Int J Clin Exp Med 2020;13(12):9857-9863
www.ijcem.com /ISSN:1940-5901/IJCEM0118106

Original Article

Correlation analysis between hyperlipidemia and prognosis of epithelial ovarian tumors

Qian Qiu, Xiangqin Zheng

Department of Gynaecology Area 2, Fujian Maternal and Child Health Hospital, Fuzhou, Fujian, China

Received July 13, 2020; Accepted August 30, 2020; Epub December 15, 2020; Published December 30, 2020

Abstract: Objective: The purpose of this study was to analyze the correlation between hyperlipidemia and prognosis of epithelial ovarian tumors. Methods: A total of 176 patients with epithelial ovarian tumors were collected from January 2014 to January 2015 and were divided into the benign group (BG, n=90) and the malignant group (MG, n=86). General clinical indicators, serum lipid levels including total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C) were compared between the two groups. The correlation between hyperlipidemia and prognosis of epithelial ovarian tumors was analyzed. Results: The systolic blood pressure, diastolic blood pressure, BMI and hyperlipidemia rate in the MG were significantly higher than those in the BG (P<0.05). The TC and HDL-C in the MG were significantly lower than those in the BG (P<0.05). In the MG, the levels of TC, HDL-C, LDL-C in patients with hyperlipidemia were significantly lower than those in patients without hyperlipidemia (P<0.05). The lipoprotein A [LP (a)] levels in patients with hyperlipidemia were significantly higher than those in patients without hyperlipidemia (P<0.05). In the MG, there were significant differences in tissue differentiation level, depth of invasion and TNM staging between patients with hyperlipidemia and non-hyperlipidemia (P<0.05). In the MG, there was no significant difference between the two groups in 1-year survival rate and 2-year survival rate (P > 0.05). The 3-year survival rate, 4-year survival rate and 5-year survival rate of patients with hyperlipidemia were lower than those of patients without hyperlipidemia (P<0.05). Conclusion: Dyslipidemia was greatly related to the development and prognosis of epithelial ovarian tumors. Patients without hyperlipidemia had more sever malignance, worse prognosis and lower survival rate.

Keywords: Hyperlipidemia, epithelial ovarian tumor, prognosis, total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), correlation

Introduction

Epithelial ovarian tumor, a common reproductive system tumor in females, originates from the ovarian surface [1]. Epithelial ovarian tumors account for about 60% of the total ovarian tumors, of which malignant tumors account for about 85% of the total ovarian malignant tumors [2]. Lipids play an essential role in metabolism and maintenance of biological structures [3]. The correlation between hyperlipidemia and prognosis of epithelial ovarian tumors has not been reported. However, in recent years, relevant studies have reported that lipid metabolism is closely related to the occurrence and development of tumors. In order to meet the needs of rapid tumor growth, tumor cells acquire and consume nutrients to the greatest extent, leading to changes in serum lipid levels of the body [4]. Meanwhile, some studies have revealed that most patients with epithelial ovarian tumors are complicated with metabolic disorder of serum lipids, which is closely related to the degree of tumor development, and hyperlipidemia is also associated with the recurrence, metastasis and death of breast cancer patients [5, 6]. Consequently, we speculated that hyperlipidemia may affect the prognosis of epithelial ovarian tumors. Therefore, we aimed to analyze the correlation between hyperlipidemia and epithelial ovarian tumors.

Materials and methods

General clinical indicators

A total of 176 patients with epithelial ovarian tumors admitted to Fujian Maternal and Child

Health Hospital from January 2014 to January 2015 were selected as observation subjects and divided into the benign group (BG, n=90) and the malignant group (MG, n=86). This study has been approved by the Ethics Committee of Fujian Maternal and Child Health Hospital. All study participants provided written informed consent prior to participating in the study.

Inclusive criteria: (1) patients without surgery, radiotherapy, chemotherapy and other treatments before diagnosis; (2) those with surgical treatment and clear surgical pathology results after diagnosis; and (3) those with complete follow-up data.

Exclusive criteria: (1) patients with cardiovascular and cerebrovascular diseases; (2) those with endocrine system diseases like diabetes and thyroid disease; (3) those with other tumors; (4) those with polycystic ovarian syndrome or other diseases related to lipid metabolism; (5) those with dysfunction of liver, lung and kidney; and (6) those with acute and chronic systemic infection were excluded.

