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ABDOMINAL IMAGING

ORIGINAL ARTICLE



# Association of body composition and systemic inflammation for patients with locally advanced cervical cancer following concurrent chemoradiotherapy

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**PURPOSE**

Systemic inflammation and body composition are associated with survival outcomes of cancer patients. This study aimed to examine the combined prognostic value of systemic inflammatory markers and body composition parameters in patients with locally advanced cervical cancer (LACC).

**METHODS**

Patients who underwent concurrent chemoradiotherapy (CCRT) for LACC at a tertiary referral teaching hospital between January 2010 and January 2018 were enrolled. A predictive model was established based on systemic immune-inflammation index (SII) and computer tomography-derived visceral fat-to-muscle ratio (vFMR). Overall survival (OS) and progression-free survival (PFS) were assessed using the Kaplan–Meier method and Cox regression models. The model performance was assessed using discrimination, calibration, and clinical usefulness.

**RESULTS**

In total, 212 patients were enrolled. The SII and vFMR were closely related, and both independently predicted survival ($P < 0.05$). A predictive model was established based on the above biomarkers and included three subgroups: high-risk [both high SII (>828) and high vFMR (>1.1)], middle-risk (either high SII or high vFMR), and low-risk (neither high SII nor high vFMR). The 3-year OS (PFS) rates for low-, middle-, and high-risk patients were 90.5% (86.0%), 73.9% (58.4%), and 46.8% (36.1%), respectively ($P < 0.05$). This model demonstrated satisfactory predictive accuracy (area under the curve values for predicting 3-year OS and PFS were 0.704 and 0.718, respectively), good fit (Hosmer–Lemeshow tests: $P > 0.05$), and clinical usefulness.

**CONCLUSION**

Systemic inflammatory markers combined with body composition parameters could independently predict the prognosis of patients with LACC, highlighting the utilization of commonly collected indicators in decision-making processes.

**CLINICAL SIGNIFICANCE**

The SII and vFMR, as well as their composite indices, were promising prognostic factors in patients with LACC who received definitive CCRT. Future studies are needed to explore novel therapies to improve the outcomes in high-risk patients.

**KEYWORDS**

Cervical cancer, concurrent chemoradiotherapy, systemic inflammation, body composition, prognosis

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Cervical cancer is the fourth most frequently diagnosed malignancy in women, causing an estimated 342,000 deaths worldwide in 2020.[1] Patients with early stage disease generally have a favorable prognosis, whereas those with locally advanced disease experience a high risk of treatment failure.[2] Concurrent chemoradiotherapy (CCRT) remains the cornerstone of treatment for patients with locally advanced cervical cancer (LACC). However, even with the same tumor stage and similar treatments, there is significant heterogeneity in prognosis.[3] Great efforts have been made to improve survival, and the identification of factors affecting patient prognosis is crucial for ensuring proper treatment.

Cumulative evidence has demonstrated that systemic inflammation and sarcopenia are closely associated with poor prognosis in various malignant tumors.[4-6] Activation of the systemic inflammatory response plays a vital role in tumorigenesis, progression, and metastasis.[7] Pretreatment blood biomarkers [e.g., systemic immune-inflammation index (SII)] are commonly used to predict the prognosis of patients with cervical cancer.[8] Sarcopenia is characterized by the progressive loss of skeletal muscle mass and is associated with poor outcomes in patients with LACC.[9-11] A deeper understanding of systemic inflammation and sarcopenia, as well as their interplay, may facilitate more accurate prognostic stratification.

Visceral obesity has been associated with a poor prognosis in several gynecologic malignancies, including cervical cancer.[12,13] Visceral fat-to-muscle ratio (vFMR), which is based on body composition, has been reported to be associated with the prognosis of patients with ovarian cancer.[14] In this study, we examine the prognostic significance of vFMR and its association with the SII in patients with LACC.

**Main points**

- Both the systemic immune-inflammation index (SII) and computed tomography-derived visceral fat-to-muscle ratio (vFMR) were independent prognostic factors in patients with locally advanced cervical cancer who underwent concurrent chemoradiotherapy.
- The SII and vFMR were closely related; a higher SII was significantly associated with a higher vFMR and vice versa.
- The composite indices of SII and vFMR enabled accurate prognostic stratification and could serve as a complement to the International Federation of Gynecology and Obstetrics staging.

## Methods

### Patients and treatment

This retrospective study identified 234 patients with biopsy-confirmed LACC [IB2-IVA disease according to the 2009 International Federation of Gynecology and Obstetrics (FIGO) staging criteria] who underwent definitive radiotherapy (RT) or CCRT with curative intent at Xingtai Third Hospital between January 2010 and January 2018. Among them, 22 patients were excluded from the analysis because of concurrent malignant tumors of other organs (n = 2), incomplete clinical data (n = 5), absence of abdominal enhanced computed tomography (CT) images obtained before treatment (n = 13), or inflammatory conditions before treatment (e.g., acute infections) (n = 2). A total of 212 patients were included in the final analysis (Figure 1). This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Xingtai Third Hospital (approval number: 2023Y0668, date: 12/8/2023). Informed consent was not required due to the retrospective and observational nature of this study.

