Systemic immune-inflammation index as a prognostic marker in patients with newly diagnosed metastatic nasopharyngeal carcinoma: a propensity score-matched study

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Background: Systemic immune-inflammation index (SII) is significantly associated with poor survival in variety of cancers. However, SII has not yet been investigated in patients with newly diagnosed metastatic nasopharyngeal carcinoma (mNPC). Thus, our aim is to explore the role of SII in metastatic Nasopharyngeal Carcinoma.

Methods: Two hundred and forty-three patients with newly diagnosed mNPC were retrospectively enrolled. The Kaplan-Meier analysis and Cox regression analysis was performed to evaluate the prognostic value of SII in overall survival (OS) and progression-free survival (PFS). Heterogeneity of factors was balanced by using propensity score-matched (PSM) analysis (1:1 for high SII versus low SII).

Results: Kaplan-Meier analysis showed that patients with high SII were associated with poor median OS (18.0 vs. 36.0 m, P<0.001) and PFS (10.0 vs. 22.0 m, P<0.001) in mNPC. The Cox regression analysis suggested that high SII was a prognostic factor for OS (HR 1.75, 95% CI: 1.22–2.52, P=0.001) and PFS (HR 1.69, 95% CI: 1.22–2.35, P=0.002). PSM analysis still confirmed that SII was an independent marker for OS (HR 1.86, 95% CI: 1.22–2.83, P=0.004) and PFS (HR 1.84, 95% CI: 1.23–2.77, P=0.003).

Conclusions: SII is an independent prognostic biomarker for poor OS and PFS in patients with newly diagnosed mNPC and might be a promising tool for guiding treatment strategy decisions.

Keywords: Nasopharyngeal carcinoma (NPC); systemic immune-inflammation index (SII); biomarker; prognosis

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Introduction

Nasopharyngeal carcinoma (NPC) is a common cancer in southern China, with an annual incidence of roughly 15–30 per 100,000 (1). Approximately 6% of NPC patients develop metastases at the time of diagnosis (2), indicating a poor prognosis. The median OS of metastatic NPC (mNPC) is only 15.5 or 21.4 months when receiving chemotherapy alone or radiotherapy combined with chemotherapy, respectively (3). With the advance of intensity modulated radiotherapy (IMRT), the overall survival prognosis for early or locally advanced NPC has improved significantly. However, patients with mNPC appear to benefit the least from IMRT (4). Therefore, it is of the utmost importance to explore novel prognostic markers, such as serum lactic dehydrogenase, haemoglobin and alkaline phosphatase, to better improve stratification and treatment in patients with
It is now well acknowledged that inflammation play a crucial role in the proliferation and progression of cancer (7,8). And inflammation is thought to be a hallmark of cancer, presenting a tumor-promoting inflammatory microenvironment and a reaction of host immune response (9,10). Of note, systemic inflammation, including small inflammatory proteins, acute-phase proteins, circulating cytokines and circulating immune cells, is a good biomarker of prognosis in cancers (7). Recently, several systemic inflammation markers, like platelet lymphocyte ratio (PLR), neutrophil lymphocyte ratio (NLR), derived NLR (dNLR) and systemic immune-inflammation index (SII) have been found to a novel prognostic marker in a variety of cancers (11,12), including NPC (13-18). However, SII has not been reported in mNPC. Therefore, the aim of this study was to evaluate the prognostic value of SII in newly diagnosed mNPC patients.

**Methods**

**Patients**

From January 2007 to July 2015, 243 patients with metastatic Nasopharyngeal carcinoma (mNPC) were enrolled in Fujian Cancer Hospital, China. Inclusion criteria included: (I) patients were newly and histologically diagnosed with mNPC; (II) patients should receive radiotherapy or at least one cycle of chemotherapy. Exclusion criteria included: (I) patients with NPC developed metastasis after first-line therapy; (II) patients with other types of cancer; (III) patients refuse any anti-tumor treatment all the way, including radiotherapy, chemotherapy or best support care; (IV) patients who were lost in the follow up.

All patients received a complete pre-treatment evaluation, including medical history and physical examination, nasopharyngeal fiberoptic endoscopy examination, standard hematology and blood biochemistry tests, magnetic resonance imaging (MRI) or computed tomography (CT) scan of the head and neck, chest X-ray photography, ultrasound examination of the liver and abdomen and whole-body bone scan. Thoracic and abdominal CT scans, MRI of the bone or liver and positron emission tomography/computed tomography (PET/CT) were applied when clinically indicated. This study was approved by the Ethical Review Committee of Fujian Cancer Hospital (No. SQ2019-031-01). All of the participants signed an informed consent form.