Methods

Detection of serum lipid level: 5 ml of peripheral venous blood was extracted in a fasted state in the morning and placed in a coagulation-promoting tube. The blood was centrifuge at 3000 r/min for 10 min within 2 h to extract supernatant. The levels of total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and lipoprotein A [LP (a)] were measured by automatic biochemical analyzer.

Patients with hyperlipidemia and non-hyperlipidemia were refered to the relevant standards of the World Health Organization: (1) TC > 6.84 mmol/L and (or) LDL-C > 3.8 mmol/L; (2) TG > 1.76 mmol/L; (3) HDL-C ≤ 1.04 mmol/L. Any one of the above meets the diagnosis of hyperlipidemia, and the absence of any of the above is considered non-hyperlipidemia.

Evaluation criterion

(1) General clinical indicators including menarche age, onset age, time of pregnancy, the systolic blood pressure, diastolic blood pressure, BMI and hyperlipidemia were compared between the BG and the MG. (2) Serum lipid levels such as TC, TG, HDL-C, LDL-C, and LP (a) were compared between the BG and the MG. (3) General clinical indicators were compared between the hyperlipidemia group and the non-hyperlipidemia group in the MG. (4) Serum lipid levels such as TC, TG, HDL-C, LDL-C, and LP (a) were compared between the hyperlipidemia group and the non-hyperlipidemia group in the MG. (5) The survival rate between the hyperlipidemia group and the non-hyperlipidemia was compared. (6) The correlations between TC, TG, HDL-C, LDL-C, LP (a) and the prognosis were analyzed.

Statistical analysis

Data were analyzed by SPSS 25.0 and Graph Pad Prism 5 Demo. Measurement data were expressed as the form of $\bar{x} \pm s$, and Student's t Test was employed to compare differences between the two groups. Enumeration data were expressed as the form of %, and Chi-squared test was adopted to compare differences between the two groups. Logistic regression analysis was adopted to analyze the correlation between epithelial ovarian cancer and TC, TG, HDL-C, LDL-C, LP (a).

Results

General clinical indicators between the BG and the MG

There was no significant difference between the BG and the MG in menarche age, onset age, the time of pregnancy ($P > 0.05$). The systolic blood pressure, diastolic blood pressure, BMI and hyperlipidemia rate in the MG were significantly higher than those in the BG ($P<0.05$) (**Table 1**).

Serum lipid level between the BG and the MG

The TC and HDL-C in the MG were significantly lower than those in the BG ($P<0.05$). There was no significant difference between the BG and the MG in TG, LDL-C, LP (a) ($P > 0.05$) (**Figure 1**).

Serum lipid levels between the malignant patients with hyperlipidemia and non-hyperlipidemia

In the MG, The TC, HDL-C, LDL-C in patients with hyperlipidemia were significantly lower than those in patients without hyperlipidemia ($P<0.05$). The LP (a) in patients with hyperlipidemia were significantly higher than those in patients without hyperlipidemia ($P<0.05$).

Table 1. General clinical indicators between the benign group and the malignant group ($\bar{x} \pm s$)

Group	*n*	Menophania (year)	Onset age (year)	Pregnancy (time)	Systolic pressure (mmHg)	Diastolic pressure (mmHg)	BMI (kg/m^2)	Hyperlipidemia
Malignant group	86	11.95±2.18	49.02±7.57	4.56±2.05	121.36±12.33	85.63±9.17	25.93±2.34	32 (37.21)
Benign group	90	12.27±2.36	49.75±6.63	3.97±2.67	112.19±11.64	76.29±8.55	22.27±2.82	13 (14.44)
t		0.933	0.681	1.639	5.075	6.992	9.347	11.976
P		0.352	0.497	0.103	0.000	0.000	0.000	0.001

