Association Between Serum Lipid Profiles and Colorectal Adenoma in Chinese Population

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Abstract

Background: Dyslipidemia may play an important role in the development of colorectal adenomas. This study aims to investigate the serum lipid profiles in patients with colorectal adenomas and determine correlation between dyslipidemia and colorectal adenomas.

Methods: This retrospective case - control study included 2,960 patients with colorectal adenomas, and 1,263 participants with normal colonoscopy results served as controls. The serum levels of lipids were measured and comparison was made between patients and controls. The association between serum lipid levels, as well as other factors and colorectal adenoma was evaluated by multivariate regression logistic analysis.

Results: The serum levels of total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDL-C) and apoliprotein B (ApoB) were significantly elevated in patients with colorectal adenomas compared with controls. The proportions of subjects with high LDL, high TC, high TG or multiple abnormality were significantly larger in adenoma group than the control group. Multivariate analysis suggested that serum levels of TC and TG were in significant associations with risk of both nonadvanced and advanced colorectal adenoma.

Conclusions: Abnormal lipid profiles are associated with the risk of colorectal adenoma. Elevated serum TC and TG were correlated with the occurrence of adenoma, thus may serve as practical markers for classifying risk of colorectal adenoma.

Introduction

Colorectal cancer (CRC) is the second most common cancer in women and the third most in men. It was estimated that colorectal cancer contributed to about 10% of new cancer cases and cancer-related deaths annually (1). In China, CRC ranks as the fifth most common cancer, and causing fifth most deaths. Notably, the incidence and mortality rates of CRC steadily went up in China in the past decades, which may be attributed to the lifestyle and dietary changes (2). Many large-scale randomized controlled trials have suggested that endoscopy procedure is effective in detection and removal of CRC, and have reduced the burden of CRC to a large extend (3–5). However, the colonoscopy is an invasive procedure which would cause rare but severe complications. This procedure also requires optimal bowel preparation and professional mucosal inspection. As study indicates, low participation rate is another important factor to reduce the diagnostic yield of colonoscopy screening (2).

It is well established that most CRC cases stem from a polyp and go through a adenoma-carcinoma pathway (6). The patients with large and multiple polyps, as well as advanced adenomas suffer a significant higher risk of CRC (7). Colorectal polyps are classified as four types based on pathological characters: adenomatous, inflammatory, hyperplastic, and hamartomic (8). Researchers have long been focused on identified risk factors associated with occurrence or progression of colorectal polyps in order

to prevent against CRC. The well-known risk factors for polyps include male sex, older age, smoking and obesity (9, 10).

Several studies have investigated the impact of abnormal serum lipid profiles on colorectal adenoma, but the associations remained inconsistent. Some of them suggested that elevated serum triglyceride (TG) and total cholesterol(TC) levels increased the risk of colorectal adenoma (11–13), while others found negative or even inverse relationship (14, 15). Moreover, to our knowledge, only a few of such studies were conducted in Chinese population, and most of them were designed with small sample size. On the other hand, the development of society brings sharp increase in number of population with dyslipidemia and obesity (16, 17). These facts highlight the importance to clarify the relationship between serum lipid levels and formation of colorectal adenoma.

In the present study, we retrospectively reviewed the serum lipid levels of patients with colorectal adenoma, and compared them with normal controls. The purpose of this study is to clarify the association between serum lipids and colorectal adenoma in Chinese population, and make a contribution to prevention of CRC.

Materials And Methods

Study subjects

The participants of this retrospective study were selected from patients who attended Gastroenterology Department of Meizhou People's Hospital Affiliated to Sun Yat-Sen University from 1st May 2018 to 1st. May 2020. Each participant underwent at less one colonoscopy during this period. The adenoma group were patients with abnormal findings in colonoscopy examination and followed by diagnosis with colorectal adenoma by experienced pathologists. The control group were individuals with normal colonoscopy results. All of the eligible participants should be free from present/previous malignancies, heart or pulmonary diseases or continued taking of lipid-lowering agents. The ethic approval for this study was obtained from the Ethics Committee of Meizhou People's Hospital Affiliated to Sun Yat-Sen University.