Peripheral blood was administrated and tested for SII before radiotherapy. The SII was defined as follows: $SII = P \times N/L$, where P, N and L was the absolute preoperatively peripheral platelet, neutrophil and lymphocyte counts, respectively (19).

**Clinical data and treatment**

Among 243 patients, 55 (22.6%) patients suffered from multiple organ metastases. One hundred and five and 112 patients received two-dimensional radiotherapy (2DRT) or IMRT of the primary tumor, respectively. The planning and delivery of 2DRT and IMRT were applied as previous study (20,21). The median dose was 69.75 Gy (range, 6–79.55 Gy) in the above 217 patients. 100% patients received at least one induction chemotherapy. The regimen of induction chemotherapy was platinum-based two or three drugs combination chemotherapy. Eighty-four (34.6%) patients received concurrent chemoradiotherapy, and 100 (41.2%) patients received concurrent chemotherapy. As to the metastatic foci, 64 patients with bone metastasis and 3 patients with distant lymph nodes were treated with local radiotherapy. Percutaneous alcohol injection therapy was applied to 4 patients with localized liver metastatic lesions. 8 patients underwent radiotherapy or resection of metastatic lung lesions.

**Follow-up**

Patients were evaluated every 3 months for the first 2 years, every 6 months from year 3–5, and then every 12 months. The overall survival (OS) was measured from the date of diagnosis to the date of death or the last follow up. The progression-free survival (PFS) was measured from the date of diagnosis to the time of document treatment failure or last follow up. The last follow up time was June, 2018. The median follow-up period was 77 months (range, 2.0–135.0).

**Statistical analysis**

Data analysis was performed using SPSS version 22 software (SPSS Inc., Chicago, IL, USA). The relationship between SII and clinicopathologic characteristics was analyzed using $\chi^2$ test or Fisher's exact test. Kaplan-Meier survival method and log-rank test were used to compare the survival rates between different groups. Univariate and multivariate
analyses were calculated using the Cox proportional hazards model. Variables with statistical significance (P<0.05) in Univariate analyses were further included in multivariate analyses. Survival tree analysis was performed and recursive-partitioning analysis (RPA) was used to identify the optimal cutoff thresholds of SII as we previously described (22). A P value of less than 0.05 was considered statistically significant.

### Results

#### Characteristics of patients

The characteristics of mNPC are shown in (Table 1). The staging of mNPC was classified according to the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC), 8th Edition. Of

| Variables | Total (%) | Unmatched data | P | PSM matched data | P |
|-----------|-----------|----------------|---|------------------|---|
|           |           | SII ≤930 | SII >930 |       | SII ≤930 | SII >930 |       |
| Sex       |           |          |         | 0.686 | 1.000 |          |         | 0.686 | 1.000 |
| Female    | 39 (24.3) | 29       | 10      | 47    | 47  |          |         | 47    | 47  |
| Male      | 184 (75.7)| 157      | 47      | 10    | 10  |          |         | 10    | 10  |
| Age, years|           |          |         | 0.096 | 1.000 |          |         | 0.096 | 1.000 |
| ≤50       | 134 (55.1)| 97       | 37      | 37    | 37  |          |         | 37    | 37  |
| >50       | 109 (44.9)| 89       | 20      | 20    | 20  |          |         | 20    | 20  |
| T category|           |          |         | 0.499 | 0.706 |          |         | 0.499 | 0.706 |
| T1        | 30 (12.3) | 24       | 6       | 7     | 6   |          |         | 7     | 6   |
| T2        | 54 (22.2) | 45       | 9       | 11    | 9   |          |         | 11    | 9   |
| T3        | 88 (36.2) | 65       | 23      | 17    | 23  |          |         | 17    | 23  |
| T4        | 71 (29.2) | 52       | 19      | 22    | 19  |          |         | 22    | 19  |
| N category|           |          |         | 0.047 | 0.906 |          |         | 0.047 | 0.906 |
| N0        | 2 (0.8)   | 2        | 0       | 0     | 0   |          |         | 0     | 0   |
| N1        | 33 (13.6) | 29       | 4       | 5     | 4   |          |         | 5     | 4   |
| N2        | 92 (37.9) | 75       | 17      | 18    | 17  |          |         | 18    | 17  |
| N3        | 116 (47.7)| 80       | 36      | 34    | 36  |          |         | 34    | 36  |
| Histology |           |          |         | 0.498 | 0.549 |          |         | 0.498 | 0.549 |
| I         | 4 (1.6)   | 3        | 1       | 0     | 1   |          |         | 0     | 1   |
| II        | 17 (7.0)  | 15       | 2       | 3     | 2   |          |         | 3     | 2   |
| III       | 222 (91.4)| 168      | 54      | 54    | 54  |          |         | 54    | 54  |
| ECOG      |           |          |         | 0.195 | 0.616 |          |         | 0.195 | 0.616 |
| 0         | 209 (86.0)| 163      | 46      | 49    | 46  |          |         | 49    | 46  |
| 1         | 34 (14.0) | 23       | 11      | 8     | 11  |          |         | 8     | 11  |
| IMRT      |           |          |         | 0.002 | 0.321 |          |         | 0.002 | 0.321 |
| No        | 131 (53.9)| 90       | 41      | 35    | 41  |          |         | 35    | 41  |
| Yes       | 112 (46.1)| 96       | 16      | 22    | 16  |          |         | 22    | 16  |

