Original Article

Lipid profile and survival time in patients with terminal cancer: a cross-sectional study

Dong-Yeon Lee[1], Hae-Jin Ko[1]^, A-Sol Kim[2]^

[1]Department of Family Medicine, School of Medicine, Kyungpook National University, Kyungpook National University Hospital, Daegu, South Korea; [2]Department of Family Medicine, School of Medicine, Kyungpook National University, Kyungpook National University Chilgok Hospital, Daegu, South Korea

Contributions: (I) Conception and design: AS Kim; (II) Administrative support: AS Kim; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: DY Lee, HJ Ko; (V) Data analysis and interpretation: DY Lee, AS Kim; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: A-Sol Kim, MD, PhD. Department of Family Medicine, School of Medicine, Kyungpook National University, Kyungpook National University Chilgok Hospital, 807 Hoguk-ro, Buk-gu, Daegu 41404, South Korea. Email: deepai@knu.ac.kr.

Background: Lipid profile as a prognostic factor in terminal cancer patients is controversial. This study aimed to provide useful information related to the treatment of patients with terminal cancer by examining lipid profiles and their association with survival time.

Methods: We retrospectively reviewed the medical records of 428 inpatients who died while receiving palliative care a university hospital in Daegu during September 2015–September 2020 and then analyzed differences in survival times and the relative risk associated with lipid profiles.

Results: The mean survival of subjects with low low-density lipoprotein cholesterol (LDL-C) (<130 mg/dL) was 30.10 days, which was significantly shorter than that of subjects without (P<0.001). The mean survival of subjects with high triglyceride (TG) levels (≥150 mg/dL) was 32.95 days, which was shorter than subject without (P=0.006). The difference in survival time according to total cholesterol (TC) and high-density lipoprotein cholesterol (HDL-C) levels was not statistically significant (P=0.068 and P=0.425, respectively). Multivariate Cox regression analysis showed that the hazard ratios of low LDL-C levels and high TG levels in relation to shorter survival times were 4.201 [95% confidence interval (CI), 2.578–6.259] and 1.492 (95% CI, 1.063–2.195), respectively.

Conclusions: Low LDL-C levels and high TG levels are correlated with survival time. However, a follow-up study on the lipid profile as a predictor of the survival time of patients with terminal cancer is necessary.

Keywords: Lipid profiles; low-density lipoprotein cholesterol (LDL-C); triglyceride (TG); terminal cancer; survival time

Submitted Mar 21, 2022. Accepted for publication Jul 27, 2022.
doi: 10.21037/apm-22-366
View this article at: https://dx.doi.org/10.21037/apm-22-366

Introduction

Cancer has a high prevalence and is one of the leading causes of death worldwide (1). Accordingly, many advances in cancer treatment have been made including chemotherapy and radiation therapy (2). However, the patient's treatment strategy or prognosis in clinical practice is almost always dependent on the tumor-node-metastasis (TNM) stage, as determined by imaging tests, such as computer tomography and magnetic resonance imaging (MRI) (3-5). As TNM staging does not always accurately

^ ORCID: Hae-Jin Ko, 0000-0003-4460-1476; A-Sol Kim, 0000-0003-2497-9500.

predict the prognosis, it is important to find new biomarkers that are useful in screening patients who would benefit from treatment and to predict prognosis (6).

The lipid profile usually includes the levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), and low-density lipoprotein cholesterol (LDL-C) (7). Disorders of lipid metabolism are strongly related to metabolic syndromes, such as obesity, hypertension, and diabetes mellitus, and dyslipidemia causes atherosclerosis, which eventually leads to cardiovascular diseases, such as angina and myocardial infarction, and cerebrovascular diseases, such as stroke. In addition, the importance of lipid profiles is currently attracting attention in various diseases, including cancer (8,9).

Many studies have shown that abnormal lipid metabolism might be involved in carcinogenesis and cancer prognosis (3,10,11). In a recent meta-analysis, patients with a higher TC level before diagnosis had a lower hazard ratio for overall survival, and patients with higher HDL-C levels had a reduced risk of death compared with those with lower HDL-C levels (3). Some studies support a positive correlation between a high level of TC and the mortality rate of patients with cancer (12,13), but in contrast, other studies claim that cholesterol levels and mortality rate are not related or that they exhibit an inverse association (14,15). In addition, one retrospective cross-sectional study reported a significant association between an increased risk of metastasis and high serum levels of LDL-C (16), but another study showed that patients with lower LDL-C levels tended to have a higher risk of malignancy (17).

Since studies on the relationship between cancer and lipid profiles have often shown conflicting results, further research is needed (18). Therefore, we aimed to investigate the relationship between survival time and lipid profile results, including LDL-C, HDL-C, and TG levels, in patients with terminal cancer and to confirm whether serum lipid parameters are suitable as prognostic factors. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-366/rc).

