

# Clinical Significance of Preoperative Serum High Density Lipoprotein Cholesterol Levels in Soft Tissue Sarcoma

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**Abstract:** The prognostic value of lipid profile remains unclear in soft tissue sarcoma. The aim of the present study was to validate the prognostic value of preoperative plasma lipid profile (high density lipoprotein-cholesterol [HDL-C], low density lipoprotein-cholesterol [LDL-C], cholesterol, and triglycerides) levels on disease-free survival (DFS) and overall survival (OS) in soft tissue sarcoma (STS) patients undergoing extensive and radical surgical resection.

The preoperative plasma lipid profile levels of 234 STS patients, who were operated on between 2000 with 2010, were retrospectively evaluated. Kaplan-Meier curves and multivariate Cox proportional models were calculated for DFS and OS.

In univariate analysis, a decreased HDL-C level was significantly associated with decreased OS (hazard ratio [HR], 3.405; 95% confidence interval (CI), 1.445–8.021,  $P=0.005$ ) and remained significant in the multivariate analysis (HR, 5.615; 95% CI, 1.243–25.378,  $P=0.025$ ). Patients with HDL-C < 1.475 mmol/L showed a median OS of 71 months. In contrast, patients with HDL-C  $\geq$  1.475 mmol/L had a median OS of 101 months. In univariate analysis, a decreased HDL-C level was significantly associated with decreased DFS (HR, 2.085; 95% CI, 1.271–3.422,  $P=0.004$ ) and remained significant in the multivariate analysis (HR, 1.808; 95% CI, 1.118–2.924,  $P=0.016$ ). Patients with HDL-C < 1.475 mmol/L presented with a median DFS of 47 months, whereas patients with HDL-C  $\geq$  1.475 mmol/L had a median DFS of 78 months. In univariate analysis and multivariate analyses regarding OS and DFS, there was no significant association between the groups in terms of LDL-C, CHO and TG.

Our study investigated the potential prognostic utility of preoperative plasma HDL-C levels as an independent factor in STS patients who had undergone radical surgical resection.

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**Abbreviations:** AJCC = American Joint Committee on Cancer, CHO = cholesterol, CI = confidence interval, DFS = disease-free-survival, FNCLCC = French Federation of Cancer Centers, HDL = high density lipoprotein, HRs = hazard ratios, LDL = low density lipoprotein, OS = overall survival, STS = soft tissue sarcoma, TG = triglyceride.

## INTRODUCTION

Soft tissue sarcomas (STSs) are a group of rare neoplasms of mesenchymal origin and account for approximately for 1.5% of all human malignancies.<sup>1</sup> Surgery remains the radical treatment modality of choice in patients with localized tumors, and complete resection may afford the significant survival benefit.<sup>2</sup> However, STS patients are at a great risk of recurrence and distant metastasis after resection.<sup>3</sup> Currently, a variety of biomarkers have been introduced to predict clinical outcome in sarcoma patients. For instance, Kikuta established nucleophosimin as a candidate prognostic marker for Ewing's sarcoma patients by measuring its levels in biopsy samples before treatment.<sup>4</sup> Additionally, Bui suggested a possible oncogenic and prognostic role for cytoplasmic Cx43 and Cx26 in EWS/PNET.<sup>5</sup> Yang found that DR6 serum protein may be a tool for diagnosing some sarcomatous tumors, and that elevated DR6 levels may predict non-response to therapy.<sup>6</sup> However, their utility is limited by complicated detection techniques and expensive costs. Therefore, reliable and convenient prognostic markers are urgently needed for predicting and identifying the patients at high risk of relapse and metastasis.

