CURRENT ONCOLOGY
A Canadian Cancer Research Journal

ORIGINAL ARTICLE

Sentinel node necrosis is a negative prognostic factor in patients with nasopharyngeal carcinoma: a magnetic resonance imaging study of 252 patients

L. Lu MD PhD,* X. Wei MD PhD,† Y.H. Li MD PhD,† and W.B. Li MD PhD†‡

ABSTRACT

Purpose We explored the patterns of sentinel node metastasis and investigated the prognostic value of sentinel node necrosis (SNN) in patients with nasopharyngeal carcinoma (NPC), based on magnetic resonance imaging (MRI).

Methods This retrospective study enrolled 252 patients at our institution who had metastatic lymph nodes from biopsy-confirmed NPC and who were treated with definitive radiation therapy, with or without chemotherapy. All participants underwent MRI before treatment, and the resulting images were reviewed to evaluate lymph node status. The patients were divided into SNN and non-SNN groups. Overall survival (OS), tumour-free survival (TFS), regional relapse–free survival (RRFS), and distant metastasis–free survival (DMFS) were calculated by the Kaplan–Meier method, and differences were compared using the log-rank test. Factors predictive of outcome were determined by univariate and multivariate analysis.

Results Of the 252 patients, 189 (75%) had retropharyngeal lymph node metastasis, and 189 (75%) had level IIA or IIB lymph node necrosis. The incidence of SNN was 43.4% (91 of 210 patients with lymph node metastasis or necrosis, or both). After a median follow-up of 54 months, the 5-year rates of OS, TFS, RRFS, and DMFS in the SNN and non-SNN groups were, respectively, 79.4% and 95.3%, 73.5% and 93.3%, 80.4% and 96.6%, and 75.5% and 95.3% (all $p < 0.01$). Age greater than 40 years, SNN, T stage, and N stage were significant independent negative prognostic factors for OS, TFS, RRFS, and DMFS.

Conclusions Metastatic retropharyngeal lymph nodes and necrotic level II nodes both seem to act as sentinels. Sentinel node necrosis is an negative prognostic factor in patients with NPC. Patients with SNN have a worse prognosis.

Key Words Sentinel node necrosis, nasopharyngeal carcinoma, prognosis, survival

Curr Oncol. 2017 June;24(3):e220-e225 www.current-oncology.com

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a prevalent and malignant head-and-neck tumour in southern China[1]. The incidence of cervical lymph node metastasis at the time of diagnosis is higher in NPC than in other head-and-neck cancers[2]. Metastatic involvement of the lymph nodes has been shown to have a major negative prognostic effect on patient survival[3]. Efferent lymphatic flow from solid tumours is not random; rather, it follows a pattern in which there is spread to an initial node[4]. From there, secondary spread occurs to other nodes[4].

The sentinel lymph node is defined as the first relay in the lymphatic drainage of the tumour. Retropharyngeal lymph nodes had been regarded as the "first echelon" nodes in NPC[5,6,7], but the findings of Ng *et al.*[8] indicated that the retropharyngeal lymph nodes are less frequently involved than are the cervical nodes. Whether retropharyngeal lymph nodes are the first-echelon nodes remains controversial.

Accurate evaluation of sentinel node metastasis is critical for evaluating treatment options in patients with NPC. In melanoma, sentinel node metastasis has been determined to be the single most important prognostic factor. Nodal necrosis, which has been used to distinguish

Correspondence to: Wenbin Li, Department of Radiology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, No. 600, Yi Shan Road, Shanghai 200233 P.R.C. E-mail: liwenbin@sjtu.edu.cn **DOI:** https://doi.org/10.3747/co.24.3168

between benign and malignant lymph nodes, is one of the most important node imaging features. The reported incidence of nodal necrosis in patients with NPC ranges from 20% to 42%[5,9,10]. However, the prognostic value of sentinel node necrosis (SNN) in patients with NPC remains poorly understood. Our study therefore aimed to explore patterns of sentinel node metastasis and to investigate the prognostic value of SNN, as determined by magnetic resonance imaging (MRI), in patients with NPC.

