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Prognostic Value and Grading of MRI-Based T Category in Patients With Nasopharyngeal Carcinoma Without Lymph Node Metastasis Undergoing Intensity-Modulated Radiation Therapy

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Abstract: We investigated the prognostic value and gradation of the T category in N0 nasopharyngeal carcinoma (NPC) patients undergoing magnetic resonance imaging (MRI) and intensity-modulated radiotherapy (IMRT).

A total of 749 patients were retrospectively reviewed, and a total of 181 N0 NPC patients were included in this retrospective study. All patients were restaged according to the 7th edition of the American Joint Committee on Cancer staging system. The following endpoints were estimated: overall survival (OS), progression-free survival (PFS), locoregional relapse-free survival (LRFS), and distant metastasis-free survival (DMFS).

The 5-year survival rates for T1 to T4 were: OS (97.3%, 100.0%, 86.1%, and 82.8%; $P=0.007$), PFS (94.6%, 96.9%, 76.5%, and 76.7%; $P=0.002$), LRFS (98.5%, 100.0%, 92.2%, and 86.7%; $P<0.001$), and DMFS (97.3%, 96.9%, 85.5%, and 85.7%; $P=0.042$), respectively. Pairwise comparisons showed that the OS, PFS, and LRFS rates were significantly poorer in the advanced T categories (T3 and T4) than the early ones (T1 and T2), and no significant differences between T1 and T2, and T3 and T4 were found. In Cox's proportional hazard analysis, T category was found to be an independent prognostic factor only for PFS ($P=0.003$). According to the primary tumor extent, we then graded all 181 N0 patients into 3 groups: group 1, early T category (n = 107); group 2, low-risk advanced T category (n = 35); and group 3, high-risk advanced T category (n = 39). The 5-year survival rates for the 3 groups were: OS (98.1%, 94.1%, and 76.3%; $P<0.001$), PFS (95.3%, 88.2%, and 66.2%; $P<0.001$), LRFS (99.0%, 97.0%, and 83.4%; $P<0.001$), and DMFS (97.2%, 91.1%, and 80.4%; $P=0.002$). The 5-year OS, PFS, and LRFS rates of group 3 differed significantly from those of groups 1 and 2, and a significant difference was observed in the DMFS rate only between groups 3 and 1. In Cox's proportional hazard analysis, the 3-grade T category was an independent prognostic factor for OS ($P=0.002$), PFS ($P<0.001$), and LRFS ($P=0.002$).

The 3-grade T category, using MRI according to the site of invasion, has prognostic value for the outcome of IMRT treatment in N0 NPC, and could aid in developing individualized treatment strategies.

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Abbreviations: AC = adjuvant chemotherapy, CCRT = concurrent chemoradiotherapy, CI = confidence interval, DMFS = distant metastasis-free survival, HR = hazard ratio, IMRT = intensity-modulated radiotherapy, LRFS = locoregional relapse-free survival, MRI = magnetic resonance imaging, NACT = neoadjuvant chemotherapy, NPC = nasopharyngeal carcinoma, NS = not significant, OS = overall survival, PET–CT = positron emission tomography–computed topography, PFS = progression-free survival, RT = radiotherapy, SPECT = SYSUCC = single photon emission computed tomography, Sun Yat-Sen University Cancer Center, UICC/AJCC = International Cancer Control/American Joint Committee On Cancer, WHO = World Health Organization.

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a squamous-cell carcinoma with uneven worldwide distribution and a high prevalence in southern China, where the incidence ranges 15 to 50 per 100,000 of the population.[1] Radiotherapy (RT) is the mainstay treatment modality for nondisseminated NPC.[2]

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Currently, the extent of disease, as embodied by the tumor-node-metastasis (TMN) staging system, is most commonly used to evaluate prognosis, facilitate the stratification of treatment, and aid in treatment planning. However, some clinical trials exploring the optimal therapeutic regimens for patients with different stages of NPC have reached inconsistent conclusions.[3] One reason for these discrepancies may be the insufficiency of the staging systems used to categorize patients into similar risk groups.[4] For example, it has been demonstrated that NPC patients with the same T category, as defined by the 7th edition of the Union for International Cancer Control/American Joint Committee on Cancer (UICC/AJCC) staging system,[5] could have different treatment outcomes.[6] There is still room for improvement in the correlation between the TMN staging system and prognosis.

