ORIGINAL RESEARCH

Predictive Value of Preoperative Controlling Nutritional Status Score Combined with Fibrinogen–Albumin Ratio in Postoperative Local Recurrence-Free Survival of Patients with Retroperitoneal Liposarcoma

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Background: Previous studies have shown that nutrition and systemic inflammation plays an essential role in the development of soft tissue sarcoma. However, few studies have explored the association of clinicopathologic features and local recurrence with nutritional and inflammatory markers in retroperitoneal liposarcoma (RPLS). This study sought to evaluate the prognostic value of the preoperative nutritional and inflammatory markers for local recurrence-free survival (LRFS) among surgical RPLS patients.

Methods: The study included 111 RPLS patients who underwent surgery between May 2010 and June 2019 at the Peking University Cancer Hospital Sarcoma Center. Time-dependent receiver operating characteristic (time-ROC) curve analysis was conducted to evaluate the ability of markers to predict LRFS. The associations of the CONUT-FAR score with clinicopathological variables and LRFS were evaluated.

Results: In the time-ROC curve analysis, the CONUT-FAR score was superior to other nutritional and inflammatory markers in predicting LRFS. The CONUT-FAR score was the only nutritional and inflammatory marker that independently predicted LRFS in the multivariate analysis, and patients with a high CONUT-FAR score (> 11) showed significantly decreased LRFS. Although the CONUT-FAR score failed to discriminate patients with low grade (G1) (p = 0.327) or undergoing incomplete (R2) resection (p = 0.072), it stratified patients with high grade (G2 and G3) or undergoing complete resection (R0/R1) into subgroups with significantly distinct LRFS (p < 0.001). The CONUT-FAR score also showed good clinical utility among patients with different clinical characteristics.

Conclusion: The preoperative CONUT-FAR score reflects both nutritional and inflammatory factors and is an effective predictor of LRFS for surgical RPLS patients.

Keywords: nutritional status, fibrinogen–albumin ratio, retroperitoneal liposarcoma, prognostic factor, time-dependent ROC

Introduction

Retroperitoneal sarcoma (RPS) is a rare and heterogeneous disease that accounts for approximately 15% of soft tissue sarcomas diagnoses.[1] Liposarcoma is the most common histological type of RPS, accounting for approximately 40–60% of RPS.[2] Since retro-peritoneal liposarcoma (RPLS) is relatively insensitive to chemotherapy or radiotherapy,

extensive resection is the primary curative treatment.[3] Considering that retroperitoneal anatomy limits the ability to achieve wide resection margins, local recurrence after surgery remains the main cause of treatment failure and the primary cause of disease-specific death, with rates ranging from 30% to 50%.[4] Hence, a reliable prognostic indicator is needed to identify patients at high risk of recurrence and optimize their follow-up strategy and adjuvant therapies.

RPLS tends to present as a large, painless mass that compresses the gastrointestinal tract, which can lead to elevated systemic inflammation and malnutrition.[5,6] Therefore, the nutritional and inflammatory status play critical roles in tumor progression and prognosis.[5,7] Peripheral blood parameters such as neutrophil count, lymphocyte count, platelet count, serum albumin (ALB) levels, fibrinogen levels, and total cholesterol (TC) are prognostic determinants and have clinical utility according to several studies.[8–12] Several methods for the assessment of inflammatory and/or nutritional status, which are mainly derived from routine blood examinations, have been explored, including the neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), fibrinogen–albumin ratio (FAR), and controlling nutritional status (CONUT) score.[12–15] The CONUT score, which is calculated from ALB, total lymphocyte count (TLC), and TC, was developed to assess nutritional status.[13] Multiple studies have revealed that malnutrition and elevated inflammatory status significantly increase postoperative complications and have a negative impact on the survival of patients with soft tissue sarcoma.[14,16,17] However, to our knowledge, few studies have explored the association of clinicopathologic features and local recurrence with the nutritional and inflammatory markers in RPLS.

This study therefore aimed to evaluate the prognostic relevance of the preoperative nutritional and inflammatory markers in predicting local recurrence for surgical RPLS patients.

Patients and Methods

The study was supported by the Ethics Committee of the Peking University Cancer Hospital, and informed consent was obtained from all patients prior to participation in this study.

Patients

From May 2010 to June 2019, data of 125 consecutive patients who underwent surgical resection for RPLS at the Peking University Cancer Hospital Sarcoma Center were carefully reviewed. The eligibility criteria were as follows: (1) pathologically confirmed RPLS; (2) absence of metastasis; (3) available medical records and follow-up data; and (4) no preoperative chemotherapy, radiotherapy or targeted therapy. Patients who were lost to follow-up (n=1), received preoperative targeted therapy (n=5), were diagnosed with acute infection or chronic inflammatory diseases (n=3) or had incomplete laboratory data (n=5) were excluded. Finally, 111 patients were included for analysis.