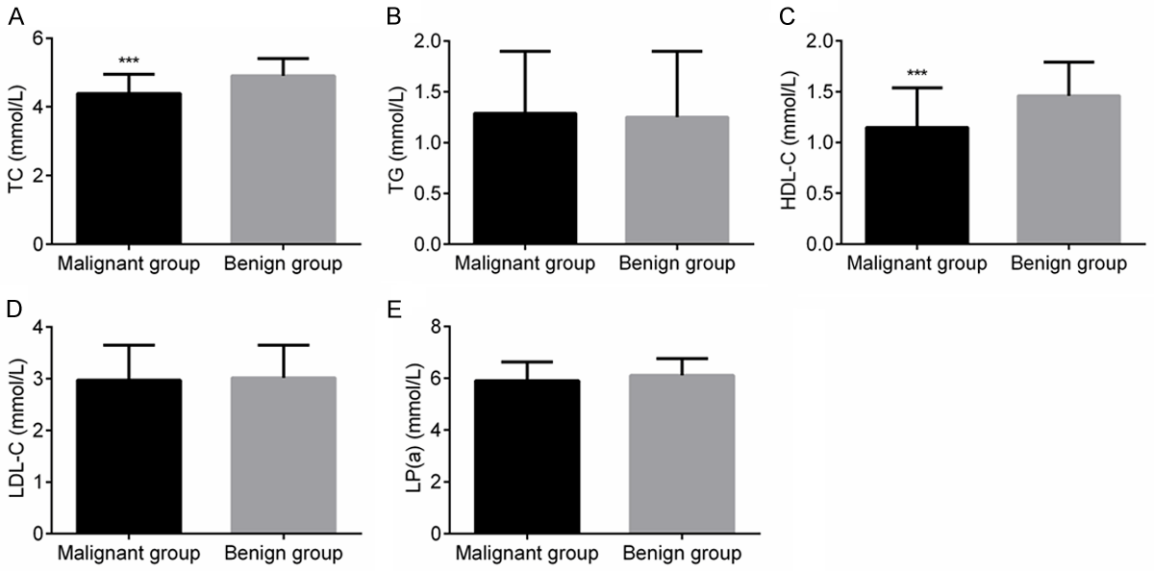

Figure 1. Serum lipid levels between the benign group and the malignant group. A: TC level in the malignant group was lower than that in the benign group; B: There was no statistical difference in TG level between the two groups; C: HDL-C level in the malignant group was lower than that in the benign group; D: There was no statistical difference in LDL-C level between the two groups; E: There was no statistical difference in LP level between the two groups. Compared with the benign group, ***P<0.001.

There was no significant difference in TG between patients with hyperlipidemia and non-hyperlipidemia (P > 0.05) (**Figure 2**).

General clinical indicators between the malignant cancer patients with hyperlipidemia and non-hyperlipidemia

In the MG, there were significant differences in tissue differentiation level, depth of invasion and TNM staging between patients with hyperlipidemia and non-hyperlipidemia (P<0.05). There was no significant difference in the onset age between patients with hyperlipidemia and non-hyperlipidemia (P > 0.05) (**Table 2**).

Survival rate between the malignant cancer patients with hyperlipidemia and non-hyperlipidemia

In the MG, there was no significant difference in 1-year survival rate and 2-year survival rate between the two groups (P > 0.05). The 3-year survival rate, 4-year survival rate and 5-year survival rate of patients with hyperlipidemia were lower than those of patients without hyperlipidemia (P<0.05) (**Table 3**).

Logistic regression analysis of prognosis and serum lipid indicators

The correlations between TC, TG, HDL-C, LDL-C, LP (a) and the prognosis were analyzed, suggesting that the HDL-C and LDL-C were highly correlated with 5-year survival rate of patients (P<0.05) (**Table 4**).

Discussion

Epithelial ovarian tumors are a common gynecological oncology and malignant epithelial ovarian tumors account for most of the mortalities in gynecological oncology [7]. Epithelial ovarian tumors are hard to be detected, so