The chart indicating the selection of final participants is shown in **Fig. 1**. A total of 4,965 patients with colorectal polyps were found during this period, and 3,220 of them were diagnosed with colorectal adenomas. After excluded for indicated reasons, there were 2,960 eligible patients for analysis, including 921 with advanced adenomas and 2,039 with nonadvanced adenomas. For the control group, a total of 3,600 individuals were observed with normal colonoscopy results, and finally 1,263 participants were selected.

Colonoscopy procedure

All patients who were supposed to undergo colonoscopy were required to eat a low fibre diet 24 hours before examination. Patients took mannitol solution to empty bowel and obtained standard bowel

preparation. Colonoscopies were performed by experienced endoscopist, putting a colonoscope into back passage and passing it along the bowel, checking from rectum to cecum. Abnormal findings were carefully checked following clinical procedure. Visualized lesions were removed by endoscopic mucosal resection (EMR) and used for pathology diagnosis.

According to their size and histology, colorectal adenomas were classified as advanced and nonadvanced. Advanced adenomas were defined if adenomas with a diameter of ≥ 10 mm, or with villous component (> 25%) or with high-grade dysplasia (18).

Serum lipid profiles testing

The serum lipid profiles were examined using commercial kits following manufacture's instruction as previously described (19). Fasting blood sample was collected from each participant within 24 hour after admission. Serum levels of TC, TG, high-density lipoprotein cholesterol (HDL-C), and low density lipoprotein cholesterol (LDL-C) were assayed by selective solubilization (AU5800 analyzer; Beckman Coulter, Brea, CA, USA). Serum levels of apolipoprotein A1 (ApoA1) and apolipoprotein B (ApoB) were assayed by standard turbidimetric immunoassays (AU5800 analyzer; Beckman Coulter).

Dyslipidemia is defined based on the Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults(20). Participants were classified as dyslipidemia if TC ≥ 5.17 mmol/L, and/or TG ≥1.7 mmol/L, and/or LDL-C level of ≥ 3.37 mmol/L, and/or HDL-C level of < 1.04 mmol/L. Multiple abnormality is defined if two or more types of serum lipid levels were abnormal.

Clinical data collection

Clinical data were collected from patients' medical records. Data were de-identity to keep privacy before analysis. Drink was defined as past/present consuming alcohol > 30 g/day. Smoke was defined as past/present taking cigarette > 1 pack/day. Hypertension was diagnosed as blood pressure of ≥ 130/85 mmHg or taking antihypertensive treatment. Diabetes mellitus was diagnosed if the patient had a fasting blood glucose level of ≥ 126 mg/dL, a random glucose level of ≥ 200 mg/dL, or was taking an antidiabetic medication (21).

Statistical analysis

Data was statistically analyzed by SPSS software version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation (SD), and categorical variables were presented as percent. Kolmogorov–Smirnov test was used to judge the normality of the distribution of continuous variables. Differences of continuous variables were examined either by Student's t test between two groups or by one-way ANNOV for three groups. Differences of categorical variables were examined by chi-square (χ^2) test. Logistic regression analysis was used to evaluate the association of variables and occurrence of nonadvanced or advanced adenomas. Odds ratios (ORs) and 95 % confidence intervals

(CIs) were calculated by adjusting for variables that were distributed differently between cases and controls. Two-sided *P* values < 0.05 were considered as statistically significant.

Results

Baseline characteristics

A total of 4,223 participants were selected for analysis in the present study, including 2,960 with colorectal adenomas and 1,263 with normal colonoscopy results. The basic characteristics of participants are presented in Table 1. The mean age and BMI of patients with colorectal adenomas were significantly higher than those of the controls (57.4 ± 11.5 *vs.* 48.2 ± 15.8, *P* < 0.001; 22.93 ± 3.28 *vs.* 22.45 ± 4.75, *P* = 0.001); Compared with participants without any colorectal adenomas, patients with colorectal adenomas showed larger proportions of male sex (62.05% *vs.* 49.56%, *P* < 0.001), drink (9.2% *vs.* 2.8%, *P* < 0.001), smoke (19.4% *vs.* 7.5%, *P* < 0.001), hypertension (21.2% *vs.* 13.4%, *P* < 0.001), diabetes mellitus (8.4% *vs.* 5.6%, *P* = 0.002), and dyslipidemia(70.4% *vs.* 58.6%, *P* < 0.001).

