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CLINICAL TRIALS STUDY

Lipid levels in serum and cancerous tissues of colorectal cancer patients

Xin Zhang, Xian-Wen Zhao, Dong-Bo Liu, Cun-Zhi Han, Li-Li Du, Jie-Xiang Jing, Yan Wang

Xin Zhang, Dong-Bo Liu, Department of Anus and Intestine Surgery, Provincial Cancer Hospital of Shanxi Province, Taiyuan 30013, Shanxi Province, China
Xian-Wen Zhao, Cun-Zhi Han, Li-Li Du, Jie-Xiang Jing, Yan Wang, Laboratory of Cancer Etiology, Provincial Cancer Institute of Shanxi Province, Taiyuan 30013, Shanxi Province, China
Author contributions: Zhang X and Du LL designed the study in addition to providing financial support for this work; Liu DB collected materials from the patients and obtained patient information; Han CZ, Du LL and Wang Y performed the majority of experiments; Jing JX and Zhao XW provided key reagents and analytical tools and were also involved in editing the manuscript; Du LL and Han CZ wrote the manuscript.
Correspondence to: Li-Li Du, Associate Senior Technologist, Laboratory of Cancer Etiology, Provincial Cancer Institute of Shanxi Province, Zhigong New Street 3, Taiyuan 30013, Shanxi Province, China. byshcz@vip.163.com
Telephone: +86-351-4651480 Fax: +86-351-4651480
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Abstract

AIM: To investigate the correlations between lipid metabolism disorder and the occurrence and development of colorectal cancer by monitoring the alterations in lipid levels in cancerous tissue and serum in patients with colorectal cancer.

METHODS: The levels of total and free cholesterol (TCH and FCH), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C), high density lipoprotein- cholesterol (HDL-C), apolipoprotein A1 (ApoA-1) and ApoB in serum of 206 patients with colorectal cancer, 70 patients with benign colorectal disease and 300 healthy participants, and in the cancerous tissue and paracancerous tissue of 152 patients with colorectal cancer were measured with an Olympus 600 auto-biochemical analyzer. The obtained data were statistically analyzed.

RESULTS: Serum FCH level was significantly higher (1.9 ± 0.4 mmol/L *vs* 1.3 ± 0.3 mmol/L, 1.9 ± 0.4 mmol/L *vs* 1.2 ± 0.4 mmol/L, $P < 0.05$), whereas serum levels of TCH, LDL-C, ApoA-I and ApoB were significantly lower in patients with colorectal cancer than in patients with benign colorectal disease and healthy controls. The levels of FCH and TG in cancerous tissue were significantly lower (14.5 ± 9.6 μmol/g *vs* 19.3 ± 13.9 μmol/g, $P < 0.05$; 16.3 ± 19.8 μmol/g *vs* 44.1 ± 38.1 μmol/g, $P < 0.05$), whereas HDL-C level was significantly higher (7.9 ± 4.5 μmol/g *vs* 5.7 ± 3.9 μmol/g, $P < 0.01$) in cancerous tissue than in paracancerous tissue. The levels of TCH and TG in serum and the levels of TCH and HDL-C in cancerous tissue in patients with colorectal cancer were significantly correlated with TNM stage. The levels of TCH and LDL-C in serum were significantly lower, whereas HDL-C level in cancerous tissue was significantly higher in patients with lymph node metastasis than in patients without lymph node metastasis. The levels of TCH, FCH, TG, HDL-C and LDL-C in cancerous tissue were not significantly different from those in paracancerous tissue. The serum levels of FCH and TG were significantly higher, whereas serum HDL-C levels were significantly lower in patients with rectum cancer than in patients with colon cancer.

CONCLUSION: The disordered and abnormally altered levels of lipids in cancerous tissue and serum of patients with colorectal cancer may be correlated with the occurrence and development of colorectal cancer.