Growing evidence has shown the role of lipid metabolism in different cancers.<sup>7,8</sup> According to a study published in *Gut*, high serum levels of HDL cholesterol are associated with a reduced risk of developing colon cancer, which could be explained by the effects of HDL cholesterol in regulating the levels of proinflammatory cytokines and modulating oxidative stress.<sup>9</sup> In neoplastic disease, membrane biogenesis requires large amounts of lipids, including total cholesterol, lipoproteins and triglycerides.<sup>10,11</sup> A decreased level of preoperative HDL-C was found to be associated with poor survival in patients with NSCLC.<sup>12</sup> Low HDL-C is also associated with increased postmenopausal breast cancer risk<sup>13</sup> and high LDL-C levels promote breast cancer progression.<sup>14</sup> In hematological cancers, the lipid profile is closely related with the risk of cancer and the prognosis,<sup>15–17</sup> some have reported that HDL-C was found to be a valuable independent prognostic factor in extranodal natural killer/T cell lymphoma.<sup>18</sup> In addition, some researchers have found that cholesterol synthesis is enhanced in cancer cells compared normal cells. However, HDL-C was considered to be a risk prognostic factor regarding the prostate cancer based on some limited data from experimental studies.<sup>19</sup> Thus, the prognostic

**TABLE 1.** Baseline Patient Characteristics

	N	%
Age at operation (years)		
<65	216	92.3
≥65	18	7.7
Gender		
Female	101	43.2
Male	133	56.8
BMI		
<25	184	78.6
≥25	50	21.4
Tumor grade		
G1	66	28.2
G2	107	45.7
G3	37	15.8
Unknown	24	10.3
Tumor size		
<5 cm	107	45.7
≥5 cm	127	54.3
Tumor site		
Upper extremity	23	9.8
Lower extremity	63	26.9
Thoracic/trunk	81	34.6
Intra-abdominal	38	16.2
Head/neck	29	12.4
AJCC stage		
IA+IB	69	29.5
IIA+IIB	115	49.1
III+IV	35	15.0
Unknown	15	6.4

N = number, AJCC = American Joint Committee on Cancer.

value of HDL-C is still unknown in cancers. Recently, some studies have been examined the plasma lipid profile in sarcoma patients, and the results show that sarcoma patients have a highly significant reduction in serum levels of triglycerides and cholesterol and a moderate decrease in LDL-cholesterol and HDL-cholesterol when compared with normal control subjects.<sup>20</sup> However, there is little information on the influence of lipid profile on clinical outcome in STS patients. Thus, predicting the survival of STS patients by measuring their lipid profile (HDL-cholesterol, LDL-cholesterol, cholesterol and triglycerides) may be helpful for prognostic assessment.

The aim of the current study was to assess the predictive value of the lipid profile for disease-free-survival (DFS) and overall survival (OS) in a cohort of STS patients who had undergone extensive and radical surgical resection.

## PATIENTS AND METHODS

### Patient Selection

A total of 234 STS patients who had undergone extensive and radical resection at Sun-Yat-sen University Cancer Center, Guangzhou, China from 2000 to 2010 were enrolled in this study. Written informed consent was obtained from each patient. Ethical approval was given by the medical ethics committee of Sun Yat-sen University Cancer Center IRB. All patients met the following eligibility criteria: all patients had

confirmed STS, with no previous cancer; none had received treatment before serum collection; Sera were obtained from all patients before therapy, and the levels of HDL-C, LDL-C, CHO, and TG were measured using a Hitachi 7600–020 automatic biochemical analyzer. Follow-up examinations were conducted at regular intervals (3-month intervals during years 1 to 3, 6-month intervals during years 4 to 5, and 12-month intervals during years 6 to 15 after diagnosis).

Clinical information, including treatment scheme and histopathological diagnosis, were obtained from the patients' history. For the present study all histologic specimens were centrally re-reviewed by an independent experienced pathologist specialized in diagnosing STS at the Sun-Yat-sen University Cancer Center. The stage was classified according to the American Joint Committee on Cancer (AJCC) 7th Edition<sup>21</sup> and tumors were graded according to the French Federation of Cancer Centers Sarcoma group (FNCLCC) grading system.<sup>22</sup>

### Statistical Analysis

Overall survival (OS), the primary end point of our study, was estimated in days from the time of radical operation until the time of death. The secondary end point was disease-free survival (DFS), which was determined from the date of curative resection to the date of the tumor recurrence or distant metastasis. We performed a receiver operating curve (ROC) analysis to determine the optimal cutoff values for the lipid profile. Chi-square<sup>2</sup> test was used for analyzing the relationship between HDL-C level and clinic-pathological parameters. Kaplan-Meier method was used to calculate the survival probabilities and log-rank test was used to compare survival curves. The significance of the variables for survival was analyzed using the Cox proportional hazards model (univariate and multivariate analysis). A  $P < .05$  was considered statistically significant. All statistical analyses were performed using the SPSS software package (SPSS Statistics 17.0).