Methods

Subjects

In total, 2,365 patients with stage 4 cancer who died after admission to a university hospital in Daegu, South Korea during September 2015–September 2020 were the subjects of this study. The medical records of all subjects were retrospectively assessed. Patients were included in this study if all of the following criteria were met: (I) inpatients who received palliative care; (II) those who died of cancer; (III) those with availability of lipid profile results. However, patients with an end-of-life status at the time of hospitalization, those treated with lipid-lowering medications, those with uncontrolled blood sugar (random blood sugar ≥300 mg/dL) (19), and those with uncontrolled high blood pressure (hypertensive urgencies or emergencies) (20) were excluded from this study. Therefore, 428 patients (223 men and 205 women) were included for the analysis (*Figure 1*). The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study protocol was approved by the Kyungpook National University Chilgok Hospital Institutional Review Board (No. 2021-02-011). The requirement for informed patient consent was waived because of the retrospective study design.

Data measurements

Basic patient information, including age, sex, primary cancer site, presence or absence of metastasis, treatment history and accompanying chronic diseases, was obtained from the personal medical history of patients. Lipid profiles and various laboratory parameters, such as hemoglobin level, white blood cell (WBC) count, neutrophil and lymphocyte count and fraction, creatinine level, and albumin and C-reactive protein (CRP) levels, among others, were evaluated. The neutrophil-to-lymphocyte ratio (NLR) was calculated based on the counts of neutrophils and lymphocytes. Based on previous study findings, the NLR cutoff value used in this study was set at 4.0, which is known to affect the survival of patients with cancer (21). In addition, since the degree of pain and activity are important factors in determining the condition of patients with cancer, we obtained this information from a questionnaire completed by patients and their caregivers. Pain was measured according to the Numerical Rating Scale (NRS), and the degree of activity was scored using the Palliative Performance Scale (PPS). The NRS was used to rate the degree of pain on a scale of 0 to 10, where 0 indicates no pain, 1–3 indicates mild pain, 4–6 indicates moderate pain, and 7–10 indicates severe pain. The PPS scores ranged from 0 to 100, and the degree of activity was scored based on the patient's ambulation, disease activity, self-care, and intake; the lower the score, the more restrictive the activity (22).

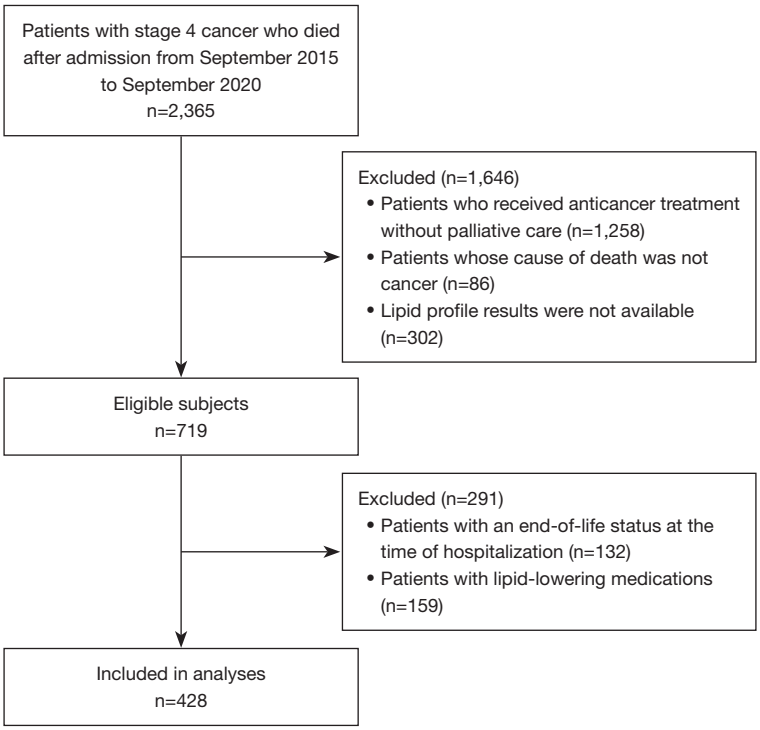

Figure 1 Flow chart of subject selection.

Study design

To determine the relationship between lipid profiles (TC, LDL-C, TG, and HDL-C) and the survival time in patients with cancer, lipid profiles were categorized according to the following cutoff values: TC (≥200 mg/dL, <200 mg/dL), LDL-C (≥130 mg/dL, <130 mg/dL), TG (≥150 mg/dL, <150 mg/dL), and HDL-C (≤40 mg/dL, >40 mg/dL). In this study, the cutoff value of each lipid parameter was used as a reference point to define risk factors for cardiovascular diseases (23). Lipid profiles were measured when patients were hospitalized, and the patients' survival time was calculated from the date of hospitalization until the date of death.