Diagnosis and Treatment

A diagnosis of RPLS was confirmed based on the histopathologic evidence. The histological subtypes were classified according to the 2013 World Health Organization classification.[18] Considering the rarity of the retroperitoneal pathological subtypes, the myxoid/round cell subtype was considered a continuum. The RPLS was therefore classified into four histologic subtypes: 1) well-differentiated (WDLPS), 2) myxoid/round cell (MLPS), 3) dedifferentiated (DDLPS), and 4) pleomorphic (PLPS). The histological grade was determined based on the French Federation of Cancer Centers Sarcoma Group (FNCLCC).[19] The variables retrieved from the medical records included sex, age, presentation status, size, multifocality, histological subtypes, FNCLCC grade, and extent of resection.

The decision to conduct surgical resection was made by a multidisciplinary team. R0/R1 and R2 resection were defined as complete resection and incomplete resection, respectively.[3] For presentation status, the study identified sarcomas as primary when diagnosed without previous surgical resection, and as recurrent when the sarcomas presented at least three months after curative resection. Multifocality was defined as more than one noncontiguous tumor through pathological confirmation.

Definition of Preoperative Nutritional and Inflammatory Indicators

Blood test results, including serum fibrinogen, ALB, white blood cell count, platelet count and TC, were collected within two weeks before surgery. Nutritional and inflammatory biomarkers were calculated as follows: NLR = neutrophil count/lymphocyte count; PLR = platelet count/ lymphocyte count; FAR = fibrinogen/ALB×100; CONUT score = ALB score + total lymphocyte score + TC score. The CONUT score was determined based on previously described methods (details shown in Table S1).[13]

Patients were dichotomized into low and high FAR groups according to the cut-off value. Based on the median of CONUT score, the low FAR group and high FAR group scores were 4 and 8, respectively. The COUNT-FAR score was defined as the CONUT score + the FAR score.

Follow-Up

Patients were regularly evaluated every three months during the first two years after discharge and every six months thereafter. At each follow-up, routine hematology (complete blood count), serum biochemistry (liver and renal function test), and abdominopelvic contrast-enhanced CT or MRI were performed. The primary end-point of the study was local recurrence-free survival (LRFS, defined as the time from surgery to the first local recurrence). Local recurrence was defined as the presence of new lesions revealed by imaging. Survival outcomes were collected from the outpatient clinic visits and telephone interviews.

Statistical Analysis

Continuous variables were presented as median (interquartile range [IQR]) and were evaluated using the Mann–Whitney U-test, whereas categorical data were summarized as numbers (proportions) and were analyzed by the two-sided Chi-square test or Fisher's exact test. Time-dependent receiver operating characteristic (ROC) curve analysis was performed via the inverse probability of censoring weighting approach and the area under the ROC curve (AUC) was estimated to compare the ability of nutritional and inflammatory biomarkers in predicting LRFS.[20] The optimal cut-off value of nutritional and inflammatory biomarkers is determined by the largest point of the log-rank statistic for 5-year LRFS by applying X-tile analysis.[21] LRFS rates were calculated using the Kaplan–Meier method and were compared between groups by the Log rank test. Multivariate Cox regression analysis was conducted to determine the independent predictors of LRFS. Hazard ratios (HRs) estimated from the Cox analysis were reported as relative risks with corresponding 95% confidence intervals (95% CIs). Time-dependent ROC curve analysis was performed with the "time-ROC" package in R version 3.6.1 (http://www.r-project.org/); X-tile analysis was conducted using X-tile software (version v3.6.1, Yale University); and other statistical analyses were carried out using SPSS software (version 24.0, Chicago, IL, USA). A p-value < 0.05 was considered statistically significant.

Results

Patient Characteristics

The detailed baseline characteristics of the 111 patients are summarized in Table 1. The majority of patients were male (56.8%) and the median age was 57 years (IQR 48–63). Fifty-nine patients (53.2%) presented with recurrence, and the remaining 52 patients (46.8%) had primary tumors. G1, G2 and G3 tumors were found in 22 (19.8%), 49 (44.1%) and 40 (36.0%) patients, respectively. The median tumor size was 20 cm (IQR 14–28). The pathological subtypes were identified as follows: WDLPS (n=24, 21.6%), DDLPS (n=61, 55.0%), MLPS/RLPS (n=17,15.3%) and PLPS (n=9, 8.1%). The proportion of multifocality was 85.6%, and 14.4% of patients underwent incomplete resection. The median levels of the FAR, NLR, PLR, and CONUT scores were 10.8 (IQR 7.8–17.9), 2.5 (IQR 1.6–3.6), 167.6 (IQR 133.9–254.9), and 4 (IQR 3–5), respectively.

