Prognostic value of ^{18}F-fluorodeoxyglucose PET parameters and inflammation in patients with nasopharyngeal carcinoma

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Abstract. The aim of the present study was to investigate the association between positron emission tomography (PET) parameters and peripheral inflammatory markers, and assess their prognostic value in nasopharyngeal carcinoma (NPC). A total of 121 patients with non-disseminated NPC were recruited. Pretreatment maximum standardized uptake values (SUVmax) of PET and peripheral inflammatory factors (leukocyte, neutrophil and monocyte counts) were recorded. Kaplan-Meier and multivariate analyses were used to identify predictors for progression-free survival (PFS), overall survival (OS), distant metastasis-free survival (DMFS) and locoregional recurrence-free survival (LRFS). The results of the present study revealed that SUVmax at the primary tumor was positively correlated with leukocytes (P=0.025), neutrophils (P=0.009) and monocytes (P=0.043). SUVmax at regional lymph nodes (SUVmax-N) was significantly associated with monocytes (P=0.024). Kaplan-Meier analysis demonstrated that SUVmax-N (>10.15) significantly predicted PFS (P=0.004) and DMFS (P=0.003). In addition, neutrophils (>5.18) were significantly associated with PFS (P=0.001), DMFS (P=0.013) and LRFS (P<0.001). Multivariate analysis revealed that SUVmax-N and neutrophils retained independent prognostic significance for PFS (SUVmax-N, P=0.026; and neutrophils, P=0.033) and DMFS (SUVmax-N, P=0.026; and neutrophils, P=0.032). Furthermore, patients with SUVmax-N ≤10.15 and neutrophils ≤5.18 had significantly improved prognosis in PFS (96.4 vs. 58.5%, P<0.001), OS (95.7 vs. 81.1%, P=0.044), DMFS (96.4 vs. 67.0%, P<0.001) and LRFS (100 vs. 90.2%, P=0.036) compared with those with SUVmax-N >10.15 or neutrophils >5.18. In conclusion, SUVmax may be significantly associated with cancer-associated inflammation. SUVmax-N and neutrophils were independent prognostic indicators for PFS and DMFS. Combined assessment of SUVmax-N and neutrophils may lead to refinement of risk stratification in NPC.

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Introduction

Nasopharyngeal carcinoma (NPC) may be distinguished from other types of head and neck cancer based on its unbalanced endemic distribution, pathology and clinical attributes (1). NPC is an endemic neoplasm in southern China, with incidence rates of 20-30 per 100,000 being reported in certain areas of Guangdong province (2,3). Currently, the prognosis of patients with NPC is evaluated based primarily on the Union for International Cancer Control/American Joint Cancer Committee (UICC/AJCC) tumor node metastasis (TNM) staging system (4). However, there is a discrepancy between actual clinical outcome and anatomically based TNM stage, indicating that clinical staging is insufficient for the precise prediction of prognosis (5). It is therefore critical to investigate alternative factors in order to accurately predict the outcome for patients with NPC.

^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/computerized tomography (CT) is a synergistic combination of functional and anatomical imaging, and serves a growing role in the diagnosis, staging and prognosis of patients with NPC (6,7). ^{18}F-FDG uptake using maximum standardized uptake values (SUVmax) has been reported to be correlated with tumor proliferation rates, metastatic potential, sensitivity to radiotherapy/chemotherapy and clinical outcomes (8,9). Furthermore, previous studies have revealed that patients with NPC who exhibit high SUVmax generally exhibit less favorable outcomes (10,11). However, due to the heterogeneity of these patients, the use of SUVmax alone to complement the TNM classification and refine risk stratification remains inadequate (12).

It has been suggested that cancer-associated inflammation represents a hallmark of malignant tumors (13,14). Infiltrating leukocytes in the tumor microenvironment promote tumor development, invasion and metastasis (15,16). Previous studies have identified that complete blood count (CBC) parameters associated with systemic inflammation, including leukocytes and their differential counts, are clearly correlated with prognosis in patients with a variety of neoplasms (17-20), including

NPC (21,22). However, previous studies on NPC usually utilize limited endpoints, including overall survival (OS) and progression-free survival (PFS) (21,22). The prognostic value of peripheral leukocytes and differential counts of neutrophils and monocytes in patients with NPC has not been sufficiently evaluated.

Previous studies have reported that a substantial component of ^{18}F-FDG uptake in tumor tissues is a result of activity localized to peri-tumoral inflammatory cells (23-25). However, studies on the association between PET parameters and cancer-associated inflammation are lacking. The present study investigated the association between PET SUVmax, peripheral inflammatory markers and TNM stage. The prognostic power of SUVmax and inflammation for predicting various survival endpoints in patients with NPC was also investigated. The combined use of PET parameters and blood inflammatory markers may improve prognostic stratification and individually tailored treatment in patients with NPC.