Statistical analysis

Baseline demographics were analyzed using an independent *t*-test and analysis of variance. Correlation and multiple regression analyses were performed to determine the relationship between each independent variable that can affect survival. Moreover, Cox regression analysis was performed to confirm the correlation between lipids and survival. To verify the effect of lipid parameters on the survival, the stepwise forward selection method was used for analysis. In addition, each factor that could affect survival time was analyzed using the enter method, and significant variables were identified using the stepwise backward elimination method. All statistical analyses were performed using SPSS for Windows version 26.0 (IBM SPSS Statistics, RRID: SCR_016479) with statistical significance set at $P<0.05$.

Results

Demographic characteristics

The clinical characteristics of the subjects suitable for this study and their survival times are reported in *Table 1*. Of the 428 subjects, 223 were male and 205 were female; 278 were aged 65 years or older and accounted for approximately 65% of the total. The most common primary cancer sites were the lung, colon, hepatobiliary system, and stomach in that order. In terms of surgery, chemotherapy, and radiotherapy as previous treatments for cancer, chemotherapy was the most common (368 patients), followed by surgery and radiotherapy. In addition, most patients (n=387) had metastasis. In total, 73 and 125 subjects

Table 1 Mean survival according to demographic and clinical characteristics

Characteristics	n	Survival (mean ± SD, days)	P value[†]
Sex			0.105
Male	223	34.75±36.69	
Female	205	36.20±37.29	
Age, years			0.921
≤65	150	35.68±35.22	
>65	278	35.40±33.03	
Primary cancer site			0.785[‡]
Lung	128	34.92±32.33	
Colon	89	36.12±22.31	
Hepatobiliary	70	33.84±34.27	
Stomach	49	34.78±35.27	
Other	92	35.15±33.39	
Previous treatment			
Surgery			0.337
No	287	35.41±37.04	
Yes	141	34.04±25.04	
Chemotherapy			0.607
No	60	34.978±34.16	
Yes	368	35.99±35.12	
Radiotherapy			0.548
No	300	34.52±31.90	
Yes	128	36.52±31.23	
Metastasis			0.785
Absent	41	35.15±32.39	
Present	387	34.98±35.09	
History of diabetes			0.885
Absent	355	34.93±32.10	
Present	73	35.32±33.18	
History of hypertension			0.564
Absent	303	35.12±31.52	
Present	125	34.68±32.15	
Pain (NRS)			<0.001[‡]
0–3	78	43.17±12.24	
4–6	252	32.75±32.43	
7–10	98	27.35±96.02	
PPS score			<0.001
>50	72	64.44±54.92	
≤50	356	29.58±22.91	

[†], independent *t*-test; [‡], one way-ANOVA. NRS, Numeric Rating Scale; PPS, Palliative Performance Scale; SD, standard deviation.

had a history of diabetes and hypertension, respectively. The presence or absence of chronic diseases did not significantly affect the survival time (P=0.885 for diabetes and P=0.564 for hypertension). At the time of admission, pain was evaluated using the NRS, and 43.17±12.24, 32.75±32.43, and 27.35±96.02 scored 0–3 points, 4–6 points, and 7–10, respectively. The survival time was shorter in the group with higher pain scores, which was statistically significant (P<0.001). Patients with PPS scores less than 50 (29.58±22.91) had a shorter survival time than those with PPS scores higher than 50 (64.44±54.92) (P<0.001).

Relationship between laboratory tests and cancer survival time

Table 2 shows the mean survival time according to the serologic characteristics. The twelve blood test items included WBC count and levels of hemoglobin, creatinine, albumin, liver enzyme, sodium, potassium, and CRP. Among these, survival time was shorter in patients with anemia (30.98±35.58, P=0.003), leukocytosis (26.05±25.37, P<0.001), hypoalbuminemia (28.10±22.10, P<0.001), hyperbilirubinemia (23.73±35.18, P=0.001), liver enzyme elevation (30.56±32.50, P=0.002), CRP elevation (33.90±29.12, P<0.001), and NLR elevation (29.30±23.85, P<0.001) than that of patients with none of these, and these differences were statistically significant.