Key words: Colorectal cancer; Correlation; Lipid level; Occurrence; Progression

Core tip: The disordered and abnormally altered levels of lipids in cancerous tissue and serum of patients with colorectal cancer may be correlated with the occurrence and development of colorectal cancer.

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INTRODUCTION

In recent years, a large number of studies have demonstrated that abnormal levels of lipids are closely correlated with the initiation and progression of breast cancer[1,2]. In particular, there have been a number of reports in the literature regarding the relationship between abnormal lipid levels and colorectal cancer[3-6]. Dessi *et al*[7,8] observed changes in cholesterol levels in both an *in vitro* experimental study on cancer cells and an experimental study on the proliferation of normal cells. However, there have been inconsistencies as to whether this relationship is due to the altered lipid metabolism taking place after tumor formation or due to altered lipid metabolism favorable for tumor formation. In order to clarify the association between abnormal lipid metabolism and colorectal cancer, this study was designed to elucidate the associations between abnormal alterations in *in vivo* lipid metabolism and the occurrence and development of colorectal cancer by examining alterations in the levels of a number of relevant lipids in cancerous tissue, paracancerous tissue and serum in patients with colorectal cancer and compare them with those from patients with benign colorectal disease and healthy participants.

MATERIALS AND METHODS

Clinical data

Patient group: A total of 260 patients with colorectal cancer including 166 patients with rectum carcinoma and 94 patients with colon cancer were recruited for this study. These patients were inpatients with colorectal cancer who were admitted to the Department of Anus and Intestine Surgery, Provincial Cancer Hospital of Shanxi Province from March 2008 to May 2010. Of these patients, 152 were male and 108 were female with a median age of 54 years, ranging from 35 to 75 years. Seventy patients with benign colorectal disease were also enrolled, including 20 with colonic polyps, 14 with adenoma of the colon, 21 with chronic colitis and 15 with ulcerative colitis. Of these patients, 45 were male and 25 were female with a median age of 53 years, ranging from 36 to 70 years. Disease in all the recruited patients was pathologically confirmed by both biopsy and colonoscopy, and by post-operative histopathologic examination.

Control group: A total of 300 healthy participants were recruited as controls, including 80 who accompanied the inpatients and 220 who were considered healthy following physical examination. Of these participants, 170 were male and 130 were female with a median age of 52 years, ranging from 35 to 70 years. A history of colorectal cancer in these participants was eliminated.

The protocols for this study were approved by The Ethic Committee of the Provincial Cancer Hospital of Shanxi Province. Informed consent was obtained from each of the recruited patients and the healthy participants.

Collection of serum samples, cancerous tissue and paracancerous tissue

Approximately 3 mL of venous blood was drawn from each of the patients with colorectal cancer and from the patients with benign colorectal disease who had not received any pre-operative therapies as well as the healthy participants who had fasted in the morning. The blood samples were centrifuged at 3000 rpm for 10 min. The separated serum samples were saved for subsequent measurement of blood lipid levels. Approximately 0.5 g of cancerous tissue and normal tissue at a distance of about 4 cm from the cancerous tissue (paracancerous tissue) were collected from 152 patients with colorectal cancer. These tissue samples were first rinsed with physiological saline solution and then frozen at -80 ℃ for the subsequent biochemical and histological examinations described below.

Experimental methods

Treatment of patient biopsies: The frozen cancerous tissue and paracancerous tissue were removed from the freezer and thawed naturally. Approximately 0.2 g of the thawed samples was taken from each sample and ground in a grinder with a small amount of arenaceous quartz into a homogeneous paste and 2 mL of ethanol-petroleum ether (1:1) mixture was added. This homogenate mixture was transferred to a 10-mL centrifuge tube, mixed thoroughly, extracted by shaking in an oscillator for 2 min and then centrifuged at 3000 rpm for 10 min. Approximately 0.5 mL of the supernatant was taken from each sample to measure the lipid levels in these tissues.