**TABLE 2.** Histologic Type

	N	%
Undifferentiated pleomorphic sarcoma/MFH	63	26.9
Fibrosarcoma	20	8.5
Dermatofibrosarcoma protuberans	28	12.0
Well-differentiated liposarcoma	14	6.0
Myxoid liposarcoma	12	5.1
Pleomorphic liposarcoma	5	2.1
Leiomyosarcoma	13	5.6
Rhabdomyosarcoma	10	4.3
Synovial sarcoma	30	12.8
Epithelioid sarcoma	1	0.4
Angiosarcoma	8	3.4
Alveolar soft part sarcoma	5	2.1
MPNST	12	5.1
PNET	8	3.4
Malignant Triton tumor	1	0.4
Mesenchymal chondrosarcoma	4	1.7

MFH = malignant fibrous histiocytoma, MPNST = malignant peripheral nerve sheath tumor, N = number, PNET = primitive neuroectodermal tumor.

**RESULTS**

**Patient Characteristics and Histologic Subtype**

In our study, 234 patients underwent extensive and radical surgical resection for soft tissue sarcoma and their general characteristics are presented in Table 1. The pathological subtype of soft tissue sarcoma was summarized<sup>3</sup> and shown in Table 2. The median age at time of surgery was 41 years (range from 5 to 78 years) and the median follow-up period was 79 months (range from 1 to 176 months). After performing receiver operating curve (ROC) analysis, the optimal cutoff value for HDL was 1.475 mmol/L (AUC: 0.655, 95% CI = 0.563–0.748), for LDL was 2.895 mmol/L (AUC: 0.545mmol/L, 95% CI = 0.452–0.648), for CHO was 4.120 mmol/L (AUC: 0.578mmol/L, 95% CI = 0.479–0.677), and for TG was 0.815 mmol/L (AUC: 0.532, 95% CI = 0.434–0.631).

**Relationship Between the HDL-C Level and Other Clinical Characteristics**

The HDL-C level was significantly associated with gender ( $P = 0.001$ ) and tumor site ( $P = 0.034$ ). Females tended to have a higher level of HDL-C than males. None of the other clinicopathological parameters was associated with an HDL-C <1.475 mmol/L, including age at operation, tumor grade, BMI, tumor size, tumor histology and AJCC stage (Table 3).

**Prognostic Significance of the Clinical Characteristics in STS**

In univariate analyses, we found significant associations of tumor grade, tumor size, tumor site, AJCC stage and HDL-C level with DFS and OS. In the multivariate analysis we observed significant associations of tumor grade, tumor site and HDL-C level with OS and DFS (Tables 4 and 5). The multivariate analysis was carried out based on age at operation, gender, BMI, tumor grade, tumor size, tumor site, AJCC stage, adjuvant radiotherapy, HDL-C level, LDL-C level, CHO level and TG level.

In both univariate and multivariate analysis, we found no significant associations of BMI with DFS and OS (Tables 4 and 5). So it is indicated that BMI was not an independent prognostic factor predicting the survival of soft-tissue-sarcoma. In addition, BMI was not significantly associated with the HDL-C concentration in our manuscript (Table 3).

**Prognostic Significance of the Serum Lipid Profile in STS**

Among the 234 patients, local recurrence or metastatic disease after curative surgical resection was diagnosed in 87 of 179 (48.6%) patients with an HDL-C level <1.475 mmol/L and in 17 of 55 (32.1%) patients with an HDL-C level  $\geq$ 1.475 mmol/L ( $P = 0.021$ ). Regarding OS, death occurred in 49 of 179 (26.8%) patients with an HDL-C level <1.475 mmol/L and in 7 of 55 (13.2%) patients with HDL-C level  $\geq$  1.475 mmol/L ( $P = 0.026$ ).