METHODS

Patients

From June 2010 to December 2011, 252 patients with biopsy-proven NPC treated at our institution with definitive radiation therapy with or without chemotherapy were enrolled in our retrospective study. Median age in the cohort was 40 years (range: 19–83 years). Evaluation by MRI of the nasopharynx and cervical region showed that all patients had cervical lymph node metastasis and no distant metastasis. Clinical staging was assessed using the 2010 American Joint Committee on Cancer staging system. All patients underwent a pre-treatment evaluation that consisted of a complete history, physical examination, hematology and biochemistry profiles, MRI of the nasopharynx and neck, chest computed tomography (CT), and abdominal sonography; patients with T3 or T4 disease, low cervical metastasis, or any lymph node exceeding 4 cm in size also underwent whole-body bone scan or combined positron-emission tomography and CT[11]. Magnetic resonance images of the complete nasopharynx and cervical area were used to evaluate lymph node status[11].

MRI Acquisition

Patients were examined at 3.0 T using a head–neck coil (Magnetom Trio: Siemens Healthcare, Erlangen, Germany; Intera Achieva SMI-2.1: Philips Medical Systems, Andover, MA, U.S.A.). The imaging protocol included a T1- and T2-weighted turbo spin echo sequence (axial scanning repetition time: 2000 ms; echo time: 9 ms; matrix: 320×320; slice thickness: 3.0 mm; field of view: 240×240 mm) and a T2 turbo inversion recovery magnitude sequence (axial scanning repetition time: 4800 ms; echo time: 96 ms; matrix: 384×384; slice thickness: 3.0 mm; field of view: 240×240mm) before injection of contrast material, and then axial and sagittal T1-weighted spin echo and coronal T1-weighted fat-suppressed spin echo images after a bolus intravenous injection of 0.1 mmol/kg gadolinium-DTPA (Bayer Healthcare, Berlin, Germany). The total scan time was 6 minutes and 5 seconds.

Criterion for Cervical Lymph Node Metastases Based on MRI

Magnetic resonance images were interpreted by two experienced radiation oncologists (WBL, YHL) each with more than 7 years of clinical experience in NPC. The criteria used for retropharyngeal and neck lymph node metastatic involvement were these[11,12]:

- Any cervical lymph node with a shortest axial diameter of 10 mm or larger
- A retropharyngeal lymph node with a minimal axial diameter of 5 mm or larger in the largest plane
- Three or more lymph nodes in the same area aggregated in a cluster, with a minimal axial diameter of 8 mm or more
- Lymph nodes of any size with signs of extracapsular spread, including irregular nodal capsular enhancement, infiltration into adjacent fat or muscle, and indistinct nodal margins
- Lymph nodes of any size with central necrosis or an enhancing rim—the definition of central necrosis on magnetic resonance images being a focal area of high signal intensity on T2-weighted images or a focal area of low signal intensity on T1-weighted images with or without a surrounding rim of enhancement (Figure 1)

Treatment Protocol and Follow-Up

Patients were immobilized from head to shoulders with commercially available thermoplastic masks and an individually customized bite block. The CT images (3 mm slice thickness) were acquired from the top of the vertex to the level of the carina. The target volumes were drawn on each axial planning CT slice, based on diagnostic CT images, supplemented with diagnostic MRI or combined positron-emission tomography and CT. The gross tumour volume included the gross extent of the primary disease and involved lymph nodes. Involved lymph nodes were classified as all nodes 1 cm or larger in the short axis, those with a necrotic center, and those that were avid on fluorodeoxyglucose positron-emission tomography. The initial planning target volume (PTV) was defined by adding a 3-mm to 5-mm margin to the gross tumour volume, depending on the proximity of the gross tumour volume to critical structures. The secondary PTV covered areas at high risk