Materials and methods

Patient selection. The present study included 121 patients who had been newly diagnosed with NPC between February 2009 and December 2013 at the Nanfang Hospital of Southern Medical University (Guangzhou, China). The inclusion criteria were: Biopsy-proven primary NPC; a pretreatment whole-body ^{18}F-FDG PET/CT scan and CBC assessment; non-disseminated NPC; and receipt of definitive radiotherapy at the South Hospital of Southern Medical University. The exclusion criteria were: Simultaneous second primary tumors; clinical evidence of infection or other systemic inflammatory conditions; and incomplete treatment. Approval was granted from the Southern Medical University Institutional Review Board to proceed with this retrospective study. Written informed consent was obtained from all patients prior to enrollment in the present study.

All patients underwent PET/CT and CBC within 2 weeks prior to therapy. Other evaluations included a complete patient history, physical examination, biochemistry profiles and a magnetic resonance imaging (MRI) scan of the nasopharynx and neck. The results of the ^{18}F-FDG PET and MRI scans were analyzed in the present study. Staging was performed based on the 7th version of the UICC/AJCC TNM staging system (4).

Treatment. All patients were treated with definitive radiotherapy. The radiation dose ranges to the nasopharynx, lymph node-positive area and lymph node-negative area were 66-76, 60-70 and 50-60 Gy, respectively. The majority of the patients (79/121) were treated with intensity modulated radiation therapy, and the remaining patients were treated with 3-dimensional conformal radiation therapy. Overall, 16/121 patients (13.2%) were treated with radiotherapy alone, whilst 105/121 (86.8%) received platinum-based chemotherapy. Concurrent chemotherapy consisted of cisplatin (75 mg/m^2), cisplatin (75 mg/m^2) with 5-fluorouracil (4.0 g/m^2) or paclitaxel liposome (135 mg/m^2) on weeks 1, 4 and 7 of radiotherapy. Neoadjuvant or adjuvant chemotherapy consisted of cisplatin (75 mg/m^2) with 5-fluorouracil (4.0 g/m^2) or paclitaxel liposome (135 mg/m^2) every 3 weeks for 2 or 3 cycles.

PET/CT. All examinations were performed using a Discovery LS PET/CT scanner (GE Healthcare Bio-Sciences, Waukesha, WI, USA). Patients fasted for at least 6 h prior to the scan, and blood glucose was monitored immediately prior to the study to ensure patients had a normal blood glucose level (<7 mmol/l). An intravenous injection of 232-524 MBq (6.27-14.16 mCi) of ^{18}F-FDG was administered. Patients then waited for ~60 min prior to the whole-body PET/CT being performed, in accordance with published guidelines for tumor imaging with ^{18}F-FDG PET/CT (26).

Image acquisition using whole-body ^{18}F-FDG PET/CT included 6-8 bed positions for each unenhanced CT and PET scan, covering the entire range from the vertex of the skull to the mid thigh using head fixation. The PET images were reconstructed using a standard iterative algorithm (27) (ordered-subset expectation maximization), with the CT data used for attenuation correction (28). The captured PET and CT images were sent to the Xeleris workstation (GE Healthcare) for registration and fusion.

All images of fused PET/CT were analyzed comparatively by 2 experienced nuclear medicine physicians. The region of interest was drawn along the margin of the lesion for the measurement of SUVmax normalized to body weight. SUVmax at the primary tumor (SUVmax-P) and regional lymph nodes (SUVmax-N) was automatically calculated by the Xeleris workstation software (GE Healthcare; ADW4.1).

CBC. The CBC test was performed within a 2-week period prior to therapy, and determined by a fully automated hematology analyzer Sysmex XE-5000 (Sysmex Corporation, Kobe, Japan). Leukocyte, neutrophil and monocyte counts were recorded.

Follow-up. Patients were regularly followed up until mortality or the patients last visit. The patients were scheduled to visit the clinics every 3 months in the first 3 years, and every 6 months thereafter. The date of last follow-up was June 2015, and the median follow-up duration was 37 months (range, 4-74 months). Physical examination and nasopharyngoscopy were performed on each visit. Nasopharyngeal and neck MRIs, chest X-rays, and abdominal sonograms were performed when clinical indications suggested it was necessary. Locoregional recurrence was established by biopsy or PET/CT scans. Distant metastases were diagnosed based on clinical symptoms, physical examination and imaging methods, including chest plain film or CT scan, bone scan, and abdominal sonography or PET/CT scan.