In univariate analysis, a decreased HDL-C level was significantly associated with decreased OS (HR, 3.405; 95% CI, 1.445–8,021,  $P = 0.005$ ) (Table 4; Figure 1) and remained significant in the multivariate analysis that included tumor site, tumor grade (HR, 5.615; 95% CI, 1.243–25.378,  $P = 0.025$ ) (Table 4). Patients with HDL-C <1.475 mmol/L showed a median OS of 71 months. In contrast, patients with HDL-C  $\geq$ 1.475 mmol/L had a median OS of 101 months. In univariate analysis, a decreased HDL-C level was significantly associated

**TABLE 3.** Relationship Between HDL Concentration and Clinical Characteristics in 234 Patients With Soft-Tissue-Sarcoma

Characteristics	HDL-C <1.475 (mmol/L)	HDL-C $\geq$ 1.475 (mmol/L)	P
Age at operation(years)			
<65	165	51	1.000
$\geq$ 65	14	4	
Gender			
Female	67	34	0.001
Male	112	21	
BMI			
<25	141	43	0.926
$\geq$ 25	38	12	
Tumor grade			
G1+G2	130	43	0.522
G3	31	6	
Unknown	18	6	
Tumor size			
<5 cm	78	29	0.233
$\geq$ 5 cm	101	26	
Tumor site			
Upper extremity	17	6	0.034
Lower extremity	44	19	
Thoracic/trunk	58	23	
Intra-abdominal	36	2	
Head/neck	24	5	
Tumor histology			
Fibrosarcoma	35	13	0.824
Liposarcoma	23	8	
UPS	51	12	
Synovial sarcoma	24	6	
Others	46	16	
AJCC stage			
IA+IB	49	20	0.638
IIA+IIB	90	25	
III+IV	28	7	
Unknown	12	3	

AJCC = American Joint Committee on Cancer, UPS = undifferentiated high-grade pleomorphic sarcoma.

with decreased DFS (HR, 2.085; 95% CI, 1.271–3.422,  $P = 0.004$ ) (Table 5; Figure 2) and remained significant in the multivariate analysis that included tumor grade, tumor size and tumor site (HR, 1.808; 95% CI, 1.118–2.924,  $P = 0.016$ ) (Table 5). Patients with HDL-C <1.475 mmol/L presented with a median DFS of 47 months, whereas patients with HDL-C  $\geq$ 1.475 mmol/L had a median DFS of 78 months.

In individual subgroup analyses, we found a significant association between decreased HDL-C levels and decreased OS in  $> = 5$  cm tumors in univariate analysis (HR, 6.402; 95% CI, 1.963–20.880,  $P = 0.002$ ) and in multivariate analysis (HR, 9.667; 95% CI, 1.155–80.918,  $P = 0.036$ ). Patients with decreased HDL-C levels shown decreased OS also in I+II stage in univariate analysis (HR, 8.624; 95% CI, 2.049–36.301,  $P = 0.003$ ) and in multivariate analysis (HR, 6.355; 95% CI, 1.395–28.957,  $P = 0.017$ ) (see Supplementary Table 1, <http://links.lww.com/MD/A270>, Supplemental digital content, <http://links.lww.com/MD/A270>, which shown the association between HDL-C levels and OS in individual subgroup).