As lymph node involvement (N1–3) is associated with an increased risk of distant failure in NPC,[7] the T category, which reflects primary tumor extent and risk of locoregional recurrence, primarily predicts the clinical outcomes of patients without lymph node metastasis (N0). According to the 7th UICC/AJCC system, tumor restricted to nasopharynx, oropharynx, and/or nasal cavity was defined as T1 category; if parapharynx is invaded, then the tumor is defined as T2 category. T3 is defined as the invasion of paranasal sinuses and/or skull-base bone, while tumor with further invasion (eg, intracranial invasion, involvement of cranial nerves, orbit, hypopharyngeal area, or masticator space/infratemporal fossa) is defined as T4. With the introduction of new diagnostic technologies and therapeutic interventions (eg, magnetic resonance imaging [MRI] and intensity-modulated radiotherapy [IMRT]), the prognosis of NPC patients, especially the locoregional control of tumor, has been significantly improved.[8] To the best of our knowledge, no study has evaluated the prognostic value of the T category specifically in N0 patients, and it is unclear whether NPC patients with the N0 category diagnosed by the use of MRI would have a different prognosis according to the site of invasion, when they are treated by IMRT.

Thus, in order to permit better characterization of N0 NPC, in this study we assembled a large and robust data set from N0 NPC patients undergoing MRI and IMRT, and investigated the prognostic value and gradation of T category in these patients.

MATERIALS AND METHODS

Patient Characteristics

Between January 2003 and December 2007, 749 patients with newly diagnosed, biopsy-proven, nonmetastatic NPC treated using IMRT at Sun Yat-Sen University Cancer Center (SYSUCC) were potentially eligible for inclusion in this retrospective study. A total of 181 N0 patients ages ≥18 years were eventually included; all patients had World Health Organization pathology type II/III NPC. The patients included in the study completed a pretreatment evaluation, including a complete patient history, hematology and biochemistry profiles, physical examination, an MRI scan of the nasopharynx and neck, chest X-ray, abdominal sonography, and a single photon emission computed tomography (SPECT). Positron emission tomography–computed topography (PET–CT) was performed in 33 of the 181 patients (18.2%). All patients were restaged according to the 7th edition of the UICC/AJCC staging system.[5] Table 1 shows the clinicopathological features of these patients. The ethics committee of SYSUCC approved this retrospective analysis; informed consent was obtained from all patients.

TABLE 1. Clinical Features of the 181 N0 Nasopharyngeal Carcinoma Patients Included in the Study

Characteristics	Number of Patients (%)
Age, yr	
≤50	118 (65.2)
>50	63 (34.8)
Gender	
Male	148 (81.2)
Female	33 (18.2)
T category*	
T1	75 (41.4)
T2	32 (17.7)
T3	44 (24.3)
T4	30 (16.6)
Stage*	
I	75 (41.4)
II	32 (17.7)
III	44 (24.3)
IVA	30 (16.6)
IVB	0
Chemotherapy	
Radiotherapy alone	109 (60.2)
Chemoradiotherapy	72 (39.8)

* According to the American Joint Committee on Cancer, 7th edition.

Imaging Protocol

All patients underwent the 1.5-T system MRI (Signa CV/i; General Electric Healthcare, Chalfont St. Giles, UK).

A head-and-neck combined coil examined the region from the suprasellar cistern to the inferior margin of the clavicle. Before the contrast material injection, T1-weighted fast spin-echo (FSE) images in 3 planes (axial, coronal, and sagittal) (the repetition time is 500–600 msec, and the echo time is 10–20 msec), and T2-weighted FSE images in the axial plane (the repetition time is 4000–6000 msec, and the echo time is 95–110 msec) would be obtained. After gadopentetic acid (Gd-DTPA) intravenous injection (0.1 mmol/kg body weight), spin-echo T1-weighted sequences (axial and sagittal, and fat-suppressed coronal) were performed sequentially. The 5 and 6 mm thick sections with a 1-mm interslice gap were used for imaging in the axial plane, and the coronal and sagittal planes, respectively.

