The Breast 32 (2017) 1–6

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Original article

The effect of preoperative serum triglycerides and high-density lipoprotein-cholesterol levels on the prognosis of breast cancer

Xing Li [1], Hailin Tang [1], Jin Wang [1], Xinhua Xie, Peng Liu, Yanan Kong, Feng Ye, Zeyu Shuang, Zeming Xie, Xiaoming Xie*

Department of Breast Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, Guangzhou, Guangdong, 510060, PR China

ARTICLE INFO

Article history:
Received 21 September 2016
Received in revised form
26 November 2016
Accepted 30 November 2016

Keywords:
Breast cancer
Lipids
Lipoproteins
Prognosis

ABSTRACT

Objectives: Although dyslipidemia has been documented to be associated with several types of cancer including breast cancer, it remains uncertainty the prognostic value of serum lipid in breast cancer. The purpose of this study is to evaluate the association between the preoperative plasma lipid profile and the prognostic of breast cancer patients.

Methods: The levels of preoperative serum lipid profile (including cholesterol [CHO], Triglycerides [TG], high-density lipoprotein-cholesterol [HDL-C], low-density lipoprotein-cholesterol [LDL-C], apolipoprotein A-I [ApoAI], and apolipoprotein B [ApoB]) and the clinical data were retrospectively collected and reviewed in 1044 breast cancer patients undergoing operation. Kaplan-Meier method and the Cox proportional hazards regression model were used in analyzing the overall survival [OS] and disease-free survival [DFS].

Results: Combining the receiver-operating characteristic and Kaplan-Meier analysis, we found that preoperative lower TG and HDL-C level were risk factors of breast cancer patients. In multivariate analyses, a decreased HDL-C level showed significant association with worse OS (HR: 0.528; 95% CI: 0.302–0.923; P = 0.025), whereas a decreased TG level showed significant association with worse DFS (HR: 0.569; 95% CI: 0.370–0.873; P = 0.010).

Conclusions: Preoperative serum levels of TG and HDL-C may be independent factor to predict outcome in breast cancer patient.

1. Introduction

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer-related death among women worldwide. According to the American Cancer Society, breast cancer alone is expected to account for 29% all new cancer diagnoses in women and lead to 40,890 deaths in the United States in 2016 [1]. Although death rates for female breast cancer are down 36% from peak rates as a result of early diagnosis and treatment [2], it is still a heavy burden on patients. Thus, it is important to search for minimally invasive methods and prognostic factors to identify breast cancer.

Abnormal lipid and lipoprotein metabolism, as a result of high-fat diet as well as physical inactivity, was considered to be related to several types of cancer [3–5]. Cholesterol plays an important role in cellular structure and function, especially the synthesis of steroid hormones, which may implicate in the etiology of breast cancer [6,7]. A previous research revealed that oxysterol 27-hydroxycholesterol, the primary metabolite of cholesterol, can increase tumor growth and metastasis in mouse models of breast cancer [8], meanwhile abnormal cholesterol biosynthesis contribute to breast cancer development and progression [9]. Furthermore, prospective clinical studies data have provided that high level of total cholesterol [TC] may increase both breast cancer

* Corresponding author. Department of Breast Oncology, Sun Yat-sen University Cancer Center, State Key Laboratory of Oncology in South China, Collaborative Innovation Center for Cancer Medicine, 651 East Dongfeng Road, Guangzhou, Guangdong, 510060, PR China.

E-mail addresses: lixing@sysucc.org.cn (X. Li), tanghl@sysucc.org.cn (H. Tang), wangjin@sysucc.org.cn (J. Wang), xiexh@sysucc.org.cn (X. Xie), liupeng@sysucc.org.cn (P. Liu), kongyn@sysucc.org.cn (Y. Kong), yefeng@sysucc.org.cn (F. Ye), shuangzy@sysucc.org.cn (Z. Shuang), xiezm@sysucc.org.cn (Z. Xie), xiexm@sysucc.org.cn (X. Xie).

[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.breast.2016.11.024
0960-9776/

incidence [10,11] and overall mortality [12]. However, the other authors showed that negative association between TC levels and breast cancer [13,14], on the contrary, high level of TC even have a protective effect [15].

High and low density serum lipoproteins play a fundamental role in supplying of cholesterol to cancer cells and tumors, potentially via receptor mediated mechanisms [16]. However, researches about the effect of lipoproteins in breast cancer were also contradictory. Regarding high density serum lipoproteins, some prospective studies showed that low level can increase breast cancer risk [17,18] and high level may be a protective effect in premenopausal patient [19]; while other studies revealed that a positive correlation between high level and breast cancer risk [20]. Regarding low density serum lipoproteins, it has been reported that high level at diagnosis was associated with poor disease free survival [21]. The aim of this study was to investigate the prognostic value of serum lipids and lipoproteins in patients of breast cancer.