ECOG, Eastern Cooperative Oncology Group performance; IMRT, intensity modulated radiotherapy; SII, systemic immune-inflammation index; I, Keratinizing squamous cell carcinoma; II, non-keratinizing differentiated carcinoma; III, non-keratinizing undifferentiated carcinoma.
all 243 patients, the median age was 48 years (range, 17–81 years), and the proportion of male (75.7%) were three times that of female (39%). Non-keratinizing undifferentiated carcinoma accounts for more than 90% of all NPC. At last follow up, 178 (73.3%) patients had died. The median OS and PFS for all patients was 31.5 (range, 2–135) months and 19.0 (range, 1–135) months, respectively. The estimated OS for 1-, 3- and 5-year was 79.8%, 43.5% and 31.5%, respectively.

**Association between SII and characteristics in mNPC**

Optimal cutoff thresholds of SII is determined by High SII (>930) was present in 57 (23.46%) mNPC patients (Table 1). High SII was associated with advanced N stage (P=0.047) and patients without IMRT therapy (P=0.002). No statistically significant difference was observed between SII level and gender, age at diagnosis, T classification, pathological type and ECOG score (Table 2).

**The prognostic significance of SII in patients with mNPC**

The Kaplan-Meier analysis indicated that high SII were closely associated with poor median OS (18.0 vs. 36.0 m, P<0.001) and PFS (10.0 vs. 22.0 m, P<0.001) (Figure 1).

As shown in Table 2 and Table 3, Univariate analysis indicated that SII were significantly associated with worse median OS (HR 2.04, 95% CI: 1.47–2.82, P<0.001) and PFS (HR 1.84, 95% CI: 1.34–2.54, P<0.001). Multivariate analysis further identified that SII was an independent prognostic factors for OS (HR 1.75, 95% CI: 1.22–2.52, P=0.001) and PFS (HR 1.69, 95% CI: 1.22–2.35, P=0.002), as well as IMRT.

**Propensity score matching (PSM) analysis**

In order to eradicate the imbalance of N category and IMRT between SII ≤930 and SII >930, we performed PSM analysis. One hundred and fourteen mNPC were enrolled and all variables were distributed equally in both group (P>0.3). Kaplan-Meier analysis indicated that low SII were significantly associated with prolonged median OS (P=0.001) and PFS (P=0.002) (Figure 2).

Univariate analysis suggested SII were associated with OS and PFS (Tables 4, 5). Multivariable analyses still demonstrated that SII were independent prognostic factors for OS (HR 1.86, 95% CI: 1.22–2.83, P=0.004) and PFS (HR 1.84, 95% CI: 1.23–2.77, P=0.003).