Statistical analysis. The primary endpoint was PFS, and the secondary endpoints were OS, distant metastasis-free survival (DMFS) and locoregional recurrence-free survival (LRFS). PFS was calculated from the first day of treatment to the date of relapse at any site, mortality or the last follow-up appointment. For the remaining endpoints, the duration was measured from the first day of treatment to the date of the target event or censored at the last follow-up date. The Spearman's rank correlation test was applied to assess the association of PET SUVmax, circulating inflammation makers and TNM stage. The receiver operating characteristic (ROC) curve analysis was subjected to the selection of cut-off points to stratify

patients at a high risk of progression. Kaplan-Meier analysis and log-rank test were used to compare the difference between survival rates. Multivariate Cox proportional hazards models were used to identify independent prognostic factors. P<0.05 was considered to indicate a statistically significant difference. All statistical analyses were performed using SPSS version 17.0 (SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics. Patients' clinical characteristics are shown in Table I. Results of the follow-up revealed that out of the 121 patients, 19 had developed distant metastasis, 7 exhibited locoregional recurrence, 3 showed distant metastasis and locoregional recurrence and mortality had occurred in 12 patients. The 3-year PFS, 3-year OS and 3-year DMFS for all 121 patients were 77.9, 88.9 and 82.6%, respectively. A total of 9 patients were unavailable for follow-up.

Association among PET parameters, peripheral inflammatory markers and TNM stage. The association between SUVmax and CBC inflammatory makers is shown in Table II. Increased SUVmax-P was associated with increased leukocytes (r=0.203, P=0.025), neutrophils (r=0.238, P=0.009) and monocytes (r=0.185, P=0.043). Patients with increased SUVmax-N had significantly increased monocytes (r=0.206, P=0.024). However, no significant association of SUVmax-N with leukocytes and neutrophils was observed.

In addition, the association of TNM stage with PET parameters and CBC variables is shown in Table III. Higher T stage was significantly associated with increased SUVmax-P (r=0.526, P<0.001) and neutrophils (r=0.207, P=0.023). Similarly, N stage was positively correlated with SUVmax-N (r=0.622, P<0.001) and monocytes (r=0.222, P=0.014). Compared with patients with early disease, those with advanced NPC had increased SUVmax-P (r=0.264, P=0.003), SUVmax-N (r=0.280, P=0.002) and monocytes (r=0.245, P=0.007).

Univariate analysis of PET parameters and peripheral inflammatory markers as prognostic factors for PFS, OS, DMFS and LRFS. As PFS was the primary endpoint, the present study took the values of PET parameters and CBC variables showing the best trade-off between sensitivity and specificity for PFS as the cut-off values, which were determined by ROC analysis. The cut-off values of SUVmax-P, SUVmax-N, leukocytes, neutrophils and monocytes were 12.35, 10.15, 8.19, 5.18 and 0.59, respectively.

As revealed in Fig. 1, Kaplan-Meier survival curves for PFS differed significantly when patients were stratified according to the cut-off points of SUVmax-N (3-year PFS 86.4 vs. 62.4%, P=0.004), leukocytes (84.3 vs. 58.5%, P=0.014) and neutrophils (85.7 vs. 53.1%, P=0.001). Significance was not identified between PFS and SUVmax-P or between PFS and monocytes (P>0.05). In addition, patients with increased values of neutrophils demonstrated a tendency towards poorer OS (P=0.071). No significant association was identified between the remaining parameters and OS (data not shown).

As shown in Fig. 2, SUVmax-N (P=0.003) and neutrophils (P=0.013) were significantly associated with DMFS.

Table I. Patient characteristics.

Characteristic	N (%)
Age (years)[a]	44 (17-76)
Gender	
Male	98 (81.0)
Female	23 (19.0)
Histology	
WHO I	9 (7.4)
WHO IIA-B	112 (92.6)
Tumor stage	
I	27 (22.3)
II	18 (14.9)
III	55 (45.5)
IV	21 (17.4)
Node stage	
0	27 (22.3)
1	33 (27.3)
2	49 (40.5)
3a	3 (2.5)
3b	9 (7.4)
Clinical classification	
I	4 (3.3)
II	18 (14.9)
III	67 (55.4)
IVa	20 (16.5)
IVb	12 (9.9)
Treatment outcome	
Distant metastasis	19 (15.7)
Locoregional recurrence	7 (5.8)
Mortality	12 (9.9)

[a]Data are presented at the median and range. WHO, World Health Organization.

