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Research Article

Lipid Profile an Important Risk Factor in Patients with Ovarian Tumors: A Meta-Analysis

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Abstract

Introduction

In the literature ovarian tumors are know to be one of the deadliest gynecological malignancies [1-4]. In US this type of malignancy represents 2.3 % of all cancer-related death and about 4 % of all new cancer cases among women. There are several studies that have reported the role of lipid profiles and it's role in ovarian tumorigenesis. Fatty acids are essential for cancer cells progression[4-8]. In our study we investigated the true differance in circulating lipid profiles (total cholesterol TC, triglyceride TG, high-density lipoprotein cholesterol HDL, low density lipoprotein cholesterol LDL) among patients with and without ovarian tumors (OT) using a meta-analytical approach.

Methods

The meta-analysis was conducted using the MOOSE guidelines. PubMed, EMBASE and Cochrane Library were extensively searched (with a period of publication restriction between 2007 and 2019) to indetify published studies using the following keywords: " total cholesterol ", "high-density lipoprotein", " triglycerides ", " low-density lipoprotein ", " ovarian cancer", " ovarian tumor ", " lipid profile ". The search methodology is shown in Fig. 1 and all references of retrieved articles were searched manually.

Results

Seven studies, involving 1542 OT cases and 2195 non-cases of OT were included in this meta-analysis and I^2 statistics ranged between 97 and 99%. Mean circulating TC and HDL were significantly lower among OT cases compared to non-OT cases (P<0.04 and P<0.005).

Conclusion

There is a modest significant association between circulating HDL and risk of ovarian tumor but it is crucial to elucidate the implications of HDL in tumor manifestations and growth.

Keywords: ovarian tumor; lipid profile; total cholesterol; triglycerides; low-density lipoprotein

Introduction

In the literature ovarian tumors are know to be one of the deadliest gynecological malignancies. In US this type of malignancy represents 2.3 % of all cancer-related death and about 4 % of all new cancer cases among women. In the latest statistical cohort, there was an incidence of 11.6 cases/100.000 women per year, with an estimated 224.940 women living with this disease in the world. The simptomatology in ovarian tumors is hidden and about 70 % of patients are diagnosed in advanced stage, wich underlines that ovarian tumors are a serious public health concern. As we all know lipids are biologically important hydrophobic moleculs vital for energy storage, cell signalling and maintenance of cell membrane

integrity. Lipids are transported in the bloodstream with the aid of lipoprotein. Lipids are widely distributed in cellular organells and used as biologically vital active molecules. There are several studies that have reported the role of lipid profiles and it's role in ovarian tumorigenesis. Fatty acids are essential for cancer cells progression. In our study we investigated the true differance in circulating lipid profiles (total cholesterol TC, triglyceride TG, high-density lipoprotein cholesterol HDL, low density lipoprotein cholesterol LDL) among patients with and without ovarian tumors (OT) using a meta-analytical approach.

Materials and methods

The meta-analysis was conducted using the MOOSE guidelines. PubMed, EMBASE and Cochrane Library were extensively searched (with a period of publication restriction between 2007 and 2019) to indetify published studies using the following keywords: " total cholesterol ", "high-density lipoprotein", " triglycerides ", " low-density lipoprotein ", " ovarian cancer", " ovarian tumor ", " lipid profile ". The search methodology is shown in Fig. 1 and all references of retrieved articles were searched manually.

Study selection

Criteria of inclusion in the meta-analysis:

- Case control studies in human population that investigated the association between lipid profile and ovarian tumors
- Studies that compared women with ovarian tumor with women without ovarian tumor
- Studies that compared lipid profile (TC, HDL, LDL, VLDL, TG) between women with ovarian tumor with women without ovarian tumor

The magnitude of variation across studies was assessed ussing I^2 test statistics and a random-effects model was used to obtain mean estimates under considerable heterogeneity (I^2-test >50% or P<0.05)

Data extraction

Name of authors, year of publication (after 2007), country, study population, sample size, lipid profile, criteria for case definition, mean values (with standard deviation SD, standard error of mean SEM, confidence interval CI) of serum lipid profile (TC, LDL, HDL, TG) were extracted independently by two reviewers and differences in data extractions were resolved in recourse to a third reviewer. We establish that mean values of TC were transformed to mg/dl, but TG, HDL and LDL were transformed to mmol/L. Also, all values reported as SEM and CI were transformed into SD.

Results

We have done a literature research and indentified through electronic catalogue searching on PUBMED, EMBASE, COCHRANE library a number of 1704 studies from the primary ture search. About 384 were duplicates and we have excluded 1201 after examining titles and abstarcts. After full-text evaluation were excluded 112 studies and in this meta-analysis we included 7 studies (Table 1) that matched the inclusion criteria comprising 1542 ovarian tumor casess and 2195 non-ovarian tumor cases.