Comparison of the Ability of Nutritional and Inflammatory Indicators in Predicting Local-Recurrence-Free Survival (LRFS)

The AUC of the CONUT-FAR score for predicting LRFS was significantly higher than those of the NLR, PLR, FAR and CONUT score at all tested timepoints (Figure 1). Therefore, the CONUT-FAR score was superior for predicting LRFS in surgical RPLS patients than any other markers assessed. The AUCs of the CONUT-FAR in predicting the 1-, 3-, and 5-year LRFS were 0.776, 0.704, and 0.796, respectively. The data for the NLR, PLR, FAR and CONUT scores were shown in Table S2.

The Optimal Cut-off Values of Nutritional and Inflammatory Indicators

X-tile analysis for 5-year LRFS was used to determine the optimal cut-off value of nutritional and Inflammatory markers. The high and low groups were created based on the markers' respective optimal cut-off values. The optimal cut-off values of NLR, PLR, FAR, CONUT score, and CONUT-FAR score were 3.6, 153.3, 16.9, 5 and 11, respectively (Figure S1). Therefore, for the CONUT-FAR score, patients were divided into low (≤11, n = 85) and high (>11, n = 26) CONUT-FAR groups.

Table 1 Baseline Characteristics of Total 111 Patients with Retroperitoneal Liposarcoma, as Well as Patients in the High (> 11) and Low (≤11) CONUT-FAR Score Groups

Variables	Total (n=111)	Low CONUT-FAR (n=85)	High CONUT-FAR (n=26)	p-value
Sex				0.548[a]
Male	63 (56.8)	48 (56.5)	15 (57.7)	
Female	48 (43.2)	37 (43.5)	11 (42.3)	
Age (yrs) [median (IQR)]	57 (48–63)	57 (48–63)	57 (49–64)	0.927[b]
Presentation status				0.017[a]
Primary	52 (46.8)	45 (52.9)	7 (26.9)	
Recurrence	59 (53.2)	40 (47.1)	19 (73.1)	
Size (cm) [median (IQR)]	20 (14–28)	19 (14–28)	20.5 (14–28.5)	0.335[b]
Multifocality				0.006[a]
Yes	95 (85.6)	33 (38.8)	18 (69.2)	
No	16 (14.4)	52 (61.2)	8 (30.8)	
Histological subtypes				0.086[a]
Well-differentiated	24 (21.6)	22 (25.9)	2 (7.7)	
Dedifferentiated	61 (55.0)	44 (51.8)	17 (65.4)	
Myxoid/Round cell	17 (15.3)	14 (16.5)	3 (11.5)	
Pleomorphic	9 (8.1)	5 (5.9)	4 (15.4)	
FNCLCC grade				0.167[a]
G1	22 (19.8)	20 (23.5)	2 (7.6)	
G2	49 (44.1)	37 (43.5)	12 (46.2)	
G3	40 (36.0)	28 (33)	12 (46.2)	
Extent of resection				0.000[a]
Complete (R0/R1)	95 (85.6)	80 (94.1)	15 (57.7)	
Incomplete (R2)	16 (14.4)	5 (5.9)	11 (42.3)	
FAR [median (IQR)]	10.8 (7.8–17.9)	9.5 (7.3–11.6)	21.5 (19.3–26.1)	0.000[b]
NLR [median (IQR)]	2.5 (1.6–3.6)	2.3 (1.5–3.1)	3.6 (2.6–8.5)	0.000[b]
PLR [median (IQR)]	167.6 (133.9–254.9)	151.7 (127.6–211.2)	290.9 (173.9–400.8)	0.000[b]
CONUT [median (IQR)]	4 (3–5)	4 (3–5)	7 (5–8)	0.000[b]
CONUT-FAR [median (IQR)]	9 (8–13)	8 (7–10)	15 (13–16)	0.000[b]

Notes: Values were shown as n (%), or median (interquartile range). [a]Using the two-sided Chi-square test; [b]Using the Mann–Whitney U-test.
Abbreviations: FNCLCC, French Federation of Cancer Centers Sarcoma Group; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; FAR, fibrinogen–albumin ratio; CONUT, Controlling Nutritional Status.

Correlation Between the CONUT-FAR Score and Clinicopathologic Characteristics

As presented in Table 1, the following variables were significantly different between the low and high CONUT-FAR groups: presentation status (p = 0.032), multifocality (p = 0.012), and extent of resection (p < 0.001). However, the groups were similar in terms of sex, age, tumor size, proportion of histological subtypes and FNCLCC grade (p > 0.05 for all). In addition, the high CONUT-FAR group also had a significantly elevated FAR (p < 0.001), elevated NLR (p < 0.001), elevated PLR (p < 0.000) and elevated CONUT score (p < 0.001).