Compared with patients who had SUVmax-N ≤10.15 (3-year DMFS, 89.2%), those with SUVmax-N >10.15 had a 3-year DMFS of 70.1%. Furthermore, patients with neutrophils ≤5.18 (3-year DMFS, 86.8%) had an improved DMFS compared with those with neutrophils >5.18 (3-year DMFS, 67.0%). The 3-year LRFS rates differed significantly when patients were stratified according to the cut-off points of leukocytes (98.8 vs. 83.8%, P<0.001), neutrophils (98.8 vs. 82.4%, P<0.001) and monocytes (97.8 vs. 84.7%, P=0.007). Patients with increased SUVmax-P (>12.35) experienced poorer LRFS compared with patients with SUVmax-P ≤12.35 (3-year LRFS, 98.3 vs. 90.9%), but this difference was not statistically significant (P=0.096). SUVmax-P did not exhibit a significant difference for DMFS and SUVmax-N demonstrated no significant difference in LRFS (data not shown).

Multivariate Cox regression analysis. To discriminate the independent prognostic indicators of various outcomes, significant factors identified in univarite analysis were subsequenly

Table II. Association between positron emission tomography parameters and peripheral inflammatory markers.

	Maximal standardized uptake values at the primary tumor		Maximal standardized uptake values at regional lymph nodes	
Cell type	r-value	P-value	r-value	P-value
Leukocytes	0.203	0.025	0.068	0.46
Neutrophils	0.238	0.009	0.023	0.802
Monocytes	0.185	0.043	0.206	0.024

Table III. Association between tumor node metastasis stage, positron emission tomography parameters and peripheral inflammatory markers.

	Tumor stage		Node stage		Clinical stage	
Factor	r-value	P-value	r-value	P-value	r-value	P-value
Maximal standardized uptake values at the primary tumor	0.526	<0.001	0.070	0.447	0.264	0.003
Maximal standardized uptake values at regional lymph nodes	0.061	0.503	0.622	<0.001	0.280	0.002
Leukocytes	0.146	0.110	0.045	0.621	0.128	0.160
Neutrophils	0.207	0.023	0.012	0.894	0.143	0.118
Monocytes	0.167	0.067	0.222	0.014	0.245	0.007

put into a Cox proportional hazards model. Adjustments were also made for age, gender, histological type, T stage and N stage. The results of multivariate survival analysis are shown in Table IV. Increased values of SUVmax-N (hazard ratio, 2.572, P=0.026) and neutrophils (hazard ratio, 3.684, P=0.033) retained their independent prognostic significance for poorer PFS. In addition, SUVmax-N (hazard ratio, 3.065, P=0.026) and neutrophils (hazard ratio, 2.888, P=0.032) were independent predictive factors for DMFS. By contrast, leukocytes, neutrophils and monocytes lost their prognostic significance for LRFS (data not shown).

Furthermore, when patients were stratified by SUVmax-N and neutrophils, it was revealed that patients with lower levels of SUVmax-N and neutrophils (SUVmax-N ≤10.15 and neutrophils ≤5.18) had significantly improved prognosis in PFS (96.4 vs. 58.5%, P<0.001; Fig. 3A), OS (95.7 vs. 81.1%, P=0.044; Fig. 3B), DMFS (96.4 vs. 67.0%, P<0.001; Fig. 3C) and LRFS (100 vs. 90.2%, P=0.036; Fig. 3D) compared with those with SUVmax-N >10.15 or neutrophils >5.18.

Discussion

NPC treatment remains challenging due to a high tendency to relapse, particularly in the form of distant metastasis. Identification of prognostic factors is important for risk stratification and the potential improvement of treatment outcomes (29). It is particularly beneficial if identification prognostic factors are achieved noninvasively. To the best of our knowledge, this is the first study to evaluate PET SUVmax and inflammation simultaneously as prognostic markers in patients with NPC.

Inflammation is closely associated with malignant tumors. Multiple mechanistic similarities are now recognized between inflammatory and malignant cells in terms of the underlying metabolic pathways (30,31). High glucose metabolism and consequent high ^{18}F-FDG accumulation are not unique phenomena for malignant cells. Inflammation also demonstrates increased ^{18}F-FDG uptake, which is mainly caused by inflammatory cells (32,33). Previous studies (23-25) have reported that the infiltrating inflammatory cells, particularly macrophages, serve an important role in ^{18}F-FDG uptake in tumor tissue. However, to the best of our knowledge there have been no studies addressing the association between PET SUVmax and circulating inflammatory cells in cancer. The present study initially identified that SUVmax-P had a weak association with peripheral leukocytes, neutrophils and monocytes. SUVmax-N was significantly associated with monocytes. Patients with active infections were excluded from the present study. Blood leukocytes, neutrophils and monocytes may partially reflect the infiltration of inflammatory cells around tumor tissue. This may partially explain the present observation that SUVmax may be associated with blood inflammatory cells.

