Prognostic Factors Affecting the Outcome of Nasopharyngeal Carcinoma

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Background: The aim of the study is to evaluate patients with nasopharyngeal carcinoma treated with multisegmental intensity-modulated radiotherapy with or without chemotherapy and analyze patient, tumor and treatment characteristics, determining outcome.

Methods: From June 1999 through to April 2003, we treated in our institution 83 patients with nasopharyngeal carcinoma, 70 males and 13 females, their ages ranging from 25 to 85 years (median, 48 years). Nineteen patients had T1 tumors, 35 had T2 tumors, six had T3 tumors and 23 had T4 tumors. Sixty-four patients had cervical lymph node metastasis. Twenty patients were treated with radiation therapy alone and 63 patients with concurrent chemoradiotherapy. Cumulative radiation dose to primary tumor ranged from 70.2 to 77.4 Gy (median, 75.6 Gy). Follow-up ranged from 3 to 41.53 months (median, 17 months).

Results: Local complete response was achieved in 81 patients (97.5%). Local failure was observed in two patients, nodal failure in one patient and systemic failure in 14 patients. Overall survival, disease-free survival and disease-specific survival were 83, 84 and 93%, respectively, at 1 year, 82, 74 and 88%, respectively, at 2 years and 81, 61 and 88%, respectively, at 3 years. In univariate analysis, T stage of disease was a significant predictor of disease-free survival favoring those with early-stage (T1 + T2) disease (P = 0.040). Cumulative radiation dose to primary tumor was a significant predictor of disease-specific survival favoring those with >75.6 Gy (P = 0.010). Stage of disease (P = 0.007), N-classification (P = 0.046) and cumulative dose to primary tumor (P = 0.046) were significant prognostic factors for overall survival.

Conclusions: High locoregional control for nasopharyngeal carcinoma was achieved with multisegmental intensity-modulated radiotherapy. Distant metastases are still the main impact on survival. More effective chemotherapy regimens and other systemic agents are needed to decrease the rate of distant metastasis.

Key words: nasopharynx – carcinoma – prognostic factors – intensity-modulated radiotherapy

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is unique and distinct from other malignant tumors arising from head and neck because of its epidemiology, histopathological spectrum, clinical characteristics and biological behavior (1,2). In the Western world, nasopharyngeal carcinoma is an uncommon type of tumor, representing <1% of all cancers in the USA, and the annual incidence in the USA and Europe varies between 0.22 and 0.5 per 100 000 population (3–5). However, it is more common among the Southern Chinese, Southeast Asian, Northern African and Eskimo populations (6). Researchers have advanced differences in diet, such as the popularity of salted or smoked fish in southern China, and genetics as potential explanations for the large epidemiologic difference (7). In Taiwan, nasopharyngeal carcinoma has a relatively high prevalence with an annual incidence rate of 5.4 per 100 000 (8). In the Hong Kong Chinese population, the annual incidence rate is even higher at 19.2–22 per 100 000 (9,10).

Because of the anatomic location of nasopharyngeal tumors, radiotherapy is the primary mode of treatment for patients with cancer of the nasopharynx, with surgery usually being limited to a biopsy (6,11). Surgery plays no role in treating primary nasopharyngeal carcinoma but may help in removing residual...
Prognostic factors of NPC neck nodes after irradiation (8). Although nasopharyngeal carcinoma is markedly radiosensitive, there is a high rate of treatment failure because of its metastatic behavior (2). While radiotherapy is the cornerstone in the treatment of nasopharyngeal carcinoma, adjunctive chemotherapy has shown some promise in improving tumor control and possibly survival with advanced nasopharyngeal carcinoma (5).

For early-stage nasopharyngeal carcinoma, the standard treatment is radiotherapy alone; for advanced nasopharyngeal carcinoma, the current standard treatment consists of definitive radiotherapy plus cisplatin-based chemotherapy (4,12). Identification of prognostic indicators that more accurately correlate with outcome would help in identifying which patients with nasopharyngeal carcinoma might benefit from adjuvant systemic therapy, because they are at a high risk for distant metastasis, locoregional recurrence and death (2). We carried out the present study to analyze the results of multisegmental static intensity-modulated radiation therapy (IMRT) for patients with nasopharyngeal carcinoma and to evaluate the prognostic factors that affect the results and determine the outcomes.

