·Nasopharyngeal Carcinoma Column·

A clinical verification of the Chinese 2008 staging system for nasopharyngeal carcinoma

Yan-Ping Mao,[1,2] Wen-Fei Li,[1,2] Lei Chen,[1,2] Ying Sun,[1,2] Li-Zhi Liu,[1,3] Ling-Long Tang,[1,2] Su-Mei Cao,[1,4] Ai-Hua Lin,[5] Ming-Huang Hong,[1,4] Tai-Xiang Lu,[1,2] Meng-Zhong Liu,[1,2] Li Li[1,3] and Jun Ma[1,2]

1. State Key Laboratory of Oncology in South China, Guangzhou, Guangdong, 510060, P. R. China
2. Department of Radiation Oncology, Cancer Center, Sun Yat-sen University, Guangzhou 510060, P. R. China
3. Department of Radio Diagnosis and Radiation Intervention, Cancer Center, Sun Yat-sen University, Guangzhou 510060, P. R. China
4. Department of Nasopharyngeal Carcinoma, Cancer Center, Sun Yat-sen University, Guangzhou 510060, P. R. China
5. The School of Public Health of Sun Yat-sen University, Guangzhou 510080, P. R. China

Correspondence to: Jun Ma
Tel.: 86.20.87343469
Fax: 86.20.87343295
Email: majun2@mail.sysu.edu.cn

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[Abstract] Background and Objective: The Chinese 2008 staging system for nasopharyngeal carcinoma (NPC) was a common set of recommendations by initial revision of the previous '92 staging system. This study was to verify the Chinese 2008 staging system and to provide evidence for its further revision. Methods: Between January 2003 and December 2004, 924 consecutive patients with newly diagnosed, nondisseminated biopsy-proven NPC, presented at the Department of Radiation Oncology, Cancer Center, Sun Yat-sen University, were entered into our study. All patients received magnetic resonance imaging examination of the neck and nasopharynx before treatment. According to the principle of the staging system, the indices of hazard consistency, hazard discrimination, prognostic value, and distribution were used to evaluate the Chinese 2008 staging system. Results: According to the Chinese 2008 staging system, the distribution of stage group for the whole series was 4.9% for the stage I, 22.6% stage II, 38.0% stage III, and 34.5% stage IVA. As for hazard discrimination, the 4-year local relapse-free survival (LRFS) rates for T1-T4 patients were 95.4%, 93.7%, 90.5% and 79.1%, respectively. Although the separation of LRFS for all subclassifications of T-stage showed reasonable, the differences among the subgroups T1, T2, and T3 were still lack of significant statistically. The 4-year distant metastasis failure-free survival (DMFS) rates for N0-N3 patients were 89.4%, 84.3%, 73.6, and 59.2%, respectively. The 4-year overall survival (OS) rates for stage Ⅰ-Ⅳ patients were 96.7%, 94.1%, 82.6% and 67.1%, respectively. As for hazard consistency, the distinctions between T3 with skull base involvement and T3 with medial pterygoid muscle in the hazard ratios of local failure (1.628 vs. 3.905) and disease failure (1.630 vs. 3.288) were large. Multivariate analyses showed that cervical nodal level, extranodal neoplastic spread, and laterality were independent prognostic factors for OS and DMFS, but maximal axial diameter was not. Conclusion: Using the Chinese 2008 staging system for NPC produces an acceptable distribution of patient numbers. Stage group, T classification, and N classification represent independent prognosis factors for major endpoints. However, our study reveals several deficiencies in the current system yet.

Key words: nasopharyngeal neoplasm, magnetic resonance imaging (MRI), tuomor stage, stage parameters

The 2008 staging system for nasopharyngeal carcinoma (NPC), as recommended by the Chinese Committee for Clinical Staging of Nasopharyngeal Carcinoma, was a consensus based on evidence-based medicine and primary revisions made on the 1992 staging system after adequate consultation.[1] Herein, we conducted a retrospective study on NPC based on a large scale data under modern diagnostic and treatment models, to provide a clinical verification on the prognostic value of the 2008 staging system for NPC.