In agreement with previous studies (10,34), the present study identified that increased SUVmax-N was significantly associated with a higher N stage. SUVmax-P was positively correlated with T stage. Similar to the T and N classification in the TNM stage system, metabolic parameters of the primary tumor and regional lymph nodes appear to represent different prognostic properties. In the present study, SUVmax-N was an independent prognostic marker for PFS and DMFS, but demonstrated no significant difference in locoregional control. Patients with increased SUVmax-P

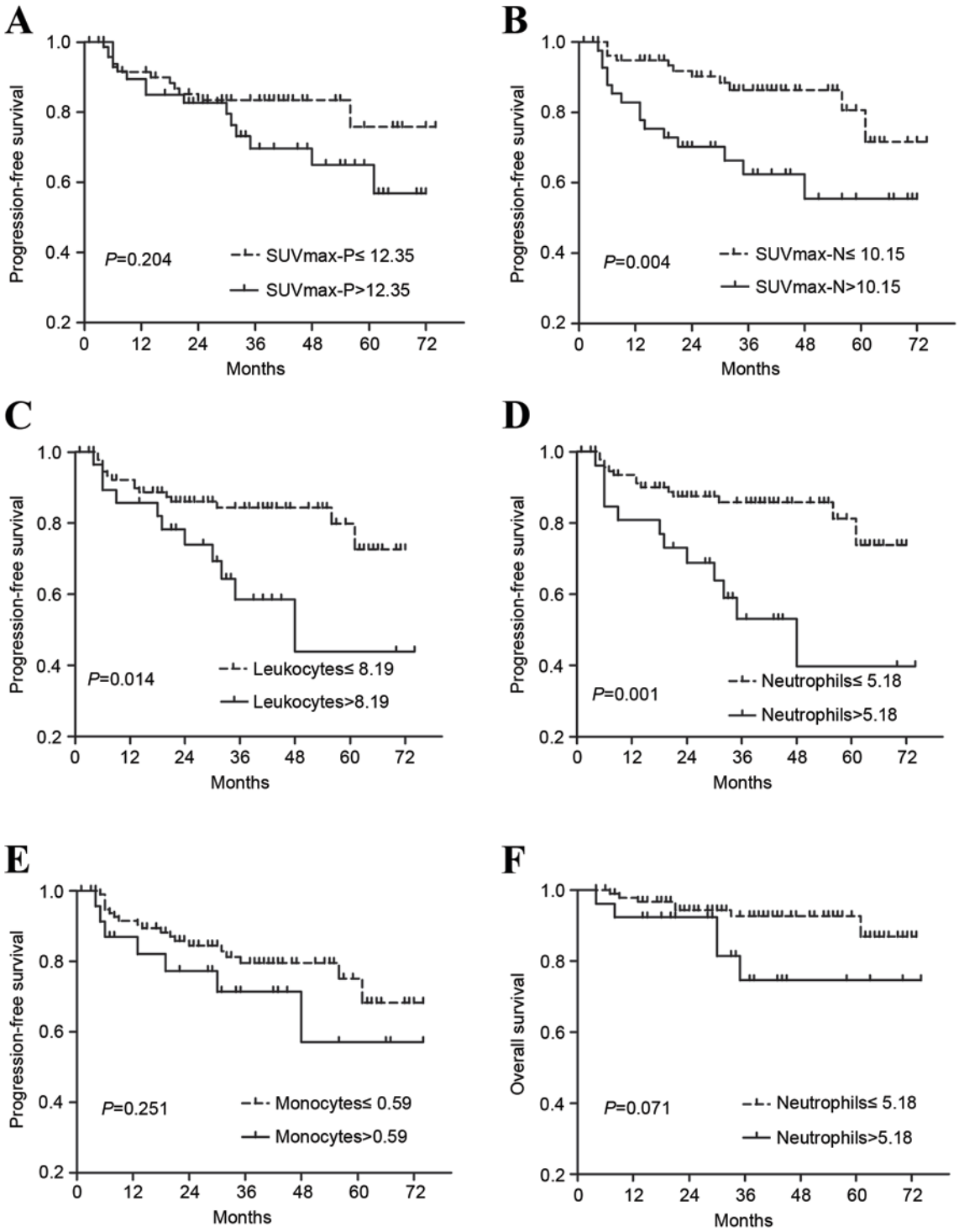

Figure 1. Kaplan-Meier analysis of PFS and OS. (A) Comparison of PFS according to the cut-off values of SUVmax-P. (B) Comparison of PFS according to the cut-off values of SUVmax-N. (C) Comparison of PFS according to the cut-off values of leukocytes. (D) Comparison of PFS according to the cut-off values of neutrophils. (E) Comparison of PFS according to the cut-off values of monocytes. (F) Comparison of OS based on neutrophil level. PFS, progression-free survival; OS, overall survival; SUVmax, maximum standardized uptake values; SUVmax-P, SUVmax at the primary tumor; SUVmax-N, SUVmax at regional lymph nodes.

had reduced LRFS, but this difference was not statistically significant, possibly due to the small sample size for locoregional recurrence. Compared with SUVmax-P, SUVmax-N had reduced predictive value for LRFS, but increased value for DMFS. In line with the present results, Chan *et al* (12) reported that SUVmax-N appeared to be more powerful in predicting distant failure than SUVmax-P. This phenomenon has also been noted in previous studies of non-NPC head and neck cancer (35-37).

