Colon & Rectum. 1986;29(12):831–5.
7. Arebi N, Swain D, Suzuki N, Fraser C, Price A, Saunders BP. Endoscopic mucosal resection of 161 cases of large sessile or flat colorectal polyps. Scandinavian Journal of Gastroenterology. 2007;42(7):859–66.
8. Boix J, Lorenzo-Zuniga V, Moreno de Vega V, Ananos FE, Domenech E, Ojanguren I, et al. Endoscopic removal of large sessile colorectal adenomas: Is it safe and effective? Digestive Diseases and Sciences. 2007;52(3):840–4.
9. Hao Y, Wang Y, Qi M, He X, Zhu Y, Hong J. Risk Factors for Recurrent Colorectal Polyps. Gut and Liver. 2020;14(4):399–411.
10. Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, et al. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. New England Journal of Medicine. 2000;342(16):1149–55.
11. Reid ME, Marshall JR, Roe D, Lebowitz M, Alberts D, Battacharyya AK, et al. Smoking exposure as a risk factor for prevalent and recurrent colorectal adenomas. Cancer Epidemiology Biomarkers & Prevention. 2003;12(10):1006–11.
12. Tiemersma EW, Wark PA, Ocke MC, Bunschoten A, Otten MH, Kok FJ, et al. Alcohol consumption, alcohol dehydrogenase 3 polymorphism, and colorectal adenomas. Cancer Epidemiology Biomarkers & Prevention. 2003;12(5):419–25.

13. Liu B, Wen P, Gu X, Weng R, Liu S. Elevated serum triglyceride predicts recurrence of colorectal polyps in patients with advanced adenomas. Lipids in Health and Disease. 2020;19(1).
14. Chen K, Guo J, Zhang T, Gu J, Li H, Wang J. The Role of Dyslipidemia in Colitis-Associated Colorectal Cancer. Journal of Oncology. 2021;2021.
15. Chung YW, Han DS, Park YK, Son BK, Paik CH, Lee HL, et al. Association of obesity, serum glucose and lipids with the risk of advanced colorectal adenoma and cancer: A case-control study in Korea. Digestive and Liver Disease. 2006;38(9):668–72.
16. Kono S, Ikeda N, Yanai F, Yamamoto M, Shigematsu T. SERUM-LIPIDS AND COLORECTAL ADENOMA AMONG MALE SELF-DEFENSE OFFICIALS IN NORTHERN KYUSHU, JAPAN. International Journal of Epidemiology. 1990;19(2):274–8.
17. Saydah SH, Platz EA, Rifai N, Pollak MN, Brancati FL, Helzlsouer KJ. Association of markers of insulin and glucose control with subsequent colorectal cancer risk. Cancer Epidemiology Biomarkers & Prevention. 2003;12(5):412–8.
18. Tsushima M, Nomura AMY, Lee J, Stemmermann GN. Prospective study of the association of serum triglyceride and glucose with colorectal cancer. Digestive Diseases and Sciences. 2005;50(3):499–505.
19. Dayton S, Pearce ML, Hashimot.S, Dixon WJ, Tomiyasu U. A CONTROLLED CLINICAL TRIAL OF A DIET HIGH IN UNSATURATED FAT IN PREVENTING COMPLICATIONS OF ATHEROSCLEROSIS. Circulation. 1969;40(1S2):II1-&.
20. Oliver MF, Heady JA, Morris JN, Cooper MJ. WHO COOPERATIVE TRIAL ON PRIMARY PREVENTION OF ISCHEMIC-HEART-DISEASE WITH CLOFIBRATE TO LOWER SERUM-CHOLESTEROL - FINAL MORTALITY FOLLOW-UP. Lancet. 1984;2(8403):600-4.
21. Atkin WS, Valori R, Kuipers EJ, Hoff G, Senore C, Segnan N, et al. European guidelines for quality assurance in colorectal cancer screening and diagnosis. First Edition Colonoscopic surveillance following adenoma removal. Endoscopy. 2012;44:SE151-SE63.
22. Martinez ME, Sampliner R, Marshall JR, Bhattacharyya AB, Reid ME, Alberts DS. Adenoma characteristics at baseline colonoscopy as risk factors for recurrence of advanced adenomas. Cancer Epidemiology Biomarkers & Prevention. 2001;10(2):157-.
23. Bruenderman EH, Martin RCG, II. High-risk population in sporadic pancreatic adenocarcinoma: guidelines for screening. Journal of Surgical Research. 2015;194(1):212–9.
24. Morson B. POLYP-CANCER SEQUENCE IN LARGE BOWEL. Proceedings of the Royal Society of Medicine-London. 1974;67(6):451-7.
25. Kronborg O, Fenger C. Clinical evidence for the adenoma-carcinoma sequence. European Journal of Cancer Prevention. 1999;8:S73-S86.
26. Hyman NH, Anderson P, Blasyk H. Hyperplastic polyposis and the risk of colorectal cancer. Diseases of the Colon & Rectum. 2004;47(12):2101–4.
27. Bosman FT. The hamartoma-adenoma-carcinoma sequence. Journal of Pathology. 1999;188(1):1–2.