All patients underwent external beam radiotherapy (EBRT) of the pelvis and brachytherapy. The clinical target volume (CTV) covered the gross tumor, uterus, cervix, parametrium, upper half of the vagina, uterosacral ligaments, and pelvic lymph node region. The para-aortic region was also covered in the CTV when there was evidence of para-aortic lymph node involvement or enough of a risk of microscopic disease (e.g., common iliac node involvement).[15] Intensity-modulated RT was used for external irradiation, which was planned using the RT treatment planning system (Varian Eclipse software; Varian Medical Systems Inc., Palo Alto, CA, USA). The EBRT was administered with a fraction of 1.8 Gy for a total dose of 45–50.4 Gy. Intracavitary brachytherapy was prescribed to point A with a fraction of 6 Gy for a total dose of 30–36 Gy. Cisplatin-based chemotherapy was administered concurrently with RT (40 mg/m$^2$ intravenously weekly). After treatment, all patients were followed up every 3 months for the first 2 years and every 6 months for the next 3 years. The final follow-up evaluation was conducted in January 2021.

### Definitions

The primary outcomes of this study included overall survival (OS) and progression-free survival (PFS), with the former defined as the time interval from the date of diagnosis to death from any cause or last follow-up, and the latter as the interval from the date of diagnosis to the date of disease progression or recurrence.

Laboratory parameters were obtained within 1 week prior to treatment. The SII was calculated as neutrophil count × platelet count/lymphocyte count.[16] Pre-treatment CT images were used for body composition

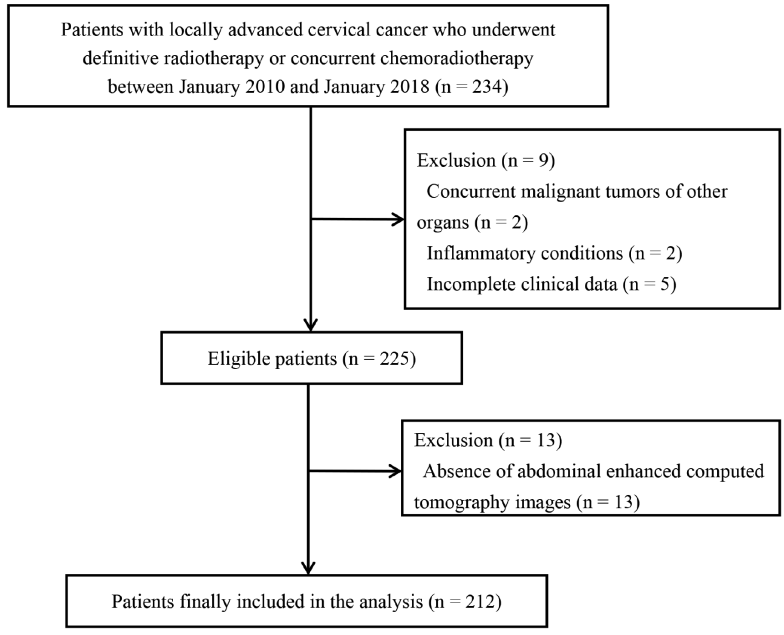


**Figure 1.** Diagram of study population.

measurements. A single CT slice of the third lumbar vertebra was selected to quantify the fat and muscle compartments. These images were analyzed by an experienced radiologist who was blinded to patient information using the sliceOmatic software (TomoVision). According to the standard density thresholds, skeletal muscle area was identified with a radiation density ranging from −29 to 150 Hounsfield units (HU), and visceral adipose area was identified with a radiation density ranging from −150 to −50 HU (Supplementary Figure 1). Both of the areas (in centimeters squared) were converted into indexes (skeletal muscle index and visceral adipose index) after dividing by height in meters squared. The vFMR was calculated by dividing the visceral adipose area by the skeletal muscle area.[14]

### Statistical analysis

Data were described as frequencies (percentages) for categorical variables and means [standard deviation (SD)] or medians [interquartile range (IQR)] for continuous variables. The Shapiro–Wilk test was used to verify the normality of variable distribution. Inter-group differences were evaluated using the chi-square test or t-test. The optimal cut-off values of the SII and vFMR for OS were determined by selecting the minimum *P* value with the maximum chi-square value in all possible subdivisions of the populations using X-tile software.[17] Spearman's coefficient was calculated to evaluate the correlation between SII and vFMR. Moreover, OS and PFS were evaluated using the Kaplan–Meier method, and differences were compared using the log-rank test. Multivariate Cox regression models were used to identify the independent risk factors for OS and PFS. Variables with a *P* value of <0.1 in the univariate analysis were included in the multivariate analysis. Receiver operating characteristic curves were used to evaluate the predictive accuracy by calculating the area under the curve (AUC). The Hosmer–Lemeshow test was used to evaluate the goodness of fit, and a *P* value of >0.05 was considered a good fit. Decision curve analysis was used to evaluate clinical usefulness by calculating the net benefit of prediction models at different threshold levels.[18] This allowed for the comparison of net benefits between different models to select the optimal model.

Statistical significance was set at two-tailed $P < 0.05$. All statistical analyses were performed using R software, version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Clinicopathological characteristics

The clinicopathological characteristics of the study cohort (n = 212) are summarized in Table 1. The mean (SD) age of the patients was 58.8 (10.6) years, and the mean (SD) body mass index was 23.1 (3.1) kg/m$^2$. Most of the patients (85.8%) underwent CCRT.