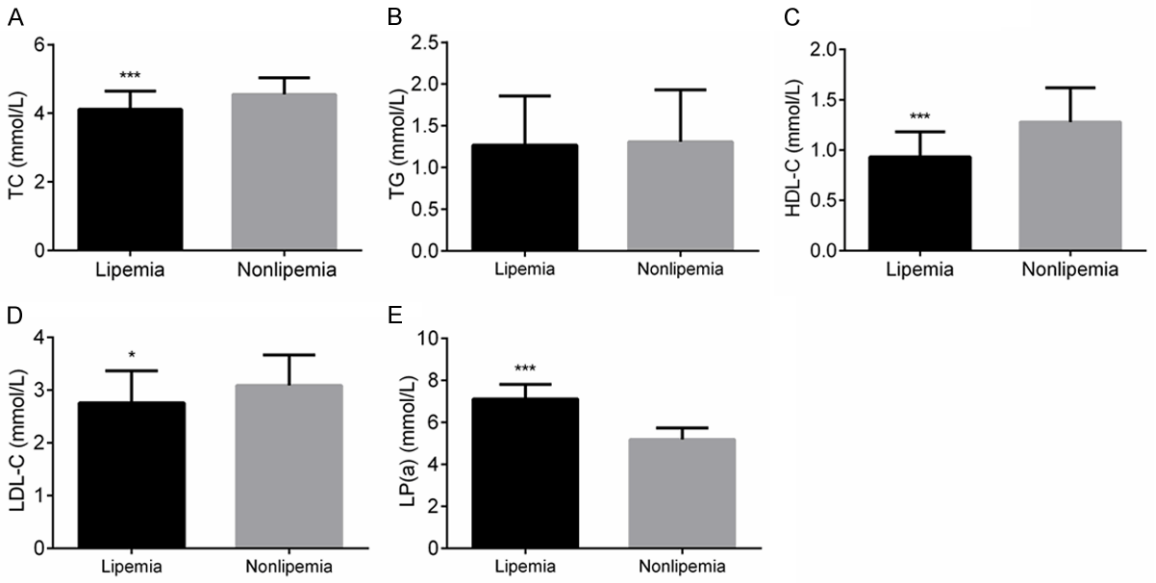

Figure 2. Serum lipid levels between the malignant patients with hyperlipidemia and non-hyperlipidemia. A: The TC in patients with hyperlipidemia was significantly lower than that in patients non-hyperlipidemia in the malignant group ($P<0.05$). B: There was no significant difference in TG between patients with hyperlipidemia and non-hyperlipidemia ($P > 0.05$). C: The HDL-C in patients with hyperlipidemia was significantly lower than that in patients non-hyperlipidemia in the malignant group ($P<0.05$). D: The LDL-C in patients with hyperlipidemia was significantly lower than that in patients with non-hyperlipidemia in the malignant group ($P<0.05$). E: The LP (a) in patients with hyperlipidemia were significantly higher than those in patients non-hyperlipidemia ($P<0.05$). Compared with patients with non-hyperlipidemia, $^{*}P<0.05$, $^{***}P<0.001$.

Table 2. General clinical indicators between the malignant patients with hyperlipidemia and non-hyperlipidemia [$\bar{x} \pm s$, n (%)]

Feature	Hyperlipidemia group (n=32)	Non-hyperlipidemia group (n=54)	t/χ^2	P
Onset age (year)	47.29±7.96	50.05±7.64	1.594	0.115
Degree of tissue differentiation				
Low	23 (71.87)	12 (22.22)	20.525	0.000
Medium + High	9 (28.13)	42 (77.78)		
Depth of invasion				
T1-T3	10 (31.25)	36 (66.67)	10.131	0.002
T4	22 (68.75)	18 (33.33)		
Staging				
I-II	7 (21.88)	31 (57.41)	10.287	0.001
III-IV	25 (78.13)	23 (42.59)		

most patients are diagnosed in advanced stages. When tumors metastasize to the peritoneum or distant organs, patients are more likely to relapse with high mortality, having a 5-year survival rate of 29%, and a poor prognosis [7, 8]. The prognosis of malignant epithelial ovarian tumors is influenced by tremendous risk factors such as the time of pregnancy, surgical staging III-IV, peritoneal metastasis, and chemo sensitivity [9]. Further clinical studies on epithelial ovarian tumor place emphasis on the impact of lipid metabolism on the prognosis.

Relevant studies have shown that there are significant differences in lipid metabolism in patients with benign and malignant ovarian tumors, among which most patients with malignant epithelial ovarian tumors have abnormal lipid levels, manifested as decreased TC and HDL-C [10, 11], In this study, we revealed that compared to the patients with benign

Table 3. Survival rate between the malignant patients with hyperlipidemia and non-hyperlipidemia [*n* (%)]

Feature	*n*	1 year survival	2 year survival	3 year survival	4 year survival	5 year survival
Hyperlipidemia group	32	30 (93.75)	26 (81.25)	19 (59.38)	13 (40.62)	9 (28.13)
Non-hyperlipidemia group	54	52 (96.30)	49 (90.74)	43 (79.63)	37 (68.52)	30 (55.56)
T		0.000	0.883	4.097	6.424	6.100
P		1.000	0.203	0.043	0.011	0.014

Table 4. Logistic regression analysis of blood lipid indicators and prognosis of patients