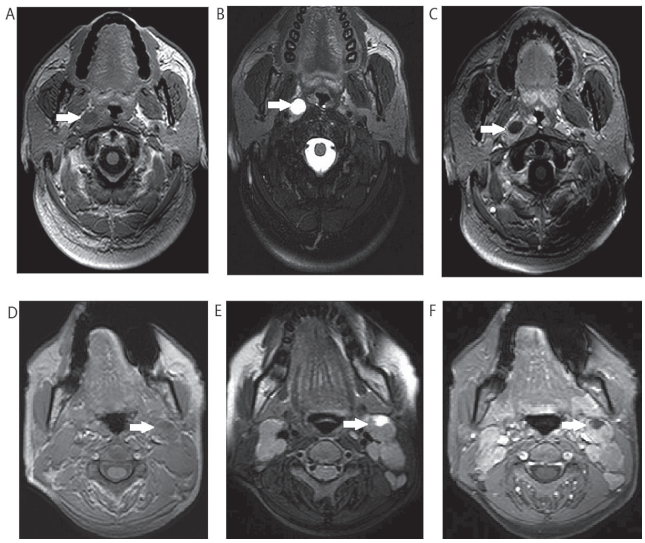

FIGURE 1 Magnetic resonance images demonstrate sentinel node necrosis in 2 patients with nasopharyngeal cancer. (A–C) In a 52-year-old man, necrosis is seen in the right retropharyngeal lymph nodes (arrows). (A) Axial T1-weighted. (B) Axial T1-weighted. (C) Contrast-enhanced T1-weighted. (D–F) In a 49-year-old woman, necrosis is seen in the lymph node in the left level II area (arrows). (D) Axial T1-weighted. (E) Axial T1-weighted. (F) Contrast-enhanced T1-weighted.

for potential microscopic disease. The tertiary PTV included the clinically negative bilateral cervical lymphatics down to the supraclavicular fossae ("elective PTV"). Organs at risk were outlined in three dimensions with an estimated planning organ-at-risk volume margin of 2–10 mm.

Intensity-modulated radiation therapy plans were generated by the Pinnacle treatment planning system (version 8.0m: Philips Healthcare, Amsterdam, Netherlands). Irradiation was delivered by linear accelerator using 6 MV photon energy. The goals were to deliver the prescription dose to at least 95% of the PTV, and 95% of the prescribed dose to at least 99% of the PTV, while meeting the following normal-tissue constraints:

- Spinal cord maximum dose less than 45 Gy
- Brainstem maximum dose less than 54 Gy
- Temporal lobe maximum dose less than 54 Gy
- Eyeball maximum dose less than 54 Gy
- Optic nerve maximum dose less than 54 Gy
- Mandible maximum dose less than 70 Gy
- Dose to 50% of the parotids volume less than 30 Gy, or mean dose less than 26 Gy
- Dose to the lens as little as possible

We also attempted to keep the volume of tissue receiving more than 110% of the prescribed dose to less than 1 mL. For patients with stages III–IV disease, 6 cycles of 5-fluorouracil–cisplatin were planned. Intravenous cisplatin 25 mg/m^2 was delivered daily on days 1–3, and intravenous 5-fluorouracil 525 mg/m^2 was administered on days 1–3. Chemotherapy was stated on the first day of radiotherapy, and each cycle was repeated every 4 weeks. The first 2 cycles of chemotherapy were therefore concurrent with radiation. Patients had a 2-week rest after completion of radiotherapy and then received the additional 4 cycles of chemotherapy. We did not modify the planned dose of chemotherapy in response to specific adverse events. However, when encountering grade 3 or greater toxicities, the cycles were postponed until the nonhematologic toxicities recovered to grade 1 or less, and neutrophil and platelet counts increased to more than 2.0×10^9/L and 100×10^9/L respectively. If a chemotherapy cycle had to be postponed for more than 2 weeks, the chemotherapy was stopped.

Follow-up started on the day of radiation therapy completion and continued to the date of an event or the last follow-up visit. All patients were followed monthly for the first 3 months, every 3 months for the subsequent year, every 6 months for the subsequent 2 years, and then annually.

Statistical Analysis

Statistical analyses were performed using the SPSS Statistics software application (version 17: SPSS, Chicago, IL, U.S.A.). The survival analysis used the Kaplan–Meier method to assess the effect of various variables on overall survival (OS), tumour-free survival (TFS), regional relapse–free survival (RRFS), and distant metastasis–free survival (DMFS). Differences between groups were compared using the log-rank test. Factors that could have affected OS, TFS, RRFS, and DMFS were analyzed by univariate analysis and confirmed by chi-square test. Multivariate analyses were performed to assess the relationship between survival and several variables simultaneously. For those analyses, Cox proportional hazards models were used. The chi-square test was used to compare patterns of treatment failure between the SNN and non-SNN groups. A p value less than 0.05 was considered statistically significant.

RESULTS

Patient Characteristics

Table I shows the characteristics and clinical features of the patients. The male-to-female ratio was 2.45:1 (179 men, 73 women). Of the 189 patients with retropharyngeal lymph node metastasis, 189 had level II (IIA or IIB) nodal metastasis, 71 had level III nodal metastasis, 9 had level IV nodal metastasis, and only 2 had level V or supraclavicular nodal metastasis. Retropharyngeal lymph node metastasis was present in 107 patients without level II nodal metastasis, and 103 patients had level II (IIA or IIB) nodal metastasis without retropharyngeal lymph node metastasis. Of the 210 patients with retropharyngeal or level II lymph node metastasis, 43.3% (n = 91) had necrotic lymph nodes.