Material and Methods

Clinical data. Between January 2003 and December 2004, 924 naive patients with pathologically diagnosed NPC, without distant metastasis, treated at the Department of Radiation Oncology, Sun Yat-sen University Cancer Center, were entered into our study. Of the 924 patients, 685 were men and 239 were women, with a male to female ratio of 2.9:1, and the median age was 45 years (range, 11-78 years). Histologically, 911 (98.6%) patients had WHO type II disease, seven (0.8%) had WHO type I disease and four (0.4%) had WHO type III disease, and two (0.2%) had well differentiated adenocarcinoma. All patients received physical examinations, nasopharyngofiberscopy, chest X-ray, abdominal ultrasound, and MRI scan of the nasopharyx and neck. All patients with N2-3 disease underwent whole-body bone scan; 56 (6.1%) patients underwent positron emission tomography-computed tomography (PET-CT) examination.

MRI scanning. MRI scanning was conducted using the superconductive magnetic resonance imaging system GE1.5T on transversal, sagittal and coronal planes under routine SE sequence. The parameters in the scanning were as follows: T1WI TR = 400-600; TE = 15-25 ms; T2WI TR = 1800-3000; TE = 90-150 ms; flip angle: 90°; slice thickness/gap: 5 mm/1 mm; matrix 256×256; FOV: 210 mm. A standard quadrature head coil was used. Transversal scanning started from the upper margin of frontal sinus and ended at clavicular level, and additional sagittal and coronal scanning were performed on nasopharynx and skull base. After plain scanning, bolus injection of Gd-DTPA (0.1 mmol/kg) was given, then transversal and sagittal T1WI scanning was performed as that in plain scanning; TIWI fat-suppression sequence was used in the coronal scanning.

Clinical staging. All MRI data were reviewed separately by two experienced radiologists (Any disagreements were resolved by consensus of the study team). Medical records (such as cranial nerve erosion) and imaging studies were analyzed retrospectively, and the patients were staged according to the 2008 staging system for nasopharyngeal carcinoma.[1] The 2008 staging system for NPC was shown in Table 1.

Image assessment and criteria for staging variables in the 2008 staging system for nasopharyngeal carcinoma. Parapharyngeal space, nasal cavity, oropharynx and masticator space were defined according to the 2008 staging system.[1] The skull base included basilar part of sphenoid bone, petrous apex, clivus, foramen lacerum, greater wing of sphenoid bone, foramen rotundum, foramen ovale, foramen spinosum, jugular foramen, hypoglossal canal and pterygoid process (including medial and lateral plates of pterygoid process, and basilar part of pterygoid process). Paranasal sinus included ethmoid

Table 1 Criterions of the Chinese 2008 nasopharyngeal carcinoma staging systems

T-Stage	2008 staging systems[1]
T1	Tumor confined to the nasopharynx
T2	Nasal cavity, oropharynx, parapharyngeal extension
T3	Skull base, medial pterygoid muscle extension
T4	Cranial nerves, paranasal sinuses, masticator space excluding medial pterygoid muscle, intracranial (cavernous sinus, dural meninges) extension
N-Stage	
N0	No regional lymph node metastasis
N1a	Retropharyngeal lymph node involvement
N1b	Unilateral level Ⅰb, Ⅱ, Ⅲ, and Va involvement, and diameter≤3 cm;
N2	Bilateral level Ⅰb, Ⅱ, Ⅲ, and Va involvement, or diameter>3 cm or with extranodal neoplastic spread;
N3	Level Ⅳ, Vb involvement
M-Stage	
M_0	Without metastases
M_1	With metastases
Clinical Stage	
Ⅰ	$T_1N_0M_0$
Ⅱ	$T_1N_{1a\sim1b}M_0$, $T_2N_{0\sim1b}M_0$
Ⅲ	$T_{1\sim2}N_2M_0$, $T_3N_{0\sim2}M_0$
Ⅳa	$T_{1\sim3}N_3M_0$, $T_4N_{0\sim3}M_0$
Ⅳb	Any T, N and M_1

sinus, maxillary sinus, frontal sinus and sphenoid sinus.

Diagnostic criteria for retropharyngeal and cervical lymph node metastasis were as follows:[2] ① any lymph node with a minimal axial diameter (MID) in the largest plane of an individual node at least 10 mm (11 mm for level IIa; ② lymph nodes of any size with central necrosis or a contrast-enhancing rim; ③ nodal grouping, the presence of three or more contiguous and confluent lymph nodes, each of which should have a MID of 8 to 10 mm; ④ lymph nodes of any size with extracapsular spread, the presence of indistinct nodal margins, irregular nodal capsular enhancement or infiltration into the adjacent fat or muscle; ⑤ retropharyngeal lymph nodes with MID in the largest plane of an individual node at least 5 mm.