Measurement of lipid levels: Total cholesterol (TCH), free cholesterol (FCH) and triglyceride (TG) were measured using enzymatic methods. High density lipoprotein-cholesterol (HDL-C) and low density lipoprotein-cholesterol (LDL-C) were measured using the three generation of homogeneous method. Apolipoprotein A1 (ApoA-1) and apolipoprotein B (ApoB) were measured using immunoturbidimetry.

Instruments and reagents: An Olympus 600 auto-biochemical analyzer was obtained from the Olympus Corporation (Tokyo, Japan). All the reagents used in this study were provided by DiaSys Diagnostic Systems (Shanghai) Co., Ltd (Shanghai, China).

Table 1 Comparison of serum lipid levels in patients with colorectal cancer, patients with benign colorectal disease and healthy participants (mmol/L)

Items	Patients with colorectal cancer (n = 260)	Patients with benign colorectal disease (n = 70)	Healthy participants (n = 300)	P value
TCH	4.8 ± 0.9[1,2]	5.9 ± 0.7	5.7 ± 0.9	< 0.05 < 0.01
FCH	1.9 ± 0.4[1,2]	1.3 ± 0.3	1.2 ± 0.4	< 0.01 < 0.01
TG	1.5 ± 0.9	1.4 ± 0.5	1.5 ± 0.7	> 0.05
HDL-C	1.4 ± 0.4	1.4 ± 0.2	1.4 ± 0.3	>0.05
LDL-C	3.1 ± 0.8[1,2]	3.9 ± 0.8	4.3 ± 0.8	< 0.01 < 0.01
ApoA-I (g/L)	1.4 ± 0.2[1,2]	2.1 ± 0.4	2.2 ± 1.5	< 0.01 < 0.001
ApoB (g/L)	0.9 ± 0.3[1,2]	1.8 ± 0.2	1.7 ± 0.3	< 0.01 < 0.01

[1]Comparison between patients with colorectal cancer and patients with benign colorectal disease, $P < 0.05$ and $P < 0.01$, respectively; [2]Comparison between patients with colorectal cancer and healthy participants, $P < 0.01$ and $P < 0.01$, respectively. ApoA-1: Apolipoprotein A1; ApoB: Apolipoprotein B; FCH: Free cholesterol; HDL-C: High density lipoprotein-cholesterol: LDL-C: Low density lipoprotein-cholesterol; TCH: Total cholesterol; TG: Triglyceride.

Statistical analysis

SPSS13.0 software was used to perform t-test, variance and correlation analyses. The difference(s) between groups with $P < 0.05$ were regarded as statistically significant.

RESULTS

Comparison of the serum levels of lipids in patients with colorectal cancer, patients with benign colorectal disease and healthy participants

The serum levels of TCH, LDL-C, ApoA-I and Apo-B in patients with colorectal cancer were significantly lower than those in patients with benign colorectal disease and healthy participants ($P < 0.05$), whereas the serum level of FCH was significantly lower in patients with colorectal cancer than in patients with benign colorectal disease and healthy participants ($P < 0.01$). However, there were no statistically significant differences in the serum levels of TG and HDL-C among the three groups ($P < 0.05$). There were no statistically significant differences in the serum levels of all lipids examined (TCH, FCH, TG, HDL-C, LDL-C, ApoA-I and Apo-B) between the patients with benign colorectal disease and the healthy participants ($P < 0.05$). These data are presented in Table 1.

Comparison of the levels of lipids in cancerous tissue and paracancerous tissue of patients with colorectal cancer

The levels of TCH, FCH and TG in cancerous tissue were lower, whereas HDL-C level was significantly higher in cancerous tissues than those in paracancerous tissue of patients with colorectal cancer ($P < 0.05$ and $P < 0.01$, respectively). However, there was no statistically significant difference in LDL-C between the two types of tissues ($P > 0.05$). These data are presented in Table 2.