### Overall survival and progression-free survival

The median (IQR) follow-up duration was 47 (40–63) months. The 3-year OS and PFS rates for all the patients were 82.1% and 73.6%, respectively. The optimal cutoff values of SII and vFMR were calculated to be 828 and 1.1, respectively (Supplementary Figure 2). A higher SII (>828) was significantly associated with poorer OS [88.3% vs. 62.1%; hazard ratio (HR): 3.399, 95% confidence interval (CI): 1.924–6.003, $P < 0.001$] and PFS (80.8% vs. 49.3%; HR: 3.347, 95% CI: 2.005–5.587, $P < 0.001$). Patients with a higher vFMR (>1.1) also exhibited significantly poorer OS (86.2% vs. 65.4%; HR: 3.443, 95% CI: 1.944–6.095, $P < 0.001$) and PFS (80.4% vs. 48.3%; HR: 3.398, 95% CI: 2.025–5.701, $P < 0.001$). Factors significantly associated with survival also included histology, FIGO stage, pelvic lymph node, squamous cell carcinoma antigen level, and CCRT ($P < 0.05$). In the multivariate analysis, SII and vFMR were both independent risk factors for OS and PFS ($P < 0.05$) (Table 2).

### Correlation between systemic immune-inflammation and visceral fat-to-muscle ratio

There was a significant linear association between the SII and vFMR (Spearman $r = 0.198$, $P = 0.004$) (Figure 2). A higher SII was

**Table 1.** Clinicopathological variables

| Characteristics | Overall (n = 212) |
|---|---|
| **Age, mean ± SD, yrs** | 58.8 ± 10.6 |
| **BMI, mean ± SD, kg/m$^2$** | 23.1 ± 3.1 |
| **ECOG performance status, n (%)** | |
| 0 | 139 (65.6) |
| 1 | 73 (34.4) |
| **Histology, n (%)** | |
| Squamous cell carcinoma | 193 (91.0) |
| Adenocarcinoma | 19 (9.0) |
| **FIGO stage, n (%)** | |
| IB-II | 158 (74.5) |
| III-IVA | 54 (25.5) |
| **Pelvic lymph node, n (%)** | |
| Negative | 106 (50.0) |
| Positive | 106 (50.0) |
| **SCC-Ag level, n (%)** | |
| <10 ng/mL | 146 (68.9) |
| >10 ng/mL | 66 (31.1) |
| **Concurrent chemotherapy, n (%)** | |
| No | 30 (14.2) |
| Yes | 182 (85.8) |
| **SII level, median (IQR)** | 518.5 (358.2–835.1) |
| **SMI, median (IQR), cm$^2$/m$^2$** | 46.7 (39.1–54.0) |
| **VAI, median (IQR), cm$^2$/m$^2$** | 32.7 (13.4–53.9) |
| **vFMR level, median (IQR)** | 0.68 (0.34–1.10) |

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; SCC-Ag, squamous cell carcinoma antigen; SII, systemic immune-inflammation index; SMI, skeletal muscle index; VAI, visceral adipose index; vFMR, visceral fat-to-muscle ratio; SD, standard deviation; IQR, interquartile range.

significantly associated with a higher vFMR (35.2% vs. 17.7%, $P = 0.008$); however, there were no significant associations between SII and other clinicopathological characteristics ($P > 0.05$) (Supplementary Table 1). Patients with a higher vFMR were more likely to be older (mean: 63.5 vs. 57.4 years, $P < 0.001$), and have a more advanced FIGO stage (36.2% vs. 22.4%, $P = 0.056$), pelvic lymph node involvement (61.7% vs. 46.7%, $P = 0.069$), and a higher SII score (40.4% vs. 21.2%, $P = 0.008$) (Supplementary Table 2).

### Establishment of the systemic immune-inflammation and fat-to-muscle ratio score

The SII and vFMR were combined and four subgroups were generated. Patients with a higher SII and vFMR exhibited the worst survival, whereas those with a lower SII and vFMR survived the longest ($P < 0.001$). The OS and PFS of patients with a higher SII and lower vFMR were similar to those of patients

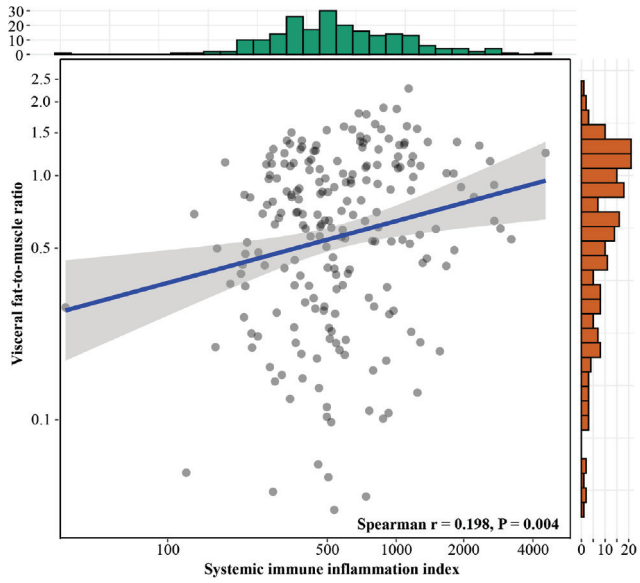


**Figure 2.** Scatter plot between systemic immune-inflammation and visceral fat-to-muscle ratio. Both parameters were normalized by natural logarithmic (ln) transformation.