Image Assessment

Two radiologists specializing in head and neck cancers independently evaluated all scans; they were blinded to the clinical findings. Any disagreements were resolved by consensus. Details regarding the diagnostic criteria for primary tumor extension have been published previously.[9]

Treatment

All patients underwent radical radiation therapy. The nasopharyngeal and upper neck areas above the caudal edge of the cricoid cartilage were treated using IMRT for the entire treatment course. For the lower neck, a conventional anterior or anteroposterior opposing cervical technique was used. All patients were treated with 1 fraction daily for 5 days per week. Further details of the IMRT treatment in our institution have been previously reported.[8] During the including period (between January 2003 and December 2007), our institute recommended RT alone for stages I to IIA NPC patients, concurrent chemoradiotherapy (CCRT) for stage IIB NPC patients, and CCRT alone, or with the addition of induction or adjuvant chemotherapy (AC) for stages III to IV NPC patients. All stages were defined according to 6th UICC/AJCC system. Concomitant chemotherapy was cisplatin administered weekly or every 3 weeks; induction chemotherapy or AC were cisplatin + 5-FU or cisplatin + taxanes for 2 to 3 cycles. In total, chemotherapy was administered to 75.7% (56/74) of the patients with stages III to IV disease in our study.

Follow-Up

The median follow-up was 86 months (range 7–127 months). The duration of patient follow-up was calculated from the first day of therapy to either the day of last examination or the day of death. Patients were seen at least every 3 months during the first 2 years and every 6 months thereafter until death.

Statistical Analysis

SPSS version 19.0 software was used. Kaplan–Meier curves were used to estimate the survival rates, and log-rank test was used to compare differences.[10] Estimated endpoints in this study included: overall survival (OS), progression-free survival (PFS), locoregional relapse-free survival (LRFS), and distant metastasis-free survival (DMFS). OS was counted from the start of treatment to death from any cause; PFS was counted from the start of treatment to failure or death. LRFS and DMFS were counted from the start of treatment to the first locoregional and distant recurrence, respectively. Multivariate analyses used the adjusted Cox's proportional hazards model (backward elimination).[11] The following parameters were included in the model as covariates: age ($>$50 vs $\leq$50 years), sex (male vs female), chemotherapy (with vs without), and T category. Two-tailed P values $<$ 0.05 were considered statistically significant.

RESULTS

Patterns of Treatment Failure and Survival

A total of 13/181 (7.2%) patients died and 20/181 (11.0%) patients experienced treatment failure during the follow-up period, including locoregional recurrence in 10/181 (5.5%) patients and distant metastasis in 13/181 (7.2%) patients. For the entire cohort, the 5-year survival rates were: OS (92.7%), PFS (87.7%), LRFS (95.4%), and DMFS (92.6%).

Prognostic Significance of T Category in N0 Patients

The 5-year survival rates for T1 to T4 were: OS (97.3%, 100.0%, 86.1%, and 82.8%; $P = 0.007$), PFS (94.6%, 96.9%, 76.5%, and 76.7%; $P = 0.002$), LRFS (98.5%, 100.0%, 92.2%, and 86.7%; $P < 0.001$), and DMFS (97.3%, 96.9%, 85.5%, and 85.7%; $P = 0.042$), respectively. Pairwise comparisons showed that OS, PFS, and LRFS rates were significantly poorer in the advanced T categories (T3 and T4) than the early ones (T1 and T2), and no significant differences between T1 and T2, and T3 and T4 were found (Figure 1A–C). In terms of DMFS, the survival rates of T3 and T4 were significantly poorer than that of T1 ($P = 0.018$ and 0.026), and had a tendency to be significantly poorer than that of T2 ($P = 0.106$ and 0.117; Figure 1D). Cox's proportional hazard analysis was performed to adjust for various prognostic factors. The following parameters were included in the model as covariates: age ($>$50 vs $\leq$50 years), sex (male vs female), chemotherapy (with vs without), and T category (T1–4). The results are shown in Table 2. T category was found to be an independent prognostic factor only for PFS (Table 2).