Table 2 Mean survival according to serologic characteristics

Characteristics	n	Survival (mean ± SD, days)	P value†
Anemia			0.003
Hemoglobin ≥10 g/dL	235	39.12±35.30	
Hemoglobin <10 g/dL	193	30.98±35.58	
Leukocytosis			<0.001
WBC ≤10.0×10^3/μL	278	40.51±33.66	
WBC >10.0×10^3/μL	150	26.05±25.37	
Neutrophilia			0.008
Neutrophils ≤75%	135	42.16±42.33	
Neutrophils >75%	293	32.65±27.56	
Lymphocytopenia			0.170
Lymphocytes ≥20%	45	41.33±41.12	
Lymphocytes <20%	383	34.75±29.29	
Thrombocytopenia			0.221
Platelet >50×10^3/μL	395	36.12±30.55	
Platelet ≤50×10^3/μL	33	27.35±21.52	
Hypercreatininemia			0.584
Creatinine <2.0 mg/dL	396	35.45±31.83	
Creatinine ≥2.0 mg/dL	32	35.36±32.73	
Hypoalbuminemia			<0.001
Albumin >3.0 g/dL	157	48.12±40.44	
Albumin ≤3.0 g/dL	271	28.10±22.10	
Hyperbilirubinemia			0.001
Total bilirubin <2.0 mg/dL	326	39.11±30.93	
Total bilirubin ≥2.0 mg/dL	102	23.73±35.18	
Liver enzyme elevation			0.002
ALT ≤41 U/L	376	36.13±32.07	
ALT >41 U/L	52	30.56±32.50	
Hyponatremia			0.008
Sodium ≥135 mmol/L	198	38.12±36.87	
Sodium <135 mmol/L	230	33.14±25.39	
Hyperkalemia			0.342
Potassium ≤5.5 mmol/L	419	35.69±31.77	
Potassium >5.5 mmol/L	9	23.98±19.69	
CRP elevation			<0.001
CRP <0.5 mg/dL	27	58.24±56.17	
CRP ≥0.5 mg/dL	401	33.90±29.12	
NLR elevation			<0.001
NLR <4.0	71	39.21±28.66	
NLR ≥4.0	357	29.30±23.85	

†, independent *t*-test. WBC, white blood cell; ALT, alanine aminotransferase; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; SD, standard deviation.

Factors that could be associated with survival and the relationship between lipids

To confirm the correlation and multicollinearity between the lipid parameters—which are the main variables set in this study—and the factors that could be associated with the serum lipid concentration and survival time, correlation analysis and multiple regression analysis were performed. The history of diabetes and hypertension and albumin, hemoglobin, creatinine, total bilirubin, alanine aminotransferase (ALT), CRP, and NLR levels showed no significant correlation with the lipid profile. Moreover, there was no multicollinearity between each of the four lipid parameters and other variables (Tables S1-S5).

Relationship between lipid profiles and cancer survival time

The results of the comparison of mean survival time according to lipid levels as seen in lipid profiles are shown in *Table 3*. First, survival times were not significantly associated with either TC or HDL-C levels. In contrast, when LDL-C was divided according to a cutoff value of 130 mg/dL, 187 patients had levels above 130 mg/dL and 241 patients had levels below 130 mg/dL, and survival times for these groups were 42.32±32.30 and 30.10±36.58 days (P<0.001). In other words, the survival time of patients with terminal cancer was shorter when their LDL-C levels were low. In addition, the survival times of patients with high (≥150 mg/dL) and low TGs were 32.95±25.37 and 38.11±32.16 days, respectively, indicating a significant

Table 3 Mean survival according to lipid profile

Characteristics	n	Survival (mean ± SD, days)	P value†
Total cholesterol			0.068
≥200 mg/dL	167	35.78±31.32	
<200 mg/dL	261	34.25±35.10	
LDL-C			<0.001
≥130 mg/dL	187	42.32±32.30	
<130 mg/dL	241	30.10±36.58	
Triglycerides			0.006
≥150 mg/dL	207	32.95±25.37	
<150 mg/dL	221	38.11±32.16	
HDL-C			0.425
≤40 mg/dL	345	35.46±32.13	
>40 mg/dL	83	34.37±34.78	

†, independent *t*-test. LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; SD, standard deviation.

Table 4 Relative risks of the lipid profiles that affect survival according to a Cox proportional hazard model with stepwise forward selection method

Variables	HR	95% CI	P value
Model 1†			
LDL-C <130 mg/dL	4.126	3.276–5.985	0.001
Model 2†			
LDL-C <130 mg/dL	4.425	3.081–6.356	<0.001
Triglycerides ≥150 mg/dL	1.569	1.129–2.118	0.009
Model Extra‡			
LDL-C <130 mg/dL	4.056	0.976–7.187	0.785
Triglycerides ≥150 mg/dL	1.395	0.722–4.128	0.658
Total cholesterol <200 mg/dL	1.016	0.425–3.342	0.615
HDL-C <40 mg/dL	1.284	0.394–2.703	0.416

†, Models 1 and 2 were derived using the forward stepwise selection method; ‡, Model Extra was derived using the enter method. There was no statistical significance (P>0.005). LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; CI, confidence interval.

difference in survival time according to TG level (P=0.006).

Relative risks of lipid profiles on cancer survival rate

The relative risk in terms of survival rate according to lipid profiles was analyzed using the Cox proportional hazard model, which is a notable result of this study. Model 1 and 2 used the forward stepwise selection method, and the Model Extra used an enter method with all four lipid parameters as variables. Model 1 selected LDL-C as the most important variable among lipid profiles. In Model 1, if the LDL-C was less than 130 mg/dL, the hazard ratio was 4.126 (95% CI, 3.276–5.985, P=0.001). In Model 2, LDL-C and TGs were selected as important variables, and in cases where LDL-C was less than 130 mg/dL, the hazard ratio was statistically significant at 4.425 (95% CI, 3.081–6.356, P<0.001). Model Extra, which used all four lipid parameters as variables, did not demonstrate any statistical significance (*Table 4*).