**Table 2.** Univariate and multivariate analysis of clinicopathologic variables in relation to overall survival and progression-free survival

| Variables | Overall survival | | | | Progression-free survival | |
|---|---|---|---|---|---|---|
| | Univariate | | Multivariate | | Multivariate | |
| | HR (95% CI) | *P* value | HR (95% CI) | *P* value | HR (95% CI) | *P* value |
| Age, per 1 year | 1.008 (0.981–1.036) | 0.550 | | | | |
| **Histology** | | 0.028 | | 0.579 | | 0.134 |
| Squamous cell carcinoma | Reference | | Reference | | Reference | |
| Adenocarcinoma | 2.235 (1.097–5.015) | | 1.259 (0.558–2.845) | | 1.722 (0.846–3.506) | |
| **FIGO stage** | | <0.001 | | 0.001 | | 0.001 |
| IB-II | Reference | | Reference | | Reference | |
| III-IVA | 5.019 (2.820–8.931) | | 2.985 (1.534–5.809) | | 2.810 (1.546–5.107) | |
| **Pelvic lymph node** | | 0.005 | | 0.158 | | 0.062 |
| Negative | Reference | | Reference | | Reference | |
| Positive | 2.398 (1.302–4.416) | | 1.621 (0.829–3.169) | | 1.762 (0.973–3.190) | |
| **SCC-Ag level** | | 0.017 | | 0.210 | | 0.848 |
| <10 ng/mL | Reference | | Reference | | Reference | |
| >10 ng/mL | 2.004 (1.135–3.536) | | 1.468 (0.806–2.673) | | 1.055 (0.608–1.833) | |
| **Concurrent chemotherapy** | | 0.027 | | 0.293 | | 0.548 |
| No | Reference | | Reference | | Reference | |
| Yes | 0.467 (0.238–0.918) | | 0.672 (0.320–1.410) | | 0.813 (0.414–1.597) | |
| **SII level** | | <0.001 | | <0.001 | | <0.001 |
| <828 | Reference | | Reference | | Reference | |
| >828 | 3.399 (1.924–6.003) | | 2.976 (1.647–5.378) | | 2.776 (1.629–4.728) | |
| **vFMR level** | | <0.001 | | 0.049 | | 0.031 |
| <1.1 | Reference | | Reference | | Reference | |
| >1.1 | 3.443 (1.944–6.095) | | 2.803 (1.005–7.817) | | 2.689 (1.093–6.616) | |
| **SMI, per 1 $cm^2/m^2$** | 0.985 (0.956–1.015) | 0.327 | | | | |
| **VAI, per 1 $cm^2/m^2$** | 1.015 (1.004–1.026) | 0.008 | 0.996 (0.976–1.015) | 0.660 | 0.996 (0.979–1.014) | 0.663 |

FIGO, International Federation of Gynecology and Obstetrics; SCC-Ag, squamous cell carcinoma antigen; SII, systemic immune-inflammation index; vFMR, visceral fat-to-muscle ratio; SMI, skeletal muscle index; VAI, visceral adipose index; HR, hazard ratio; CI, confidence interval.

with a lower SII and higher vFMR (Figure 3a, c). Based on the above results, we defined three risk groups according to the SII and vFMR [systemic immune-inflammation and fat-to-muscle ratio (SFMR)]: patients with both lower SII and vFMR were regarded as low-risk, patients with either a higher SII or vFMR were regarded as middle-risk, and patients with both higher SII and vFMR were regarded as high-risk. Patients with a higher risk according to SFMR score were more likely to be older ($P = 0.013$) and obese ($P = 0.065$), and have a more advanced FIGO stage ($P = 0.081$) (Supplementary Table 3).

### Prognostic value of systemic immune-inflammation and fat-to-muscle ratio

The 3-year OS rates for low-, middle-, and high-risk patients were 90.5%, 73.9%, and 46.8%, respectively ($P < 0.05$); the 3-year PFS rates for low-, middle-, and high-risk patients were 86.0%, 58.4%, and 36.1%, respectively ($P < 0.05$) (Figure 3b, d). After adjusting for FIGO stage and lymph node status, SFMR was found to be an independent risk factor for both OS and PFS (middle-risk vs. low-risk: HR: 3.783, 95% CI: 2.095–6.829; high-risk vs. low-risk: HR: 6.062, 95% CI: 2.888–12.723; $P < 0.001$) (Table 3).

The AUC values of SFMR for predicting 1-year, 3-year, and 5-year OS were 0.847, 0.704, and 0.730, respectively. The AUC values of SFMR for predicting 1-year, 3-year, and 5-year PFS were 0.723, 0.718, and 0.728, respectively (Figure 4). Hosmer–Lemeshow tests showed that SFMR was a good fit for predicting OS and PFS ($P = 0.975$ and 0.432, respectively). As depicted in Figure 5, the curve corresponding to the SFMR combined with FIGO stages was above, and the area under the decision curve it formed with the "treat none" and "treat all" lines was larger than that of the FIGO stages alone. Therefore, the clinical model consisting of the SFMR and FIGO stages has a higher net benefit compared with the FIGO stages, making it the superior model.

## Discussion

This is the first study to demonstrate the prognostic value of vFMR and its combined effect with the SII in patients with LACC undergoing definitive CCRT. Moreover, we found that the co-occurrence of a high SII and vFMR (SFMR: high-risk) was related to a six-fold risk of death or progression in these patients. Our results suggest that these two easily identifiable biomarkers have great potential for prognostic stratification.