### Table 2 Univariate and multivariate analysis of overall survival in patients with metastatic nasopharyngeal carcinoma patients (unmatched data)

| Variables             | Univariate analysis | Multivariate analysis |
|-----------------------|---------------------|-----------------------|
|                       | HR (95% CI)         | P         | HR (95% CI) | P         |
| Sex                   | 0.094               |          |            |          |
| Female vs. male        | 0.70 (0.46–1.06)    | 0.056    |            |          |
| Age, years             | 1.33 (0.99–1.79)    | 0.056    |            |          |
| T classification       |                     |          |            |          |
| T1                    | 1                   |          |            |          |
| T2                    | 0.89 (0.51–1.54)    | 0.666    |            |          |
| T3                    | 1.14 (0.69–1.87)    | 0.616    |            |          |
| T4                    | 1.11 (0.66–1.85)    | 0.695    |            |          |
| N classification       | 0.017               |          |            |          |
| N0                    | 1                   |          |            |          |
| N1                    | 0.86 (0.12–6.41)    | 0.881    |            |          |
| N2                    | 1.16 (0.52–2.22)    | 0.886    |            |          |
| N3                    | 1.69 (0.24–12.15)   | 0.602    |            |          |
| Histology              | 0.08                |          |            |          |
| I                     | 1                   |          |            |          |
| II                    | 0.52 (0.25–1.01)    | 0.053    |            |          |
| III                   | 0.67 (0.17–2.69)    | 0.567    |            |          |
| ECOG                   | 0.08                |          |            |          |
| 1 vs. 0               | 1.41 (0.95–2.10)    | <0.001   | <0.001     |          |
| IMRT                   | <0.001              |          |            |          |
| Yes vs. no             | 0.49 (0.36–0.66)    | 0.53     | (0.39–0.73) |          |
| SII                   | <0.001              | 0.001    |            |          |
| ≥930 vs. <930          | 2.04 (1.47–2.82)    | 1.75     | (1.22–2.52) |          |

ECOG, Eastern Cooperative Oncology Group performance; IMRT, intensity modulated radiotherapy; HR, hazard ratio; CI, confidence interval. SII, systemic immune-inflammation index.
Discussion

It is now well established that inflammation can increase cancer risk by causing oncogenic mutations, genomic instability, tumor promotion, angiogenesis and metastasis, and can lead to an immunosuppressive microenvironment (9,10). During the inflammatory process, different subtypes of inflammatory and immune cells were released and involved in tumor-promoting inflammation and anti-tumor immunity. Therefore, it is meaningful to explore a tool that can simply and accurately predict the state of inflammation according to these inflammatory and immune cells in cancers.

Table 3 Univariate and multivariate analysis of progression-free survival in patients with metastatic nasopharyngeal carcinoma patients (unmatched data)

| Variables     | Univariate analysis | Multivariate analysis |
|---------------|---------------------|-----------------------|
|               | HR (95% CI)         | P         | HR (95% CI) | P         |
| Sex           | 0.286               |          |            |
| Female vs. male| 0.81 (0.54–1.20)   |          |            |
| Age, years    | 0.112               |          |            |
| >50 vs. ≤50   | 1.26 (0.95–1.67)    |          |            |
| T classification|                     |          |            |
| T1            | 1                   |          |            |
| T2            | 1.00 (0.58–1.71)    | 0.994    |            |
| T3            | 1.33 (0.81–2.18)    | 0.261    |            |
| T4            | 1.20 (0.73–2.00)    | 0.472    |            |
| N classification|                     |          |            |
| N0            | 1                   |          |            |
| N1            | 1.21 (0.16–9.01)    | 0.852    |            |
| N2            | 1.58 (0.22–11.39)   | 0.649    |            |
| N3            | 2.47 (0.34–17.72)   | 0.369    |            |
| Histology     | 0.38                |          |            |
| I             | 1                   |          |            |
| II            | 0.55 (0.29–1.05)    | 0.07     |            |
| III           | 0.79 (0.255–2.48)   | 0.69     |            |
| ECOG          | 0.034               |          |            |
| 1 vs. 0       | 1.19 (0.80–1.77)    |          |            |
| IMRT          | 0.004               | 0.034    |            |
| Yes vs. no    | 0.66 (0.49–0.88)    | 0.73     | (0.54–0.98) |
| SII           | <0.001              | 0.002    |            |
| ≥930 vs. <930 | 1.84 (1.34–2.54)    | 1.69     | (1.22–2.35) |

ECOG, Eastern Cooperative Oncology Group performance; IMRT, intensity modulated radiotherapy; HR, hazard ratio; CI, confidence interval. SII, systemic immune-inflammation index.
Recently, SII, based on 3 immune inflammatory cells (lymphocyte, neutrophil and platelet) from peripheral blood, was considered to be a promising inflammatory marker. Accumulated data have proved that SII was a novel prognostic indicator in various cancers, including non-small cell lung cancer (23-26), hepatocellular carcinoma (19,27,28), esophageal cancer (29-32), colorectal cancer (33), gastric cancer (34-36), renal cell cancer (37), prostate cancer (38) and pancreatic cancer (39). However, SII has not been thoroughly studied in NPC. Previous studies have focused on prognostic significance of NLR\PLR and percentages of neutrophil and lymphocyte in NPC (16,18,40). In addition, the roles of SII were just reported in two studies in NPC and no detailed examination in mNPC patients (13,41). It is worth noting that mNPC were more in need of prognostic biomarkers, as those patients have a median OS of only 12-15 months with platinum-based chemotherapy (42).