28. Rose G, Blackburn H, Keys A, Taylor HL, Kannel WB, Paul O, et al. COLON CANCER AND BLOOD-CHOLESTEROL. Lancet. 1974;1(7850):181–3.
29. Chung YW, Han DS, Park YK, Son BK, Paik CH, Jeon YC, et al. Association of Obesity, Serum Glucose and Lipids with the Risk of Advanced Colorectal Adenoma and Cancer: A Case-Control Study in Korea. Gastrointestinal Endoscopy. 2006;63(5):AB212-AB.
30. Pan J, Cen L, Xu L, Miao M, Li Y, Yu C, et al. Prevalence and risk factors for colorectal polyps in a Chinese population: a retrospective study. Scientific Reports. 2020;10(1).
31. Kim Y-J, Lee K-J, Park S-Y, Han J-H, Kwon K-Y, Kim J-H. Association between Dyslipidemia and the Prevalence of Colon Polyps Based on a Health Evaluation of Subjects at a Hospital. Korean journal of family medicine. 2014;35(3):143–51.
32. Burchfiel CM, Abbott RD, Curb JD, Sharp DS, Rodriguez BL, Arakaki R, et al. Association of insulin levels with lipids and lipoproteins in elderly Japanese-American men. Annals of Epidemiology. 1998;8(2):92–8.
33. Esteve E, Ricart W, Fernandez-Real JM. Dyslipidemia and inflammation: an evotutionary conserved mechanism. Clinical Nutrition. 2005;24(1):16–31.
34. Sparks JD, Sparks CE. APOLIPOPROTEIN-B AND LIPOPROTEIN METABOLISM. Advances in Lipid Research. 1985;21:1–46.
35. Olofsson SO, Boren J. Apolipoprotein B: a clinically important apolipoprotein which assembles atherogenic lipoproteins and promotes the development of atherosclerosis. Journal of Internal Medicine. 2005;258(5):395–410.
36. Xie C, Wen P, Su J, Li Q, Ren Y, Liu Y, et al. Elevated serum triglyceride and low-density lipoprotein cholesterol promotes the formation of colorectal polyps. BMC gastroenterology. 2019;19(1):195-.
37. Katzke VA, Sookthai D, Johnson T, Kuhn T, Kaaks R. Blood lipids and lipoproteins in relation to incidence and mortality risks for CVD and cancer in the prospective EPIC-Heidelberg cohort. Bmc Medicine. 2017;15.
38. Siddiqui A, Nazario HE, Patel M, Mahgoub A, Spechler SJ. Reduction in Low-Density Lipoprotein Cholesterol Levels During Statin Therapy Is Associated With a Reduced Incidence of Advanced Colon Polyps. American Journal of the Medical Sciences. 2009;338(5):378–81.
39. Swamy MV, Patlolla JMR, Steele VE, Kopelovich L, Reddy BS, Rao CV. Chemoprevention of familial adenomatous polyposis by low doses of atorvastatin and celecoxib given individually and in combination to APC(min) mice. Cancer Research. 2006;66(14):7370–6777.
40. Teraoka N, Mutoh M, Takasu S, Ueno T, Yamamoto M, Sugimura T, et al. Inhibition of Intestinal Polyp Formation by Pitavastatin, a HMG-CoA Reductase Inhibitor. Cancer Prevention Research. 2011;4(3):445–53.
41. Huang EH, Johnson LA, Eaton K, Hynes MJ, Carpentino JE, Higgins PDR. Atorvastatin Induces Apoptosis In Vitro and Slows Growth of Tumor Xenografts but Not Polyp Formation in Min Mice. Digestive Diseases and Sciences. 2010;55(11):3086–94.