Gradation of T Category in N0 Patients

In N0 NPC patients, it seemed reasonable to merge T1 and T2 into the early T category and merge T3 and T4 into the advanced category. Thus, the early T category was defined as primary tumor involvement confined to the nasopharynx, oropharynx, nasal cavity, and/or parapharynx. With respect to the advanced T category, these patients had an unfavorable prognosis and to subclassify them might help to enhance prediction of treatment outcomes. The categorization of the sites of involvement in the 74 N0 NPC patients with advanced T category is shown in Table 3. A study by Tian et al[12] has shown that in NPC patients with T3 to T4 categories, paranasal sinus invasion has a relatively better prognosis than intracranial extension, and the findings of our previous studies suggest that the subclassification of skull-base invasion and of T4 category enables more accurate prognostication in NPC.[6,13] Therefore, we subclassified patients with advanced T category into 2 grades according to the sites of invasion: the low-risk advanced T category was defined as involvement of the paranasal sinus, the mild type of skull-base erosion (including the pterygoid process, base of sphenoid bone, petrous apex, clivus, and foramen lacerum), infratemporal fossa, and/or cranial nerve only; the high-risk advanced T category was defined as involvement of the severe type of skull-base erosion (including the great wing of the sphenoid bone, pterygopalatine fossa, foramen ovale, pterygoid canal, foramen rotundum, foramen spinosum, hypoglossal canal, jugular foramen, foramen magnum, and facial canal), intracranial region, orbit, and/or hypopharynx. Hence, all 181 N0 patients in this series were graded into 3 groups: group 1, early T category (n = 107); group 2, low-risk advanced T category (n = 35); and group 3, high-risk advanced T category (n = 39).

Prognostic Significance of the 3-Grade T Category in N0 Patients

The 5-year survival rates for groups 1 to 3 by gradation of T category were: OS (98.1%, 94.1%, and 76.3%; $P < 0.001$), PFS (95.3%, 88.2%, and 66.2%; $P < 0.001$), LRFS (99.0%, 97.0%, and 83.4%; $P < 0.001$), and DMFS (97.2%, 91.1%, and 80.4%; $P = 0.002$), respectively. With respect to all outcomes, there were no significant differences between groups 1 and 2, and patients in group 3 had significantly lower survival rates than those in group 1 (Figure 2). In addition, patients in group 3 had significantly lower OS, PFS, and LRFS rates than those in group 2 (Figure 2). Cox's proportional hazard analysis was performed to adjust for various prognostic factors. The following parameters were included in the model as covariates: age ($>$50 vs $\leq$50 years), sex (male vs female), chemotherapy (with vs without), and T category (groups 1–3). The results are shown in Table 4. The 3-grade T category was found to be an independent predictive factor for OS, PFS, and LRFS. Compared with patients in group 1, patients in group 3 had an increased risk of death, disease progression, and locoregional recurrence (Table 4).