Table 1
Baseline characteristics between controls and patients

Characteristics	**Control (n = 1,263)**	**Colorectal adenoma (n = 2,960)**	***P* value**
Age (yrs, mean ± SD)	48.2 ± 15.8	57.4 ± 11.5	< 0.001
Male (n, %)	626(49.56%)	1836(62.05%)	< 0.001
BMI (kg/m^2)	22.45 ± 4.75	22.93 ± 3.28	0.001
Drink (n, %)	35(2.8%)	271(9.2%)	< 0.001
Smoke (n, %)	95(7.5%)	573(19.4%)	< 0.001
Hypertension (n, %)	169(13.4%)	627(21.2%)	< 0.001
Diabetes Mellitus (n, %)	71(5.6%)	248(8.4%)	0.002
Dyslipidemia (n, %)	740(58.6%)	2085(70.4%)	< 0.001
BMI: body mass index; SD: standard deviate			

Comparison of serum lipid profiles between patients with colorectal adenomas and controls

We analyzed the serum lipid levels in patients with nonadvanced or advanced colorectal adenomas, and compared them with individuals without adenomas. As shown in Table 2, the serum levels of TC, LDL-C and TG in patients with nonadvanced or advanced colorectal adenoma were significantly higher than those in subjects without adenomas. Meanwhile, patients with nonadvanced or advanced colorectal

adenomas had elevated levels of ApoB than the controls. There was no significant difference between patients with nonadvanced and advanced colorectal adenoma group in lipid and lipoprotein levels except for TG, which increased in patients with advanced colorectal adenomas.

Table 2
Comparison of serum lipids profiles between patients with nonadvanced or advanced colorectal adenomas and controls

Variables	Control (n = 1,263)	Nonadvanced colorectal adenoma (n = 2,039)	Advanced colorectal adenoma (n = 921)	*P* value
TC (mmol/L)	4.88 ± 1.22	5.28 ± 1.20	5.24 ± 1.15	< 0.001
LDL-C (mmol/L)	2.67 ± 0.81	2.95 ± 0.82	2.90 ± 0.82	< 0.001
HDL-C (mmol/L)	1.35 ± 0.37	1.36 ± 0.36	1.34 ± 0.37	0.513
TG (mmol/L)	1.45 ± 1.58	1.64 ± 1.54	1.73 ± 1.64*	< 0.001
ApoA1 (g/L)	1.24 ± 0.36	1.25 ± 0.32	1.24 ± 0.34	0.83
ApoB (g/L)	0.86 ± 0.27	0.97 ± 0.30	0.96 ± 0.29	< 0.001

***:** $P < 0.05$ for comparison between nonadvanced colorectal adenoma and advanced colorectal adenoma by Student's *t* test.

TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

Lipid abnormality in patients with colorectal adenomas

According to the Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults, low HDL (< 1.04 mmol/L), high LDL (> 3.37 mmol/L), high TG (> 1.7 mmol/L) and high TC (> 5.17 mmol/L) were regarded as major types of lipid abnormality. Multiple abnormality was defined if two or more types of lipid abnormality was occurred to a patient. The distributions of lipid abnormality in patients with colorectal adenomas were shown in Table 3. High TC was the most common type of lipid abnormality in both patients with colorectal adenomas and controls, followed by multiple abnormality in the second place. Compared with controls, a larger proportion of colorectal adenoma patients suffered from high LDL, high TG and high TC, except for low HDL. Also, multiple abnormality was more frequent in patients with colorectal adenomas than in individuals without adenomas.