Excessive or persistent systemic inflammation, represented by the ratio of circulating blood cell counts, plays a significant role in cancer development and progression.[19] Calculated using peripheral neutrophil, lymphocyte, and platelet counts, SII has been demonstrated to be a powerful prognostic factor for various human malignancies.[20] Cumulative evidence has indicated a significant association between the SII and survival in cervical cancer.[16,21,22] In this study, it was found that a higher SII was independently associated with poorer OS and PFS. These findings can be attributed to the prognostic value of each SII component. Lymphocytes play a vital role in cell-mediated immune responses and secrete antitumor cytokines. Therefore, lymphocytopenia can lead to an unfavorable prognosis.[23] Second, neutrophils may promote a tumor-favorable environment by promoting neovascular-

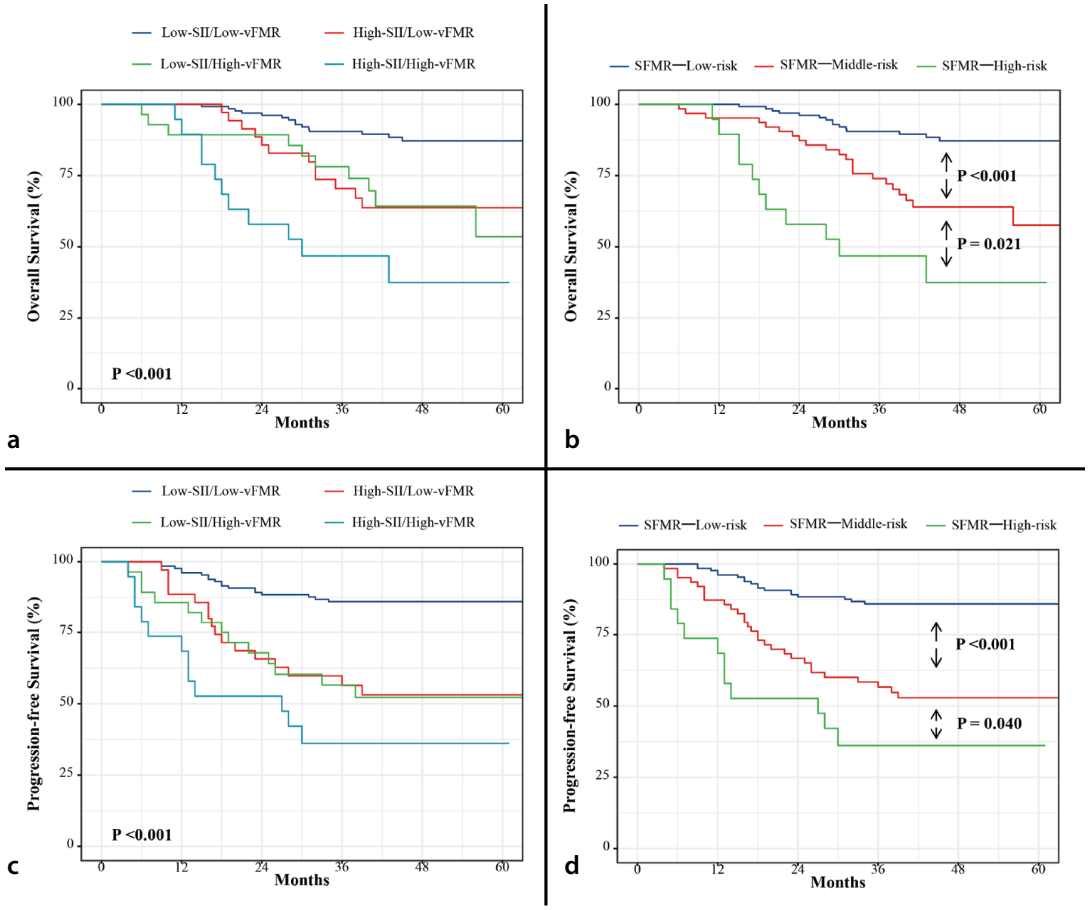


**Figure 3.** Kaplan–Meier curves for overall survival **(a+b)** and progression-free survival **(c+d)** according to the combination of systemic immune-inflammation (SII) and visceral fat-to-muscle ratio (vFMR) **(a+c)** and systemic immune-inflammation and fat-to-muscle ratio (SFMR) **(b+d)**. The *P* values were calculated using the log-rank test.

ization and suppressing lymphocyte-mediated cytolysis.[24] Third, an increase in the number of platelets can directly promote tumor growth, invasion, and angiogenesis.[25] Hence, the SII, which is based on the three aforementioned types of blood cells, can more effectively demonstrate the equilibrium between antitumor and pro-tumor immune statuses.

Sarcopenia is an early manifestation of cancer and cachexia. Cumulative studies have demonstrated that pretreatment sarcopenia is significantly associated with survival outcomes in patients with gastrointestinal[26] and gynecological tumors.[27] The prognostic value of pretreatment sarcopenia has also been extensively investigated in LACC, but with mostly negative results.[9,28,29] In addition, previous studies have reported the prognostic significance of the visceral fat area in various cancers.[30-32] Similarly, the prognostic value of adiposity in patients with LACC remains controversial.[9,22] We speculated that considering individual muscle or fat parameters alone might not accurately describe the distribution of body composition, which could weaken the prognostic prediction ability. Therefore, we investigated the combined index of muscle and fat areas, vFMR, and confirmed its prognostic value. A feasible explanation is that patients with sarcopenia and/or visceral obesity are more likely to experience treatment-related adverse events, leading to low compliance with planned treatments.[33-35] The association between vFMR and CCRT response should be investigated further.