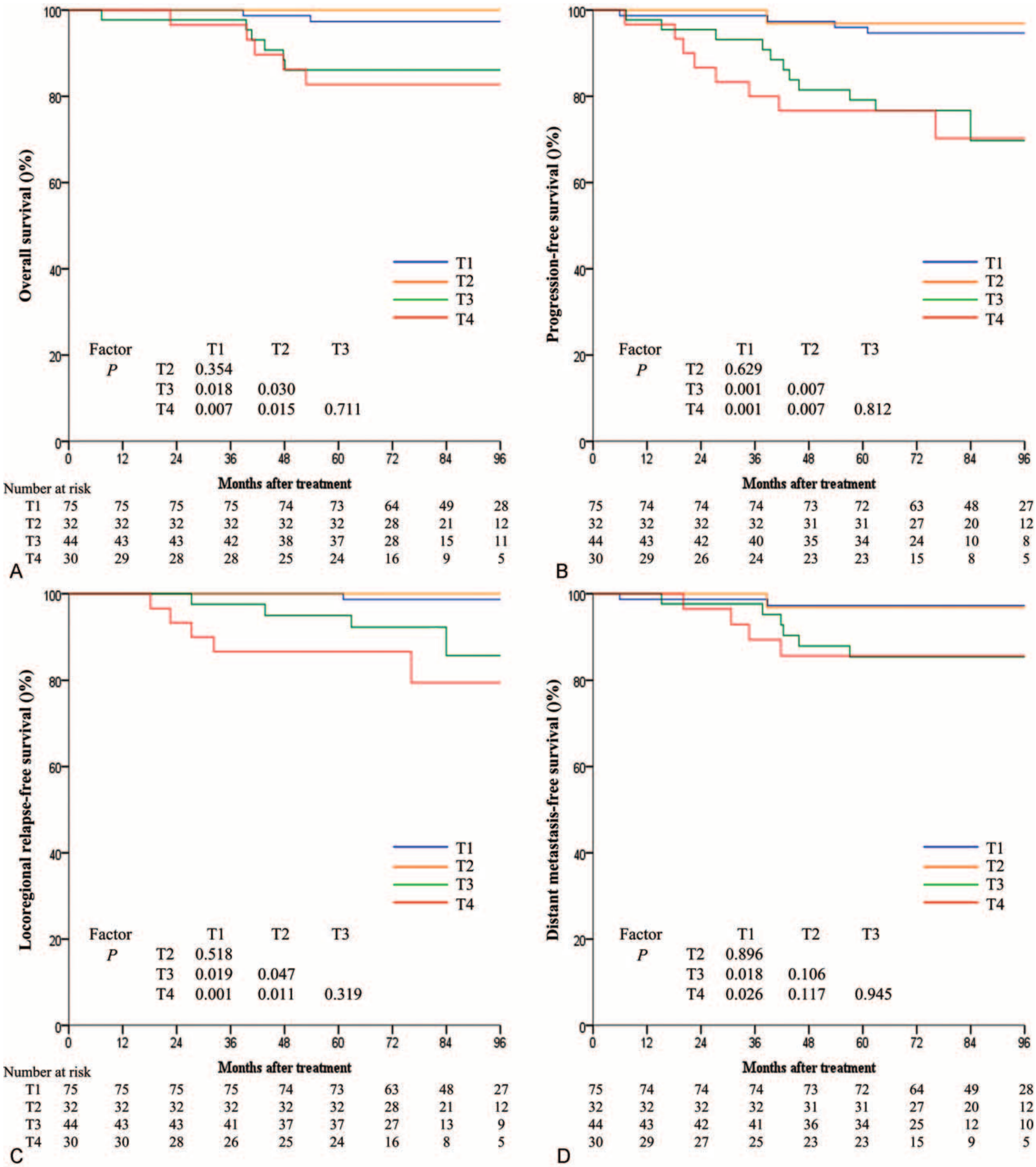

FIGURE 1. Kaplan–Meier survival curves for overall survival (A), progression-free survival (B), locoregional relapse-free survival (C), and distant metastasis-free survival (D) in different T categories in all 181 N0 nasopharyngeal carcinoma patients. All categories are based on the 7th edition of the Union for International Cancer Control/American Joint Committee on Cancer staging system.

DISCUSSION

We used a 3-grade T category to investigate the prognostic value of primary tumor extent in N0 NPC patients treated with IMRT. The 3-grade T category was a significant predictive factor for OS, PFS, and LRFS. In addition, the 5-year OS, PFS, and LRFS rates of the high-risk advanced T category (group 3) differed significantly from those of the early (group 1) and the low-risk advanced T category (group 2).

Lymph nodes play an important role in the immune response to cancer, as they contain special immune cells that can trap tumor cells traveling through the body. The spread of NPC usually follows an orderly progression, and metastasis of

TABLE 2. Cox's Proportional Hazard Analysis of T Category in 181 N0 Nasopharyngeal Carcinoma Patients

Endpoint	Variable	HR (95% CI)	*P* Value†
OS	Age (>50 vs ≤50 yr)	4.176 (1.231–14.162)	0.022
	T category		0.142
	T1	Reference	
	T2	–*	0.973
	T3	6.506 (1.305–32.431)	0.022
	T4	5.238 (1.005–27.306)	0.049
PFS	T category		0.003
	T1	Reference	
	T2	0.584 (0.065–5.226)	0.631
	T3	5.525 (1.753–17.419)	0.004
	T4	6.172 (1.853–20.563)	0.003
LRFS	T category		0.090
	T1	Reference	
	T2	–*	0.982
	T3	8.435 (0.938–75.872)	0.057
	T4	16.188 (1.875–139.740)	0.011
DMFS	Chemotherapy (with vs without)	9.520 (2.109–42.966)	0.003
	T category		NS
	T1	Reference	
	T2	NS	NS
	T3	NS	NS
	T4	NS	NS

CI = confidence interval; DMFS = distant metastasis-free survival; HR = hazard ratio; LRFS = locoregional relapse-free survival; NS = not significant; OS = overall survival; PFS = progression-free survival.
* HR and 95% CI were unavailable to be calculated because of the small number of events.
† *P* values were calculated with an adjusted Cox's proportional hazards model.