PATIENTS AND METHODS
From June 1999 through to April 2003, 103 patients with nasopharyngeal carcinoma received radiotherapy with/without chemotherapy at the Department of Radiation Oncology, Changhua Christian Hospital, Taiwan. Six patients with distant metastases, seven patients with local recurrence who were previously treated with radiotherapy and seven patients who did not complete the course of radiotherapy were excluded. Pretreatment evaluation consisted of a complete history, physical examination, including flexible fiberoptic endoscopy, complete blood counts, liver function tests, chest X-ray, CT or MRI scans of the nasopharynx and neck and dental evaluation. Bone scans and CT scans of the abdomen and chest were obtained when there was elevated alkaline phosphatase, abnormal liver function tests, or abnormal chest X-rays or when clinically indicated. The disease was staged according to the 1997 American Joint Committee on Cancer (AJCC) staging classifications (13). Eighty-three patients received segmental IMRT. Seventy were male (84%), 13 were female (16%). The median age was 48 years (range, 25–85 years). Histopathologically, two patients (2%) had World Health Organization (WHO) type 1, 46 (56%) had WHO type 2, and 35 (42%) had WHO type 3 carcinomas (14). Nineteen patients (23%) had T1, 35 (42%) had T2, six (7%) had T3 and 23 (28%) had T4 tumors. Nineteen patients (23%) had N0, 27 (33%) had N1, 25 (30%) had N2 and 12 (14%) had N3 cervical lymph nodes. According to the AJCC classification staging system (13), six patients (7%) were at Stage I, 25 (30%) at Stage II, 20 (24%) at Stage III and 32 (39%) at Stage IV (Table 1).

Linear accelerator with computer controlled auto-sequencing multi-leaf collimator (Siemens Medical Systems, Concord, CA, USA) was used to deliver static multisegmental IMRT. The Pinnacle-3 Treatment Planning System (ADAC Laboratories, Milpitas, CA, USA) was used to develop static multisegmental IMRT. Segmental IMRT makes use of multisegment treatment field consisting of multiple fixed portal shapes. The intensity of a field is modulated by adding additional segments to change the overall shape of dose distribution (15). The prescribed dose was 70–77 Gy to the gross target volume (GTV) and positive neck nodes and 60–65 Gy to the clinical target volume (CTV), which included the GTV plus a margin of potential microscopic spread, and 50 Gy to clinically negative neck. Dose was delivered at 1.8 Gy/fraction/day, 5 days a week. The primary tumor and the upper neck above the level of the vocal cords were irradiated using the segmental IMRT techniques.
described above. The lower neck and supraclavicular fossae were irradiated with a single anterior field. To avoid potential overlap between the beams of these two fields, a split-beam technique was used for the anterior lower neck field, and only the lower half of the anterior field was used. The primary tumor was irradiated with 6- or 15-MV photons and the lower neck was irradiated with 6-MV photons. The GTV was defined as the gross extent of the tumor shown by imaging studies (CT or MRI scan) and physical examination: this included the nasopharyngeal primary and retropharyngeal lymphadenopathy. The CTV was defined as the GTV plus margin of potential microscopic spread. In addition, surrounding critical normal structures, including the brain stem, spinal cord, optic nerves, chiasm, parotid glands, pituitary, temporomandibular joints and middle and inner ears, were outlined. The goal was to deliver a dose of 70–77 Gy to 95% or more of the GTV, 60–65 Gy to 95% or more of the CTV and to limit the maximum dose to 1% of the volume of the critical normal structures to 50 Gy for the brain stem and optic nerves, 45 Gy for the spinal cord and optic chiasm, 60 Gy for the temporal lobes and 25 Gy to 50% of the contralateral parotid gland (16). Figure 1 shows an example of a multi-segmental IMRT plan used for a patient with a stage T2bN0M0 carcinoma of the nasopharynx.

Figure 1. Isodose curves of a multi-segmental IMRT using seven coplanar gantry angles delivered for a patient with T2bN0M0 carcinoma of the nasopharynx displayed on the axial (a), coronal (b) and sagittal (c) planes and the dose-volume histogram (DVH) for the relevant structures (d).