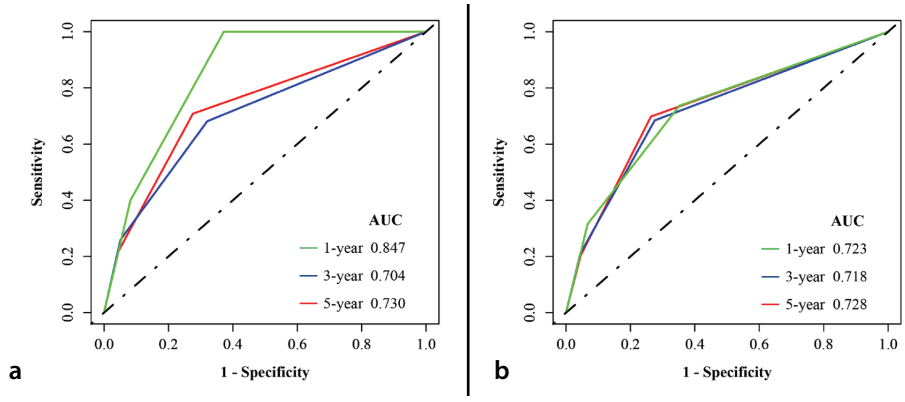


**Figure 4.** Time-dependent receiver-operating characteristic curves and area under the curves (AUCs) for predicting overall survival **(a)** and progression-free survival **(b)** by systemic immune-inflammation and fat-to-muscle ratio.

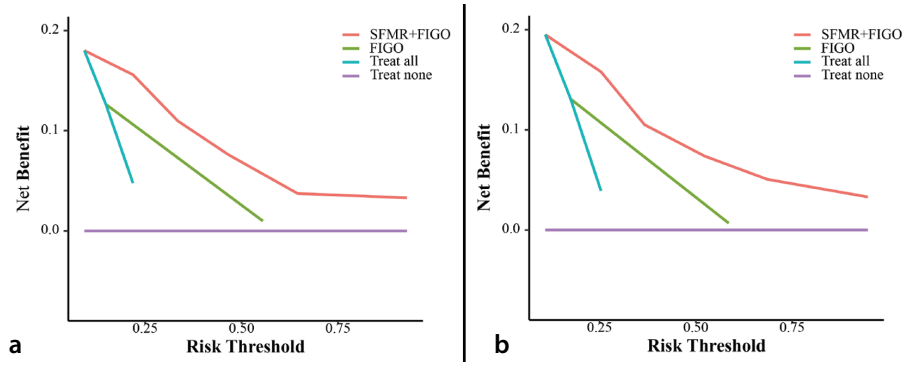


**Figure 5.** Decision curve analysis for overall survival **(a)** and progression-free survival **(b)**.

Systemic inflammation is the basis of and is intensified by sarcopenic obesity, forming a mutually reinforcing cycle that supports cancer progression. For instance, several cytokines released by inflammatory cells (e.g., interleukin 6) can regulate skeletal muscle metabolism, leading to protein degradation and decreased synthesis.[36] Excess adipose tissue is closely associated with low-grade systemic inflammation, which is characterized by abnormal cytokine production and muscle degradation.[37,38] Moreover, skeletal muscle wasting can drive local inflammation, systemic inflammation, and muscle degradation.[39] Our results also showed that higher vFMR was significantly associated with higher SII. The combination of the vFMR and SII better reflects the synergistic effect of systemic inflammation and sarcopenic obesity and exhibits promising prognostic significance.

This study has some limitations that need to be considered. First, as this was a retrospective, single-center study, selection bias and confounding factors were inevitable. Second, because all patients were Asian, the generalizability of our findings should be further confirmed. Third, although SII can possibly be influenced by various med-

**Table 3.** Multivariate analysis of clinical variables in relation to overall survival and progression-free survival

| Variables | Progression-free Survival | | |
|---|---|---|---|
| | HR (95% CI) | HR (95% CI) | *P* value |
| **FIGO stage** | | | <0.001 |
| IB-II | Reference | Reference | |
| III-IVA | 3.653 (1.983–6.730) | 3.457 (1.996–5.989) | |
| **Pelvic lymph node** | | | 0.114 |
| Negative | Reference | Reference | |
| Positive | 1.593 (0.839–3.026) | 1.594 (0.893–2.844) | |
| **SFMR** | | | <0.001 |
| Low-risk | Reference | Reference | |
| Middle-risk | 3.158 (1.633–6.108) | 3.783 (2.095–6.829) | |
| High-risk | 6.341 (2.873–13.996) | 6.062 (2.888–12.723) | |

FIGO, International Federation of Gynecology and Obstetrics; HR, hazard ratio; CI, confidence interval; SFMR, systemic immune-inflammation and fat-to-muscle ratio.

ical conditions, this inflammatory marker was calculated through routine laboratory test results. Other markers of systemic inflammation (e.g., C-reactive protein) were available for few patients and therefore not used. Fourth, laboratory blood and CT-derived body composition parameters were obtained from a single time point at the initial diagnosis. In future studies, data from subsequent CT scans should be incorporated to explore the prognostic significance of the changes in these markers. Finally, all patients received point A-based brachytherapy in this study. As image-guided brachytherapy is the current standard of treatment, further validation of our findings is needed in patients undergoing this procedure.

In conclusion, despite the above limitations, our study demonstrated that the SII and vFMR, as well as their composite indices, were independent prognostic factors in patients with LACC who received definitive CCRT. Future studies are needed to explore novel therapies to improve the outcomes in high-risk patients.

### Conflict of interest disclosure

The authors declared no conflicts of interest.