TABLE 3. Primary Tumor Extent in 74 N0 Nasopharyngeal Carcinoma Patients With an Advanced T Category Tumor

Primary Tumor Extent	Number of Patients (Incidence, %)
Paranasal sinus	31 (41.9)
Skull-base	73 (98.6)
Pterygoid process	62 (83.8)
Base of sphenoid bone	64 (86.5)
Petrous apex	45 (60.8)
Clivus	43 (58.1)
Foramen lacerum	38 (51.2)
Great wing of sphenoid bone	24 (32.4)
Pterygopalatine fossa	19 (25.7)
Foramen ovale	19 (25.7)
Pterygoid canal	18 (24.3)
Foramen rotundum	14 (18.9)
Foramen spinosum	14 (18.9)
Hypoglossal canal	10 (13.5)
Jugular foramen	6 (8.1)
Foramen magnum	6 (8.1)
Facial canal	0
Infratemporal fossa	16 (21.6)
Medial pterygoid muscle	16 (21.6)
Lateral pterygoid muscle	7 (9.5)
Cranial nerve	13 (17.6)
Intracranial region	20 (27.0)
Orbit	6 (8.1)
Hypopharynx	0

lymph nodes is strongly associated with distant failure in NPC, as normal lymph node function may be disturbed by tumor cells.[14,15]

The control of distant failure is better in NPC patients without than with lymph node metastasis. Thus, it was not surprising that the 3-grade T category could not predict DMFS well in this study. However, factors affecting locoregional recurrence, such as the grade of tumor invasion, may have a relatively greater impact on the prognosis of these patients than distant metastasis. In our analysis, we found that patients with NPC involving the nasopharynx, oropharynx, nasal cavity, and/or parapharynx had more favorable treatment outcomes. The main reason for this observation may be the excellent dose coverage of these sites provided by IMRT.[15] Thus, we defined NPC confined to these sites as the early T category (group 1) in N0 patients.

As for the advanced T category (groups 2 and 3), the sites of the severe type of skull-base erosion (group 3) were all outside the pharyngobasilar fascia compared with those of the mild type (group 2), which means that the primary tumor volume of NPC invading group 3 sites was greater.[13] Moreover, it is difficult to design a therapeutic strategy for tumors with intracranial and orbit extension, and dose escalation is limited. The intracranial region and orbit also have an anatomically rich venous plexus, which may provide potential routes of hematogenous dissemination.[16] N0 patients with NPC involving these sites had poor survival rates, and were graded as high-risk advanced T category (group 3).

By contrast, for the advanced T category graded as low-risk (group 2), paranasal sinus invasion may occur early with a small tumor volume,[12] the sites of the mild type of skull-base