Table 3
Lipid abnormality in patients with colorectal adenomas

Variables	Control (n = 1,263)	Nonadvanced colorectal adenoma (n = 2,039)	Advanced colorectal adenoma (n = 921)	*P* value
Low HDL-C	238(18.8%)	373(18.3%)	171(18.6%)	0.92
High LDL-C	240(19.0%)	597(29.3%)	240(26.1%)	< 0.001
High TG	282(22.3%)	649(31.8%)	308(33.4%)	< 0.001
High TC	486 (38.5%)	1068 (52.4%)	462(50.2%)	< 0.001
Multiple abnormality	377(29.8%)	884(43.4%)	390(42.3%)	< 0.001

TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

Association between serum levels of lipids and occurrence of colorectal adenomas

Multivariate analysis was used to determine the association of serum levels of lipids with colorectal adenoma. As shown in Table 4, older age was the most intensive risk factor for both nonadvanced adenoma (OR, 3.16; 95% CI, 2.69–3.71) and advanced adenoma (OR, 3.81; 95% CI, 3.08–4.71). Male sex, drink and smoke were risk factors that significantly increased incidence of both nonadvanced and advanced colorectal adenoma. High TG was associated with increased risk of both nonadvanced colorectal adenoma (OR, 1.36; 95% CI, 1.13–1.64) and advanced colorectal adenoma (OR, 1.40; 95% CI, 1.12–1.75). Similar association was observed for TC. High TC appeared to be a risk factor for both nonadvanced colorectal adenoma (OR, 1.35; 95% CI, 1.11–1.64) and advanced colorectal adenoma (OR, 1.38; 95% CI, 1.08–1.76). There was no significant association between serum levels of LDL-C or HDL-C and risk of colorectal adenoma.

Table 4
Multivariate analysis of risk factors associated with colorectal adenoma

Variables	Nonadvanced colorectal adenoma (n = 2,039)		Advanced colorectal adenoma (n = 921)	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Male	1.34 (1.14–1.58)	< 0.001	2.16(1.76–2.65)	< 0.001
Age (≥ 50 yrs)	3.16 (2.69–3.71)	< 0.001	3.81 (3.08–4.71)	< 0.001
BMI (≥ 25 kg/m^2)	1.22(1.01–1.47)	0.040	1.10 (0.88–1.39)	0.398
Hypertension	1.01 (0.81–1.26)	0.932	1.34(1.04–1.72)	0.023
Diabetes mellitus	1.10 (0.80–1.49)	0.565	0.97 (0.68–1.40)	0.879
Smoke	2.09 (1.59–2.75)	< 0.001	1.58 (1.14–2.18)	0.006
Drink	1.65 (1.09–2.49)	0.019	2.08 (1.30–3.31)	0.002
TG (≥ 1.7 mmol/L)	1.36 (1.13–1.64)	0.001	1.40 (1.12–1.75)	0.003
TC (≥ 5.17 mmol/L)	1.35 (1.11–1.64)	0.003	1.38 (1.08–1.76)	0.003
LDL-C (≥ 3.37 mmol/L)	1.16 (0.93–1.45)	0.19	1.04 (0.79–1.37)	0.757
HDL-C (≤ 1.04 mmol/L)	0.82 (0.67–1.01)	0.067	0.80 (0.62–1.03)	0.079

OR: odd ratio; CI: confidence index; BMI: body mass index; TC, total cholesterol; TG, triglyceride; HDL, high-density lipoprotein cholesterol; LDL, low density lipoprotein cholesterol.

Discussion

In the present study, we investigated the serum lipid profiles in patients with colorectal adenomas in Chinese population, and analyzed the association between dyslipidemia and colorectal adenoma. This large-scale study revealed that (i) dyslipidemia was more prevalent among patients with colorectal adenomas, and (ii) elevated serum TG and TC were associated with increased risk of both nonadvanced and advanced colorectal adenomas in Chinese population.