Among the total 83 patients, sixty-three (76%) with advanced disease (T1-4N1, T1-4N2, T1-4N3, T2-4N0) received concurrent chemotherapy according to the Head and Neck Intergroup Protocol 0099. Two (2%) patients with early disease (T1N0) underwent IMRT alone. Eighteen (22%) patients with advanced disease (T1-4N1, T1-4N2, T1-4N3, T2-4N0) refused concurrent chemotherapy and underwent IMRT only. Chemotherapy consisted of: cisplatin 100 mg/m² on days 1, 22 and 43 during radiotherapy; postradiotherapy, chemotherapy with cisplatin 80 mg/m² on day 1 and 5-fluorouracil (5-FU) 1000 mg/m²/day on days 1–4 was administered every 4 weeks for three courses (6). Among 63 patients receiving concurrent chemotherapy, 51 (81%) completed the six courses of chemotherapy, eight (13%) completed five courses and four (6%) completed four courses.

FOLLOW-UP

The follow-up period ranged from 3 to 41.53 months (median, 17 months). During radiotherapy, patients were evaluated once a week. After completion of radiotherapy, patients were evaluated every 1–2 months for the first year, every 3 months for the next year, then every 6 months thereafter. Physical examination, including flexible fiberoptic endoscopy and palpation of the neck, was performed at each follow-up visit. A post-treatment MRI scan of the nasopharynx and neck was obtained within 3–4 months after completion of radiotherapy and then
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every 6 months or when clinically indicated. Acute and late normal tissue effects were graded according to the Radiation Therapy Oncology Group (RTOG) radiation morbidity scoring criteria (17).

STATISTICAL ANALYSIS

Overall survival was defined as the time from diagnosis to death resulting from any cause. Patients who were alive were classified as censored observations at the time of last follow-up for overall survival. Disease-free survival was defined as the time from diagnosis to local failure, nodal failure, systemic failure or death resulting from any cause, whichever occurred first. Patients who were alive without local failure, nodal failure or systemic failure were classified as censored observations at the time of last follow-up for disease-free survival. Disease-specific survival was defined as the time from diagnosis to death from nasopharyngeal carcinoma. Patients who were alive were classified as censored observations at the time of last follow-up and patients dying from any cause other than nasopharyngeal carcinoma were classified as censored observations at the time of death for disease-specific survival. Patients dying before evaluation of response were classified as uncensored observations for overall survival, disease-free survival and disease-specific survival. Survival estimations were performed using the method of Kaplan and Meier (18), univariate analysis using the log rank test and multivariate analysis using the Cox proportional hazards model (19).

RESULTS

SURVIVAL

Overall survival, disease-free survival and disease-specific survival were 83, 84 and 93%, respectively, at 1 year, 82, 74 and 88%, respectively, at 2 years and 82, 61 and 88%, respectively, at 3 years (Fig. 2). Sex, age, histopathology, T-classification, N-classification, radiation dose and treatment with chemotherapy in combination with radiation therapy were evaluated as prognostic factors for survival.

PROGNOSTIC FACTORS FOR OVERALL SURVIVAL

In univariate analysis, stage of disease ($P = 0.007$), N-classification ($P = 0.046$) and cumulative dose to primary tumor ($P = 0.046$) were significant prognostic factors for overall survival; favoring early stage (stage I + II), N0, and dose $\geq 75.6$ Gy, respectively. Stage I + II had a 3-year overall survival rate of 90% versus stage III + IV, with a rate of 80%. N0 had a 3-year overall survival rate of 88% versus N1 + N2, with a rate 85%, and N3, with a rate of 58%. Dose $\geq 75.6$ Gy had a 3-year overall survival rate of 86% versus dose $\leq 75.6$ Gy, with a rate of 60%.

In multivariate analysis, stage of disease ($P = 0.023$), N-classification ($P = 0.041$) and cumulative radiation dose to primary tumor ($P = 0.029$) still predicted overall survival.
PROGNOSTIC FACTORS FOR DISEASE-FREE SURVIVAL

T-stage of disease was a significant predictor of disease-free survival favoring those with early-stage (T1 + T2) disease ($P = 0.040$). T1 + T2 had a 3-year disease-free survival rate of 68% versus T3 + T4, with a rate of 49%.

PROGNOSTIC FACTORS FOR DISEASE-SPECIFIC SURVIVAL

Cumulative radiation dose to primary tumor was a significant predictor of disease-specific survival favoring those with dose $\geq 75.6$ Gy ($P = 0.010$). Dose $\geq 75.6$ Gy had a 3-year disease-specific survival rate of 93% versus dose $\leq 75.6$ Gy, with a rate of 61%. In multivariate analysis, cumulative radiation dose to primary tumor still predicted disease-specific survival ($P = 0.020$).