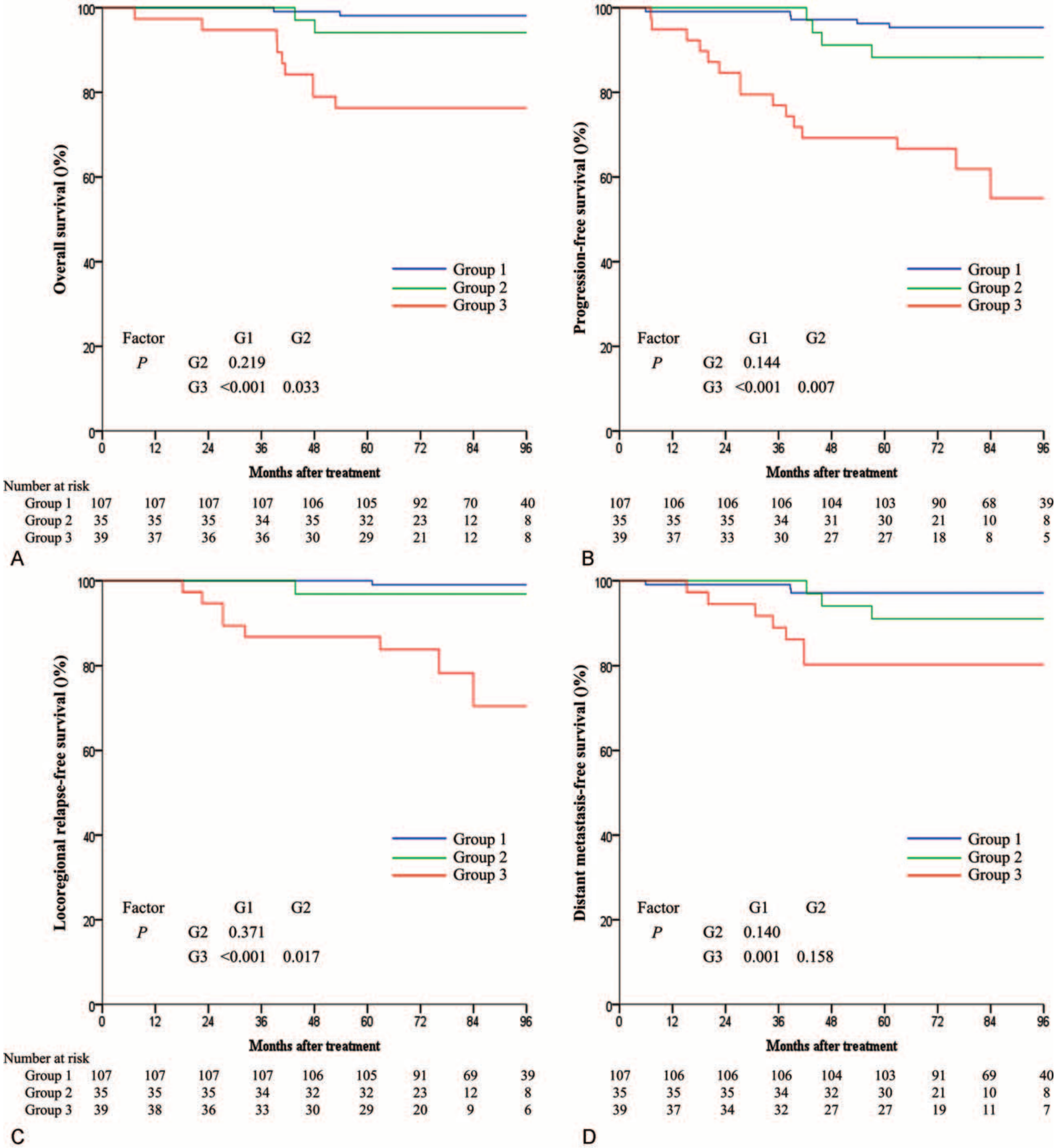

FIGURE 2. Kaplan–Meier survival curves for overall survival (A), progression-free survival (B), locoregional relapse-free survival (C), and distant metastasis-free survival (D) in different groups in all 181 N0 nasopharyngeal carcinoma patients. Group 1, early T category (T1 to T2); group 2, low-risk advanced T category (T3 to T4); and group 3, high-risk advanced T category (T3 to T4). All categories are based on the 7th edition of the Union for International Cancer Control/American Joint Committee on Cancer staging system.

erosion are all inside the pharyngobasilar fascia (except the clivus), and extension to only the masticator space does not frequently result in lymphatic and hematogenous dissemination.[6] These all result in better treatment planning (particularly delineation of target volume) and a more favorable prognosis. It should be noted that though lateral invasion of the masticator space (involvement of the lateral pterygoid muscle) could worsen survival as compared with medial invasion, this adverse effect mainly resulted from the increased risk of distant metastasis, and no significant differences of locoregional recurrence rates were found between the patients with lateral and medial invasions.[17] Besides, cranial nerve involvement is usually associated with a greater propensity for lymphatic metastasis but not locoregional recurrence in NPC,[16] as the tumor may

TABLE 4. Cox's Proportional Hazard Analysis of 3-Grade T Category in 181 N0 Nasopharyngeal Carcinoma Patients

Endpoint	Variable	HR (95% CI)	*P* Value*
OS	Age (>50 vs ≤50 yr)	4.048 (1.245–13.162)	0.020
	T category		0.002
	Early	Reference	
	Low-risk advanced	2.906 (0.409–20.652)	0.286
	High-risk advanced	13.316 (2.871–61.758)	0.001
PFS	T category		0.001
	Early	Reference	
	Low-risk advanced	2.683 (0.719–10.021)	0.142
	High-risk advanced	10.573 (3.929–30.031)	<0.001
LRFS	T category		0.002
	Early	Reference	
	Low-risk advanced	3.623 (0.226–58.160)	0.363
	High-risk advanced	28.064 (3.707–241.478)	0.001
DMFS	Chemotherapy (with vs without)	9.520 (2.109–42.966)	0.003
	T category		NS
	Early	Reference	
	Low-risk advanced	NS	NS
	High-risk advanced	NS	NS

CI = confidence interval; DMFS = distant metastasis-free survival; HR = hazard ratio; LRFS = locoregional relapse-free survival; NS = not significant; OS = overall survival; PFS = progression-free survival.