A classification method for cervical node recommended by the Chinese Committee for Clinical Staging of Nasopharyngeal Carcinoma was used to define the location of lymph nodes. The following nine levels were evaluated: (1) retropharyngeal region; (2) level Ia; (3) level Ib; (4) level IIa; (5) level IIb; (6) level III; (7) level IV; (8) level Va; (9) level Vb. Lymph node in the juncture of two levels would be classified into the level where its center was located.

Treatment. Of the 924 patients, 773 (83.7%) received conventional 2-dimensional radiotherapy, 118 (12.7%) received intensity-modulated radiotherapy and 33 (3.6%) received 3-dimensional radiotherapy. Of the 629 patients with stage III-IV (T3-T4 or N2-N3) disease, 517 (82.2%) were given platinum-based induction, concomitant or adjuvant chemotherapy.

For the radiotherapy, external irradiation was given with ^{60}Co γ-ray or photon beam at the dosage of 6-8 MV by a linear accelerator. During therapy, patients were immobilized by thermoplastic mask. A spiral CT system Siemens Plus4 was used to conduct constract-enhanced scanning from vertex to 1 cm below the clavicle, with a slice thickness/gap of 3 mm/3 mm. According to the definitions in the ICRU report 50, gloss tumor volume in nasopharynx (GTVnx), gloss tumor volume in cervical nodes (GTVnd), clinical target volume 1 (CTV_1), clinical target volume 2 (CTV_2) and affected organs, such as brain stem, spinal cord, optical nerve, chiasma opticum, pituitary gland, temporal lobe, lens, parotid gland, temporomandibular joint and mandible, were delineated on each slice of CT images in the CT-sim, 3D-TPS or IMRT workstation. During conventional 2-dimensional radiotherapy, isocentric therapy was given under low-melting-point lead shielding and conventional fractionation (radiotherapy was given 5 days per week at the dosage of 2 Gy). Accumulative dosage in target volume was 68-72 Gy in GTVnx, 60-70 Gy in GTVnd, 60 Gy in CTV_1 and 50 Gy in CTV_2. For those with substantial parapharyngeal invasion, an additional dosage of 8-10 Gy was given in the parapharyngeal field. For patients with intracranial or skull base invasion, additional external irradiation of 8-10 Gy was given on the skull base radiation field. For patients with invasion in nasal cavity or ethmoid sinus, electron irradiation on the ethmoid sinus was added.[3] In 3D-TPS, the ADAC laboratories Pinnacle RTP System 6.0i was used for the calculation. Prescribed dosage in target volume was 65-70 Gy in GTVnx, 60-70 Gy in GTVnd, 60 Gy in CTV60, $\geqslant$50 Gy in CTVnx50 and CTVnd50.[4] The planning and execution of IMRT scheme were conducted by the PEACOCK system (NOMOS). Prescribed dosage in target volume was 68 Gy/30 times in GTVnx, 60-66 Gy by 30 fractions in GTVnd, 60 Gy by 30 fractions in CTV_1 and 54 Gy by 30 fractions in CTV_2.[5] In case of residual carcinoma in nasal cavity at the end of external irradiation, ^{192}Ir after-loading radiotherapy was given at the dosage of 10-15 Gy by 2-3 fractions.

Follow-up and statistical methods. The follow-up duration was calculated from the first day of therapy to either the day of death or June 30th, 2009. The median follow-up for the whole group was 55 months (range, 3-73 months), and that for the survival group was 57 months (range, 3-73 months). Overall survival duration was defined as the time span from the first date of treatment to the date of death. For patients who were still alive at the end of follow-up, the survival duration data were censored. Local recurrence-free survival duration and distant metastasis-free survival duration were defined likewise. SPSS11.0 software was used for the statistical analysis; multivariate analysis was conducted with Cox proportional hazards model, and survival rate calculated by Kaplan-Meier method; log-rank test was used to reveal the significance of differences in survival rate. Based on the clinical staging principles, the staging system was evaluated by parameters including hazard consistency and hazard discrimination, prognostic value and balance of distribution.