Outcomes for Treatment and Follow-Up

All patients underwent radical radiation therapy that covered the nasopharynx and retropharyngeal lymph nodes within the primary target. Whole-neck irradiation was

TABLE I Patient characteristics

Characteristic	Value
Patients (n)	252
Sex [n (%)]	
Men	179 (71)
Women	73 (29)
Median age (years)	40
T Stage [n (%)]	
T1	14 (5.6)
T2	68 (27)
T3	118 (46.8)
T4	52 (20.6)
N Stage [n (%)]	
N1	114 (45.2)
N2	87 (34.5)
N3	51 (20.3)
Clinical stage [n (%)]	
II	36 (14.3)
III	121 (48)
IVa	44 (17.4)
IVb	51 (20.3)
Cervical node metastases [n (%)]	
Single level involved	99 (39.2)
Multiple levels involved	153 (60.8)
Sentinel node metastasis	210 (83.3)
With necrosis	91 (43.3)
Without necrosis	119 (56.7)

performed in all cases. Of the 252 patients, 58.7% (n = 148) were treated with conventional techniques, with 38.9% (98 of 252) undergoing intensity-modulated radiation therapy and 2.4% (6 of 252) undergoing three-dimensional conformal radiation therapy. Most patients (n = 216, 85.7%) received platinum-based neoadjuvant, concurrent, or adjuvant chemotherapy.

The median follow-up duration for the entire group was 54 months (range: 3–60 months), with 8 of the 252 patients (3.2%) being lost to follow-up. Table II summarizes the types of treatment failure that occurred in the cohort. By the last follow-up examination, 19.8% of the patients (n = 50) had developed treatment failure. Patients with SNN accounted for more than four fifths of those who experienced treatment failure (82%, 41 of 50). In the SNN group, 30.8% (28 of 91) developed distant metastases, with 23 developing distant metastasis alone, and 3 developing both distant metastasis and locoregional recurrence. In comparison, the distant metastasis rate in the non-SNN group was only 5.9% (7 of 119). For all patients, the estimated 5-year rates of OS, TFS, RRFS, and DMFS were, respectively, 88.8%, 85.3%, 85.3%, and 87.3%; for the SNN and non-SNN groups, the rates were 79.4% and 95.3%, 73.5% and 93.3%, 80.4% and 96.6%, and 75.5% and 95.3% respectively (all p <0.01). Figure 2 presents the Kaplan–Meier survival curves.

Univariate and Multivariate Analyses

Univariate analysis demonstrated that age greater than 40 years, SNN, and T, N, and clinical stage were associated with OS, TFS, RRFS, and DMFS (Table III). Furthermore, multivariate analysis revealed that age greater than 40 years, SNN, and T and N stage were negative prognostic factors for OS, TFS, RRFS, and DMFS. Clinical stage was not an independent prognostic factor in the multivariate analysis. Statistically significant differences were observed between the various T stages (HR: 1.82; 95% CI: 1.48 to 2.28) and N stages (HR: 1.7; 95% CI: 1.24 to 2.20). The risk for death (HR: 2.1; 95% CI: 1.57 to 2.64) and for developing distant metastasis (HR: 2.0; 95% CI: 1.51 to 2.69) was higher in the SNN than in the non-SNN group (Table IV).

TABLE II Treatment failure, all patients with sentinel node metastasis

Type of failure	Patient group			p Value
	Metastasis		Overall	
	Yes	No		
Locoregional recurrence only				<0.01
Local	7	1	8	
Regional	4	1	5	
Locoregional	2	0	2	
SUBTOTAL	13	2	15	
Distant metastases only				<0.01
Lung	10	2	12	
Bone	9	1	10	
Brain	1	0	1	
Bone and lung	3	1	4	
SUBTOTAL	23	4	27	
Locoregional recurrence and distant metastasis	5	3	8	
TOTAL	41	9	50	<0.01

DISCUSSION

Cervical node metastasis is very common in patients with NPC. King *et al.*[6] considered the retropharyngeal lymph nodes to be the first-echelon nods in NPC; however, Ng *et al.*[8] regarded only level II nodes as the first-echelon nodes in NPC. In the present study, of the 252 patients with lymph node involvement, 189 had retropharyngeal lymph node metastasis, and 189 had level II (IIA or IIB) nodal metastasis —that is, the incidences were the same. Those results indicate that the retropharyngeal lymph nodes and the cervical level II nodes might both be the first-echelon nodes in NPC, perhaps partly because the lymphatic vessels of the nasopharynx drain in two general directions, lateral and medial[5,13]. The primary drainage is the lateral pathway, which drains the lateral nasopharynx and flows into the lateral half of the upper internal jugular chain or into the lateral retropharyngeal lymph node[11].