Table 2 Lipid levels in cancerous tissue and paracancerous tissue in patients with colorectal cancer (μmol/g)

Group	Cancerous tissue (n = 152)	Paracancerous tissue (n = 152)	P value
TCH	17.8 ± 10.7	23.6 ± 18.9	< 0.05
FCH	14.5 ± 9.6	19.3 ± 13.9	< 0.01
TG	16.3 ± 19.8	44.1 ± 38.1	< 0.001
HDL-C	7.9 ± 4.5	5.7 ± 3.9	< 0.01
LDL-C	4.4 ± 3.1	4.9 ± 3.3	> 0.05

FCH: Free cholesterol; HDL-C: High density lipoprotein-cholesterol: LDL-C: Low density lipoprotein-cholesterol; TCH: Total cholesterol; TG: Triglyceride.

Correlations between lipid levels in serum and cancerous tissue in patients with colorectal cancer and TNM stages

The analysis of variance regarding lipid levels in serum and cancerous tissue of patients with colorectal cancer and TNM stages revealed that there were significant correlations between the levels of TCH, TG and HDL-C in cancerous tissue and serum of patients with colorectal cancer and clinical TNM stages of colorectal cancer. With pathogenic progression, the levels of TCH and TG in cancerous tissue and in serum of patients at TNM stages Ⅲ and Ⅳ were significantly reduced, whereas HDL-C level in cancerous tissue was significantly increased as compared to those in patients at TNM stages Ⅰ and Ⅱ ($P < 0.05$ and $P < 0.01$), respectively. These data are presented in Table 3.

Comparison of the lipid levels in cancerous tissue and serum of patients with and without lymph node metastasis

The levels of TCH and HDL-C in the cancerous tissue of patients with lymph node metastasis were significantly higher than those of patients without lymph node metastasis ($P < 0.05$), whereas TG levels in the cancerous tissue of patients with lymph node metastasis were significantly lower than those of patients without lymph node metastasis ($P < 0.01$). These data are presented in Table 4.

Comparison of the levels of various lipids in cancerous tissue, paracancerous tissue and serum samples of patients with rectal cancer and those of patients with colon cancer

There were no significant differences in the levels of FCH, TG, TCH, HDL-C and LDL-C in the cancerous tissue and paracancerous tissue between patients with rectal cancer and patients with colon cancer ($P > 0.05$). However, the levels of FCH and TG in the serum of patients with rectal cancer were 1.5 ± 0.47 mmol/L and 1.4 ± 0.59 mmol/L, respectively, which were significantly higher than those in the serum of patients with colon

Table 3 Correlations between serum lipid levels and cancerous tissue of patients with colorectal cancer with the tumor node metastasis stages

Groups	Case (*n*)	TCH	FCH	TG	HDL-C	LDL-C
Tissue (μmol/g)						
Ⅰ	15	18.3 ± 4.2	14.4 ± 8.3	17.2 ± 10.9	5.1 ± 4.3	3.9 ± 2.3
Ⅱ	66	17.9 ± 3.6	15.2 ± 9.7	16.5 ± 12.2	5.7 ± 3.6	4.2 ± 2.9
Ⅲ	53	16.3 ± 4.0	15.9 ± 13.4	14.9 ± 13.3	7.2 ± 5.2	4.5 ± 3.4
Ⅳ	18	13.5 ± 5.3[a]	13.1 ± 9.2	13.4 ± 9.4[a]	9.3 ± 3.2[a]	4.2 ± 2.7
Serum (mmol/L)						
Ⅰ	25	5.9 ± 0.8	1.5 ± 0.2	2.8 ± 1.1	1.5 ± 0.4	3.5 ± 1.3
Ⅱ	113	4.8 ± 0.9	1.4 ± 0.3	1.9 ± 0.7	1.4 ± 0.3	3.1 ± 0.9
Ⅲ	91	4.1 ± 1.0	1.4 ± 0.4	1.5 ± 0.9	1.4 ± 0.3	3.0 ± 0.9
Ⅳ	31	3.9 ± 0.9[d]	1.3 ± 0.4	1.3 ± 0.5[d]	1.1 ± 0.6	3.0 ± 0.8

[a]$P < 0.05$ *vs* the levels of total cholesterol (TCH) and high density lipoprotein-cholesterol (HDL-C) in cancerous tissues with tumor node metastasis (TNM) stages; [d]$P < 0.01$ *vs* the levels of TCH and triglyceride (TG) in serum with TNM stages. LDL-C: Low density lipoprotein-cholesterol.