Results

Case distribution and failure patterns. According to the 2008 staging system for NPC, the distribution of T- and N-categeries in 924 patients was detailed in table 1. The proportions of patients at stage I was 4.9%, stage II was 22.6%, stage III was 38.0%, and stage IVA was 34.5%. In particular, each T-staging subgroup accounted for 19.8% -29.0% of the patients, indicating proper distribution. In terms of N-staging, the highest percentage of 35.1% was seen in N2 subgroup. Till the last date of follow-up, 240 patients reported failure events, of which 92 had local recurrence, 32 had regional recurrence, 147 had distant metastasis; 196 patients died.

Hazard ratio of local failure and disease failure under the 2008 T staging. Under the framework of the 2008 T staging, all patients were assigned into seven subgroups including T1, T2, T3 with skull base erosion, T3 with medial pterygoid muscle erosion, T4 with paranasal sinus erosion, T4 with masticator space (except for medial pterygoid muscle) erosion and T4 -other subgroup. With T1 subgroup as baseline (HR=1), radiotherapy techniques and the 2008 N staging as adjustment, and gender and age as covariates, hazard ratios (HRs) of local failure and disease failure were observed. HRs of varied subgroups were shown in table 2. The HRs of local failure (1.628 vs. 3.905) and disease failure (1.630 vs. 3.288) were substantially different between T3 with skull base erosion and T3 with medial pterygoid muscle erosion.

Influence onprognosis by different lymph node parameters in NPC. The following known important prognostic variables were included in the Cox proportional hazards model: age, gender, chemotherapy, radiation techniques, T-category in the 2008 staging system for NPC, nodal variables including retropharyngeal lymph node, maximal axial diameter (MAD) of cervical lymph nodes, level of cervical lymph nodes, laterality of cervical lymph nodes, extracapsular spread. The HRs of distant metastasis and death were observed. The results suggested level, extracapsular spread and laterality of cervical lymph nodes were independent prognostic factors for overall survival rate and distant metastasis-free survival rate in NPC, whereas MAD of cervical lymph nodes was not (Table 3).

Table 2 The distribution of the Chinese 2008 staging system: cases (%)

	T1	T2	T3	T4	Total
N0	45(4.9%)	34(3.7%)	25(2.7%)	34(3.7%)	138(14.9%)
N1a	35(3.8%)	42(4.5%)	51(5.5%)	58(6.3%)	186(20.1%)
N1b	41(4.4%)	57(6.2%)	56(6.1%)	53(5.7%)	207(22.4%)
N2	50(5.4%)	74(8.0%)	95(10.3%)	105(11.4%)	324(35.1%)
N3	12(1.3%)	17(1.8%)	22(2.4%)	18(1.9%)	69(7.5%)
Total	183(19.8%)	224(24.2%)	249(26.9%)	268(29.0%)	924(100.0%)

Survival profile under the 2008 staging. The 4-year local recurrence-free survival rates of stages T1-T4 patients were 95.4%, 93.7%, 90.5% and 79.1%, respectively (Fig. 1). The survival curves for all subclassifications of T stage separated in an abnormal order. However, the differences between adjacent T categories were not significant between T1 and T2 group, T2 and T3 group, and T1 and T3 group (P=0.292, 0.442 and 0.089, respectively).

The 4-year distant metastasis-free survival rates of stages N0-N3 patients were 89.4%, 84.3%, 73.6 and 59.2%, respectively (Fig. 2). The survival curves for all subclassifications of N stage separated well. The differences between adjacent N categories were significant.

Table 3 Risk of local relapse and disease failure by T stage of the Chinese 2008 staging system

	Cases(%)	Local RecurrentHR(95%CI)	Disease failureHR(95%CI)
T1	183(19.9)	1	1
T2	224(24.2)	1.539(0.679- 3.490)	1.737(1.077-2.801)
T3			
Skull base	213(23.1)	1.628(0.706- 3.755)	1.630(1.002-2.653)
Medial pterygoid muscle	36(3.9)	3.905(1.368-11.144)	3.288(1.663-6.502)
T4			
Paranasal sinuses	110(11.9)	3.289(1.417- 7.635)	2.986(1.793-4.972)
Masticator space excluding medial pterygoid muscle	98(10.6)	6.072(2.734-13.483)	4.002(2.417-6.626)
Other	60(6.5)	3.227(1.252- 8.315)	2.424(1.345-4.369)