Our study underscores the potential of SII in mNPC, suggesting that SII was a prognostic biomarker for poor OS and PFS. This view was basically consistent with previous studies, which found that SII was unfavorable indicator for OS in all stages of NPC (14,41). While, our report found no significant relationships between SII and clinical characteristics. The discrepancies are likely due to the registration of different populations, which might lead to the different cutoff value of SII and various outcomes. More work remains to determine the different roles of inflammatory markers involved between non-metastatic NPC and mNPC.

The mechanisms why high SII results in adverse outcome may be explained by the following reasons. Firstly, patients with higher SII often have thrombocytosis, which is commonly observed in metastatic cancers (43). Platelets can significantly promote cancer in variety of ways, such as inducing angiogenesis, resisting cell death, sustaining proliferative signals, supporting cancer stem cell and evading immune detection (44). In addition, study have showed that platelets could induce the production of circulating cancer cells (CTCs) and protect CTCs from immune attacks. And platelets-derived TGF-β and PDGF could induce epithelial-mesenchymal transition (EMT) in CTCs and help them intravasation and extravasation (45). Secondly, neutrophils, as the first line of innate immune system, were proved to promote metastasis through neutrophil extracellular traps (NET). NET could wrap up CTCs and cause micrometastases spread safely to the metastatic sites (46). Consistent with platelets, subpopulations of tumor-associated neutrophils could aid tumorigenesis through plenty of ways, like promoting tumor proliferation, angiogenesis and genetic instability. More importantly, tumor-associated neutrophils will suppress CD8+ T cell, leading to immune invasion (47). Currently, there is growing evidence that neutrophils could facilitate metastasis by creating a systemic immunosuppressive microenvironment and a “pre-metastatic niche” within metastatic organs (48,49). And neutrophils were reported to be closely associated with poor prognosis of different cancers treated with radiation therapy (50). Finally, NPC is characterized by massive infiltration of lymphocytes (51).
### Table 4: Univariate and multivariate analysis of overall survival in patients with metastatic nasopharyngeal carcinoma patients (PSM matched data)

| Variables         | Univariate analysis |          | Multivariate analysis |          |
|-------------------|---------------------|----------|-----------------------|----------|
|                   | HR (95% CI)         | P        | HR (95% CI)           | P        |
| Sex               | 0.057               |          |                       |          |
| Female vs. male   | 0.56 (0.31–1.02)    | 0.35     | 0.56 (0.31–1.02)      | 0.35     |
| Age, years        | 0.35                |          |                       |          |
| >50 vs. ≤50       | 1.23 (0.80–1.89)    |          |                       |          |
| T classification  |                     |          |                       |          |
| T1                | 1                   |          |                       |          |
| T2                | 0.96 (0.44–2.11)    | 0.924    | 0.96 (0.44–2.11)      | 0.924    |
| T3                | 0.86 (0.69–1.87)    | 0.672    | 0.86 (0.69–1.87)      | 0.672    |
| T4                | 0.69 (0.66–1.85)    | 0.315    | 0.69 (0.66–1.85)      | 0.315    |
| N classification  |                     |          |                       |          |
| N1                | 1                   |          |                       |          |
| N2                | 1.19 (0.49–2.89)    | 0.704    | 1.19 (0.49–2.89)      | 0.704    |
| N3                | 1.79 (0.77–4.16)    | 0.177    | 1.79 (0.77–4.16)      | 0.177    |
| Histology         |                     |          |                       |          |
| I                 | 1                   |          |                       |          |
| II                | 0.49 (0.25–1.01)    | 0.231    | 0.49 (0.25–1.01)      | 0.231    |
| III               | 4.80 (0.65–35.73)   | 0.125    | 4.80 (0.65–35.73)     | 0.125    |
| ECOG              | 0.93                |          |                       |          |
| 1 vs. 0           | 0.98 (0.57–1.68)    |          | 0.98 (0.57–1.68)      |          |
| IMRT              | 0.013               | 0.032    |                       |          |
| Yes vs. no        | 0.55 (0.35–0.88)    | 0.60     | 0.55 (0.35–0.88)      | 0.60     |
| SII               | 0.002               | 0.004    |                       |          |
| ≥930 vs. <930     | 1.96 (1.29–2.94)    | 1.86     | 1.96 (1.29–2.94)      | 1.86     |

ECOG, Eastern Cooperative Oncology Group performance; IMRT, intensity modulated radiotherapy; HR, hazard ratio; CI, confidence interval. SII, systemic immune-inflammation index.