**TABLE 4.** Univariate and Multivariate Cox Proportional Analysis Regarding Overall Survival

Parameter	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age at operation (years)				
<65	1 (referent)	0.442	1 (referent)	0.946
≥65	1.397 (0.596–3.275)		1.039 (0.342–3.163)	
Gender				
Female	1 (referent)	0.714	1 (referent)	0.549
Male	1.110 (0.636–1.937)		1.238 (0.616–2.489)	
BMI				
<25	1 (referent)	0.382	1 (referent)	0.576
≥25	1.505 (0.648–3.225)		1.639 (0.575–4.882)	
Tumor grade				
G1	1 (referent)	0.002	1 (referent)	0.026
G2	4.429(1.688–11.618)	<0.001	5.882(1.236–27.997)	0.043
G3	7.137(2.437–20.897)		10.697(1.075–106.416)	
Tumor size				
<5 cm	1 (referent)	0.002	1 (referent)	0.265
≥5 cm	2.629 (1.420–4.867)		1.560 (0.714–3.405)	
Tumor site				
Trunk & extremity	1 (referent)	<0.001	1 (referent)	<0.001
Head/neck & intra-abdominal	4.736 (2.715–8.260)		3.759 (1.878–7.523)	
AJCC stage				
Localised at diagnosis	1 (referent)	<0.001	1 (referent)	0.676
Metastasised at diagnosis	2.584 (1.684–3.966)		0.783 (0.249–2.466)	
Adjuvant radiotherapy				
Yes	1 (referent)	0.647	1 (referent)	0.918
No	1.148 (0.635–2.076)		1.043 (0.468–2.325)	
HDL-C (mmol/L)				
<1.475	3.405 (1.445–8.021)	0.005	5.615 (1.243–25.378)	0.025
≥1.475	1 (referent)		1 (referent)	
LDL-C (mmol/L)				
<2.895	1 (referent)	0.238	1 (referent)	0.362
≥2.895	1.392 (0.803–2.412)		1.453 (0.650–3.248)	
CHO (mmol/L)				
<4.120	1 (referent)	0.960	1 (referent)	0.966
≥4.120	1.105 (0.562–1.835)		0.982 (0.415–2.321)	
TG (mmol/L)				
<0.815	1 (referent)	0.403	1 (referent)	0.528
≥0.815	1.361 (0.662–2.799)		0.730 (0.275–1.940)	

CHO = total cholesterol, CI = confidence interval, HDL-C = high-density lipoprotein cholesterol, HR = hazard ratio, LDL-C = low-density lipoprotein cholesterol, TG = triglycerides.

In addition, patients with decreased HDL-C levels showed decreased DFS in  $\geq 5$  cm tumors in univariate analysis (HR, 2.485; 95% CI, 1.307–4.723,  $P = 0.005$ ) and multivariate analysis (HR, 1.773; 95% CI, 1.016–3.096,  $P = 0.044$ ). While patients with decreased HDL-C levels shown decreased DFS in I+II stage only in univariate analysis (HR, 2.229; 95% CI, 1.226–4.053,  $P = 0.009$ ) (see Supplementary Table 2, <http://links.lww.com/MD/A270>, Supplemental digital content, <http://links.lww.com/MD/A270>, which shown the association between HDL-C levels and DFS in individual subgroup).

## DISCUSSION

Previous studies proposed that abnormal lipid profiles may be associated with the occurrence and progression of cancers.<sup>23–25</sup> In recent years, there has been increasing evidence

that HDL-C correlates with clinical outcome in patients with some cancers.<sup>26–28</sup> In gastrointestinal cancer patients, a low preoperative serum HDL-C concentration is a potential biomarker of advanced Pn2–3 stages.<sup>29</sup> Van Duijnhoven FJ reported that high concentrations of serum HDL are associated with a decreased risk of colon cancer based on cohort studies.<sup>9</sup> In lung cancer, a higher HDL-C concentration has been proven to be associated with a decreased risk of cancer overall.<sup>12,30</sup> In prostate cancer, high HDL-C is regarded as a prognostic factor indicating a poor clinical outcome.<sup>19</sup> However, in STS, there have not been any studies that have indicated an association between lipid profile and disease outcome. In this present study, we established the association between HDL-C and soft tissue sarcoma and showed that decreased pre-operative HDL-C in the peripheral blood was associated with decreased DFS and OS in STS patients following radical surgery.