Table 4 Independent effect of nodal parameters in multivariate analysis

Stage parameters	Hazard ratio for distant metastasis (95%CI)	Hazard ratio for death (95%CI)
Size		
≤30 mm	0.722	1.059
>30 mm	(0.479–1.089)	(0.751–1.493)
Level		
Ⅰb、Ⅱ、Ⅲ、Va	2.107	1.567
Ⅳ、Vb	(1.380–3.217)	(1.048–2.341)
Laterality		
Unilateral	1.204	1.113
Bilateral	(1.002–1.582)	(1.004–1.403)
ENS		
No	2.098	1.486
Yes	(1.432–3.074)	(1.066–2.070)

Abbreviations: CI =confidence interval

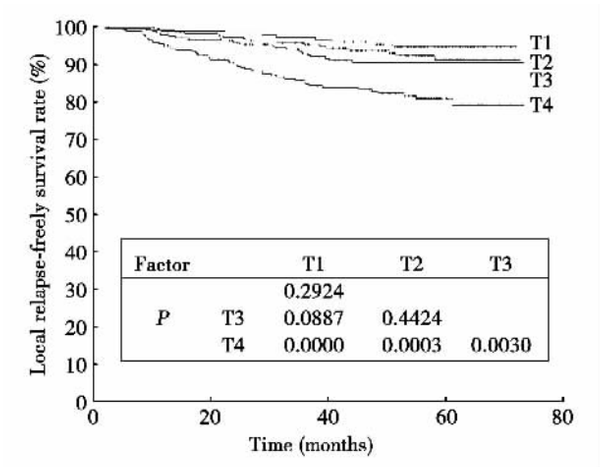

Figure 1 Local relapse-freely survival curves of the patients at different 2008 T-stages for nasopharygeal carcinoma

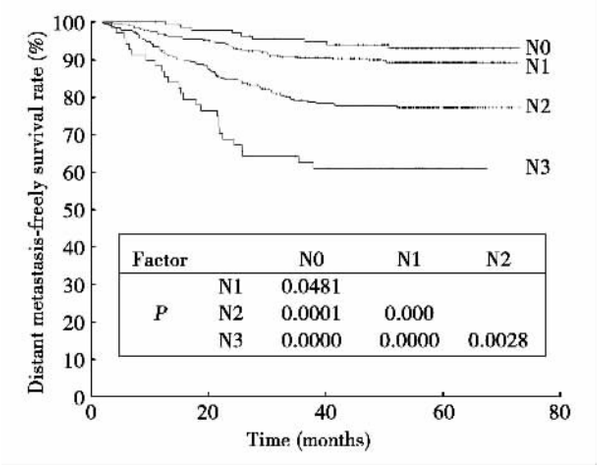

Figure 2 Distant metastasis-freely survival curves of the patients at different 2008 N-stages for nasopharyngeal carcinoma

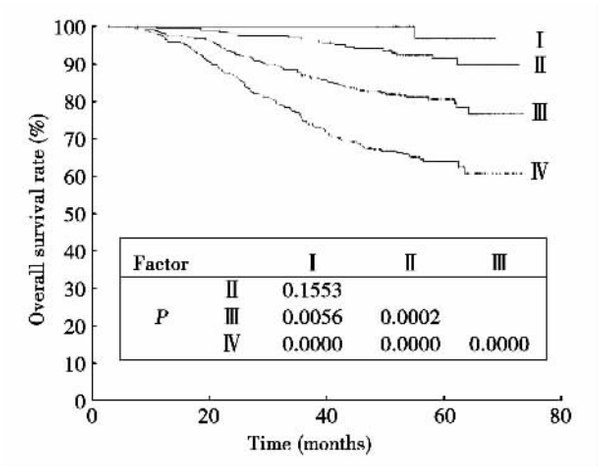

Figure 3 Overall survival curves of the patients at different 2008 clinical stages for nasopharyngeal carcinoma

The 4-year overall survival rate of stages Ⅰ–Ⅳ patients were 96.8%, 94.1%, 82.6% and 67.1%, respectively (Fig. 3). The survival curves for all subclassifications of clinical stage separated well. The differences between adjacent stages, except that between stage Ⅰ and stage Ⅱ, were significant.