The $P$ values of each variable are summarized in Table 2.

<table>
<thead>
<tr>
<th>Variable</th>
<th>LR, $P$</th>
<th>NR, $P$</th>
<th>OAS, $P$</th>
<th>DFS, $P$</th>
<th>DSS, $P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>0.536</td>
<td>0.679</td>
<td>0.558</td>
<td>0.881</td>
<td>0.775</td>
</tr>
<tr>
<td>Age</td>
<td>0.069</td>
<td>0.241</td>
<td>0.108</td>
<td>0.209</td>
<td>0.203</td>
</tr>
<tr>
<td>Histopathology</td>
<td>0.428</td>
<td>0.689</td>
<td>0.746</td>
<td>0.634</td>
<td>0.464</td>
</tr>
<tr>
<td>T-classification</td>
<td>0.293</td>
<td>–</td>
<td>0.068</td>
<td>0.040</td>
<td>0.379</td>
</tr>
<tr>
<td>N-classification</td>
<td>–</td>
<td>0.484</td>
<td>0.046 (0.023)</td>
<td>0.065</td>
<td>0.715</td>
</tr>
<tr>
<td>Stage</td>
<td>0.726</td>
<td>0.611</td>
<td>0.007 (0.041)</td>
<td>0.178</td>
<td>0.979</td>
</tr>
<tr>
<td>Cumulative radiation dose to primary tumor</td>
<td>0.219</td>
<td>–</td>
<td>0.046 (0.029)</td>
<td>0.301</td>
<td>0.010 (0.020)</td>
</tr>
<tr>
<td>Radiation dose to metastatic nodes</td>
<td>–</td>
<td>0.459</td>
<td>0.693</td>
<td>0.203</td>
<td>0.696</td>
</tr>
<tr>
<td>Concurrent chemotherapy</td>
<td>0.393</td>
<td>0.661</td>
<td>0.799</td>
<td>0.919</td>
<td>0.425</td>
</tr>
</tbody>
</table>

LR, local complete response; NR, nodal complete response; OAS, overall survival; DFS, disease free survival; DSS, disease specific survival; $P$, univariate analysis; the values in parentheses are from multivariate analysis.

PATTERNS OF FAILURE

Local complete response was achieved in 81 patients (97.5%). Local failure was found in two patients. Sex, age, histopathology, T-classification, cumulative radiation dose to primary tumor and treatment with chemotherapy in combination with radiation therapy were evaluated as prognostic factors for local response. Of 64 patients with metastatic cervical lymph nodes, nodal complete response was achieved in 98.4%. Nodal failure was observed in one patient. Systemic failure was observed in 14 patients. Eight patients had bone metastases, five had liver metastases and one had lung metastases. Eight patients died of distant metastases.

ACUTE AND LATE TOXICITY

The acute side effects of radiotherapy with or without chemotherapy were usually tolerable. The acute toxicity most frequently seen was mucositis (grade 1 in 26 patients, grade 2 in 39 patients, grade 3 in seven patients and an absence of grade 4 mucositis was noted). Normal tissue effects occurring more than 90 days were scored as late toxicity. Table 3 shows the frequency, type and grade of toxicity observed. Fatal acute toxicity was observed in two patients with concurrent chemoradiotherapy. Two patients died of cerebrovascular disease 7 and 10 months, respectively, after treatment.

DISCUSSION

Nasopharyngeal carcinoma has always been distinguished from cancers of other sites on the head and neck by its relatively higher radiocurability (5). Radiation therapy at high doses tolerated by the normal tissue is the treatment of choice for carcinoma of the nasopharynx (20). Results from the experiences of The University of California–San Francisco (UCSF) and Memorial Sloan-Kettering Cancer Center, indicated that the prescribed doses to the sites of gross disease (including primary nasopharyngeal tumor and involved regional lymph nodes) should be 65–70 Gy (4,12). Other reports concluded that radiation doses of 65–75 Gy to the nasopharynx are necessary to achieve satisfactory primary tumor control (20,21). Meanwhile, elective irradiation of the N0 neck has shown to be effective in eliminating subclinical disease (22). UCSF suggests doses of 50–60 Gy to the clinically negative neck (4). However, the nasopharynx is a mid-line structure in close proximity to many other organs. High dose radiotherapy to this region results in considerable morbidity (11). The common toxicities include mucositis, pharyngitis, xerostomia, hearing