**TABLE 5.** Univariate and Multivariate Cox Proportional Analysis Regarding Disease-Free-Survival

Parameter	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	P	HR (95% CI)	P
Age at operation (years)				
<65	1 (referent)	0.005	1 (referent)	0.083
≥65	2.354 (1.291–4.293)		1.849 (0.922–3.706)	
Gender				
Female	1 (referent)	0.733	1 (referent)	0.248
Male	1.068 (0.733–1.556)		1.297 (0.834–2.017)	
BMI				
<25	1 (referent)	0.790	1 (referent)	0.960
≥25	1.064 (0.673–1.685)		1.014 (0.600–1.711)	
Tumor grade				
G1	1 (referent)	<0.001	1 (referent)	0.022
G2	2.809 (1.602–4.927)	<0.001	3.068 (1.180–7.978)	0.003
G3	6.201 (3.312–11.642)		8.544 (2.121–34.419)	
Tumor size				
<5 cm	1 (referent)	<0.001	1 (referent)	0.001
≥5 cm	2.874 (1.902–4.345)		2.364 (1.444–3.870)	
Tumor site				
Trunk & extremity	1 (referent)	<0.001	1 (referent)	0.050
Head/neck & intra-abdominal	2.152 (1.471–3.148)		1.557 (1.000–2.425)	
AJCC stage				
Localised at diagnosis	1 (referent)	<0.001	1 (referent)	0.739
Metastatised at diagnosis	2.208 (1.644–2.965)		0.882 (0.422–1.844)	
Adjuvant radiotherapy				
Yes	1 (referent)	0.802	1 (referent)	0.710
No	0.949 (0.632–1.426)		0.911 (0.559–1.487)	
HDL-C (mmol/L)				
<1.475	2.085 (1.271–3.422)	0.004	1.808 (1.118–2.924)	0.016
≥1.475	1 (referent)		1 (referent)	
LDL-C (mmol/L)				
<2.895	1 (referent)	0.048	1 (referent)	0.196
≥2.895	1.457 (1.004–2.115)		1.506 (0.810–2.800)	
CHO (mmol/L)				
<4.12	1 (referent)	0.796	1 (referent)	0.553
≥4.12	0.950 (0.641–1.406)		0.851 (0.500–1.449)	
TG (mmol/L)				
<0.815	1 (referent)	0.229	1 (referent)	0.322
≥0.815	1.326 (0.837–2.102)		1.337 (0.752–2.377)	

CHO = total cholesterol, CI = confidence interval, HDL-C = high-density lipoprotein cholesterol, HR = hazard ratio, LDL-C = low-density-lipoprotein cholesterol, TG = triglycerides.

There are several possible reasons, which could account for the association between HDL-C levels and tumorigenesis. First, it has been established that a major function of HDL is to maintain normal cell cholesterol homeostasis by removing excess cholesterol from an intracellular pool.<sup>31,32</sup> Cancer cells need excess cholesterol and intermediates of the cholesterol biosynthesis pathway to maintain a high level of proliferation is well accepted.<sup>33–35</sup> The up-regulation of cholesterol biosynthesis and uptake are considered to be consistent with carcinogenesis. The possible factor that promote the upregulation of cellular cholesterol synthesis are the abundant availability of precursors (acetyl-CoA), via glycolysis that potentiates de novo fatty acid synthesis.<sup>11,36</sup> Based on these data, the explanation of the reduction of HDL-C levels in plasma is that the activity of HDL-C receptor pathway was enhanced to prevent the

accumulation of intracellular cholesterol during tumor development and lymphatic spread.<sup>29</sup>

Another mechanism includes the involvement of HDL in the regulation of levels of proinflammatory cytokines and modulation of oxidative stress. Decreased levels of HDL have been associated with increased circulating levels of proinflammatory cytokines such as interleukin 6 (IL-6) and tumor necrosis factor- $\alpha$  receptors, whereas increased levels of HDL-C are related to raised levels of anti-inflammatory cytokines such as IL-10.<sup>37</sup> These proinflammatory cytokines are considered to stimulate cellular proliferation and inhibit apoptosis.<sup>38</sup> In contrast, anti-inflammatory cytokines inhibit the production of these proinflammatory cytokines.<sup>39</sup> In addition, HDL protects LDL from oxidative damage,<sup>40,41</sup> which has been described as a cause of tumorigenesis.<sup>42</sup>