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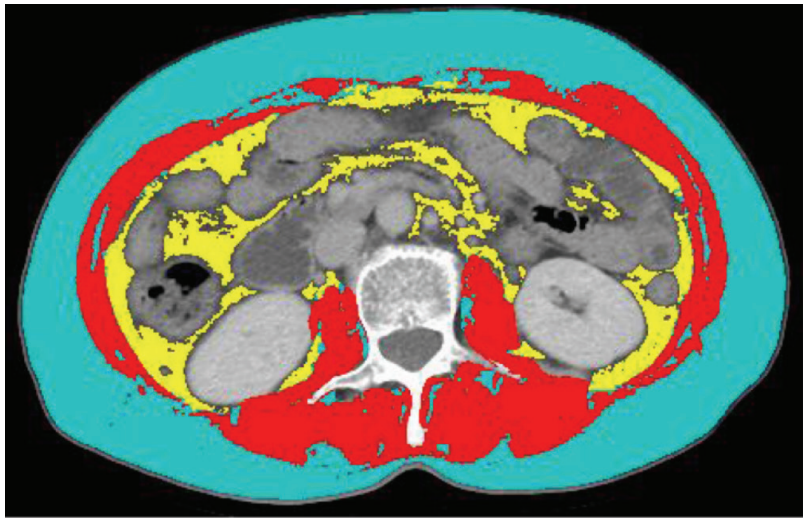
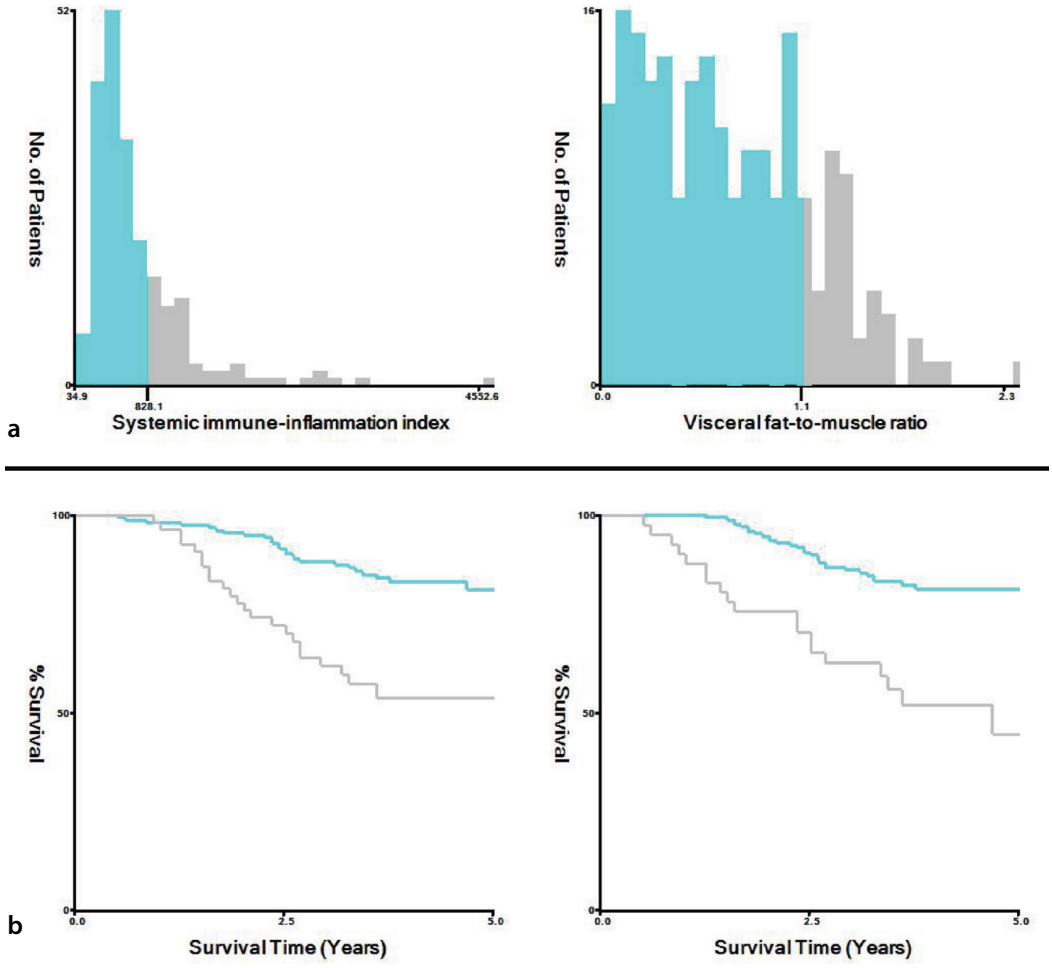


**Supplementary Figure 1.** Example of body composition analysis for measurement of tissue areas. The blue area represents subcutaneous adipose, the red area represents skeletal muscle, and the yellow area represents visceral adipose.




**Supplementary Figure 2.** X-tile software analysis to determine the optimal cut-off values for systemic immune-inflammation index (left) and visceral fat-to-muscle ratio (right). **(a)** The histogram of the both parameters. **(b)** Kaplan-Meier analysis for overall survival.

