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## Selective neck dissection for neck residue of nasopharyngeal carcinoma: A prospective study



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### ABSTRACT

**Purpose:** Cervical residue or recurrence of nasopharyngeal carcinoma (NPC) is traditionally treated with radical neck dissection (RND). Because cervical residue patients with NPC exhibit better prognoses than patients with neck recurrence, selective neck dissection (SND) rather than RND may be the optimal treatment for these patients. This study was designed to evaluate the efficacy of SND for the management of neck residue of NPC.

**Material and methods:** Between January 2008 and July 2013, a total of 69 patients were assigned to undergo either RND or SND in the Department of Head and Neck Surgery at Fudan University Cancer Center. The patients' clinical and pathological characteristics, complications, and treatment outcomes were evaluated and analyzed.

**Results:** Our study consisted of 69 patients, including 51 in the RND group and 18 in the SND group. There was no significant difference in any clinical or pathological characteristic between the two groups. The overall survival (OS), disease-free survival (DFS), and regional-free survival of all the patients were 79.70%, 61.43%, and 83.30%, respectively, at 3 years and 66.81%, 47.43%, and 78.67%, respectively, at 5 years. No statistically significant difference was found in the OS, DFS, or regional-free survival between the RND and SND groups. The total complication rate was much lower in the SND group (11.11%) than in the RND group. The patients in the RND group experienced longer hospitalization and postoperative hospitalization than those in the SND group.

**Conclusion:** SND was demonstrated to be safe and effective for the treatment of neck residue of NPC. The results indicated that patients with neck residue disease who are at stage II to III with a single enlarged lymph node (<1 cm) and only one positive pathological lymph node may benefit the most from SND.

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## 1. Introduction

Nasopharyngeal carcinoma (NPC) is a relatively rare malignant tumor and is endemic in southern China. The age-standardized incidence (per 100,000) of NPC in Europe and the United States ranges between 0.5 and 2. In southern China, the incidence is much higher, at 26.9 (Ferlay et al., 2004). Its standard initial treatment is radiotherapy (RT) for early-stage disease and concurrent chemo-

radiotherapy (Chemo-RT) for advanced local-regional disease (Chan et al., 2009). Cervical lymph node metastases occur in up to 75% of NPC patients upon initial presentation (Ma et al., 2008). For those patients with advanced nodal disease upon presentation, the incidence of failure in the neck following concurrent chemo-radiation has been reported to be as high as 33% (Palazzi et al., 2004). In the past two decades, surgery rather than reirradiation has been recommended as the first choice for cervical residue or the recurrence of NPC after initial RT or Chemo-RT. Surgery results in better tumor control and long-term survival, with minimal complications compared with re-irradiation (Chua et al., 2001). However, the type of neck dissection that should be performed remains controversial (Wei and Mok, 2007).

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In our previous retrospective study of 355 patients, a comparison of the 'residual group' with the 'recurrence group' revealed a significant difference in their survival rates (Zhang et al., 2011). Because the residual group of patients exhibited a better prognosis than the recurrence group of patients, we suggest that selective neck dissection (SND) rather than radical neck dissection (RND) may be the optimal treatment for these patients. Therefore, we conducted this prospective study to determine and confirm whether SND is the optimal procedure for residual NPC.

## 2. Material and methods

### 2.1. Study design

This prospective trial was a single-center study that compared RND with SND for the management of patients with residual NPC. NPC patients of either sex who had previously undergone either a standard RT or Chemo-RT and exhibited a previously untreated neck residue of NPC with no evidence of distant metastases were eligible to participate in this trial. Written informed consent was required from every participant according to the protocol approved by Fudan University Shanghai Cancer Center. The participants were assigned to undergo either RND or SND in the Department of Head and Neck Surgery at Fudan University Shanghai Cancer Center. The decision of the type of neck dissection was based on the surgeon's decision and patient's own wishes. The patients were followed up every 3 months after surgery.

### 2.2. Patient characteristics

Between January 2008 and July 2013, a total of 69 patients were assigned to undergo either RND or SND in the Department of Head and Neck Surgery at Fudan University Cancer Center. The clinical, pathological, and radiological data for these patients were reviewed and retrospectively classified. There were 53 males (76.8%) and 16 females (23.2%), with ages ranging from 22 to 72 years (median, 46 years). The duration after standard RT or Chemo-RT ranged from 3 to 119 months (median, 17 months).

