Background
The nasopharynx is a cubical cavity located behind the nasal cavity and superior to the soft palate. Superiorly it borders the base of skull and floor of the sphenoid sinus. Laterally it is perforated by the eustachian tubes, which connect to internal ears. Nasopharynx is rich in lymphatics. Patients with nasopharyngeal cancer may present with enlarged neck lymph nodes even in the absence of other symptoms.

Nasopharyngeal cancer is a relatively rare disease in the United States, approximately 0.6 to 0.8 per 100,000 population. The highest prevalent is in southern China, with incidence rates as high as 20 per 100,000. The incidence for descendants of southern Chinese living in other countries remains higher than the other population.

Because of the anatomic location of nasopharyngeal cancer, surgical resection of a primary lesion is successful. Radiation therapy (XRT) is considered the treatment of choice for the majority of patients with this disease. However, the local control and survival of patients with loco-regionally advanced disease treated with radiation alone remain unsatisfactory. Some Phase II trials using combination of chemotherapy (CTX) and radiation therapy have shown promising results. This led to the National Head and Neck Cancer Intergroup randomized phase III trial of advanced nasopharyngeal cancer. Southwest Oncology Group (SWOG) with participation of Radiation Therapy Oncology Group (RTOG) and Eastern Cooperative Oncology Group (ECOG) coordinated this study.

Methods
Patients with histologically proven stage III and IV nasopharyngeal cancer without evidence of systemic metastasis (M0) were enrolled in this study. The patients were randomized to 2 arms: A) XRT alone versus B) CTX concurrent with XRT. The XRT was the same for both arms, which was 1.8-2.0 Gy/day for 35 to 39 fractions for a total dose of 70Gy. The investigation arm received chemotherapy with cisplatin 100mg/m2 on days 1, 22, and 43 concurrently with XRT. CTX was continued after completion of XRT, using cisplatin 80mg/m2 on day 1 and fluorouracil 1,000 mg/m2/day on days 1 to 4 every 4 weeks for total of 3 courses. Chemotherapy dose was modified based upon the neutrophil and platelet count and renal function.

Results
A total of 193 patients were registered onto the study with 147 evaluable for primary analysis of survival and toxicity. Sixty-nine patients were in XRT group and 78 patients in CTX/XRT group. The majority of patients had stage IV disease. The performance status was 0-1 in more than 90% of patients. The median progression-free survival (PFS) time for the radiotherapy group was 15 months and had not been reached for the combined group. The 3-year actuarial PFS rates were 24% and 69%, respectively (p < 0.001). The 3-year overall survival rate was 47% and 78%, respectively (p < 0.005). CTX/XRT was associated with higher incidence of grade 3 and 4 toxicity and higher percentage of non-compliance.

Discussion
This study demonstrated that CTX/XRT was superior to XRT alone in preventing loco-regional recurrence and distant metastases. In addition, this is the first randomized study to demonstrate an overall survival benefit with the use of concurrent CTX/XRT followed by adjuvant CTX as compared with XRT alone. More effective systemic treatment is needed to reduce the high systemic recurrences to improve the results further.
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