It is generally accepted that inflammation may contribute to the initiation and progression of cancer. Systemic inflammation may also protect circulating metastatic cancer cells from natural killer cell-mediated killing, thereby overcoming immunosurveillance (38). Neutrophils in the peripheral or

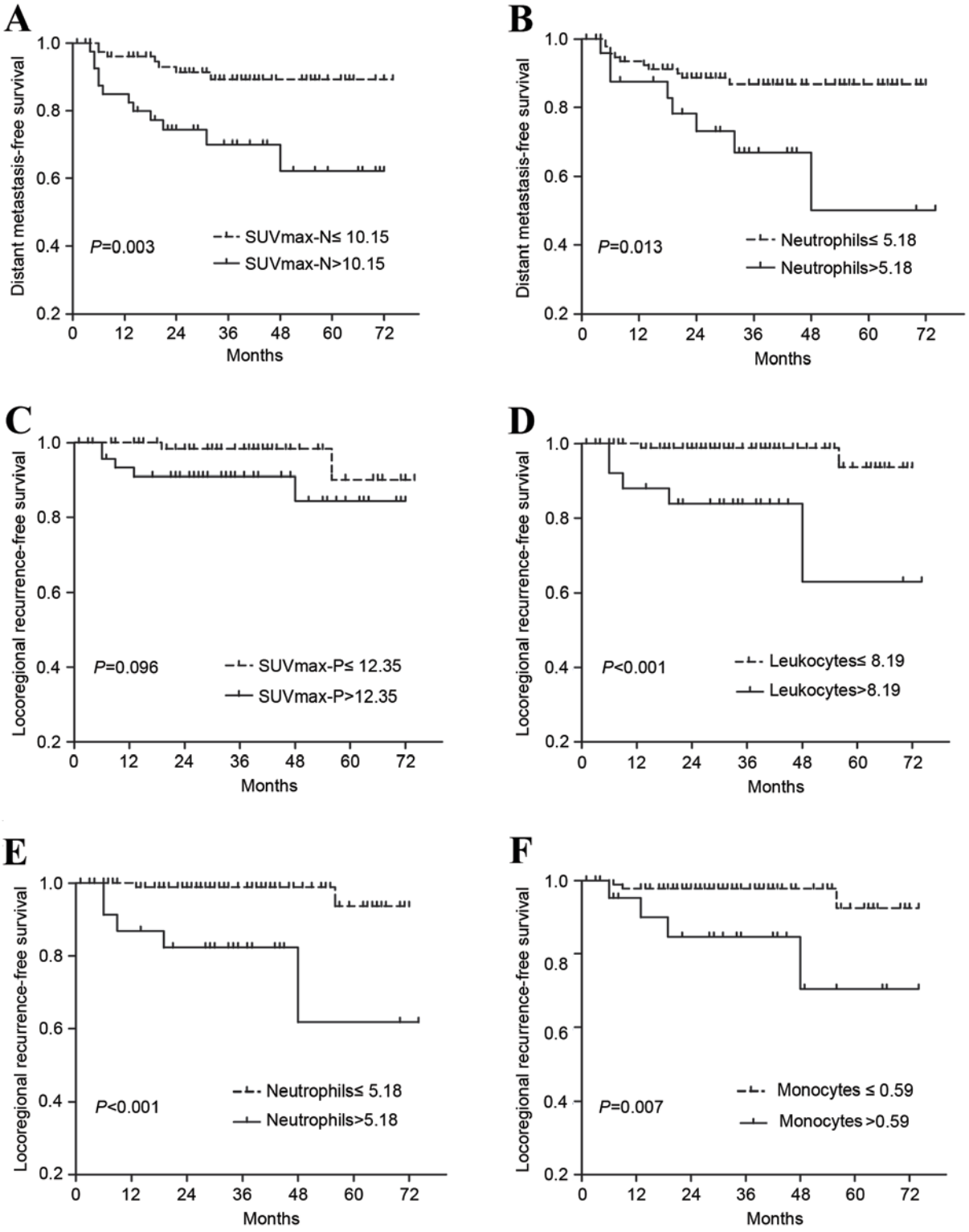

Figure 2. Kaplan-Meier analysis of DMFS and LRFS. (A) DMFS for patients stratified by the cut-off values of SUVmax-N. (B) DMFS for patients stratified by the cut-off values of neutrophils. (C) LRFS for patients stratified based on the cut-off values of SUVmax-P. (D) LRFS for patients stratified based on the cut-off values of leukocytes. (E) LRFS for patients stratified based on the cut-off values of neutrophils. (F) LRFS for patients stratified based on the cut-off values of monocytes. DMFS, distant metastasis-free survival; LRFS, locoregional recurrence-free survival; SUVmax, maximum standardized uptake values; SUVmax-N, SUVmax at the regional lymph nodes; SUVmax-P, SUVmax at the primary tumor.

tumor microenvironment have been demonstrated to produce proangiogenic factors, including vascular endothelial growth factor, to stimulate tumor development (39,40). A number of studies have shown associations between differential counts of leukocytes and the prognosis in various types of cancer, including melanoma (17), advanced non-small cell lung (18) and gastric cancer (19). A limited number of studies exist on the prognostic role of peripheral leukocytes and differential counts of neutrophils and monocytes in NPC. He *et al* (21) and Sun *et al* (22) investigated the association of neutrophils and

Table IV. Multivariate Cox regression analyses.

Factor	Progression-free survival		Distant metastasis-free survival	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Age: >45 years	2.052 (0.869-4.846)	0.101	1.694 (0.630-4.553)	0.296
Gender: Female	0.711 (0.210-2.415)	0.585	0.909 (0.259-3.189)	0.881
Histology: WHOIIa-b	1.442 (0.186-11.193)	0.727	1.170 (0.148-9.243)	0.882
T stage: T3-4	1.159 (0.468-2.872)	0.749	1.055 (0.348-3.199)	0.925
N stage: N2-3b	2.661 (1.065-6.649)	0.036	2.478 (0.880-6.983)	0.086
Maximal standardized uptake values at regional lymph nodes: >10.15	2.572 (1.121-5.898)	0.026	3.065 (1.145-8.201)	0.026
Leukocytes: >8.19	0.846 (0.261-2.745)	0.781	-	-
Neutrophils: >5.18	3.684 (1.114-12.181)	0.033	2.888 (1.093-7.634)	0.032

HR, hazard ratio; CI, confidence interval.