The associations between serum lipids and colorectal adenoma have been intensively studied, but the findings remained controversial. Yang et al. investigated the obesity and serum lipids in old Chinese people with colorectal polyps, and found that colorectal polyps were significantly associated with increased TC and TG levels(12). Another study by Passarelli et al. found that cholesterol levels were associated with advanced colorectal adenomas (22). However, some studies found no association between TC levels and colorectal adenoma (23, 24). In the present study, patients with colorectal

adenomas bared higher levels of TC. Multivariate analysis suggested that elevated TC levels significantly increased the risk of nonadvanced and advanced colorectal adenomas.

Meanwhile, our data indicated that high TG increased the risk of both nonadvanced and advanced colorectal adenomas, which was consistent with previous studies. In a large-scale cross-sectional study of 19,281 participants, Yang et al. reported that high TG levels were significantly associated with both nonadvanced and advanced colorectal adenomas (25). Another large-scale study including 1,771 adenoma cases and 4,667 controls revealed that individuals whose plasma TG ≥ 150 mg/dL were at higher risk of advanced colorectal adenomas with an OR of 1.47(26). Some researchers have reported that HDL-C levels were inversely associated with colorectal adenoma risk (27, 28),while others failed to find such association (25, 29), or even observed a positive association with colorectal adenomas(30). In our study, serum levels of HDL-C in patients with colorectal adenomas were not significantly different from normal controls. Moreover, though serum levels of LDL-C elevated in patients with colorectal adenomas, no significant relationship was observed after adjusting for other factors. The mechanisms underlying the relationship between dyslipidemia and formation of colorectal adenoma are not completely clear. One possible hypothesis is that obesity causes oxidative stress and inflammation, resulting in lipid accumulation within organs, which is known to cause insulin resistance and hyperglycemia, and induce colorectal adenomas(31).

The present study also evaluated other factors that may influence the occurrence of colorectal adenomas. Older age and male sex are prominent risk factors of both colorectal adenomas and CRC. Previous studies found that the incidence of colorectal adenoma increased dramatically after 50 years of age (10, 32). Consistently, in this study, both older age and male sex were associated with an increased risk of colorectal adenoma, and this was more pronounced for advanced colorectal adenoma cases. Several studies have suggested that larger BMI has been consistently associated with a higher risk of CRC and colorectal adenoma (33–35). We evaluated the role of overweight (BMI ≥ 25 kg/m^2) in the formation of colorectal adenomas, and found it associated with an increased risk of nonadvanced colorectal adenomas rather than advanced colorectal adenomas.

Study Strengths And Limitations

Although the associations between serum lipid profiles and risk of colorectal adenoma have been studied, there are not consistent conclusions. Especially, most clinical studies about Chinese population were conducted with small sample size, and the association remained poorly understood. In the present study, all participants had colonoscopy data, which would remove the classification bias and valid the case-control study. Meanwhile, with large-scale case-control design, the present study provides convincible evidence that elevated serum TC and TG increased the risk of colorectal adenoma in Chinese population.

There are also limitations of this study. First, the retrospective design made it impossible to collect some important information like genetic background, dietary composition, physical activity, thus may cause

possible selection biases. Second, the mechanisms underlying the association between dyslipidemia and colorectal adenoma remain unclear, and needed more experimental evidences to clarify it.

Conclusions

The present study investigated the association between serum lipid profiles and occurrence of colorectal adenoma. Multivariate analysis suggested that higher levels of serum TG and TC increased the risk of both nonadvanced and advanced colorectal adenoma. Our findings supported a significant role of serum lipids in development of colorectal adenoma, and suggested that evaluated TC and TG would practical markers for classifying risk of colorectal adenoma.

Abbreviations

CRC: colorectal cancer; 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; 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 2018-A-12). Informed consent for involvement in the study was obtained from each participant.

Availability of data and material

The datasets used and analyzed in this study will be provided by the corresponding author upon reasonable request.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Sudong Liu designed the study, reviewed the draft; Boying Liu reviewed pathology reports, analyzed the data and wrote the draft; Pingwu Wen reviewed the medical records and collected clinical data; Xiaodong Gu and Ruiqiang Weng conducted the experiment and collected the serum lipid levels.