Table 4 Lipid levels in serum and cancerous tissues of patients with and without lymph node metastasis

Group	Case (*n*)	TCH	FCH	TG	HDL-C	LDL-C
Tissue (μmol/g)						
With lymph node metastasis	74	18.4 ± 3.4	16.0 ± 13.4	14.9 ± 10.3	8.9 ± 3.8	4.5 ± 3.4
Without lymph node metastasis	78	17.5 ± 4.1	15.1 ± 11.6	17.7 ± 12.2	7.0 ± 4.9	4.2 ± 2.9
P		< 0.05[1]	> 0.05	< 0.01[1]	< 0.05[1]	> 0.05
Serum (mmol/L)						
With lymph node metastasis	127	3.2 ± 0.9	1.5 ± 0.4	1.5 ± 1.1	1.0 ± 0.4	3.2 ± 0.8
Without lymph node metastasis	133	4.9 ± 1.0	1.4 ± 0.3	1.5 ± 0.7	1.5 ± 0.4	3.0 ± 0.7
P		< 0.01[2]	< 0.05[2]	> 0.05	< 0.01[2]	> 0.05

[1]Indicates the comparison between lipid levels in cancerous tissue of patients with and without lymph node metastasis; [2]Indicates the comparison between lipid levels in serum of patients with and without lymph node metastasis. FCH: Free cholesterol; HDL-C: High density lipoprotein-cholesterol; LDL-C: Low density lipoprotein-cholesterol; TCH: Total cholesterol; TG: Triglyceride.

cancer, which were 1.4 ± 0.38 and 1.3 ± 0.36 mmol/L, respectively ($P < 0.01$). The serum HDL-C level in patients with rectum cancer was 1.21 ± 0.37 mmol/L, which was significantly lower than 1.43 ± 0.75 mmol/L in patients with colon cancer ($P < 0.01$).

DISCUSSION

Cholesterol is present in every tissue/organ and is the most abundant steroid compound in the human body. As an important component of cell membranes, cholesterol plays important physiological roles. When cholesterol is deficient in humans, cellular rigidity is increased and the cells are easily fractured. TCH is the sum of a variety of lipid molecules and lipoproteins that contain cholesterol, including FCH, HDL-C and LDL-C. Cholesterol is present in the human body in many forms. For instance, when present as HDL-C it is transported from the extrahepatic tissues *via* HLD to the liver where it is further metabolized and finally secreted out of the body. When it is present as LDL-C, it is transported *via* LDL-C to various tissues/organs. Apolipoproteins Apo-A1 and Apo-B are correlated with the metabolism and function of HDL and LDL. Both HDL and LDL are involved in cholesterol transport, and thus have certain relationships with the occurrence and progression of cancers.