Univariable and Multivariable Analyses for LRFS

In univariate analyses, the presentation, histologic subtypes, FNCLCC grade and extent of resection were significantly associated with LRFS, as were the FAR, NLR, PLR, CONUT score and CONUT-FAR score. Multivariate
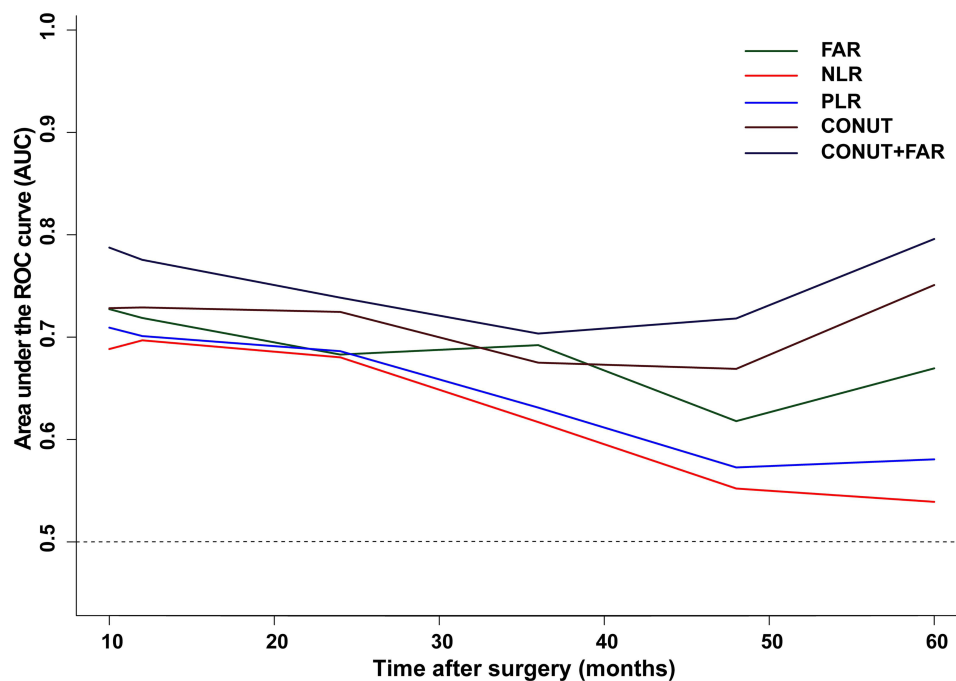
Figure 1 Time-ROC curve analysis to compare the ability of NLR, PLR, FAR, CONUT and CONUT+FAR in predicting the local recurrence-free survival. The horizontal axis depicts the time after surgery, and the vertical axis depicts the corresponding area under the ROC curve for survival at different time points.
Abbreviations: NLR, neutrophil–lymphocyte ratio; PLR, platelet–lymphocyte ratio; FAR, Fibrinogen–Albumin Ratio; CONUT, controlling nutritional status.

analysis showed that the CONUT-FAR score was an independent prognostic factor of LRFS in surgical RPLS patients (>11 vs ≤11: HR 2.552, 95% CI 1.476–4.415; p = 0.001), as were the FNCLCC grade (G3 vs G1:HR 4.798,95% CI 1.821–12.641; p = 0.005) and the extent of resection (incomplete vs complete: HR 3.849, 95% CI 2.001–7.406; p < 0.001) (Table 2).

LRFS in the High and Low CONUT-FAR Groups

With a median follow-up of 32 months (IQR 24–51), 24 patients (92.3%) in the high CONUT-FAR group developed recurrence compared with 45 (52.9%) in the low CONUT-FAR group. The median LRFS in the high CONUT-FAR group (7 months) was significantly lower than in the low CONUT-FAR group (29 months, p < 0.001) (Figure 2).

Subgroup Analyses of LRFS in Patients with High and Low CONUT-FAR According to the Extent of Resection and Histologic Grade

Considering that FNCLCC grade and extent of resection were the two most critical factors in the prognosis of RPLS, we further examined the prognostic role of the

CONUT-FAR score in RPLS patients stratified by FNCLCC grade and extent of resection.

Using the optimal cut-off value, the CONUT-FAR score stratified patients who received complete resection into two subgroups with significantly distinct LRFS (p <0.001) (Figure 3A). However, for patients who underwent incomplete R2 resection, there was no significant prognostic difference between the high CONUT-FAR score group and the low CONUT-FAR score group (p = 0.072) (Figure 3B).

Similarly, when we divided patients based on histological grade, the CONUT-FAR score stratified patients with high-grade tumors (G2 and G3) into two subgroups with significantly distinct LRFS (G2: p <0.001; G3: p<0.001) (Figure 4B and C). However, for patients with G1 tumors, the high CONUT-FAR subgroup had no significant prognostic differences than those in the low CONUT-FAR subgroup (p = 0.327) (Figure 4A).