Table 3. Frequency of worst late toxicity by type and grade

<table>
<thead>
<tr>
<th>Type</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xerostomia</td>
<td>–</td>
<td>3</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Hearing impairment</td>
<td>–</td>
<td>2</td>
<td>1</td>
<td>–</td>
</tr>
<tr>
<td>Trismus</td>
<td>–</td>
<td>1</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Subcutaneous fibrosis</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Soft tissue necrosis</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
impairment, nasopharyngeal stenosis, pain of temporomandibular joints, trismus and chondronecrosis of the torus (4). With the progress of three-dimensional conformal radiotherapy (3DCRT) and IMRT, the dose distribution is more conformal to the target tumor volume in the 3DCRT and IMRT than conventional 2D radiotherapy, and the morbidity has improved because of significant sparing of critical normal tissues such as mandible, temporomandibular joints and salivary glands (4,23,24).

Improved outcome for nasopharyngeal carcinoma may be achieved with delivery of higher radiation doses (1). Vikram et al. (25) reported that those patients who received a dose to the primary between 67 and 77 Gy had a higher rate of local control compared with those who received a dose between 57 and 67 Gy ($P = 0.08$, log rank). A high rate of local control is possible in carcinoma of the nasopharynx, even with advanced disease, if a sufficiently high dose of radiation therapy is delivered (25). Yan et al. (26) found a significant improvement in local control and survival among the group of patients who received a 20–50 Gy external boost dose for residual disease after a full 70 Gy radiation therapy. Tang et al. (27), Perez et al. (20) and Lee et al. (28) have reported on radiation dose to evaluate local response, nodal response and survival. Local control of nasopharyngeal carcinoma may improve with the increase of radiation dose or with concurrent chemotherapy (5,29). With regard to increased total dose in the reports mentioned above, the average dose delivered with the external beam radiotherapy was escalated to 75.6 Gy or more to the GTV in our institution.

With the progress in chemotherapy, the combination of chemotherapy and radiotherapy has been investigated for the treatment of patients with advanced nasopharyngeal carcinoma, while radiotherapy alone is the standard treatment for early-stage nasopharyngeal carcinoma. Geara et al. (30) reported reduced failure and improved survival with induction chemotherapy in combination with radiation therapy when compared with radiation therapy alone in a matched cohort. Improved response was also shown in the preliminary report of the Asian-Oceanian Clinical Oncology Association randomized trial, which compared cisplatin and epirubicin followed by radiotherapy versus radiotherapy alone in the treatment of patients with locoregionally advanced nasopharyngeal carcinoma. No improvement of survival was observed (31). The RTOG reported improved response, reduced failure, improved survival and insubstantial toxicity with radiation therapy and concurrent cisplatin when compared with radiation therapy alone in a matched cohort (32). The phase III randomized Intergroup study 0099 reported 3-year progression free survival rates of 69% versus 24% in two groups of 147 patients with nasopharyngeal carcinoma, 78 of them treated with CCRT and 69 of them treated with radiotherapy alone, respectively (6).

In our study, only 18 patients with advanced disease refused concurrent chemotherapy. It was a relatively small group as compared to patients with advanced disease who received concurrent chemotherapy (63 patients). This resulted in an unbalanced comparison of patients with and without concurrent chemotherapy in this retrospective study. Therefore, the analysis could not reach the level of prognostic significance of concurrent chemotherapy in overall survival, disease-free survival and disease-specific survival.

With the analysis of our present study, multi-segmental IMRT is shown to improve the outcome of nasopharyngeal carcinoma as compared to conventional radiotherapy in our previous study (33) and other series (34,35), as shown in Table 4. It might be attributed to the average dose delivered with IMRT that was escalated to be $\geq 75.6$ Gy to the GTV, and also be attributed to the fact that the majority of patients (76%) in our study received concurrent chemoradiotherapy.