Kitahara *et al*[5] conducted a 14-year follow-up in a total of 1189719 Korean adults and standardized their medical examinations once every two years. They found that a total of 53944 males and 24475 females were diagnosed with primary cancers. Among them, the occurrence of rectum cancer and prostate cancer in males and breast cancer in females was positively correlated with TCH levels with a HR value of 1.12, 95%CI of 1.00-1.25 and *P* value of 0.05 for male rectum cancer; HR value of 1.12, 95%CI: 1.07-1.44 and *P* value < 0.01 for prostate cancer, and a HR value of 1.17, 95%CI: 1.03-1.33 and $P = 0.03$ for female breast cancer, respectively. Yamada *et al*[9] also found that after adjustment for such factors as age, sex, body mass index, cigarette smoking and alcohol intake, the TCH level in serum was positively correlated with the occurrence of colorectal cancer *in situ*. A study by Chung *et al*[6] indicated a negative correlation of serum TCH level with the risk of colorectal cancer occurrence with an OR value of 0.3 and 95%CI: 0.1-0.8. The reason for this correlation may be due to nutritional alterations and abnormal metabolism in patients with colorectal cancer. Tomiki *et al*[10] conducted a case-control study and their results indicated that TCH levels in patients with colorectal cancer, gastric cancer, and esophageal cancer were significantly lower than those in healthy control participants. The study by Bird *et al*[11] indicated that after adjustment for relevant influencing factors such as obesity, physical activity, refined carbohy-

drates and alcohol intake, the serum TCH level was not inversely related to the risk of colorectal polyps. Kostić *et al*[12] performed a study on the correlations between the levels of total lipids and TCH and benign and malignant tumors of the colon and rectum. Their statistical analysis of the obtained data revealed that hypocholesterolemia was associated with the incidence of adenocarcinoma. Gaard *et al*[13] conducted a 7-13 year prospective study in 62173 participants and found 186 cases with rectum cancer and 106 cases with colon cancer. Their statistical analyses revealed no association between the levels of blood lipids and lipoproteins and the risk of rectum cancer and colon cancer. While there was a statistically significant difference in this risk among females, this was regarded as incidental. The results obtained in the present study indicated that the serum FCH level in patients with colorectal cancer was significantly increased, whereas TCH levels were significantly decreased as compared to those in patients with benign colorectal disease and healthy participants. Additionally, in this study, we also found that the FCH level in the cancerous tissue of patients with colon cancer was significantly lower than that in their paracancerous tissue. These results are completely inconsistent with those described above. This disparity requires further investigation.

TG is one of the most abundant lipids in the human body. Most tissues utilize the energy derived from the products of TG hydrolysis. Under normal conditions, the storage, transport and exchange of lipids in the human body are maintained in a state of dynamic balance. When cancer occurs, the physiological balance of lipid levels is destroyed, leading to lipid metabolism disorders. Yamada *et al*[9] found that TG level was positively correlated with the occurrence of colorectal carcinoma *in situ*. The results of a population study conducted by Sun *et al*[14] indicated that higher serum TG level was generally related to a higher risk of tubulovillous/villous adenoma in the rectosigmoid colon. A study by Chung *et al*[6] indicated that serum TG level was negatively and strongly correlated with the risk of colorectal cancer with an OR value of 0.2 and 95%CI: 0.1-0.6, whereas the study by Bird *et al*[11] indicated that after adjustment for factors such as obesity, physical activity, refined carbohydrates and alcohol intake, high serum TG level was correlated with the risk of adenomas in the left colon and rectum. A case-control study conducted by Tomiki *et al*[10] indicated no significant difference in TG between cancer-bearing cases and controls. The results of the present study revealed no statistically significant difference in serum TG level between patients with colorectal cancer, patients with benign colorectal disease and the healthy control group. These results are consistent with those reported by Tomiki *et al*[10]. The results of the present study also indicated that TG levels in cancerous tissue of patients with rectum cancer and patients with colon cancer were significantly lower than those in their corresponding paracancerous tissue. However, the mechanisms underlying these differences are not clear at present and require further investigation.