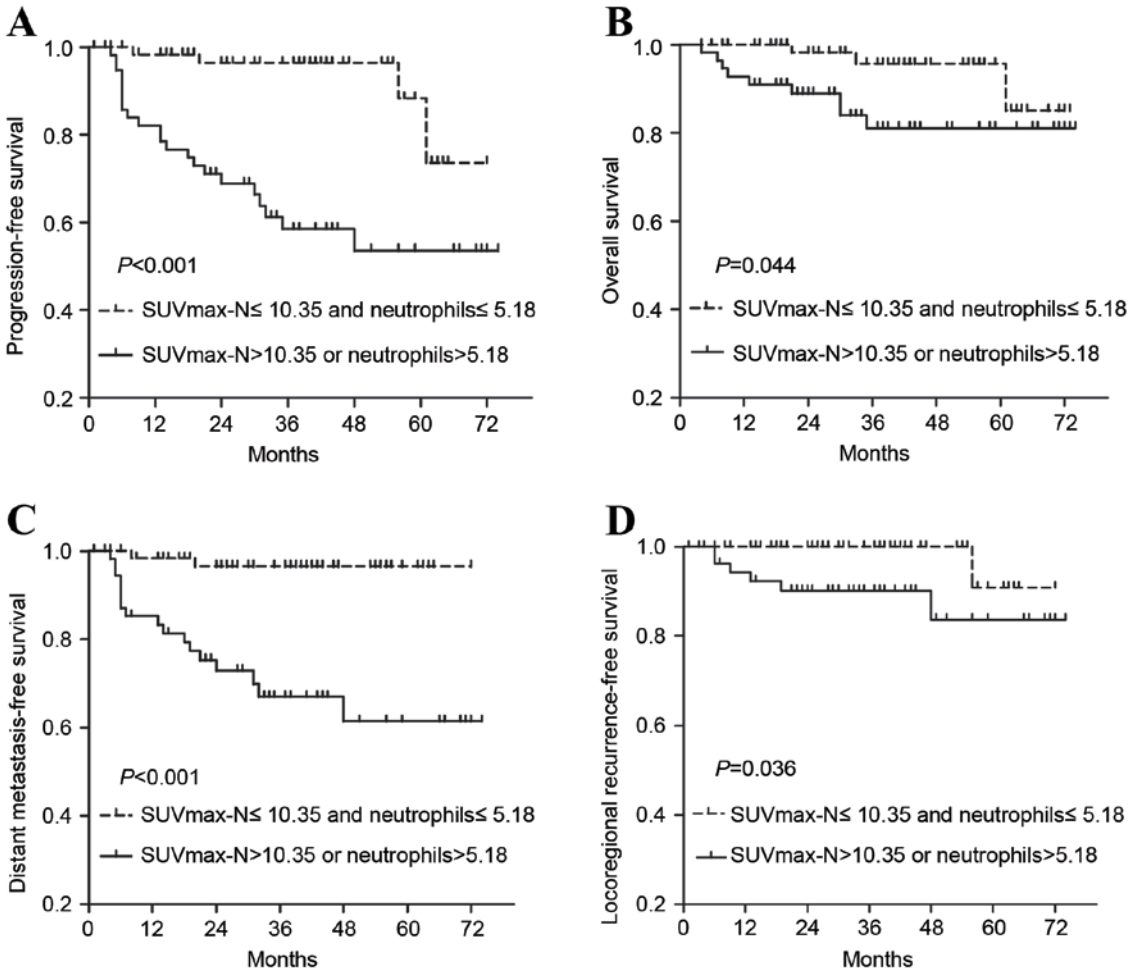

Figure 3. Kaplan-Meier analysis estimates the probabilities of survival for patients stratified by SUVmax-N and neutrophils. (A) Progression-free survival. (B) Overall survival. (C) Distant metastasis-free survival. (D) Locoregional recurrence-free survival. SUVmax, maximum standardized uptake values; SUVmax-N, SUVmax at the regional lymph nodes.

lymphocytes with PFS and OS in NPC; however, the authors did not evaluate the endpoints for distant metastasis and locoregional recurrence. The prognostic roles of leukocyte and monocyte count were not addressed in above two studies. The present study assessed the prognostic power of leukocyte, neutrophil and monocyte counts for predicting PFS, OS, DMFS and LRFS in patients with NPC. It was revealed that neutrophil count (≤5.18) was a negative prognostic

marker for PFS, DMFS and LRFS, and demonstrated a trend of poorer OS. Following multivariate adjustment, neutrophil count maintained independent prognostic significance for PFS and DMFS. Although leukocyte count was a significant prognostic factor for PFS and LRFS and monocyte count was significantly associated with LRFS, they both lost independent prognostic significance in subsequent multivariate analysis. Therefore, compared with leukocytes and monocytes, neutrophils may have an increased predictive value for NPC.

Although the majority of previous studies have focused on the prediction of poor prognosis, with the goal of identifying patients who may benefit from adjuvant chemotherapy, it is equally important that prognostic classifiers can identify patients with good prognosis who may not require further radical treatment, as the benefit of adjuvant chemotherapy in patients with NPC remains unclear (41,42). The present data demonstrated that prognostic stratification was greatly improved following the combination of SUVmax-N and neutrophils in NPC. The combined assessment provides a novel tool for reaching optimal clinical