### Table 5: Univariate and multivariate analysis of progression-free survival in patients with metastatic nasopharyngeal carcinoma patients (PSM matched data)

| Variables         | Univariate analysis |          | Multivariate analysis |          |
|-------------------|---------------------|----------|-----------------------|----------|
|                   | HR (95% CI)         | P        | HR (95% CI)           | P        |
| Sex               | 0.056               |          |                       |          |
| Female vs. male   | 0.57 (0.33–1.01)    | 0.55     | 0.57 (0.33–1.01)      | 0.55     |
| Age, years        | 0.55                |          |                       |          |
| >50 vs. ≤50       | 1.14 (0.75–1.73)    |          | 1.14 (0.75–1.73)      |          |
| T classification  |                     |          |                       |          |
| T1                | 1                   |          |                       |          |
| T2                | 0.87 (0.40–1.89)    | 0.722    | 0.87 (0.40–1.89)      | 0.722    |
| T3                | 1.03 (0.51–2.09)    | 0.928    | 1.03 (0.51–2.09)      | 0.928    |
| T4                | 0.78 (0.38–1.57)    | 0.480    | 0.78 (0.38–1.57)      | 0.480    |
| N classification  |                     |          |                       |          |
| N1                | 1                   |          |                       |          |
| N2                | 1.04 (0.43–2.51)    | 0.938    | 1.04 (0.43–2.51)      | 0.938    |
| N3                | 1.89 (0.82–4.39)    | 0.138    | 1.89 (0.82–4.39)      | 0.138    |
| Histology         |                     |          |                       |          |
| I                 | 1                   |          |                       |          |
| II                | 0.88 (0.32–2.38)    | 0.794    | 0.88 (0.32–2.38)      | 0.794    |
| III               | 2.06 (0.28–14.97)   | 0.475    | 2.06 (0.28–14.97)     | 0.475    |
| ECOG              | 0.662               |          |                       |          |
| 1 vs. 0           | 0.89 (0.52–1.52)    |          | 0.89 (0.52–1.52)      |          |
| IMRT              | 0.165               |          |                       |          |
| Yes vs. no        | 0.73 (0.47–1.14)    |          | 0.73 (0.47–1.14)      |          |
| SII               | 0.003               | 0.003    |                       |          |
| ≥930 vs. <930     | 1.84 (1.23–2.77)    | 1.84     | 1.84 (1.23–2.77)      | 1.84     |

ECOG, Eastern Cooperative Oncology Group performance; IMRT, intensity modulated radiotherapy; HR, hazard ratio; CI, confidence interval. SII, systemic immune-inflammation index.
Tumor infiltrating lymphocytes (TILs) in NPC were common significantly associated with better survival, which was supposed to be an independent and potential prognostic biomarker (52). And several data have also showed that higher peripheral blood lymphocytes predicted a favorable outcome in NPC and other head and neck cancer (18,45,53,54).

Although SII proved to be a useful tool for OS and PFS in mNPC. This research has a few limitations. Firstly, it is a retrospective study. Secondly, large heterogeneity of outcomes was noted in mNPC, since there is now no standard therapy for mNPC. Lastly, our study was in a single center and performed in popular areas of NPC. Therefore, more investigation is needed to fully define the validity and practicability of SII. The application of SII in clinical practice should be validated in large sample and randomized studies.

To our knowledge, our study is the first report to examine the role of SII in patients with newly diagnosed mNPC. Our results showed that the SII was a simple and novel tool that could serve as an independent prognostic biomarker for OS and PFS in mNPC patients. Larger model validations and deeper mechanisms underlying the associations between high SII and worse outcomes are truly warranted.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2019.09.25). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethical Review Committee of Fujian Cancer Hospital (No. SQ2019-031-01). All of the participants signed an informed consent form.

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