Apolipoproteins ApoA-I and ApoB are the major components of serum lipoproteins and are correspondingly related to the metabolism and function of HDL and LDL. They are also related, to an extent, to the occurrence and development of tumors. Kostić *et al*[12] investigated the relations between the levels of total lipids, TCH, LDL, HDL, phospholipids, gastrin and insulin and both benign and malignant tumors of the colon and rectum. After conducting statistical analyses of the obtained results, they found that only hyperlipidemic LDL-C was related to the risk of colorectal cancer. A case-control study by Tomiki *et al*[10] indicated that the levels of TC and LDL-C in the serum of patients with colorectal cancer were significantly lower than those in the controls, whereas no significant differences in serum levels of HDL-C and TG were seen between patients with gastrointestinal cancer and controls. van Duijnhoven *et al*[15] reported that the concentrations of HDL-C and ApoA-1 were negatively correlated with the risk of colorectal cancer with a RR value of 0.78 and 95%CI: 0.68-0.89 for HDL-C, and a RR value of 0.82 and 95%CI: 0.72-0.94 for ApoA-1, respectively. Their results indicate that high concentrations of serum HDL-C are related to the reduced risk of rectum cancer. However, the mechanisms underlying these correlations require further investigation. The results of the present study show that serum Apo-A1 concentration in patients with colorectal cancer was significantly lower than those in patients with benign colorectal disease and in healthy controls. These results are consistent with those reported by van Duijnhoven *et al*[15]. There were no statistically significant differences in serum HDL-C levels between these groups.

In this study, we also found that lipid alterations in patients with colorectal cancer were closely related to several clinical characteristics. With the progression of TNM stage, the serum levels of TCH and TG and the levels of TCH in cancerous tissues were decreased, whereas HDL-C levels were increased. The serum TCH and HDL-C levels in patients with lymph node metastasis were decreased, whereas HDL-C level was decreased and HDL-C in cancerous tissue was increased. There were no significant differences in the levels of lipids in both serum and cancerous tissue between the histological types. Notarnicola *et al*[16] suggested that the levels of TCH, LDL-C and the ratio of LDL-C/HDL-C were significant higher in patients with distant metastasis and in patients without distant metastasis, and the increased levels of these lipids may promote distant metastasis in patients with colorectal cancer. These results showed that lipid alterations in patients with colorectal cancer may be related to the degree of malignancy of tumors, *i.e.*, the higher the degree of malignancy and the later the TNM stage, there is a higher demand for cholesterol which is taken up by cancer cells. A case-control study conducted by Tomiki *et al*[10] indicated that in patients with earlier TNM stage, the TCH level was significantly lower. However, the low level of TCH was not correlated with clinical stage.

There are a large number of reports in the literature

indicating that abnormally altered lipid levels are related to colorectal adenoma. For instance, Shinomiya *et al*[17] conducted a comparative investigation on serum lipid levels and ApoE genotype in 205 Japanese patients with colorectal adenoma and 220 cases that were confirmed to be normal by colonoscopy, to examine the relation between both serum lipids and ApoE genotype and colorectal adenomas. They reported that after adjustment for body mass index, cigarette smoking, alcohol intake and other related factors, the odds ratios of proximal and distal adenomas were associated with the presence of allele E4. Serum levels of TC and LDL-C were not related to both proximal and distal adenomas. However, serum TG was positively related to distal adenomas. These data suggest that altered lipid metabolism may be differentially associated with tumorigenesis of the proximal and distal colorectum. The study by Zhongyin *et al*[18] indicated that the risk of colorectal adenomas for populations carrying ApoE E3/E4 genotype was lower than that for populations carrying other genotypes, and altered lipid metabolism may reduce the risk of colorectal cancer. Tabuchi *et al*[19] conducted a multiple logistic regression analysis of the correlation between the incidence of colorectal adenoma or carcinoma and fasting serum levels of TC and TG in Japanese patients and revealed that TG was an independent correlation factor in male ($P < 0.01$), but not in female patients. The TG level in patients with invasive carcinoma was not significantly higher than that in patients with adenoma, suggesting that hypertriglyceridemia may be an independent risk factor for colonic adenoma in men. In conducting an analysis of plasma lipid metabolism in patients with colorectal adenoma, Li *et al*[20] found that dyslipidemia may affect the incidence of colorectal adenoma, particularly at hypertriglyceridemia and low HDL-C levels, which may be related to the occurrence of colorectal adenoma. Yang *et al*[21] performed a large scale cross-sectional study on 19281 Korean participants and identified 5958 participants with colorectal adenomas including 5504 with non-advanced adenomas and 454 with advanced adenomas. They found that higher serum TG level was significantly associated with an increased prevalence of both non-advanced and advanced colorectal adenomas, while higher levels of ApoA-1 and HDL-C were significantly associated with an increased prevalence of non-advanced adenomas. The results of the present study showed no statistically significant differences in serum lipid levels and tissue lipid levels between patients with benign colorectal disease and healthy controls.