Cervical nodal metastasis also has a substantial role in the prognosis of patients with head-and-neck squamous cell carcinoma, including NPC. Some studies showed that rates of distant metastasis were higher in NPC patients with retropharyngeal lymph node involvement. Zoumalan *et al.*[14] and Randall *et al.*[15] reported that cervical node necrosis visible on preoperative CT was a useful indicator of extracapsular nodal spread, which was confirmed to be an important negative prognostic indicator in patients with head-and-neck squamous cell carcinoma, with a sensitivity of 91%–95% and a negative predictive value of 88%–98%[16–19]. Those studies appear to suggest that SNN might also be an unfavourable prognostic factor in patients with NPC, and the results of the present study confirmed that suggestion.

Fulmes *et al.*[20] reviewed postoperative pathology data from 48 patients with colon cancer and observed that lymph node necrosis occurred in almost 70% of patients. The 5-year OS rates for patients with and without lymph node necrosis were, respectively, 85% and 50% (p = 0.02), and the authors concluded that lymph node necrosis was a significant positive prognostic factor in patients with colon cancer, which is the opposite of our results. However, their sample size was relatively small, and only 30 patients were enrolled in the survival analysis. In patients with head-and-neck squamous cell carcinoma, the reported incidence of lymph node necrosis is 50%, and the incidence ranges from 20% to 42% in patients with NPC[9,10,12]. In a study of 786 patients with NPC and positive cervical lymph nodes, Mao *et al.*[9] reported that the incidence of lymph node necrosis was only 26.5%. In our study, the incidence of lymph node necrosis was much higher (43.3%, 91 of 210 patients) and similar to the incidence described by Lan *et al.*[11]. In the study by Mao *et al.*[9], lymph node necrosis did not have a significant association with survival in NPC patients; however, that result might reflect the analysis of a relatively small cohort. In our analysis, survival outcomes in the SNN group were substantially poorer than they were in the

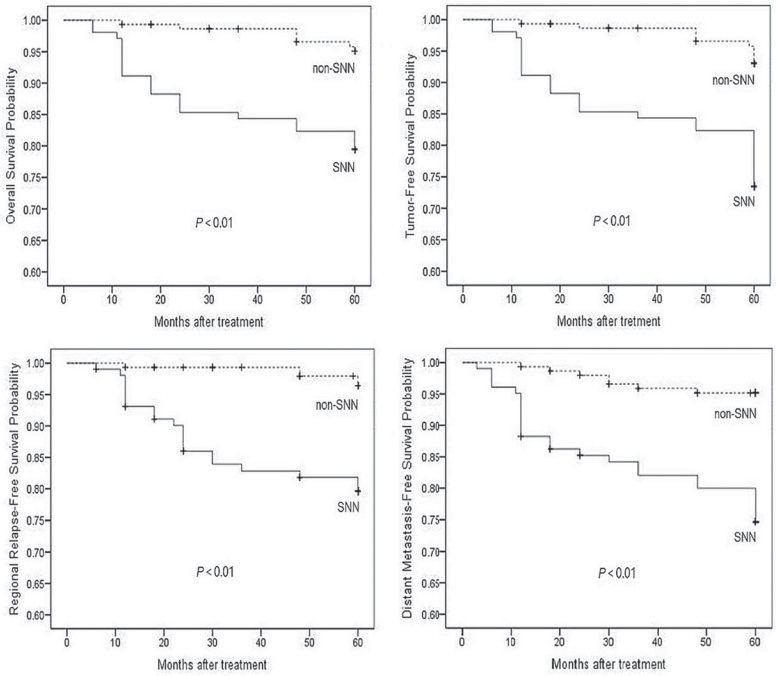

FIGURE 2 Overall, tumour-free, regional relapse-free, and distant metastasis-free survival for the groups with and without sentinel node necrosis (SNN).