Subgroup Analyses to Assess the Clinical Utility of the CONUT-FAR in Predicting LRFS

To further assess the clinical utility of the CONUT-FAR score in predicting LRFS, subgroup analyses using univariate Cox regression were conducted on the basis of sex

Table 2 Univariate and Multivariate Analyses to Determine Independent Predictors of LRFS of RPLS

Variables	Local Recurrence-Free Survival					
	Univariate			Multivariate		
	HR	95% CI	*p*-value	HR	95% CI	*p*-value
Sex (female vs male)	0.554	0.718–1.856	0.554	–	–	–
Age (years)	0.998	0.976–1.021	0.876	–	–	–
Presentation (recurrence vs primary)	1.892	1.160–3.086	0.011	1.261	0.730–2.180	0.405
Size (cm)	1.006	0.980–1.032	0.652	–	–	–
Multifocality (yes vs no)	1.959	1.216–3.155	0.006	0.748	0.411–1.359	0.340
Histology subtypes 　DD vs WD 　Myxoid/Round Cell vs WD 　Pleomorphic vs WD	 4.735 2.049 3.541	 2.111–10.622 0.779–5.391 1.233–10.175	0.001	 1.278 0.646 1.029	 0.441–3.709 0.199–2.097 0.282–3.748	0.383
FNCLCC grade 　G2 vs G1 　G3 vs G1	 3.817 6.729	 1.476–9.868 2.613–17.324	0.000	 3.086 4.798	 1.184–8.043 1.821–12.641	0.005
Extent of resection (R2 vs R0/R1)	6.655	3.653–12.124	0.000	3.849	2.001–7.406	0.000
FAR (>16.9% vs ≤16.9%)	2.772	1.688–4.552	0.000	0.901	0.257–3.155	0.870
NLR (>3.6 vs ≤3.6)	2.529	1.530–4.182	0.000	1.363	0.789–2.356	0.267
PLR (>153.3 vs ≤153.3)	2.852	1.675–4.859	0.000	1.490	0.785–2.829	0.223
CONUT (>5 vs ≤5)	2.265	1.407–3.645	0.001	0.872	0.480–1.586	0.654
CONUT-FAR (>11 vs ≤11)	3.534	2.117–5.898	0.000	2.552	1.476–4.415	0.001

Abbreviations: WD, well-differentiated; DD, dedifferentiated; FNCLCC, French National Federation of the Centers for the Fight Against Cancer; 95% CI, 95% confidence interval; HR, hazard ratio.

(female or male), age (≤ 60 or >60 years), presentation status (primary or recurrence), multifocality (no or yes), FNCLCC grade (G1, G2 or G3), and extent of resection (complete or incomplete). We found that a high CONUT-FAR score (>11) was associated with poor LRFS in nearly all subgroup analyses (Figure 5). Although it failed to obtain statistical significance in subgroup analyses of LRFS in patients with G1 sarcoma and who underwent incomplete resection, the trend of poor prognosis in patients with a high CONUT-FAR score was consistent.

Discussion

Current prognostic tools focus on tumor pathologic and histologic characteristics available only after surgery, such as the Personalised Sarcoma Care (PERSARC) model and prognostic nomograms. The recommended prognostic Sarculator used for RPS is a postoperative prognostic nomogram, which incorporated tumor size, FNCLCC grade, histologic subtype and multifocality to determine 7-year disease-free survival.[22] And the PERSARC model, which included age, size, depth, histology and radiotherapy (RT), only focused on the patients with high-grade extremity soft-tissue sarcomas after surgical resection,[23] and has limited value for RPS because of the anatomic constraints of the retroperitoneum as well as the different histologic subtype distribution. Although these postoperative prognostic models are validated, a growing body of evidence suggests that preoperative patient-specific factors, such as nutritional and systemic inflammation, can improve prognostication for STS in the preoperative setting.[12,15,17,24] However, the prognostic value of these markers in patients with RPLS is still unknown.