Under normal conditions, the storage, transport and exchange of lipids within the human body are maintained in a normal state of dynamic balance. The data obtained from the present study indicated that when colorectal cancer occurred, the serum levels of TCH, LDL-C, Apo-AI, and ApoB were reduced, whereas FCH level was increased. The levels of TCH, FCH and TG in cancerous tissue were reduced and HDL-C level was increased, indicating that when colorectal cancer developed, the physiological balance of lipids is destroyed, leading to lipid metabolism disorder. The mechanisms underlying lipid metabolism disorder are not completely understood. *In vitro* studies have confirmed that in cancer cells, in order to meet the increasing demand for cell proliferation, cholesterol anabolism in these cells is significantly enhanced, which is characterized by increased absorption, increased synthesis and increased activity of a key rate-limiting enzyme of cholesterol synthesis, 3-hydroxy-3-methylglutaryl-CoA reductase[5]. This may be the major reason for the decreased serum cholesterol level in patients with colorectal cancer. The decreased FCH level in cancerous tissue is presumed to be related to the reason why the synthesis and transport of cholesterol cannot meet the demand for the rapid proliferation of cancer cells. Dessi *et al*[22] reported that the cholesterol level in cancerous tissue was increased due to the deposition of cholesterol in this tissue. However, this appears to contradict the growth characteristics of cancer cells and requires further investigation. HDL-C level was decreased in serum, but was increased in cancerous tissue and the LDL-C level was decreased in serum, indicating that both HDL and LDL are involved in cholesterol transport during proliferation of cancerous tissue. It is likely that the rate of cholesterol transport *via* HDL from extra-hepatic tissues is reduced, whereas the rate of cholesterol *via* LDL to other tissues is accelerated. Apolipoproteins ApoA-I and ApoB serve as structural proteins for HDL and LDL, respectively. Their alteration may be related to the parallel alterations in lipoproteins. Whether the decreased TG level in cancerous tissue shares a similar mechanism remains to be investigated.

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COMMENTS

Background

Abnormal lipid metabolism has been found to be associated with several types of cancer including colorectal cancer. However, whether this association is due to the altered lipid metabolism taking place after tumor formation or due to altered lipid metabolism favorable for tumor formation is not clear and requires clarification.

Research frontiers

One of the hotspots in current cancer research is the determination of the correlations between metabolic disorders, including lipid metabolism disorders, and the occurrence and development of colorectal cancer.

Innovations and breakthroughs

This study attempted to elucidate the associations between abnormal alterations in *in vivo* lipid metabolism and the occurrence and development of colorectal cancer.

Applications

The results of this study indicate that when colorectal cancer develops in humans, the physiological balance of lipids is destroyed, leading to lipid metabolism disorders. Thus, the application of pharmacological approaches targeting abnormal lipid metabolism in cancer cells to maintain the physiological balance of lipids may be a potentially promising treatment option in patients with colorectal cancer.

Peer review

In this paper, authors compared the serum lipids levels of the colorectal cancer and benign illnesses and the health participants, also compared the lipids levels of the cancerous and paracancerous tissue. Moreover they also assessed relation between the lipids levels and the tumor node metastasis stages and lymph node metastasis in patients with colorectal cancer. Therefore authors provided a lot of useful information for readers in this paper.

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