* *P* values were calculated with an adjusted Cox's proportional hazards model.

proliferate along the nerves within the lymphatic system of the epineurium and the perineural sheaths and increase the risk of distant metastasis.[18] Thus, these factors may not have great impacts on the treatment outcomes in N0 patients, and was classified into the low-risk grade.

Nowadays, the TMN staging system is the most common method used to evaluate prognosis. However, for N0 NPC patients, it could not predict treatment outcomes well, which was only a prognostic factor for PFS. This indicates the limitation of the old T category for this subgroup of NPC patients. Thus, we refined the old T category into the 3-grade T category, and found that it could serve as prognostic factors for OS, PFS, and LRFS, and could identify low-risk patient population from those with advanced T category. The 3-grade T category may enhance better prediction of outcomes and individualized treatment for N0 NPC patients. Therefore, it may be better to evaluate prognosis for a subgroup of NPC (N0 NPC) by using the 3-grade T category, though the TNM staging system is still a universal method to indicate prognosis and aid the clinician in the planning of treatment for NPC patients.

Currently, the National Comprehensive Cancer Network recommend that the standard treatment regimen for stage I NPC is definitive RT to the nasopharynx and elective RT to the neck, while for stage II and locoregionally advanced NPC the recommended treatment is CCRT with or without AC.[2,19] According to our results, we speculate that IMRT alone may be sufficient for N0 patients with the early T category, since these patients have a lower risk of distant metastasis and locoregional control is favorable. Furthermore, overtreatment could cause unnecessary side effects, which could decrease quality of life, or may even increase the risk of noncancer death.[20] As indicated in our previous study,[19] no significant improvement was found following CCRT plus AC compared with CCRT alone for locoregionally advanced NPC, and the additional AC might increase toxic effects. Therefore, for N0 patients with the low-risk advanced T category, CCRT alone may be an optimal choice that achieves a balance between efficacy and toxicity. Nevertheless, the additional AC has the potential to improve locoregional control,[19,21] and N0 patients with the high-risk advanced T category may benefit most from this aggressive therapy (CCRT + AC). Nowadays, the impact of NACT + CCRT remained controversial. A phase III trial by Lee et al[22] found no significant difference between the efficacies of NACT + CCRT and CCRT + AC in locally advanced NPC; another phase III trial by Tan et al[23] found that NACT + CCRT did not improve survival when compared with CCRT alone. A recent meta-analysis also indicated that the efficacies of NACT + CCRT and CCRT/CCRT + AC appeared to be similar.[24] Besides, additional NACT mainly helps to reduce the distant metastasis rate,[21] and, therefore, may not be suitable for N0 patients. Thus, we did not separate patients receiving NACT + CCRT from those receiving chemotherapy in this study.

One limitation of the present study is that we enrolled patients at a single center in an NPC endemic area retrospectively. Large scale, multi-institutional prospective studies are necessary to confirm the findings. Another limitation is that NPC was treated primarily with RT, and no surgical or pathologic verification of primary tumor involvement identified through imaging studies was available. This problem is commonly encountered in imaging studies.

To the best of our knowledge, this study is the first to classify N0 NPC patients into 3 grades based on MRI findings of the site of primary tumor invasion, and to investigate the prognosis after IMRT. We found that the 3-grade T category has prognostic value for the outcomes of IMRT treatment in N0 NPC. These results may aid in developing individualized treatment strategies, and improve the prognosis of NPC patients. Biomarkers such as plasma Epstein–Barr virus DNA[25] and microRNA[26] may also be useful indicators of prognosis. Combining the use of the 3-grade T category and biomarkers might help to refine individualized treatment strategies for patients with N0 NPC.

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