To distinguish patients with good prognosis from poor prognosis would influence treatment decisions. Patients with poor prognostic factors may benefit from newer experimental treatment approaches, whereas those with better prognosis may do well with standard therapy and can be spared the severe toxic side effects of more radical therapy (36). Analyzing the prognostic factors for nasopharyngeal carcinoma, Perez et al. (20) demonstrated that the most significant prognostic factors in nasopharyngeal carcinoma were patient age, stage of the primary tumor, presence of cervical lymphadenopathy and certain technical factors of irradiation. Likewise, Sanguineti et al. (5) suggested that T-stage, N-stage and the dose to the primary site were prognostic indicators for local and regional control. On the other hand, although in Chinese series the great majority of patients with nasopharyngeal carcinoma had undifferentiated tumors (WHO type 3), no significant difference in survival and locoregional control was observed with histological tumor type or degree of differentiation (5,20). Furthermore, Cheng’s study of 149 patients with nasopharyngeal carcinoma revealed that WHO (World Health Organization) type II histology, T4 clas-

### Table 4. Overall survival rates at 3 year point

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Conventional radiotherapy</th>
<th>IMRT</th>
<th>Chemotherapy</th>
<th>Survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cooper et al. (34)</td>
<td>107</td>
<td>70 Gy</td>
<td>–</td>
<td>–</td>
<td>63%</td>
</tr>
<tr>
<td>Ozyar et al. (35)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>90</td>
<td>66 Gy</td>
<td>+</td>
<td>–</td>
<td>73%</td>
</tr>
<tr>
<td>Yeh et al. (33)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>233</td>
<td>71.6 Gy</td>
<td>+</td>
<td>–</td>
<td>57%</td>
</tr>
<tr>
<td>Liu et al. (this study)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>83</td>
<td>75.6 Gy</td>
<td>+</td>
<td>–</td>
<td>82%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Neoadjuvant or concurrent chemotherapy in N2–N3 patients.
<sup>b</sup>Neoadjuvant chemotherapy in 10 patients (4.3%).
<sup>c</sup>Concurrent chemotherapy in 63 patients (76%).
sification and parapharyngeal extension were poor prognostic factors for locoregional control; T4, N3 classifications, serum LDH level > 410 U/l, parapharyngeal extension and infiltration of the clivus were significantly associated with poor prognosis for distant metastasis (37).

In our study, the local complete response rate of 97.5% was achieved in the patients with nasopharyngeal carcinoma. Overall survival, disease-free survival and disease-specific survival were 83, 84 and 93%, respectively, at 1 year, 82, 74 and 88%, respectively, at 2 years and 82, 61 and 88%, respectively, at 3 years. With univariate analysis, T-stage of primary nasopharyngeal tumor was a significant predictor of disease-free survival, favoring those with early-stage (T1 + T2) disease \( (P = 0.040) \). Cumulative radiation dose to primary tumor was a significant predictor of disease-specific survival, favoring those with >75.6 Gy \( (P = 0.010) \). Stage of disease \( (P = 0.007) \), N-classification \( (P = 0.046) \) and cumulative dose to primary tumor \( (P = 0.046) \) were significant prognostic factors for overall survival. In multivariate analysis, stage of disease \( (P = 0.023) \), N-classification \( (P = 0.041) \) and cumulative radiation dose to primary tumor \( (P = 0.029) \) predicted overall survival. Cumulative radiation dose to primary tumor predicted disease-specific survival \( (P = 0.200) \). Although high locoregional control rate was achieved with multisegmental IMRT, distant metastases were still the major impact on patients’ survival. More effective chemotherapeutic regimens and other systemic agents are needed to decrease the rate of distant metastasis and improve survival.

References

32. Al-Sarraf M, Pajak TF, Cooper JE, Mohiuddin M, Herskovic A, Ager PJ. Chemoradiotherapy in patients with locally advanced nasopharyngeal car-
cinoma: A radiation therapy oncology group study. J Clin Oncol 1990;8: 33. Yeh CY, Chiou JF, Liu MT. Clinical studies of 283 patients with undiffer-
entiated carcinoma of the nasopharynx (UCN) treated by radiotherapy. Thera-
34. Cooper JS, Cohen R, Stevens RE. A comparison of staging systems for
35. Ozyar E, Yildiz F, Akyol FH, Atahan IL. Comparison of AJCC 1988 and
1997 classifications for nasopharyngeal carcinoma. American Joint
features and treatment outcome in locoregionally advanced nasopharyn-
geal carcinoma following concurrent chemotherapy and radiotherapy.
prognostic factors and patterns of failure in nasopharyngeal carcinoma
following concomitant radiotherapy and chemotherapy: impact on future