**Supplementary Table 1.** The relationship between systemic immune-inflammation and clinicopathological parameters

| Characteristics | SII ≤828 (n = 158) | SII >828 (n = 54) | *P* value |
|---|---|---|---|
| Age, mean ± SD, yrs | 58.6 ± 10.4 | 59.4 ± 11.1 | 0.607 |
| BMI, mean ± SD, kg/m$^2$ | 22.9 ± 3.1 | 23.7 ± 3.0 | 0.116 |
| **ECOG performance status, n (%)** | | | 0.144 |
| 0 | 108 (68.4) | 31 (57.4) | |
| 1 | 50 (31.6) | 23 (42.6) | |
| **Histology, n (%)** | | | 0.522 |
| Squamous cell carcinoma | 145 (91.8) | 48 (88.9) | |
| Adenocarcinoma | 13 (8.2) | 6 (11.1) | |
| **FIGO stage, n (%)** | | | 0.417 |
| IB-II | 120 (75.9) | 38 (70.4) | |
| III-IVA | 38 (24.1) | 16 (29.6) | |
| **Pelvic lymph node, n (%)** | | | 1.000 |
| Negative | 79 (50.0) | 27 (50.0) | |
| Positive | 79 (50.0) | 27 (50.0) | |
| **SCC-Ag level, n (%)** | | | 0.949 |
| ≤10 ng/mL | 109 (69.0) | 37 (68.5) | |
| >10 ng/mL | 49 (31.0) | 17 (31.5) | |
| **vFMR level, n (%)** | | | 0.008 |
| ≤1.1 | 130 (82.3) | 35 (64.8) | |
| >1.1 | 28 (17.7) | 19 (35.2) | |

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; SCC-Ag, squamous cell carcinoma antigen; vFMR, visceral fat-to-muscle ratio; SD, standard deviation; SII, systemic immune-inflammation.

**Supplementary Table 2.** The relationship between visceral fat-to-muscle ratio and clinicopathological parameters

| Characteristics | vFMR ≤ 1.1 (n = 165) | vFMR > 1.1 (n = 47) | *P* value |
|---|---|---|---|
| Age, mean ± SD, yrs | 57.4 ± 10.9 | 63.5 ± 7.9 | <0.001 |
| BMI, mean ± SD, kg/m$^2$ | 22.1 ± 2.9 | 22.1 ± 3.7 | 0.989 |
| **ECOG performance status, n (%)** | | | 0.949 |
| 0 | 108 (65.5) | 31 (66.0) | |
| 1 | 57 (34.5) | 16 (34.0) | |
| **Histology, n (%)** | | | 0.648 |
| Squamous cell carcinoma | 151 (91.5) | 42 (89.4) | |
| Adenocarcinoma | 14 (8.5) | 5 (10.6) | |
| **FIGO stage, n (%)** | | | 0.056 |
| IB-II | 128 (77.6) | 30 (63.8) | |
| III-IVA | 37 (22.4) | 17 (36.2) | |
| **Pelvic lymph node, n (%)** | | | 0.069 |
| Negative | 88 (53.3) | 18 (38.3) | |
| Positive | 77 (46.7) | 29 (61.7) | |
| **SCC-Ag level, n (%)** | | | 0.625 |
| ≤10 ng/mL | 115 (69.7) | 31 (66.0) | |
| >10 ng/mL | 50 (30.3) | 16 (34.0) | |
| **SII level, n (%)** | | | 0.008 |
| ≤550.1 | 130 (78.8) | 28 (59.6) | |
| >550.1 | 35 (21.2) | 19 (40.4) | |

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; SCC-Ag, squamous cell carcinoma antigen; SII, systemic immune-inflammation index; SD, standard deviation; vFMR, visceral fat-to-muscle ratio.

**Supplementary Table 3.** The relationship between the combination of systemic immune-inflammation and visceral fat-to-muscle ratio and clinicopathological parameters

| Characteristics | SFMR | | | $P_{linear}$ value |
|---|---|---|---|---|
| | Low-risk (n = 130) | Middle-risk (n = 63) | High-risk (n = 19) | |
| **Age, n (%)** | | | | 0.013 |
| <65 yrs | 95 (73.1) | 33 (52.4) | 11 (57.9) | |
| ≥65 yrs | 35 (26.9) | 30 (47.6) | 8 (42.1) | |
| **BMI, n (%)** | | | | 0.065 |
| <25 kg/m$^2$ | 99 (76.2) | 43 (68.3) | 11 (57.9) | |
| ≥25 kg/m$^2$ | 31 (23.8) | 20 (31.7) | 8 (42.1) | |
| **ECOG performance status, n (%)** | | | | 0.352 |
| 0 | 89 (68.5) | 38 (60.3) | 12 (63.2) | |
| 1 | 41 (31.5) | 25 (39.7) | 7 (36.8) | |
| **Histology, n (%)** | | | | 0.475 |
| Squamous cell carcinoma | 119 (91.5) | 58 (92.1) | 16 (84.2) | |
| Adenocarcinoma | 11 (8.5) | 5 (7.9) | 3 (15.8) | |
| **FIGO stage, n (%)** | | | | 0.081 |
| IB-II | 102 (78.5) | 44 (69.8) | 12 (63.2) | |
| III-IVA | 28 (21.5) | 19 (30.2) | 7 (36.8) | |
| **Pelvic lymph node, n (%)** | | | | 0.250 |
| Negative | 69 (53.1) | 29 (46.0) | 8 (42.1) | |
| Positive | 61 (46.9) | 34 (54.0) | 11 (57.9) | |
| **SCC-Ag level, n (%)** | | | | 0.725 |
| ≤10 ng/mL | 90 (69.2) | 44 (69.8) | 12 (63.2) | |
| >10 ng/mL | 40 (30.8) | 19 (30.2) | 7 (36.8) | |

BMI, body mass index; ECOG, Eastern Cooperative Oncology Group; FIGO, International Federation of Gynecology and Obstetrics; SCC-Ag, squamous cell carcinoma antigen; SFMR, systemic immune-inflammation and fat-to-muscle ratio