Authors	Year	Country	Cases	Control	Lipid profile	Ascertainment of ovarian tumor cases	Classification
Bukhari et al.	2016	Pakistan	30	30	TC, TG, HDL, LDL	Hospital/Medical record	NR
Camuzcuoglu et al.	2009	Turkey	24	29	TC, TG, HDL, LDL	Hospital/Medical record	FIGO
Delimaris et al.	2007	Greece	15	30	TC, HDL, LDL	Hospital confirmed	FIGO
Chen et al.	2017	China	573	1146	TG, HDL	Histopathological examinations	FIGO
Knapp et al.	2017	Poland	74	81	TC, TG	Hospital/Medical record	NR
Melvin et al.	2012	Sweden	786	829	TC, TG, HDL, LDL	Histopathological examinations	FIGO
Qadir et al.	2008	Pakistan	40	50	TC, TG, HDL, LDL	Hospital confirmed	FIGO
			1542	2195			

(Table 1)

In our meta-analysis mean total cholesterol was significantly lower among ovarian tumors cases comapare to non-ovarian tumors cases (P= 0.04) also mean HDl=L was significantly lower among OT cases compared to non-OT cases. All cases we stratified by age and this differences were insignificant. If we talk about mean TG and LDL the differences were insignificantly between OT and non-OT cases. As we

mentioned we stratified our meta-analysis by age (Table 2). In table 2 we could observed that TG profile was significantly elevated among OT cases under 49 years old 0.059 [0.54, 0.63] mmol/L $P<0.0001$ and LDL profile was significantly elevated 0.38 [0.23, 0.06] mmol/L $P<0.0001$ among OT cases over 49 years old.

In a subgroup of cases with malignant OT and/or advanced tumors TC was significantly lower ($P<0.05$) and TC and LDL profiles were insignificantly different, but HDL profile was significanlty lower between OT and non-OT cases.

	TC (mg/dL)	D	TG (mmol/L)	D2	HDL (mmol/L)	D3	LDL (mmol/L)	D4
All studies	-16,52 [-32,43 ; -0,72]	↓	0.063 [-0.19, 0.28]	↔	-0.24	↓	0.12 [-0.23, -0.09]*	↔
Age groups								
Young adults (under 49 years)	-23,34 [-57,86; 12,12]	↔	0.059 [0.54, 0.63]^	↑	≠		≠	
Old adults (over 49 years)	-19,63 [-47,12; 8,32]	↔	-0.04 [-0.3, 0.32]	↔	-.039 [-1.23, 0.38]	↔	0.38 [0.23, 0.06]^	↑
Type of tumor								
Benign	-13,21 [-39,32; 13,02]	↔	0.02 [-0.20, 0.22]	↔			≠	
Malignant	-36,98 [-69,87; -4,21]*	↓	0.14[-0.02, 0.31]	↔	-0.59 [-0.68, -0.43]	↓	≠	
Stage of cancer								
Early (under II)	≠		≠		≠		≠	
Advanced (over III)	-27.12 [-81,34; 32,1]	↔	-0.23 [-0.64, 0.24]	↔	≠		≠	
Type and/or Stage								
Benign and Early	8,23 [-32,18; 50,12]	↔	0.01 [-0.16, 0.22]	↔	-0.28 [-0.36, -0.18]	↓	≠	
Malignant and Advanced	-30,23[-60,56;	↓	-0.00 [-0.15, 0.18]	↔	-0.28 [-0.92, 0.28]	↔	≠	
Risk of Bias of included studies	-0,32]*							
Low	-15,98 [-51,1; 19,2]	↔	0.15 [-0.10, 0.39]	↔	-0.25 [-0.46, -0.03]*	↓	0.23 [-0.16, 0.69]	↔
High	-16,2 [-31,2; -0,56]*	↓	-0.00 [-0.23. 0.25]	↔	-0.25 [-0.51, -0.04]*	↓	-0.23 [-0.29, 0.15]^	↓

Mean difference and 95% CI of Lipid Profile between cases and non-cases of ovarian tumors.

D-direction of mean difference relative to non-ovarian tumour cases; TC-Total cholesterol; TG-Triglycerides; HDL-High density lipoprotein; LDL-Low density lipoprotein

*p < 0.05

^p < 0.0001

≠studies were insufficient to carry out the meta-analysis

↑mean difference significantly higher among cases than non-cases of ovarian tumour

↓mean difference significantly lower among cases than non-cases of ovarian tumour

↔mean difference insignificantly different between cases than non-cases of ovarian tumour

(Table 2)

Discussion

There are few metaanalytical studies in the literature about this topic. Lipid profile it is an important risk factor in ovarian tumorigenessis [9-14]. Total cholesterol and HDL profiles were significantly lower among patients with ovarian tumors but the profile level of TG and LDL were insignificant. Circulating lipid profiles are largely subject to alterations in occurrence of tumor events. In our meta-analysis we highlight the significance of lipids in OT outcomes. The strong affinity of cancer cells for sterols and lipids makes lipid metabolism a critical factor in cancer signaling and excessive production of lipogenic enzymes has been observed in several cancers and is linked with cancer severity and recurrance. In our meta-analysis we observed that HDL was inversely related to OT risk. This kind of observation was related by Gadomska et al. In a multidimensional analysis. As we all know the anti-inflammatory properties of HDL in inhibiting cell proliferatrion and apoptosis are crucial in preventing the increased intracellular oxidative stress that is a critical step in cancer pathogenesis [15,16]. Decreased HDL levels are associated with increased levels of proinflammatory cytokines including tumor necrosis factor-alpha and interleukin-6. Tumor cells express increased LDL receptor levels which lead to low LDL levels. Most studies included in our meta-analysis were cross-sectional and limited studies age-matched cases with controls in the eligible studies [17,18].

Conclusion

There is a modest significant association between circulating HDL and risk of ovarian tumor but it is crucial to elucidate the implications of HDL in tumor manifestations and growth and it's important to highlights the role of serum lipid profile in diagnosis, prognosis and recurrence of the disease in future studies.

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