Discussion

A staging system should be established based on the following principles: (1) advancement, that is, the revisions on a staging system should reflect improvement in diagnostic and treatment methods;[6] (2) practicality, a staging system should be simple and easy to memorized;[7] (3) objectiveness, each stage should be clearly defined, with objective diagnostic criteria; (4) scientificity, the staging system should be in accordance with the scientific principles of hazard consistency and hazard discrimination, prognostic value and balance of distribution.[8] The 2008 staging system for NPC established MRI as the standard diagnostic approach, suggesting advancement. Compared with the 1992 staging system, the revised staging system was simpler and easier to memorize. In addition, it clearly defined the boundary of parapharyngeal space, masticator space, nasal cavity and oropharynx. In accordance to the principle of scientificity of a staging system, T

stage, N stage and overall stage, as determined by the 2008 staging system for NPC, were independent prognostic factors for LRFS, DMFS and OS. Among 924 patients, patients with early or middle stage (stage I–II) disease accounted for 27.5%, and those with advanced stage disease accounted for 72.5%. In general, the staging system for NPC 2008 was an acceptable system. However, our study revealed several deficiencies of it.

Evaluation on T staging. The results of our study suggested that one of the deficiencies observed in the 2008 T –stage was a lack of hazard discrimination, that is, the differences for LRFS between adjacent T categories revealed no significant differences between T1 and T2 group, T2 and T3 group, and T1 and T3 group. With the 6th edition UICC/AJCC staging system, Cheng et al. [9] reported that the 4–year local control rate was 94%–99% for T1 –T3 patients and 83% for T4 patients treated with 2–dimensional radiotherapy. Lee et al.[10] suggested that the 4–year LRFS in NPC treated with conformal radiotherapy was as much as 98%. Tham et al. [11] reported a lack of significant differences in LRFS among T1, T2 and T3 for NPC patients treated with conformal radiotherapy, but local control in T4 subgroup were relatively poorer. It is considered the main reasons may be, first of all, the use of magnetic resonance imaging provides more sensitive and accurate delineation on tumor target volume;[12] secondly, the application of computed tomography radiation therapy planning system provides direct visualization of the tumor in a 3–dimension and thus reduces the possibility of missed irradiation; meanwhile, 3 –dimensional conformal radiotherapy and intensity–modulated radiotherapy are better than traditional 2 –dimensional radiotherapy technique in ensuring adequate dosage in skull base and parapharyngeal space; lastly, the use of combined chemotherapy also improves local control rate to a certain extent.[13] However, in some T4 NPC cases, since tumors are larger and closer to vital organs, such as brain stem and spinal cord, dosage in tumor lesion is compromised due to the limitation of tolerable dosage in the normal organs. Even if with conformal radiotherapy, local control in these patients is still poor.[11] Based on the 6th UICC/AJCC system, Mao et al. [14] revealed that, although the LRFS for T1–T3 patients were hardly separated, the disease–free survival rate between adjacent T categories revealed that T1 was closer to T2a, while T2b closer to T3. In addition, parapharyngeal space involvement was an independent prognostic factor for distant metastasis in stage I–II patients. Therefore, they suggested T1 and T2a should be incorporated as T1, and T2 with parapharyngeal space involvement and T3 with bony skull base involvement incorporated as T2, so as to increase the predicting ability of T stage. With the widespread use of intensity–modulated radiotherapy, local control rate in NPC has been further increased, and the influence of T stage on prognosis will be less and less important. Thus the T –categery shall be further modified.

The definition of infratemporal fossa in 1992 staging system[15] and the definition of masseteric space in AJCC/UICC staging system[16] were designed to describe the extent of lateral invasion from the primary lesion. However, these definitions were not completely consistent to the anatomic definitions, they might cause misunderstandings for clinicians, which had hindered the widespread use of these staging systems. Based on the anatomic definition of masticator space, the 2008 staging system for NPC has included medial pterygoid muscle into T3 subgroup and the masticator space except for medial pterygoid muscle into T4 subgroup.[1] However, the results of our study suggested the risk for local recurrence was similar for T3 with medial pterygoid muscle erosion and T4 subgroup. Therefore, inclusion of the entire masticator space into the T4 subgroup might be more reasonable and more comprehensible for clinicians.