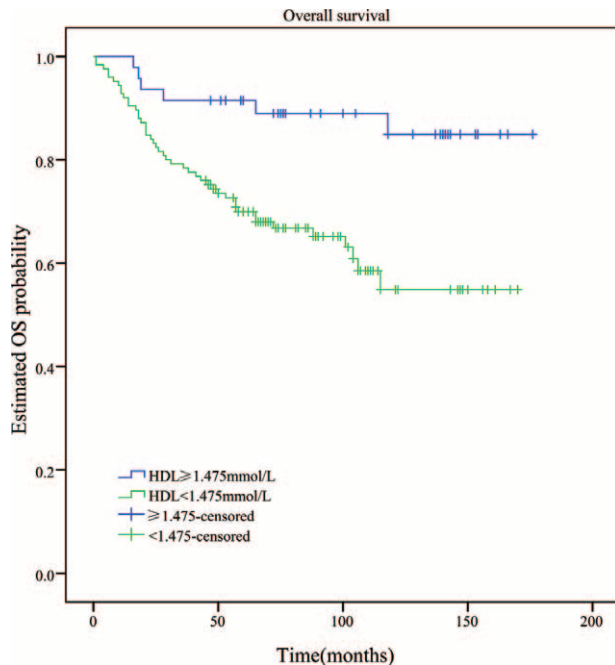


FIGURE 1. Kaplan-Meier curve for overall survival regarding low vs high HDL-C levels ( $P < 0.01$ ).

Furthermore, some other data supports the notion that cancer cells are able to uptake cholesterol from the plasma. For example, there is an increased expression of LDL-C receptor in breast cancer tissue compared to normal tissue.<sup>43</sup> These findings suggest that during the process of carcinogenesis, tumor cells exploit the cholesterol from peripheral tissues to satisfy their increased cholesterol requirements.

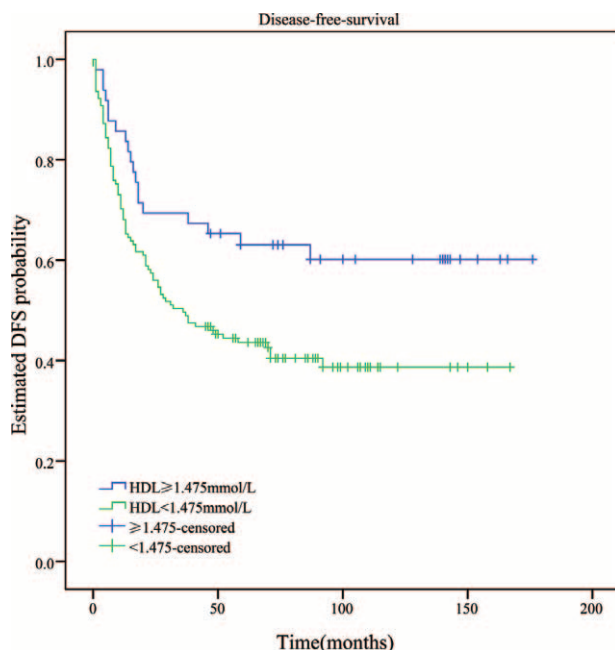


FIGURE 2. Kaplan-Meier curve for disease-free survival regarding low vs high HDL-C levels ( $P < 0.05$ ).

To our knowledge, this is the first study to explore the prognostic value of HDL-C in soft tissue sarcoma. These findings might have potentially crucial impacts, as the levels of HDL cholesterol could be useful for advising patients to lead a healthier lifestyle. Moreover, lipid metabolism plays a significant role in STS, which could provide a valuable clue in the prognosis and treatment for STS. However, there are a few limitations of the present study. It is limited mostly by its retrospective design and the heterogeneous group of histologic subtypes. However, as STSs are rare tumors, the pooling of different histological subtypes by tumor grade has been well established in prognostic studies.

In conclusion, our study clearly indicates the potential prognostic utility of pre-operative plasma HDL-C levels as an independent factor in STS patients who have undergone extensive and radical surgical resection. However, in the future, it will be necessary to conduct large-scale multicentre studies and to accumulate cases, as well as to determine the mechanistic details in vitro.

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