decisions, enabling clinicians to identify low-risk patients (SUVmax-N ≤10.15 and neutrophils ≤5.18) for mild treatment without unnecessary radical therapy. By contrast, patients with an increased level of SUVmax-N or neutrophils, may benefit from higher-dose radiation, adjuvant therapy or molecular-target therapy. However, the mechanism by which the combined assessment improves the prognostic stratification of patients with NPC is unclear. As is commonly reported, reprogramming energy metabolism and inflammation are the emerging hallmarks of cancer (14). Circulating inflammatory cells may represent a high degree of inflammatory cell infiltration in the tumor microenvironment, which may enhance tumor progression and increase glucose uptake. Markedly increased uptake of glucose can be documented readily by noninvasively visualizing glucose uptake using ^{18}F-FDG PET. The inflammation-metabolism-cancer connection may account for the present results, which observed that PET SUVmax and inflammation had a coordinated value for NPC prognosis.

The principal limitations of the present study are its retrospective nature, small sample-size, insufficient follow-up for certain patients and the inclusion of the patients from a single institution. A larger, multicentre prospective design is required for further validation.

In summary, PET SUVmax may be significantly associated with TNM stage and cancer-associated inflammation. The present study has screened out SUVmax-N and neutrophils as independent prognostic indicators for PFS and DMFS. These findings provide additional evidence supporting the use of ^{18}F-FDG PET and CBC in the clinical management of patients with NPC. Further studies are required to clarify whether the combined assessment of ^{18}F-FDG PET functional parameters and peripheral inflammatory markers can improve patient outcomes through an optimized biomarker-guided and imaging-guided treatment strategy.

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