TABLE III Univariate analyses of 5-year survival rate, by various clinical characteristics

Variable	Overall survival		Tumour-free survival		Regional relapse-free survival		Distant metastasis-free survival	
	Value (%)	*p* Value	Value (%)	*p* Value	Value (%)	*p* Value	Value (%)	*p* Value
Age group		0.013		<0.01		0.011		<0.01
≤40 Years	89.2		89		89.1		89.2	
>40 Years	83.5		83.2		82.6		83.7	
Sex		0.647		0.15		0.43		0.148
Men	86.7		85.7		86.5		86.6	
Women	86.9		86.9		86.9		86.8	
Sentinel node metastasis		<0.01		<0.01		<0.01		<0.01
Sentinel node necrosis								
Yes	74.6		74.1		74.3		74.2	
No	89.7		89.7		88.9		89.5	
T Stage		0.014		0.028		<0.01		<0.01
T1	95.6		95.7		95.5		95.6	
T2	90.8		90.9		89.9		90.7	
T3	85.4		84.4		84.2		85.3	
T4	72.1		72.3		71.9		72.3	
N Stage		0.038		0.017		<0.01		<0.01
N1	90.5		90.9		90.3		90.1	
N2	84.2		84.4		83.9		84.1	
N3	73.7		73.2		72.1		73.4	
Clinical stage		0.011		<0.01		0.004		<0.01
II	96.4		96.8		96.3		96.4	
III	89.5		89.7		88.9		89.9	
IVa	75.8		75.9		75.4		75.5	
IVb	75.6		75.7		75.3		75.2	

TABLE IV Multivariate analysis of 5-year survival, by independent variables correlated with various clinical characteristics

Variable	Overall survival			Tumour-free survival			Regional relapse-free survival			Distant metastasis-free survival		
	HR	95% CL	*p* Value	HR	95% CL	*p* Value	HR	95% CL	*p* Value	HR	95% CL	*p* Value
Age > 40 years	1.78	1.43, 2.23	<0.01	1.73	1.24, 2.42	<0.01	1.75	1.43, 2.23	<0.01	1.72	1.24, 2.43	<0.01
Sentinel node necrosis	2.1	1.57, 2.64	<0.01	2.13	1.62, 2.75	<0.01	2.1	1.57, 2.74	<0.01	2.01	1.51, 2.69	<0.01
T Stage	1.82	1.48, 2.28	<0.01	1.76	1.48, 2.18	<0.01	1.75	1.47, 2.19	<0.01	1.74	1.40, 2.21	<0.01
N Stage	1.7	1.24, 2.20	<0.01	1.73	1.28, 2.20	<0.01	1.72	1.24, 2.20	<0.01	1.71	1.24, 2.27	<0.01

HR = hazard ratio; CL = confidence limits.

non-SNN group. We suggest that it might be worth considering whether SNN should be incorporated into the American Joint Committee on Cancer staging system for NPC.

One limitation of our study is that the assessment of SNN could be reliably performed only using MRI because, unlike other head-and-neck cancers, NPC is typically treated without the use of cervical node biopsy. In addition, our study is a retrospective analysis of patients who were treated at a single centre. Furthermore, there were no significant differences between the SNN and non-SNN groups with respect to the radiation therapy dose to lymph nodes, because the doses at our centre lie within a small range. We therefore cannot propose treatment strategy adjustments on the basis of the present work.

CONCLUSIONS

In patients with NPC, SNN is a negative prognostic factor. We suggest that it might be appropriate to investigate whether SNN should be incorporated into the American Joint Committee on Cancer staging system for patients with NPC.

CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

AUTHOR AFFILIATIONS

*Department of Radiology, Nanjing First Hospital, Nanjing Medical University, Nanjing, †Department of Radiology, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, and ‡Imaging Center, Kashgar Prefecture Second People's Hospital, Xinjiang, P.R.C.