This study investigated the prognostic significance of preoperative nutritional and inflammatory markers in surgical RPLS patients. We found that the combined use of the CONUT score and the FAR is superior to the CONUT
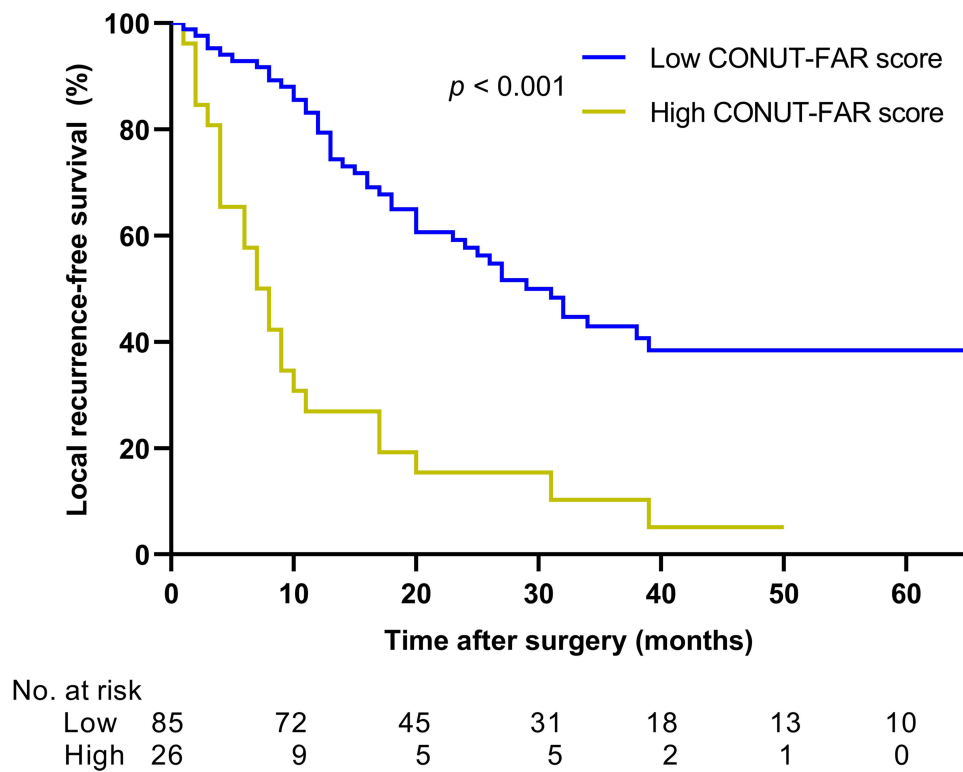
Figure 2 Comparison of local recurrence-free survival (p<0.001) between patients with high (> 11) and low (≤11) CONUT-FAR score in the entire patient cohort.
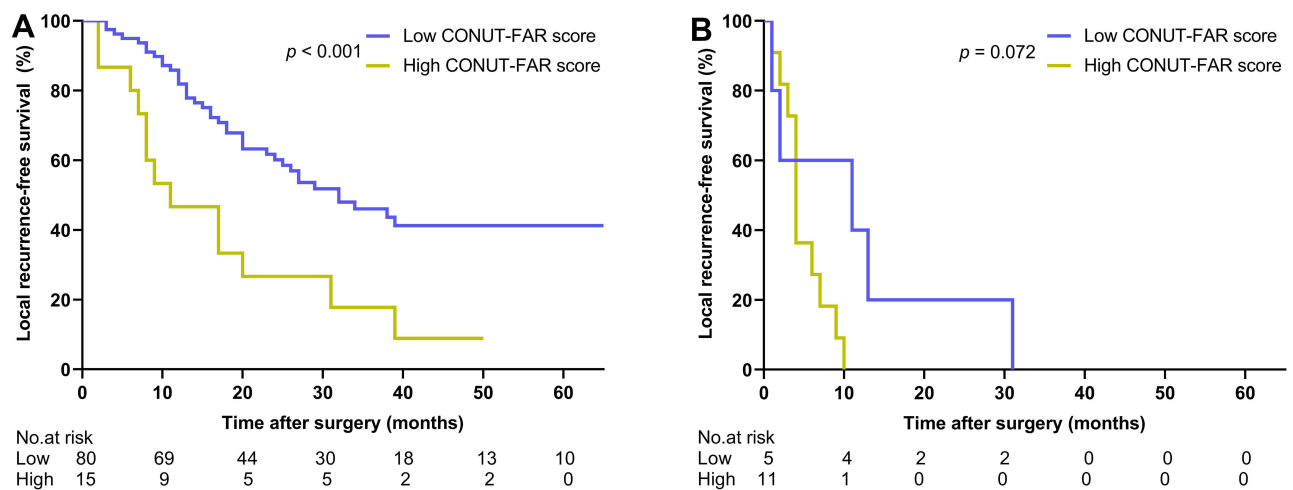

Figure 3 Subgroup analyses of LRFS in patients with high (> 11) and low (≤11) CONUT-FAR score according to the extent of resection. (**A**) LRFS in patients who received complete resection (p < 0.002); (**B**) LRFS in patients who received incomplete resection (p = 0.072).
Abbreviation: LRFS, local recurrence-free survival.

score, FAR, NLR, and PLR for predicting LRFS among RPLS patients. Moreover, the preoperative CONUT-FAR score was an independent predictor of LRFS. With the robust prognostic value in subgroup analyses of patients with different clinical characteristics, the CONUT-FAR score is a more valuable prognostic marker for RPLS

patients than other commonly used nutritional and inflammatory indicators.