42. Jung YS, Park CH, Eun CS, Park DI, Han DS. Statin use and the risk of colorectal adenoma: A meta-analysis. Journal of Gastroenterology and Hepatology. 2016;31(11):1823–30.
43. Broughton T, Sington J, Beales ILP. Statin use is associated with a reduced incidence of colorectal adenomatous polyps. International Journal of Colorectal Disease. 2013;28(4):469–76.
44. Siddiqui A, Pandove S, Mahgoub A, Spechler S, Nazario H. The long-term use of statins is associated with a decreased incidence of advanced adenomatous colon polyps. American Journal of Gastroenterology. 2008;103:S544-S.

Figures

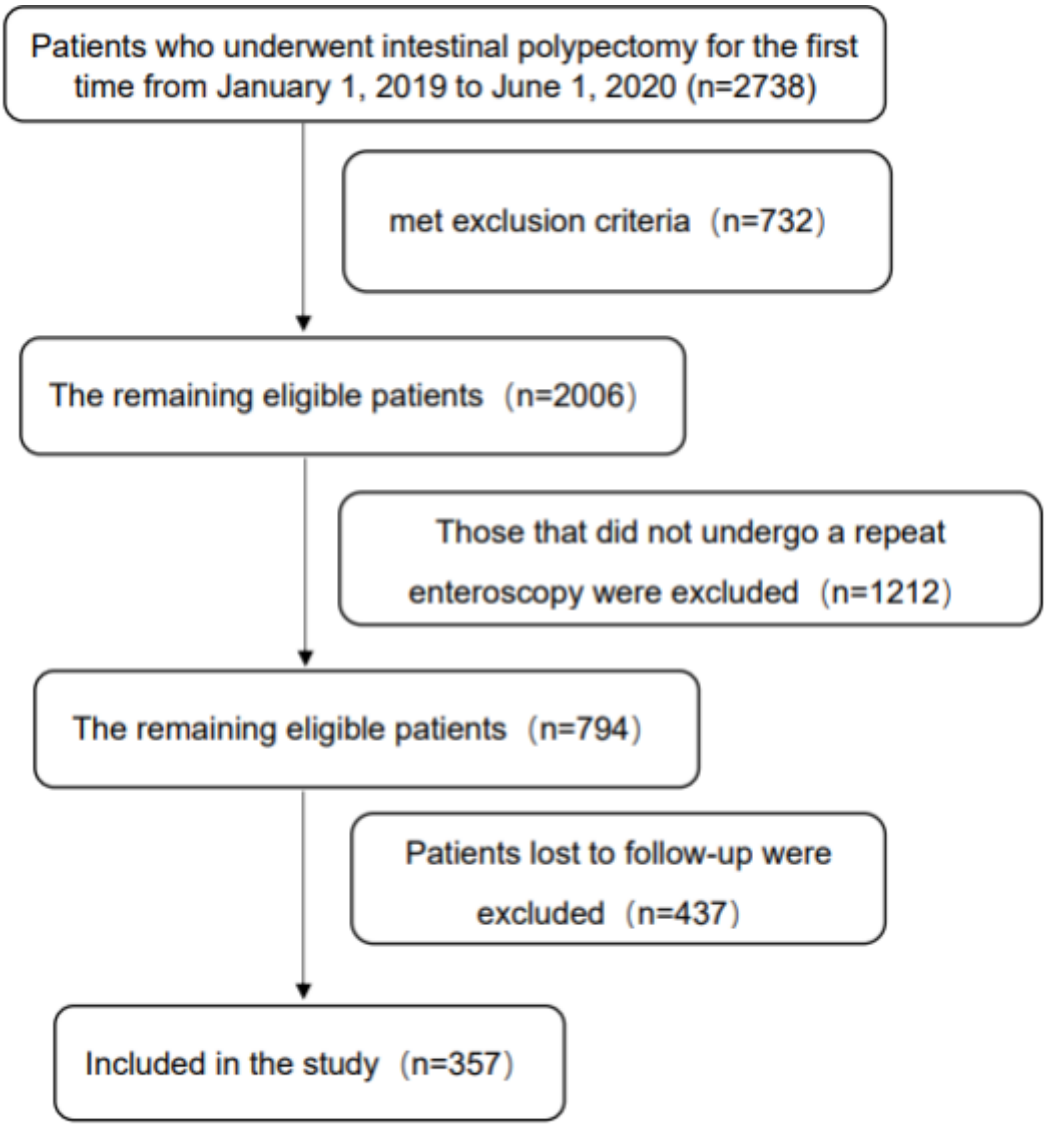

Figure 1 Inclusion and exclusion process of study participants(n， number;)

Figure 1

See image above for figure legend.