2. Methods

2.1. Patient selection and clinical data collection

A total of 1044 patients diagnosed with breast cancer who were undergoing resection of primary tumor at Sun Yat-sen University Cancer Center between 2008 and 2011 were collected in the present study. All patients were eligible for inclusion in the study: (1) without cancer history; (2)without using hormone replacement therapy influencing in lipid metabolism; (3) without distant metastases (4)serum samples (including cholesterol, triglycerides, high-density lipoprotein-cholesterol [HDL-C], low-density lipoprotein-cholesterol [LDL-C], apolipoprotein A-I [ApoAI], and apolipoprotein B [ApoB]) were collected before treatment. A blood analyzer (Hitachi Automatic Analyzer 7600-020 [Hitachi, Tokyo, Japan]) was routinely used to test the blood samples. Meanwhile, Patient clinical characteristics such as age, menopausal status, tumor size, axillary lymph nodal status, hormonal receptor and Ki-67 grade, human epidermal growth factor receptor-2 [HER2] status, date of last follow-up or breast cancer-related death and date of local recurrence or distant metastasis after radical surgical resection were collected. The tumor stages after surgery were classified according to the AJCC TNM staging system. The molecular subtypes were defined as follow: Luminal A (ER+/PR +, HER2-and Ki-67 < 14%), Luminal B (ER + and HER2 + or Ki-67 ≥ 14%), HER2 overexpressing (ER -, PR -, HER2 +) and triple-negative breast cancer [TNBC] (ER -, PR -, HER2 -). “HER2+”was defined as“3+”in immunohistochemical test or positive in HER2 fluorescence in situ hybridization test.

The study protocol was approved by the local Institute Research Ethics Committee. Written informed consent was obtained from each patient.

2.2. Patients follow up

All patients were followed up by telephone interview and medical records review. The last follow-up was completed on 1 May 2016. The primary endpoint of this study was overall survival (OS), which was defined as the time interval from diagnosis to death or the last follow-up. The secondary end point was disease-free survival (DFS), which was defined as the time interval from surgery to the date of disease recurrence or distant metastases.

2.3. Statistical analysis

All statistical analyses were performed using SPSS21.0 software. The cutoff value to stratify patients at high risk of death for serum cholesterol, triglycerides, HDL-C, LDL-C, ApoAI, and ApoB was established by receiver-operating curve [ROC] analyses. The correlations between serum lipid and clinical characteristics were tested by chi-square test. The Kaplan-Meier and log-rank test were used to calculate survival curves and to compare differences. Cox proportional hazards model was used to perform multivariate analysis and test independent significance variables. Hazard ratio (HR) was reported as relative risks with corresponding 95% confidence intervals (CIs). A P-value<0.05 was considered statistical significant.

3. Results

3.1. Characteristics of all patients

A total of 1044 patients who were diagnosed with breast cancer and underwent radical surgical resection were enrolled in the analysis. The median age was 47 years (range: 22–85 years) and nearly one-tenth patients (9.6%) were under age 35years, and 602 (57.7%) patients were premenopausal. According to the pTNM classification for breast cancer, 211(20.2%), 494(47.3%) and 287 (27.5%) were staged in I, II, III respectively. Most of the patients (767, 73.5%) molecular type pathological were Luminal type, while 115 patients (11.0%) were HER-2 over-expressing type, 162 patients (15.5%) were TNBC type. The characteristics of these patients are presented in Table 1.

3.2. Cut-off determination of serum lipid and lipoproteins

Based on receiver operating curve (ROC) analysis, the recommended cutoff value of joint maximum sensitivity and specificity were for CHO 4.40 mmol/L (AUC: 0.522, 95% CI:459–584), 1.30 mmol/L for TG (AUC: 0.552, 95% CI: 0.487–0.616), 1.02 mmol/L for HDL-C (AUC: 0.505, 95% CI: 0.434–0.577), and 2.79 mmol/L for LDL-C (AUC: 0.525, 95% CI: 0.461–0.589), 1.56 mmol/L for ApoA1 (AUC: 0.518, 95% CI: 0.451–0.584), 0.93 mmol/L for ApoB (AUC: 0.533, 95% CI: 0.474–0.592), respectively.

3.3. Relationship between different levels of TG, HDL-C and other clinical characteristics

The correlation between the different level of TG, HDL-C and the other clinical features were showed in Table 2 and Table 3 respectively. The statistical analysis presented that the TG level was significantly correlated with age (P = 0.002), menopausal status (P < 0.001), stage (P = 0.039). But there was no significant links between the TG level and the other parameters. The HDL-C level was only significantly correlated with molecular type (P = 0.044).

3.4. The prognostic impact of serum lipids on long-term outcomes of breast cancer

For OS, in the univariate Cox proportional hazards regression model analysis, the molecular type showed prognostic significance. Furthermore, according to the recommended cutoff levels of preoperative serum lipids and lipoproteins, the preoperative high level serum HDL-C was associated with better OS. In the multivariate Cox regression model analysis, the results showed that the high level HDL-C (hazard ratio [HR]: 0.528; 95% CI: 0.302–0.923; P = 0.025) was a significant independent predictors of favorable OS including molecular type. (Table 4).

For DFS, in the univariate and multivariate Cox proportional analysis, the molecular type also showed prognostic significance of DFS. Meanwhile, the results revealed that the high level TG was a significant independent predictors of better DFS in the univariate