REFERENCES

1. Wei WI, Sham JS. Nasopharyngeal carcinoma. *Lancet* 2005;365:2041–54.
2. Ho FC, Tham IW, Earnest A, Lee KM, Lu JJ. Patterns of regional lymph node metastasis of nasopharyngeal carcinoma: a meta-analysis of clinical evidence. *BMC Cancer* 2012;12:98.
3. Zheng J, Li J, Xu L, *et al*. Phosphorylated Mnk1 and eIF4E are associated with lymph node metastasis and poor prognosis of nasopharyngeal carcinoma. *PloS One* 2014;9:e89220.
4. Salguero-Fernandez I, Rios-Buceta L, Jaen-Olasolo P. Sentinel lymph node in nonmelanoma skin cancer [Spanish]. *Actas Dermosifiliogr* 2011;102:589–98.
5. Wang XS, Hu CS, Ying HM, Zhou ZR, Ding JH, Feng Y. Patterns of retropharyngeal node metastasis in nasopharyngeal carcinoma. *Int J Radiat Oncol Biol Phys* 2009;73:194–201.
6. King AD, Ahuja AT, Leung SF, *et al*. Neck node metastases from nasopharyngeal carcinoma: MR imaging of patterns of disease. *Head Neck* 2000;22:275–81.
7. Neel HB 3rd, Taylor WF, Pearson GR. Prognostic determinants and a new view of staging for patients with nasopharyngeal carcinoma. *Ann Otol Rhinol Laryngol* 1985;94:529–37.
8. Ng SH, Chang JT, Chan SC, *et al*. Nodal metastases of nasopharyngeal carcinoma: patterns of disease on MRI and FDG PET. *Eur J Nucl Med Mol Imaging* 2004;31:1073–80.
9. Mao YP, Liang SB, Liu LZ, *et al*. The N staging system in nasopharyngeal carcinoma with Radiation Therapy Oncology Group guidelines for lymph node levels based on magnetic resonance imaging. *Clin Cancer Res* 2008;14:7497–503.
10. Liu LZ, Zhang GY, Xie CM, Liu XW, Cui CY, Li L. Magnetic resonance imaging of retropharyngeal lymph node metastasis in nasopharyngeal carcinoma: patterns of spread. *Int J Radiat Oncol Biol Phys* 2006;66:721–30.
11. Lan M, Huang Y, Chen CY, *et al*. Prognostic value of cervical nodal necrosis in nasopharyngeal carcinoma: analysis of 1800 patients with positive cervical nodal metastasis at MR imaging. *Radiology* 2015;276:619. [Erratum for: Lan M, Huang Y, Chen CY, *et al*. Prognostic value of cervical nodal necrosis in nasopharyngeal carcinoma: analysis of 1800 patients with positive cervical nodal metastasis at MR imaging. *Radiology* 2015;276:536–44]
12. King AD, Tse GM, Ahuja AT, *et al*. Necrosis in metastatic neck nodes: diagnostic accuracy of CT, MR imaging, and US. *Radiology* 2004;230:720–6.
13. Lindberg R. Distribution of cervical lymph node metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. *Cancer* 1972;29:1446–9.
14. Zoumalan RA, Kleinberger AJ, Morris LG, *et al*. Lymph node central necrosis on computed tomography as predictor of extracapsular spread in metastatic head and neck squamous cell carcinoma: pilot study. *J Laryngol Otol* 2010;124:1284–8.
15. Randall DR, Lysack JT, Hudon ME, *et al*. Diagnostic utility of central node necrosis in predicting extracapsular spread among oral cavity squamous cell carcinoma. *Head Neck* 2015;37:92–6.
16. Johnson JT, Myers EN, Bedetti CD, Barnes EL, Schramm VL Jr, Thearle PB. Cervical lymph node metastases. Incidence and implications of extracapsular carcinoma. *Arch Otolaryngo* 1985;111:534–7.
17. Snyderman NL, Johnson JT, Schramm VL Jr, Myers EN, Bedetti CD, Thearle P. Extracapsular spread of carcinoma in cervical lymph nodes. Impact upon survival in patients with carcinoma of the supraglottic larynx. *Cancer* 1985;56:1597–9.
18. Puri SK, Fan CY, Hanna E. Significance of extracapsular lymph node metastases in patients with head and neck squamous cell carcinoma. *Curr Opin Otolaryngol Head Neck Surg* 2003;11:119–23.
19. Jose J, Coatesworth AP, Johnston C, MacLennan K. Cervical node metastases in squamous cell carcinoma of the upper aerodigestive tract: the significance of extracapsular spread and soft tissue deposits. *Head Neck* 2003;25:451–6.
20. Fulmes M, Setrakian S, Raj PK, Bogard BM. Cancer biology and necrotic changes in metastatic lymph nodes and survival of colon cancer patients. *Am J Surg* 2005;189:364–8.