A Comparison of Staging Systems for Nasopharyngeal Carcinoma in Taiwan

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The fifth edition of the American Joint Committee on Cancer (AJCC) staging manual defines new rules for staging nasopharyngeal carcinoma. The authors tested the value of this new system by applying these rules retrospectively to their previously treated patients and comparing the results with those obtained using the fourth edition of the AJCC staging manual.

Information from 196 patients who had biopsy-proven squamous cell carcinoma of the nasopharynx that was treated with definitive-intent radiation therapy alone or combined chemo-radiation therapy (CCRT) at one institution provided the data base for this analysis. The extent of disease of each patient was staged according to the rules of 1) the fourth edition of the AJCC staging manual, and 2) the fifth edition of the AJCC staging manual.

The new system appears to be better than the previous system. It separated patients into cohorts of more equal size than did the previous system. It also correlated with outcome for the study population more appropriately than did the fourth edition of the AJCC staging manual.

The fifth edition of the AJCC staging manual appears to be an improvement over the previous edition for the staging of nasopharyngeal carcinoma.

Key words: Nasopharyngeal carcinoma, Tumor staging, Prognosis

MATERIAL AND METHODS

A number of different staging systems of nasopharyngeal carcinoma (NPC) have been used in different parts of the world [1-4]. While the International Union Against Cancer (UICC) and American Joint Committee (AJCC) classifications are more popular in Europe and North America where the incidence of NPC is low, Ho and Changsha classifications has been widely used in Southeast Asia where the incidence of NPC is one of the world’s highest [5]. The use of different classifications causes difficulties on comparing treatment results from different centers. AJCC/UICC classifications are criticized for the skewed patient number distribution among stages and inefficacy in predicting prognosis; while, Ho’s classification for its complexity [5-7]. A refinement of Ho’s staging was proposed incorporating the radiological findings into the staging criteria [8].

In 1997, AJCC has revised the classification for NPC after the criticisms toward it in the literature and the recognition of the prognostic significance of parapharyngeal extension, cranial nerve palsy, and intracranial extension of the tumor [5-8].

Taiwan is an endemic area for NPC and the first study [9] for staging of NPC can be traced up to 1985. The sixth edition of AJCC has been published, but there is no change to 5th edition. To the best of our knowledge, there is no report for comparing 4th and 5th editions (Table 1&2) of AJCC staging manual in Taiwan.
and bone scan. Table 3 showed the clinical data of patients recruited in this study. Histologically, 98% of the patients had World Health Organization (WHO) type II or type III tumors; the rest (2%) had type I tumors [10]. All patients were treated with external beam radiotherapy using 6 MV photons generated from linear accelerator. Daily fraction was given in 1.8 or 2 Gy, five fractions per week. Patients with AJCC staging based 4th edition showed N2 and N3 disease were given cisplatin either concomitant or neoadjuvant chemotherapy regimens. Median follow-up period was 55 months (range: 3-60). None of the patients were lost to follow-up.

Comparisons were made by calculating the percentages of patients assigned to each stage by each system (Table 4), rates of loco-regional relapse (Table 5), and distant metastasis (Table 6). The Kaplan-Meier method was used to test significance of the differences between survival curves.

**RESULTS**

The reported population is typical for Chinese series [11]. As would be expected, the new system is clearly better than the 4th edition because it assigned patients to more uniform sized stage groupings (Table 2). It also resulted in an overall “down staging” of the population compared with the 4th edition of the AJCC staging system.

Furthermore, the new system correlates stage and
prognosis of survival at least as well as, and in some respects is better than the 4th edition. Figures 1 and 2 show actuarial survival by the staging. We can discriminate stage 1 vs. 3, stage 1 vs. 4, stage 2 vs. 3 and stage 2 vs. 4 in the 5th edition, whereas only stage 1 vs. 4, stage 2 vs. 4, and stage 3 vs. 4 can be discriminated in the 4th edition. It means the discriminating capacity of 5th edition is better than 4th edition. Besides, the 5th edition (Table 5) shows more powerful prediction for loco-regional relapse vs. staging especially in low tumor stages. Although the 5th edition is not perfect (e.g. stage 1 and 2 are inverted at 2 year survival), the 4th edition similarly shows the same phenomenon.