All of the patients diagnosed with NPC were treated with a standard course of conventional RT or Chemo-RT. The typical treatment regimen consisted of 65–78 Gy to the primary tumor, 60–70 Gy to the involved lymph nodes, and 50 Gy to the uninvolved neck administered as single daily fractions of 1.8–2.0 Gy for 5 days a week for 6–7 weeks. In addition, 60 patients received chemotherapy during RT. All of the patients required treatment of both sides of the neck. The responses to the treatment were evaluated according to the WHO criteria (Miller et al., 1981).

### 2.3. Surgical procedures

For the patients suffering from NPC whose neck nodes did not regress completely by 3 months after the completion of therapy, either standard RT or Chemo-RT, there is likely to be residual disease in the persistent lymph nodes. All of the patients were pathologically confirmed to exhibit malignant neck tumor based on fine-needle aspiration cytology (FNAC), which was performed with the consent of the patients. All of the pathological samples were reviewed by another independent pathologist at our hospital. Before receiving salvage treatment for neck residue, patients also underwent a complete physical examination, including nasopharyngoscopy and biopsy for suspicious nasopharyngeal lesions, magnetic resonance imaging of the nasopharynx and neck, bone scintigraphy, and ultrasound of the liver to exclude local disease and distant metastases.

Either RND or SND was performed for neck residual disease of NPC at this hospital using the conventional techniques as recommended. The extent of SND included removing level I, II, III, and IV lymph nodes. The pathological statuses of the harvested lymph nodes were postoperatively examined using hematoxylin and eosin (H&E) staining. The tumor stage was classified according to the International Union Against Cancer (UICC), 7th edition. Histopathologically, all of the patients exhibited WHO type 3 carcinoma, which is the most prevalent cancer type in southern China.

### 2.4. Statistical analysis

The  $\chi^2$  test or Fisher's exact test was used to analyze the categorical data, and descriptive statistics and T-tests were used for the between-group or within-group comparisons of independent samples. The statistical analysis was performed using SPSS 16.0 statistical software (SPSS, Inc., Chicago, IL), and the threshold value for significance was set at  $p \leq 0.05$ .

Overall survival (OS) was defined as the time from the diagnosis to death from any cause. Disease-free survival (DFS) was defined as the time from the diagnosis to local, nodal, or systemic recurrence or death from any cause, whichever occurred first. Regional-free survival was defined as the time from the diagnosis to nodal recurrence. The initial point of the follow-up period was defined as the time since the completion of the salvage treatment for the residual tumor. The end point of the follow-up period was defined as the date when the patient died or July 2014. The regional-free survival, DFS and OS rates were calculated using the Kaplan–Meier product-limit method and the log rank test. Multivariate survival analyses of the potential confounding factors were performed using the Cox proportional hazard regression model.

## 3. Results

### 3.1. General characteristics of the study population and follow-up

Our study consisted of 69 patients, including 51 in the RND group and 18 in the SND group. The descriptive characteristics of the two groups are provided in Table 1. All of the patients exhibited World Health Organization type 3 carcinoma. There was no significant difference in any clinical or pathological characteristic between the RND and SND groups of our study population. However, the median number of lymph nodes detected between the two cohorts differed, with more lymph nodes detected in the RND group than in the SND group.

The patients were reviewed every 3 months after surgery. All of the patients were followed up for at least 12 months. The duration of the follow-up period ranged from 12 months to 77 months, with a median of 36 months.

The OS, DFS, and regional-free survival of the patients were 79.70%, 61.43%, and 83.30%, respectively, at 3 years and 66.81%, 47.43%, and 78.67%, respectively, at 5 years. The OS, DFS, and regional-free survival rates of the RND and SND groups are presented in Table 2. During the follow-up period, 7 patients had neck recurrences, 2 in the SND group and 5 in the RND group. Of those 7 patients, 3 of them had contralateral level II lymph nodes recurrences, 2 of them had contralateral level II and IV lymph nodes recurrences, 1 had ipsilateral level II and III lymph nodes recurrences, and 1 had ipsilateral level IV lymph nodes recurrences. During the follow-up period, 15 of the patients died. Specifically, 2 patients died of bone metastasis, 3 patients died of liver metastasis, 4 patients died of lung metastasis, 2 patients died of neck recurrence, and 4 patients died of primary lesion recurrence. The OS, DFS, and regional-free survival curves of the RND group and SND group are shown in Fig. 1a–c, respectively ( $p = 0.68$ ,  $p = 0.70$ ,

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