Studies on N staging. The 2008 N staging has its advantages: ① N staging based on transversal images by magnetic resonance imaging and RTOG classification for cervical lymph nodes level can avoid subjectiveness and provide more accurate workup;[17] ② incorporation of laterality and extracapsular spread as parameters in N staging system has improved the predicting ability of the staging method;[17] ③ it clarified the role of retropharyngeal lymph nodes in the staging system.[18, 19] Our results showed that the survival curves for DMFS according to the 2008 N staging system were rationally distributed, and the differences between adjacent stages were significant, But the 2008 N staging still has some disadvantages. The prognostic significance of nodal size has always been reported to be much controversial. Lee et al. [20] suggested that nodal diameter of ⩾6 cm, bilateral nodal metastasis, superclavicular nodal metastasis and immobilized lymph nodes were independent

prognostic factors in NPC. Teo et al.[21] found that Hos staging, immobilized lymph nodes and contralateral nodal metastasis were independent prognostic factors, while maximal diameter of lymoh nodes was not an independent prognostic factor. Heng et al.[22] and Zong et al.[23] found that the laterality and level of lymoh nodes were independent prognostic factors, while the mobility and size of lymph nodes were not. In the study based on transversal images by MRI, Mao et al.[17] revealed that MAD of cervical lymph node was not independent prognostic factor in NPC; in addition, the MAD of the lymph node was significantly interrelated with extracapsular spread, laterality and level. Hence, the size of lymph node might be just an accompanied factor. Its inconsistent prognostic significance in NPC might be related to the variations in evaluation approaches and other factors that were included in the analysis. When using transversal image as evaluation approaches, size of lymph node should not be included as N staging criteria. Secondly, the 2008 staging system has used the classification for cervical nodes level in replacement of previous concepts of superior and inferior cervical lymph nodes and superclavicular fossa. The classification for cervical lymph nodes has gradually evolved from surgery-based method to imaging-based method, and various versions of definitions have been used in the past.[24] To avoid controversies with regard to definitions, major European and North American oncology groups including RTOG proposed a classification for negative cervical nodes in head and neck cancers, which translates surgical guidelines into into radiologic guidelines based on transversal CT images, facilitating uniform delineation of the target volumes in the neck among radiation oncologists. It was an important step in establishing consensus.[24] The 2008 staging system for NPC has defined the classification of cervical nodes based on the RTOG guidelines, but with some modifications, which might be in the way of the communications of clinical experience and the comparisons of study results among countries.

As a large scale retrospective case study in highly prevalent area of NPC with long-term follow-up and MRI-based data, our study reflected the prognosis profile under current diagnostic and treatment ability in our country. As an overall verification on the 2008 staging system, hopefully our study could provide valuable scientific evidence for further revision and improvement of the staging system.

References

[1] Committee of Chinese Clinical Staging of Nasopharyngeal Carcinoma. Report on the revision of nasopharyngeal carcinoma '92 staging [J]. Chin J Radiat Oncol, 2009,18(1):2-6. [in Chinese]

[2] Van den Brekel MW, Stel HV, Castelijns JA, et al. Cervical lymph node metastasis: assessment of radiologic criteria [J]. Radiology, 1990, 177(2):379-384.

[3] Lu LX, Zhao C, Han F, et al. Initial study of the clinical target volume delineation for radiotherapy of nasopharyngeal carcinoma [J]. Chin J Radiat Oncol, 2005,14(2):81-85. [in Chinese]

[4] Luo W, Deng XW, Lu TX, et al. Dosimetric evaluation for three dimensional conformal, conventional,and traditional radiotherapy plans for patients with early nasopharyngeal carcinoma [J]. Aizheng, 2004,23(5):605-608. [in Chinese]

[5] Zhao C, Lu LX, Han F, et al. Intensity modulated radiation therapy for 122 patients with untreated nasopharyngeal carcinoma [J]. Chin J Radiat Oncol, 2006,15(5):364-368. [in Chinese]

[6] Wei BQ. Relevant issues should be immediately resolved in staging system for nasopharyngeal carcinoma [J]. J Oncol, 2006, 12(4):259-261. [in Chinese]

[7] Mao YP, Hong MH, Sun Y, et al. Clinical staging of nasopharyngeal carcinoma based on MRI: suggestions [J]. Aizheng, 2007,26(10):1099-1106. [in Chinese]

[8] Groome PA, Schulze K, Boysen M, et al. A comparison of published head and neck stage groupings in carcinomas of the oral cavity [J]. Head Neck, 2001, 23(8):613-624.