Indicator	*B* Value	Wald χ^2	*P* Value	*OR* Value	95% *CI*	
					Lower limit	Upper limit
TC	-0.159	3.549	0.086	0.530	0.128	1.069
TG	0.612	2.101	0.127	1.799	0.937	5.261
HDL-C	2.027	25.176	0.001	6.932	3.859	15.662
LDL-C	1.633	7.362	0.013	4.726	1.715	21.253
LP (a)	-0.625	3.279	0.072	0.835	0.289	1.054

tumors, the blood pressure, BMI, and hyperlipidemia rate were higher in patients with malignant tumors. The TC and HDL-C were lower in patients with malignant tumors, suggesting that lipid metabolism disorder may play an essential role in the oncogenesis. The mechanism of the decline of TC and HDL-C may be attributed to the fact that during the growth and proliferation of cancer cells, a large amount of cholesterol is needed to synthesize new cell membranes, leading to a decrease in TC levels [12, 13]. HDL-C is needed in order to maintain the balance of TC in cells, where it binds to cellular surface receptors and causes excessive TC flowing out of cells. Similarly, the progression of tumors activates the signaling pathway of HDL-C receptors, leading to a decrease in HDL-C [14-16].

Recently, the role of lipid metabolism in the development and metastasis of ovarian tumors has attracted more attention. Kouba and colleagues [17] reported that the expression of Ca^{2+} and K activated Ca channels were regulated by lipids, causing upregulation of Ca^{2+}, which further led to proliferation and migration of tumors. Ladanyi and colleagues [18] revealed that the fatty acid receptor CD36 was highly expressed in the plasma membrane of ovarian cancer cells, and inhibition of CD36 could reduce the accumulation of TC and lipid droplets induced by adipocytes, thereby inhibiting the adhesion, invasion and migration of ovarian cancer cells. Furthermore, Hiramatsu and other scholars [2] showed that inhibition of lipid uptake suppressed the tumor growth in the treatment of epithelial ovarian tumors. These studies suggest that lipid metabolism may play a vital role in the development, metastasis and death of epithelial ovarian tumors. By the analysis of general clinical indicators in epithelial ovarian tumor patients with hyperlipidemia and non-hyperlipidemia, this study showed that compared with non-hyperlipidemia patients, patients with hyperlipidemia had decreased TC, HDL-C, LDL-C, increased LP (a), more sever tissue differentiation level, depth of invasion and TNM staging, and lower survival rate. The mechanism may be involved in LDL-C serving as carrier of TC, which is responsible for transporting TC to peripheral tissues. With tumor growth, differentiation and invasion, tumor cells need to absorb more LDL-C from the periphery to synthesize cell membranes, leading to the decrease of LDL-C level [19-21]. LP (a) is composed of apolipoprotein A and low density lipoprotein, and is highly homologous with fibrinolytic enzymes. LP (a) can bind platelets to form a network structure of tumor thrombus, which facilitates the adherence of tumor cells to and outside blood vessels in the process of tumor cell metastasis, and provides tumor cells with growth factors and nutrients, so as to facilitate the proliferation of tumor cells [22-24]. This mechanism may be responsible for the more serious degree of tissue differentiation, depth of infiltration, and TNM staging in

patients with malignant epithelial ovarian tumors complicated with hyperlipidemia. This study shows from another point of view that lipid metabolism disorder leads to tumor development, metastasis and death. Meanwhile, logistic regression analysis showed that HDL-C and LDL-C were correlated to the 5-year survival rate of patients with ovarian epithelial tumors, and the lower HDL-C and LDL-C represented higher mortality rates and lower 5-year survival rates. As a result, HDL-C and LDL-C may become a new targets for clinical intervention in patients with ovarian epithelial tumors complicated with hyperlipidemia.

In conclusion, dyslipidemia is closely related to the development and prognosis of epithelial ovarian tumors. Patients with epithelial ovarian tumors complicated with dyslipidemia have worse prognosis and lower survival rate. Therefore, dealing with dyslipidemia may be a new target for the treatment of epithelial ovarian tumors and prolongation of survival. However, this study also has some deficiencies, such as small sample size and being from a single center, so it is still necessary to expand the sample size in the future in order to obtain more valuable results. More work such as increasing the sample volume is planned in future experiments.

Disclosure of conflict of interest

None.

Address correspondence to: Xiangqin Zheng, Department of Gynaecology Area 2, Fujian Maternal and Child Health Hospital, No. 18 Daoshan Road, Fuzhou 350000, Fujian, China. Tel: +86-0591-83372215; E-mail: dp6vrc@163.com

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