Table 5 shows the results of Cox regression analysis performed with enter method and backward stepwise method using all variables that could be associated with survival. Among the lipid parameters, TC was excluded because of the multicollinearity with other parameters. In the full model, low LDL-C, low hemoglobin, high CRP, and high TG levels were significantly associated with survival. The hazard ratio of the variables remaining after removal by the backward stepwise elimination was 4.201 (95% CI, 2.578–6.259) for low LDL-C, 2.616 (95% CI, 1.451–3.875) for high CRP, 1.607 (95% CI, 1.126–2.214) for low hemoglobin, and 1.492 (95% CI, 1.063–2.195) for high TG.

Discussion

The importance of lipid profiles is increasing in various diseases, including cancer, and as lipid profiles are specifically related to carcinogenesis and cancer progression, they are attracting attention as a potential prognostic factor. However, the exact mechanism has not been identified, and the relationship between the lipid profile and the survival and prognosis of patients with cancer is inconsistent (10,11,18). Therefore, we conducted this retrospective study to investigate the serum lipid profile levels when patients with terminal cancer, including hospice patients, were admitted to the hospital for palliative care. The survival time was calculated from the hospitalization date to the date of death, and we sought to determine the correlation with the lipid profile. The results of this study confirmed that the patients' survival times were shorter when their LDL-C

Table 5 Multivariate Cox regression analysis of the lipid profile and the factors likely to be correlated with lipids as a risk factor contributing to survival

Covariates	Full model		Stepwise backward elimination	
	HR	95% CI	HR	95% CI
Diabetes	1.001	0.971–1.029	–	–
Hypertension	0.987	0.589–1.687	–	–
Albumin ≤3.0 g/dL	2.641	2.154–4.541	–	–
Hemoglobin <10 g/dL	1.562	1.071–2.158	1.607	1.126–2.214
Creatinine ≥2.0 mg/dL	1.100	0.785–1.2351	–	–
Total bilirubin ≥2.0 mg/dL	1.106	0.987–1.358	–	–
ALT >41 U/L	1.58	0.997–1.968	–	–
CRP ≥0.5 mg/dL	2.586	1.256–3.995	2.616	1.451–3.875
NLR ≥4.0	1.685	0.879–2.567	–	–
LDL-C <130 mg/dL	4.158	2.578–6.966	4.201	2.578–6.259
Triglyceride ≥150 mg/dL	1.412	1.235–2.895	1.492	1.063–2.195
HDL-C ≤40 mg/dL	1.055	0.328–2.168	–	–

ALT, alanine aminotransferase; CRP, C-reactive protein; NLR, neutrophil-to-lymphocyte ratio; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HR, hazard ratio; CI, confidence interval.

levels were low (<130 mg/dL) and when their TG levels were high (≥150 mg/dL); these parameters are therefore likely prognostic factors in patients with cancer.

The cutoff values of the lipid parameters used in this study were set to the same values as the well-known cardiovascular risk factors. Lipids have not been established as prognostic factors in patients with cancer. However, the same reference values as ours was selected for the investigation in some previous studies (7,24). Given that the reference value suggested metabolic problems, such as chronic inflammation in relation to the survival of patients with cancer (25), it was determined that it was sufficient as the reference point for our study.

A possible explanation of the results of this study is that in the case of rapidly proliferating tumor cells, cholesterol requirements for the synthesis of new membranes increase. As a result, the LDL receptor expression is increased, and this increases cholesterol influx into cells, which can in turn leads to hypocholesterolemia. If the cholesterol concentration in the serum is low, the following may occur. First, immune system functions may be impaired (3). Second, susceptibility to oxidative stress may be increased. Finally, the concentration of inflammatory proteins, such as interleukin-6, which is associated with carcinogenesis and cancer progression, may be increased. Impaired immune function, oxidative stress, and inflammatory proteins have been shown to exert harmful effects on the body and may also affect cancer progression (26,27).

As for TG, in our study, patients with high TG levels (≥150 mg/dL) had a shorter survival time. In one retrospective case-control study, the cancer group had a higher TG level than the control group (28), whereas another study found that when the serum TG level in patients with advanced breast cancer was examined, higher concentrations were found in cases of cancer progression or recurrence (29). However, opposite results were also reported. In a study of breast cancer patients, when the preoperative serum TG level was high, patients had better disease-free survival, and therefore, the serum TG level was shown to be a possible prognostic factor (30). In addition, TG levels tend to have different results depending on the type of cancer. In a large-scale cohort study, high TG levels were associated with an increased risk of lung, thyroid, and rectal cancers, whereas the opposite was found for prostate cancer and non-Hodgkin's lymphoma (31). Several studies have reported conflicting results regarding TG levels and cancer progression, and thus, the mechanism and association are still unclear (32,33).