[9] Cheng SH, Yen KL, Jian JJ, et al. Examining prognostic factors and patterns of failure in nasopharyngeal carcinoma following concomitant radiotherapy and chemotherapy: Impact on future clinical trials [J]. Int J Radiat Oncol Biol Phys, 2001, 50(3):717-726.

[10] Lee N, Xia P, Quivey JM, et al. Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: An update of the UCSF experience [J]. Int J Radiat Oncol Biol Phys, 2002, 53(1):12-22.

[11] Tham IW, Hee SW, Yeo RM, et al. Treatment of nasopharyngeal carcinoma using intensity-modulated radiotherapy-The National Cancer Centre Singapore experience [J]. Int J Radiat Oncol Biol Phys, 2009, 20. [Epub ahead of print]

[12] Liao XB, Mao YP, Liu LZ, et al. How does of magnetic resonance imaging influence on the 6th edition of the AJCC staging system for nasopharyngeal carcinoma compared to computed tomography? [J]. Int J Radiat Oncol Biol Phys, 2008, 72(5):1368-1377.

[13] Lee AW, Lau WH, Tung SY, et al. Preliminary results of a randomized study on therapeutic gain by concurrent chemotherapy for regionally-advanced nasopharyngeal carcinoma: NPC-9901 trial by the Hong Kong Nasopharyngeal Cancer Study Group[J]. J Clin Oncol, 2005, 23(): 6966-6975.

[14] Mao YP, Xie FY, Liu LZ, et al. Re-evaluation of 6th edition of AJCC staging system for nasopharyngeal carcinoma and proposed improvement based on magnetic resonance imaging [J]. Int J Radiat Oncol Biol Phys, 2009, 73(5):1326-1334.

[15] Qing MH, Hong MH, Ma J, et al. A New Staging System for Nasopharyngeal Carcinoma in China [J]. Int J Radiat Oncol Biol Phys, 1994, 30(5):1037-1042.

[16] Cooper J, Fleming ID, Henson DE, editors. American Joint Committee on Cancer manual for staging of cancer [M]. 6th ed. Philadelphia: JB Lippincott, 2002.

[17] Mao YP, Liang SB, Liu LZ, et al. The N-staging system in nasopharyngeal carcinoma with RTOG guidelines for lymph node levels based on magnetic resonance imaging [J]. Clinical Cancer Research, 2008, 14(22):7497-7503.

[18] Ma J, Liu L, Tang L, et al. Retropharyngeal lymph node metastasis in nasopharyngeal carcinoma: prognostic value and staging categories [J]. Clin Cancer Res, 2007, 13(5):1445-1452.

[19] Tang LL, Li Li, Mao YP, et al. Retropharyngeal lymph node metastasis in nasopharyngeal carcinoma detected by MRI: prognostic value and staging categories[J]. Cancer, 2008, 113(2):347-354.

[20] Lee AW, Foo W, Poon YF, et al. Staging of nasopharyngeal carcinoma: evaluation of N-staging by Ho and UICC/AJCC systems [J]. Clin Oncol, 1996, 8():146-154.

[21] Teo P, ShiuW, Leung SF, et al. Prognostic factors in nasopharyngeal carcinoma investigated by computer tomography: an analysis of 659 patients [J]. Radiother Oncol, 1992, 23(1):79-93.

[22] Heng DMK,Wee J, Fong KW, et al. Prognostic factors in 677 patients in Singapore with nondisseminated nasopharyngeal carcinoma [J]. Cancer, 1999, 86():1912-1920.

[23] Zong JX, Ma J, Tang LL, et al. A study of the combined treatment strategy for patients with nasopharyngeal carcinoma based on the analysis of the treatment results from 749 cases [J]. Bulletin Chin Cancer, 2005,14(8):538-542. [in Chinese]

[24] Grégoire V, Levendag P, Ang KK, et al. CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines [J]. Radiother Oncol, 2003, 69:227-236.