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Original Article

Preoperative serum lipid profile and outcome in nonmetastatic colorectal cancer

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Abstract

Objective: A large portion of non-metastatic colorectal cancers (non-mCRCs) recur after curative surgery. In addition to the traditional tumor-related factors, host-related factors are also required to accurately predict prognosis. A few studies have shown an association between the serum lipid profile and the survival and treatment response of patients with colorectal cancer.

Methods: We retrospectively evaluated the prognostic significance of the preoperative serum lipid profile [total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)] in patients with non-mCRC treated with curative surgery. The Spearman rank correlation test was used to analyze associations between lipid levels and categorical variables. Lipid levels were modeled as four equal-sized quartiles based on the distribution among the whole cohort. Kaplan-Meier curves were used to estimate survival probabilities, and the log-rank test was used to detect differences between them. Multivariate fractional polynomial (MFP) analysis was used to model any non-linear effects and avoid categorization. To evaluate the added prognostic value of lipids, the predictive power of two models (with and without lipids as covariates) was compared by using Harrell's C-statistic and the Akaike information criterion (AIC).

Results: A total of 266 patients with non-mCRC were enrolled in the present study. Spearman rank correlation test showed that TG levels inversely correlated with N stage ($r = -0.20$, $P = 0.00$) and Tumor-Node-Metastasis (TNM) stage ($r = -0.19$, $P = 0.00$). HDL-C levels positively correlated with perineural invasion (PNI) ($r = 0.15$, $P = 0.02$), and LDL-C levels inversely correlated with lymphovascular invasion (LVI) ($r = -0.12$, $P = 0.04$). None of the four lipids predicted overall survival (OS) in univariate or multivariate analyses adjusted for age, gender, T stage, N stage, TNM stage, histological grade, tumor deposits, LVI, PNI, and adjuvant treatment (all $P > 0.05$). In agreement, the Kaplan-Meier curves for OS according to the lipid quartiles were not significantly different, as confirmed by the log-rank test (all $P > 0.05$). MFP analysis also found no significant associations between lipid levels and OS (all $P > 0.05$). A prognostic model that included lipids had a higher Harrell's C-statistic and a lower AIC value than did a model that did not include lipids (for Harrell's C-statistic: 0.82 *vs*. 0.77; for AIC: 398 *vs*. 432).

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Conclusion: Measuring preoperative serum lipid levels may be a simple and cost-effective way of increasing prognostic accuracy in patients with non-mCRC treated with curative surgery.

Keywords: Serum lipids; Colorectal cancer; Overall survival; Prognostic model

Introduction

Colorectal cancer (CRC) remains one of the leading causes of cancer-related death worldwide despite a significant decrease in its mortality rate in recent years. Although non-metastatic CRC (non-mCRC) can be potentially cured via radical surgery and adjuvant therapy, this cancer often recurs. Several pathological characteristics of CRC have prognostic significance including Tumor-Node-Metastasis (TNM) staging, histological grade, resection marginal status, perineural invasion (PNI), and lymphovascular invasion (LVI). However, the identification of additional factors is required to fine-tune prognostic accuracy, and both tumor-related and host-related factors should be considered.

The serum lipid profile [total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C)] is one of the few host-related factors whose relationship with CRC prognosis has been investigated. Lipids, as key components of the cell membrane, are required for tumor growth. Moreover, as an epidemiological observation, statins, a class of drugs that lower LDL-C levels, have been shown to reduce CRC risk[1−4] and mortality rates.[5,6] However, whether these protective effects result from LDL-C depletion[7,8] or other mechanisms[9,10] is unclear.

Dyslipidemia has been associated with an increased risk for CRC.[11,12] However, whether it increases,[6,8,13−16] decreases,[17−20] or has no effect[21] on mortality rates is still controversial. In patients with metastatic CRC (mCRC) with elevated LDL-C levels, a high LDL-C/HDL-C ratio predicted poor prognosis.[22] In patients with non-mCRC, investigation of the usefulness of serum lipids as prognostic indicators showed that adjuvant chemotherapy-related elevations in HDL-C levels correlated with longer disease free-survival and overall survival (OS) time[23]; TC independently predicted tumor regression after neoadjuvant chemoradiotherapy[24]; dyslipidemia predicted a favorable prognosis in one study[15] and a poor prognosis in another[18]; and low pretreatment serum levels of C-reactive protein and cholesterol indicated a poor prognosis.[14]

To further clarify the prognostic role of serum lipids in CRC, we conducted a retrospective cohort study that examined the effects of preoperative serum lipid levels on the outcome of patients with non-mCRC after curative surgery.

Material and methods

Patients

We retrospectively collected, reviewed, and analyzed the medical information of all patients treated with curative surgery for CRC at the Department of Surgical Oncology at the Fourth People's Hospital of Wuxi from January 2009 to December 2014. Patients were excluded if they were diagnosed with other malignancies; died within 1 month after surgery; had a metastatic disease, multiple synchronous CRCs, or a history of diabetes mellitus or hypertension; had received neoadjuvant treatment; or had an unknown survival status. The following information was collected from the medical charts and recorded: the patient's name, age, and gender; the site and histology of the CRC; the depth of the primary tumor invasion; the number of metastatic lymph nodes, total lymph nodes sampled, and tumor deposits; the histology grade; PNI; LVI; tumor necrosis; and adjuvant treatment. Patients were classified according to the guidelines of the 7th edition of American Joint Committee on Cancer TNM Staging Manual. Patients with preoperative measurement of the four lipids (TC, TG, LDL-C, or HDL-C) were eligible for the study. Since the patients in our study were not prospectively followed up, their survival status was determined by consulting the death information registry at the Bureau of Public Security in Wuxi. If the patient was not listed in this registry, we interviewed via telephone either the patient or a close relative.

This study was approved by our hospital's ethics review board.