Studies examining the association between the NLR or PLR and prognosis in STS have found widely divergent results.[12,14,16,25,26] In the present study, we confirmed that the NLR and PLR were not independently associated with
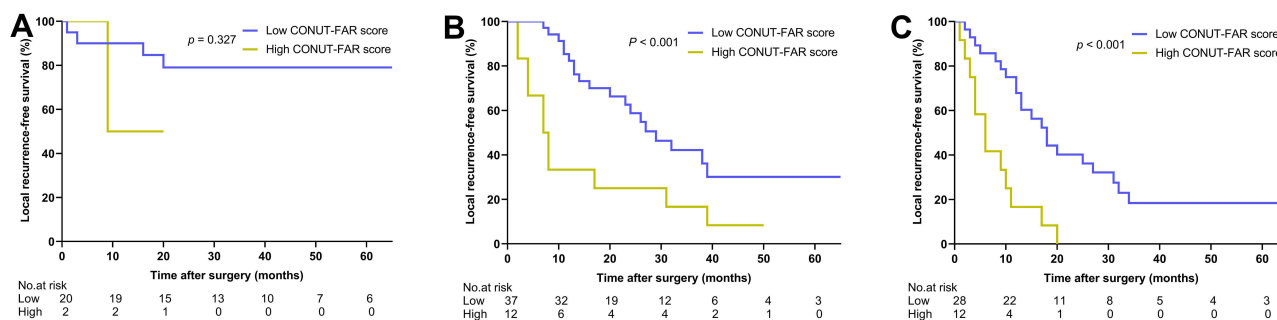
Figure 4 Subgroup analyses of LRFS in patients with high (> 11) and low (≤11) CONUT-FAR score according to FNCLCC grade. (**A**) LRFS in patients with G1 tumor (p = 0.327); (**B**) LRFS in patients with G2 tumor (p < 0.001); (**C**) LRFS in patients with G3 tumor (p < 0.001).
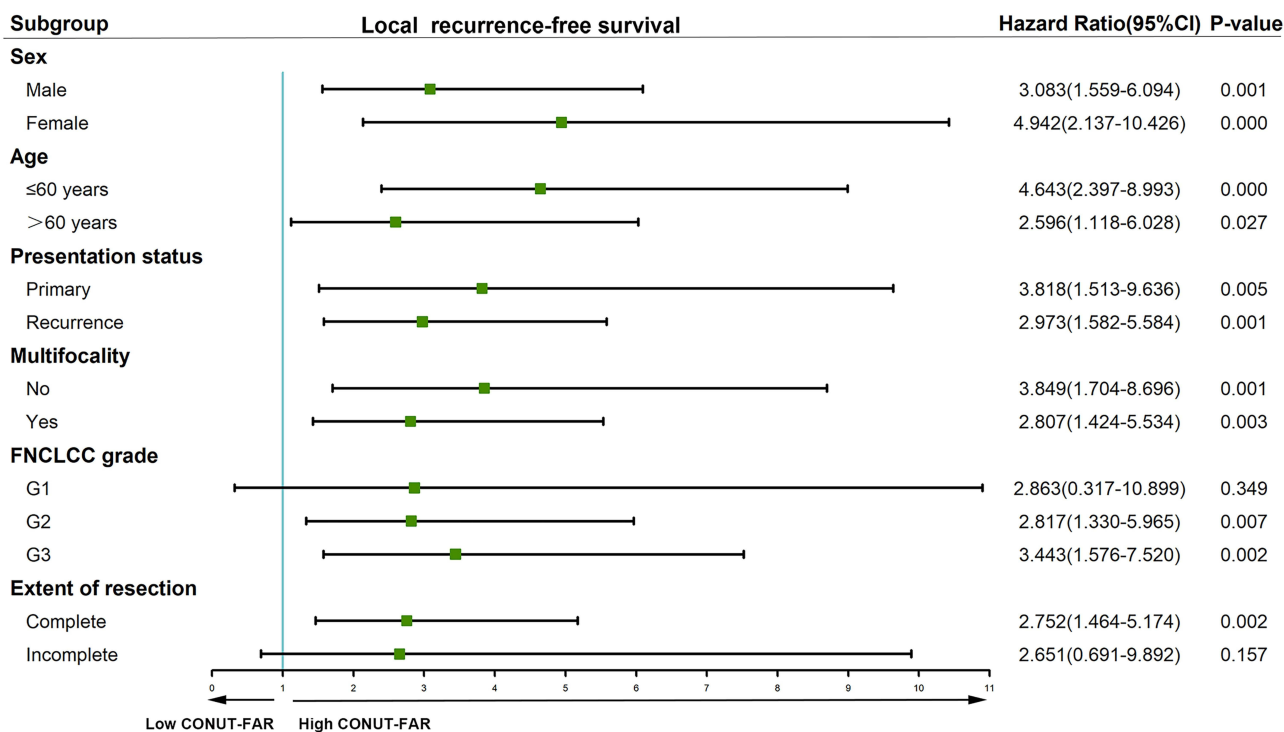**Abbreviation**: FNCLCC, French Federation of Cancer Centers Sarcoma Group.

Figure 5 Subgroup analyses using univariate Cox regression to assess the discrimination ability of the CONUT-FAR score for LRFS in patients with different clinical characteristics.
Abbreviations: FNCLCC, French Federation of Cancer Centers Sarcoma Group; 95% CI, 95% confidence interval.