In our study, no significant results were obtained for the association of HDL-C level and survival time of patients

with cancer. However, HDL-C exhibits not only an anti-atherogenic function as well as anti-inflammatory and antiangiogenic properties (24), and a previous study has shown that HDL-C may be related to carcinogenesis and cancer progression (25). According to a retrospective analysis, patients with extremely low serum HDL-C levels (≤20 mg/dL) had an increased risk of death, sepsis, and malignancy compared with patients with elevated HDL-C levels (≥65 mg/dL) (34,35). Other studies showed that the level in patients with cancer was lower than that of controls and that the HDL-C level decreased as cancer progressed, whereas when chemotherapy was successful, the level increased (28,36). Therefore, HDL-C is also expected to be a cancer prognostic factor.

In general, lipid profiles are closely related to nutritional status (37). Albumin is representative as an indicator reflecting nutritional status, and hemoglobin can reflect overall nutritional status. As this study investigated lipid parameters as factors affecting the survival, it was essential to consider the nutritional status that can affect the lipid concentrations as well as the survival. In this study, there was no significant correlation between lipid parameters and albumin or hemoglobin, and there was no multicollinearity. The mean survival time of the subjects in this study was approximately 35 days, which is relatively late stage of life. It is judged that indicators such as albumin and hemoglobin did not reflect only the nutritional status, but were also affected by overall organ dysfunction due to cancer (33). Therefore, it is believed that there was no direct correlation of survival time with lipid.

In this study, along with LDL-C and TG levels, CRP was found to be a factor influencing the survival time. High CRP is an indicator of systemic inflammation along with the NLR. In addition, it is a well-known prognostic factor for terminal cancer (38). Systemic inflammatory status can also influence lipid parameters (39). However, there was no significant correlation between lipid parameters and CRP or NLR, and there was no multicollinearity in this study. To establish lipid parameters as prognostic factors for terminal cancer, future studies considering the relationship with inflammatory markers are needed.

According to some previous studies, the lipid profile can serve as a prognostic marker in cancer (12,18,33), and thus, it may help evaluate the condition of cancer patients and predict the prognosis and treatment of patients in the future. However, as discussed previously, the study results are controversial, and large-scale studies on this topic are required. It will also be necessary to clarify a mechanism that can explain the results.

This study has some limitations. First, various factors, such as age, sex, cancer type, stage, nutritional status, comorbid diseases, smoking status, alcohol consumption, and exercise, could affect the survival of patients with cancer, but we were limited in considering all these factors. Second, this was a single-center study. Third, it was impossible to consider the amount of nutrients supplied by the patient and the type of nutrition being supplied (for example, whether nutrients were supplied by parenteral nutrition or enteral nutrition). Furthermore, the ratio of carbohydrates, proteins, and lipids of each nutrient supplied was not identified.

Despite the above limitations, this study has some strengths. This study included patients in hospice care, which is novel because studies of patients in hospice have not been active until now. Another strength of this study is that it is not just a simple study, but rather, it is worthwhile because it involves topics that can be useful in the treatment of patients with cancer. We expect that the lipid profile, together with the TNM stage, will be considered in understanding the disease state and predicting the prognosis of patients with cancer, and that this will contribute to determining the patients' treatment plan and direction.

Conclusions

In conclusion, our study shows that low LDL-C and high TG levels are associated with survival time in patients with terminal cancer. Based on this finding, lipid profiles appear to have potential as new prognostic biomarkers in patients with cancer. Thus, further follow-up studies are needed to resolve the current controversy and to confirm the ability of lipid profiles to serve as predictors of the survival of patients with terminal cancer.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-366/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-366/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-366/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work while ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study protocol was approved by the Kyungpook National University Chilgok Hospital Institutional Review Board (No.2021-02-011). The requirement for informed patient consent was waived because of the retrospective study design. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