Table 5. Comparison of the tumor stage and ratio of loco-regional relapse according to the AJCC 4th and 5th editions

<table>
<thead>
<tr>
<th>Stage</th>
<th>4th Ratio of local failure</th>
<th>Percentage</th>
<th>5th Ratio of local failure</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>4/32</td>
<td>12.5%</td>
<td>7/65</td>
<td>10.8%</td>
</tr>
<tr>
<td>T2</td>
<td>5/53</td>
<td>9.4%</td>
<td>10/54</td>
<td>18.5%</td>
</tr>
<tr>
<td>T3</td>
<td>23/54</td>
<td>42.6%</td>
<td>10/26</td>
<td>38.5%</td>
</tr>
<tr>
<td>T4</td>
<td>27/57</td>
<td>47.4%</td>
<td>32/51</td>
<td>62.7%</td>
</tr>
</tbody>
</table>

Table 6. Comparison of the nodal stage and the ratio of the distal metastasis

<table>
<thead>
<tr>
<th>Nodal Stage</th>
<th>4th Ratio of metastasis</th>
<th>Percentage</th>
<th>5th Ratio of metastasis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>4/72</td>
<td>5.6%</td>
<td>4/72</td>
<td>5.6%</td>
</tr>
<tr>
<td>N1</td>
<td>2/29</td>
<td>6.9%</td>
<td>3/41</td>
<td>7.3%</td>
</tr>
<tr>
<td>N2</td>
<td>9/72</td>
<td>12.5%</td>
<td>8/60</td>
<td>13.3%</td>
</tr>
<tr>
<td>N3</td>
<td>6/23</td>
<td>26.0%</td>
<td>6/23</td>
<td>26.0%</td>
</tr>
</tbody>
</table>

DISCUSSION

Throughout the four previous editions of the AJCC staging manual (1977, 1983, 1988, and 1992), there have been relatively few changes in the staging rules for nasopharyngeal carcinoma. The groupings of T category, N category, and M category into stages have not changed and the definitions of T and N have remained relatively constant. In the first edition, T category was based on the size of the primary tumor whereas in the later three editions the T category was based on anatomic lesion extent starting from the third edition, bilateral lymph involvement was moved from N3b to N2c.

The TN groupings of 5th edition are different from the previous editions. The TN groupings of 5th edition, which facilitated a step-by-step grouping (overall stage=T-stage and /or N-stage+1), showed good regularity [11].

One purpose of staging is to create subgroups of patients that have similar prognosis. For the system to be useful clinically, each subgroup should have a reasonable number of patients. An ideal system would assort patients into equal-sized group [13]. Subgrouping of T2 category is a new classification dependent on the parapharyngeal extension. The prognostic significance of parapharyngeal extension appears too uncertain to warrant upstaging at present. The study by Teo et al. [14] and Lee did not show any significant effect on survival, which are in contrast to the studies by Sham and Choy [15] and Chua et al. [16]. One possible explanation is that parapharyngeal involvement has been defined differently in different studies. The current edition of TNM designates para-
pharyngeal tumor extension as T2b, so as to facilitate further evaluation.

The loco-regional relapse and distant metastasis are the prognostic factors in patients with NPC [17]. Table 5 shows the 5th edition provides better predictive capacity for loco-regional relapse, whereas we can not see any significant difference of prediction for distant metastasis between 4th and 5th. One possible explanation is that there is no obvious change in N0 and N3 definition.

**CONCLUSIONS**

The 5th edition for NPC was published in 1997 in accordance with the regulation following the last 10 years of the 4th edition in use since 1988. The 6th edition of AJCC staging manual has been published in 2002 without change in staging criteria from the 5th edition. It is important that the new system be adapted worldwide to facilitate communications, data reporting, and clinical decisions among oncologists. Although it remains to be improved, the 5th edition of AJCC staging manual is prognostically useful for the Taiwanese patient populations on the basis of our current data. It seems reasonable that every oncology center should stage the NPC patients with the new system before a better stage classification emerging for the 5th and 6th editions.

**REFERENCES**

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鼻咽癌分期系統之比較

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本研究主要目的為探討第五版（1997）美國癌症聯合委員會(AJCC)鼻咽癌分期手冊是否更適用於台灣鼻咽癌病人。本研究共有一百九十六位經切片檢查證實為鼻咽癌病患。所有病人皆具備頭頸部之電腦斷層或磁振造影、胸部X光片、腹部超音波，及骨骼核子掃描的資料。所有影像資料皆存入電腦並依照AJCC第四版及第五版鼻咽癌分期系統做癌症分期。所得之結果以病人之五年存活率、局部復發，及遠端轉移來做比較。結果顯示，第五版AJCC鼻咽癌分期手冊對五年存活率及局部復發情形有較好之預測率。遠端轉移率則無顯著差別。所得到的結論為第五版AJCC鼻咽癌分期手冊比第四版更適合台灣地區的病例。

註：第六版 (2002) 與第五版完全相同

關鍵詞：鼻咽癌，腫瘤分期，預後