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Figures

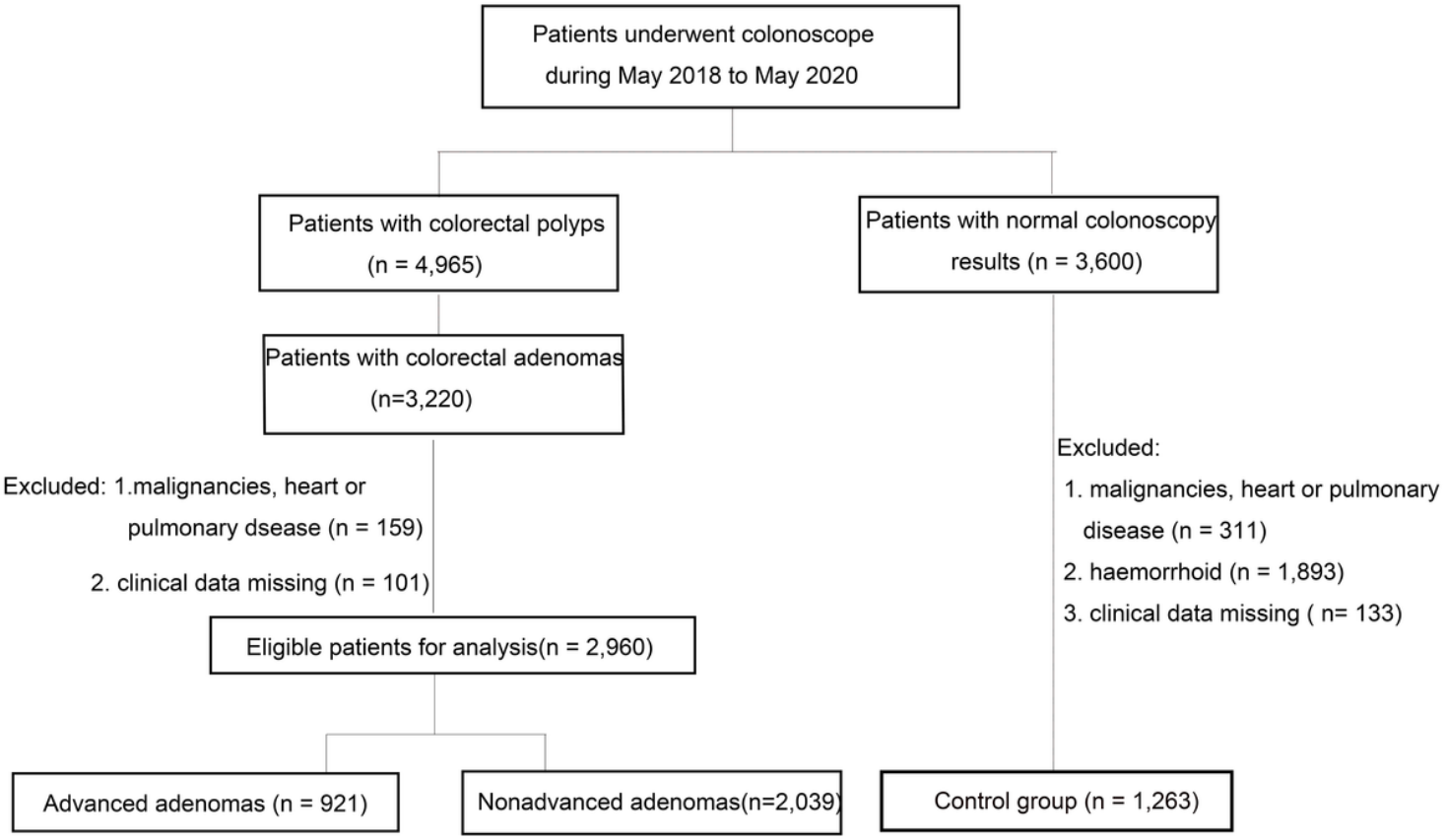

Figure 1

Inclusion and exclusion criteria of the study participants.