References

1. Heron M, Anderson RN. Changes in the Leading Cause of Death: Recent Patterns in Heart Disease and Cancer Mortality. NCHS Data Brief 2016;(254):1-8.
2. Baskar R, Lee KA, Yeo R, et al. Cancer and radiation therapy: current advances and future directions. Int J Med Sci 2012;9:193-9.
3. Zhou P, Li B, Liu B, et al. Prognostic role of serum total cholesterol and high-density lipoprotein cholesterol in cancer survivors: A systematic review and meta-analysis. Clin Chim Acta 2018;477:94-104.
4. Joo I, Lee JM, Kim JH, et al. Prospective comparison of 3T MRI with diffusion-weighted imaging and MDCT for the preoperative TNM staging of gastric cancer. J Magn Reson Imaging 2015;41:814-21.
5. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part I. Development, growth, and spread: key pathologic and imaging aspects. Radiology 2014;272:635-54.
6. Heijnen LA, Maas M, Beets-Tan RG, et al. Nodal staging in rectal cancer: why is restaging after chemoradiation more accurate than primary nodal staging? Int J Colorectal Dis 2016;31:1157-62.
7. Parsa N, Taravatmanesh S, Trevisan M. Is low cholesterol a risk factor for cancer mortality? Eur J Cancer Prev 2018;27:570-6.
8. Shabana, Shahid SU, Sarwar S. The abnormal lipid profile in obesity and coronary heart disease (CHD) in Pakistani subjects. Lipids Health Dis 2020;19:73.
9. Markelić I, Hlapčić I, Rogić D, et al. Lipid profile and atherogenic indices in patients with stable chronic obstructive pulmonary disease. Nutr Metab Cardiovasc Dis 2021;31:153-61.
10. Long J, Zhang CJ, Zhu N, et al. Lipid metabolism and carcinogenesis, cancer development. Am J Cancer Res 2018;8:778-91.
11. Cruz PM, Mo H, McConathy WJ, et al. The role of cholesterol metabolism and cholesterol transport in carcinogenesis: a review of scientific findings, relevant to future cancer therapeutics. Front Pharmacol 2013;4:119.
12. Lin F, Zheng R, Yu C, et al. Predictive role of serum cholesterol and triglycerides in cervical cancer survival. Int J Gynecol Cancer 2021;31:171-6.
13. Panagiotakos DB, Pitsavos C, Polychronopoulos E, et al. Total cholesterol and body mass index in relation to 40-year cancer mortality (the Corfu cohort of the seven countries study). Cancer Epidemiol Biomarkers Prev 2005;14:1797-801.
14. Iso H, Ikeda A, Inoue M, et al. Serum cholesterol levels in relation to the incidence of cancer: the JPHC study cohorts. Int J Cancer 2009;125:2679-86.
15. Ukawa S, Tamakoshi A, Murakami Y, et al. Pooled Analysis of the Associations between Body Mass Index, Total Cholesterol, and Liver Cancer-related Mortality in Japan Asian Pac J Cancer Prev 2018;19:2089-95.
16. Ghahremanfard F, Mirmohammadkhani M, Shahnazari B, et al. The Valuable Role of Measuring Serum Lipid Profile in Cancer Progression. Oman Med J 2015;30:353-7.
17. Saito N, Sairenchi T, Irie F, et al. Low serum LDL cholesterol levels are associated with elevated mortality from liver cancer in Japan: the Ibaraki Prefectural health study. Tohoku J Exp Med 2013;229:203-11.
18. Cvetkovic Z, Cvetkovic B, Petrovic M, et al. Lipid profile as a prognostic factor in cancer patients. J BUON 2009;14:501-6.
19. American Diabetes Association Professional Practice Committee; Draznin B, Aroda VR, et al. 6. Glycemic Targets: Standards of Medical Care in Diabetes-2022. Diabetes Care 2022;45:S83-96.

20. Rodriguez MA, Kumar SK, De Caro M. Hypertensive crisis. Cardiol Rev 2010;18:102-7.
21. Zucker A, Winter A, Lumley D, et al. Prognostic role of baseline neutrophil-to-lymphocyte ratio in metastatic solid tumors. Mol Clin Oncol 2020;13:25.
22. Anderson F, Downing GM, Hill J, et al. Palliative performance scale (PPS): a new tool. J Palliat Care 1996;12:5-11.
23. Rhee EJ, Kim HC, Kim JH, et al. 2018 Guidelines for the management of dyslipidemia in Korea. Korean J Intern Med 2019;34:1171.
24. Shor R, Wainstein J, Oz D, et al. Low HDL levels and the risk of death, sepsis and malignancy. Clin Res Cardiol 2008;97:227-33.
25. Chien JY, Jerng JS, Yu CJ, et al. Low serum level of high-density lipoprotein cholesterol is a poor prognostic factor for severe sepsis. Crit Care Med 2005;33:1688-93.
26. Muldoon MF, Marsland A, Flory JD, et al. Immune system differences in men with hypo- or hypercholesterolemia. Clin Immunol Immunopathol 1997;84:145-9.
27. Kuroda K, Nakashima J, Kanao K, et al. Interleukin 6 is associated with cachexia in patients with prostate cancer. Urology 2007;69:113-7.
28. Muntoni S, Atzori L, Mereu R, et al. Serum lipoproteins and cancer. Nutr Metab Cardiovasc Dis 2009;19:218-25.
29. Zielinski CC, Stuller I, Rausch P, et al. Increased serum concentrations of cholesterol and triglycerides in the progression of breast cancer. J Cancer Res Clin Oncol 1988;114:514-8.
30. Li X, Tang H, Wang J, et al. The effect of preoperative serum triglycerides and high-density lipoprotein-cholesterol levels on the prognosis of breast cancer. Breast 2017;32:1-6.
31. Ulmer H, Borena W, Rapp K, et al. Serum triglyceride concentrations and cancer risk in a large cohort study in Austria. Br J Cancer 2009;101:1202-6.
32. Wulaningsih W, Vahdaninia M, Rowley M, et al. Prediagnostic serum glucose and lipids in relation to survival in breast cancer patients: a competing risk analysis. BMC Cancer 2015;15:913.
33. Maran L, Hamid A, Hamid SBS. Lipoproteins as Markers for Monitoring Cancer Progression. J Lipids 2021;2021:8180424.
34. Furberg AS, Jasienska G, Bjurstam N, et al. Metabolic and hormonal profiles: HDL cholesterol as a plausible biomarker of breast cancer risk. The Norwegian EBBA Study. Cancer Epidemiol Biomarkers Prev 2005;14:33-40.
35. Gonçalves RP, Rodrigues DG, Maranhão RC. Uptake of high density lipoprotein (HDL) cholesteryl esters by human acute leukemia cells. Leuk Res 2005;29:955-9.
36. Ray A, Jain D, Yadav R, et al. Effect of cancer treatment modalities on serum lipids and lipoproteins among women with carcinoma of the breast. Indian J Physiol Pharmacol 2001;45:337-44.
37. Boretti A. Nutrition, lipidic parameters, and cancer risk and progress. Nutrition 2020;69:110538. Erratum in: Nutrition 2019:110630. PMID: 31525703.
38. Kim AS, Youn CH, Ko HJ, et al. The survival time of terminal cancer patients: prediction based on clinical parameters and simple prognostic scores. J Palliat Care 2014;30:24-31.
39. Zhang C, Wang K, Yang L, et al. Lipid metabolism in inflammation-related diseases. Analyst 2018;143:4526-36.