LRFS among RPLS patients. In line with our observations, Nakamura et al examined the role of the pretreatment NLR and PLR in a cohort of 310 STS patients and observed that neither the NLR nor the PLR were independent prognostic factors for OS and DFS.[14] However, these results were not confirmed in other studies. In a cohort of 260 STS patients with limb soft tissue sarcomas, a high NLR (≥ 3.58) was significantly associated with decreased time to tumor recurrence and poor OS.[25] Similarly, in a cohort of 222 STS patients, a significantly worse disease-specific survival was observed in patients with a high PLR.[16] However,

RPLS patients accounted for only a small proportion of these cohorts.

The CONUT score is a nutritional evaluation score, based on three objective parameters (ALB, TLC, and TC).[13] Hypoalbuminemia has proved to be strongly associated with cachexia and poor survival.[8] TLC is found to be an effective detector to predict survival in sarcomas.[9] Serum TC level is correlated with tumor progression and patient survival in various cancers.[27] Therefore, the CONUT score is an effective readout of the nutritional condition. A study by Zhou et al indicated that the

CONUT score was superior to the NLR and PLR for predicting survival and was associated with OS and DFS in patients with STS.[17] A high-plasma fibrinogen level is secondary to increased systemic inflammatory responses.[28] A previous study revealed that an elevated FAR was a strong unfavorable prognostic factor in STS patients.[15] In our study, although elevated preoperative FAR and CONUT scores showed an association with decreased LRFS in univariate analysis, they were not significant in multivariate analysis. Our results probably differ from those of previous studies because those studies included various histologic and anatomic presentations of STS. This has intrinsic limitations, because the oncologic outcome of STS strongly correlates with both the site of tumor origin and the histologic subtype.[29–31] Therefore, researches focused on site-specific and histology-specific prognosis should be endorsed.

The combination of the CONUT score and FAR (CONUT-FAR score) exhibited superior prognostic ability for patients with RPLS after surgery than any single factor alone, as confirmed by the discriminatory power of time-dependent ROC analyses. In addition, the CONUT-FAR score was shown to be an independent prognostic indicator on multivariate analysis. Hence, we conclude that compared with the traditional nutritional and inflammatory markers, the CONUT-FAR score, which takes into account both the inflammatory status and nutritional status, could more accurately predict the LRFS of surgical RPLS patients.

FNCLCC grade and extent of resection are two critical and well-known prognostic factors of LRFS for RPLS patients.[32] In the present study, FNCLCC grade and extent of resection were also identified as independent predictors of LRFS. Moreover, in the subgroup analyses of the FNCLCC grade and extent of resection, an elevated CONUT-FAR score was associated with decreased LRFS among patients with high-grade tumors (G2 and G3) and those who received complete resection, and the CONUT-FAR score further stratified these patients into subgroups with significantly distinct LRFS. However, the CONUT-FAR score was not significantly associated with LRFS among patients with G1 tumors and those who received incomplete resection, probably due to the small number of patients with G1 tumors and the intrinsic tendency of recurrence after incomplete resection, respectively.

In this study, a high CONUT-FAR score (>11) was more likely to be found in patients who presented with recurrence ($p = 0.017$), had multifocality tumors ($p = 0.006$), or underwent incomplete resection ($P < 0.001$), suggesting that the CONUT-FAR score could reflect tumor progression in patients with RPLS. Additionally, the CONUT-FAR score showed good clinical utility in patients with different clinical characteristics. Further subgroup analysis revealed that a high CONUT-FAR score was associated with decreased LRFS in patients regardless of sex, age, presentation status, or multifocality. Because patients with a high CONUT-FAR score have a high risk of recurrence, more frequent follow-up and molecular analysis should be considered.

There are several limitations in this study. First, the optimal cut-off value of nutritional and inflammatory markers may fluctuate based on sample size, and could be affected by patient-specific variables, such as age, alcoholism, smoking status, mental issues, comorbidities, socioeconomic status, among others. Second, this study was a retrospective analysis and selection bias could not be avoided. Because none patients in our cohort received preoperative radiotherapy or chemotherapy, so our study lacks the power to give insight into how preoperative treatment might affect the association between nutritional and inflammatory markers and (LRFS) among surgical RPLS patients. Third, due to the low incidence of RPLS, the sample size is relatively limited. Further large-scale, multi-center studies should be performed to verify our findings.

Conclusion

In summary, the preoperative CONUT-FAR score is not only significantly associated with clinical characteristics but also a preferred predictor of LRFS for surgical RPLS patients, superior to the traditional nutritional and inflammatory markers. The CONUT-FAR score is efficient, economical, and has robust predictive ability, making it a valuable marker in monitoring local recurrence in RPLS patients after surgery. Our findings may help surgeons and oncologists to monitor disease progression accurately and to plan individualized postoperative treatment strategies.

Data Sharing Statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics

All patients provided written informed consent for participation in the study. The study protocol was in accordance with the Declaration of Helsinki, and the research ethics committee of Peking University Cancer Hospital approved this study (approval no. 2016KT41).

Disclosure

The authors declare that they have no conflicts of interest for this work.

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