Cite this article as: Lee DY, Ko HJ, Kim AS. Lipid profile and survival time in patients with terminal cancer: a cross-sectional study. Ann Palliat Med 2022;11(10):3075-3084. doi: 10.21037/apm-22-366

Supplementary

Table S1 Correlation between lipid parameters and related factors

Variables	History of diabetes	History of hypertension	Albumin	Hemoglobin	Creatinine	Total bilirubin	ALT	CRP	NLR
Total cholesterol	0.405	0.236	0.512*	0.445	0.219	0.339	0.375	0.198	0.225
LDL-C	0.398	0.255	0.523*	0.369	0.258	0.348	0.345	0.248*	0.311
Triglyceride	0.597	0.168	0.465	0.279	0.279	0.149	0.225	0.234	0.298
HDL-C	0.365	0.115	0.198	0.243	0.156	0.201	0.123	0.215	0.238

The correlation coefficient was expressed as a Point-biserial correlation coefficient or Pearson correlation coefficient. *, 0.05< P value <0.10. LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; ALT, alanine aminotransferase; CRP, C-reactive protein, NLR, neutrophil-to-lymphocyte ratio

Table S2 Multicollinearity analysis[†] of total cholesterol and related factors

Variables	Coefficient	VIF	R^2
Albumin	0.028	2.1	0.683
Hemoglobin	0.078	1.6	
Creatinine	0.002	2.4	
Total bilirubin	-0.001	1.5	
ALT	0.097	2.0	
CRP	0.000	1.6	
NLR	-0.001	1.4	

[†] Using multiple regression analysis. VIF, variance inflation factors ALT, alanine aminotransferase; CRP, C-reactive protein, NLR, neutrophil-to-lymphocyte ratio.

Table S3 Multicollinearity analysis[†] of low-density lipoprotein cholesterol and related factors

Variables	Coefficient	VIF	R^2
Albumin	0.023	3.0	0.712
Hemoglobin	0.098	2.5	
Creatinine	0.001	2.2	
Total bilirubin	0.000	1.5	
ALT	0.057	2.4	
CRP	0.000	1.9	
NLR	0.000	1.5	

[†], using multiple regression analysis. VIF, variance inflation factors ALT, alanine aminotransferase; CRP, C-reactive protein, NLR, neutrophil-to-lymphocyte ratio.

Table S4 Multicollinearity analysis[†] of triglyceride and related factors

Variables	Coefficient	VIF	R^2
Albumin	0.058	1.1	0.703
Hemoglobin	0.112	1.3	
Creatinine	0.005	2.4	
Total bilirubin	0.007	1.1	
ALT	-0.067	2.2	
CRP	-0.001	1.6	
NLR	-0.004	1.3	

[†], using multiple regression analysis. VIF, variance inflation factors ALT, alanine aminotransferase; CRP, C-reactive protein, NLR, neutrophil-to-lymphocyte ratio.

Table S5 Multicollinearity analysis[†] of high-density lipoprotein cholesterol and related factors

Variables	Coefficient	VIF	R^2
Albumin	0.019	2.0	0.533
Hemoglobin	0.058	1.7	
Creatinine	0.009	2.3	
Total bilirubin	0.002	1.5	
ALT	0.073	2.2	
CRP	0.001	1.5	
NLR	-0.002	1.5	

[†], using multiple regression analysis. VIF, variance inflation factors ALT, alanine aminotransferase; CRP, C-reactive protein, NLR, neutrophil-to-lymphocyte ratio.

https://dx.doi.org/10.21037/apm-22-366