

# Is it necessary to perform radical neck dissection as a salvage procedure for persistent or recurrent neck disease after chemoradiotherapy in patients with nasopharyngeal cancer?

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## Introduction

Nasopharyngeal carcinoma (NPC) is well known for its high propensity for nodal metastases and in up to 70% of the patients cervical lymphadenopathy may be the presenting symptom. Following standard treatment with radiotherapy or a combination of chemotherapy and radiotherapy most patients with NPC are cured from their disease. However, persistent or recurrent nodal disease following the initial treatment is not uncommon. The treatment of such persistent or recurrent neck disease following radiotherapy with or without chemotherapy is controversial.

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## The patterns of lymph node spread of NPC

NPC has a high propensity for neck metastases and the most frequently affected sites are levels II and V of the neck. Khoo et al. [1] studied retrospectively 68 patients with NPC who underwent radical neck dissection (RND) for regionally recurrent disease and evaluated the pathological status of 74 neck dissection specimens. The site of positive nodes in the neck was analyzed according to the levels of the neck. Their results indicate that level II has the highest rate for metastases: 88.2% of patients with positive adenopathy at multiple levels and 67.7% of patients with metastatic disease at a single level. However, when multiple levels were involved, the frequency of nodal metastases at any other levels was 30%. The authors conclude that RND is the treatment of choice for recurrent NPC because of the high frequency of involvement of all levels of the neck.

King et al. [2] reported on cervical node metastases from NPC diagnosed by MRI. Evidence of involvement of the retropharyngeal lymph node was present in 72% of patients with NPC and 94% of those patients with evidence of nodal disease. Metastasis outside the jugular and spinal accessory chains were rare in this series: submandibular metastases were uncommon (3%) and there were no metastases to sublevel IA. However, submental metastases from NPC have been reported, albeit very uncommon [3].

## When to perform salvage surgery

Analogous to the strategy in other primary tumors of the head and neck, the timing of and indication for salvage neck dissection after chemoradiotherapy has been a matter of debate. Usually, if a complete remission has been

obtained in the neck, no salvage surgery is considered necessary and if a metastatic mass in the neck does not disappear completely, a neck dissection is performed. Investigations for evaluation of the treatment result are performed around 12 weeks after finishing of the treatment. PET-CT in particular has a high-negative-predictive value and is considered reliable to evaluate the response to treatment.

### The type of neck dissection

An important clinical question is the extent of treatment to the neck, and which type of neck dissection is most effective, given the patterns of nodal spread and recurrences after prior (chemo)radiation for NPC.

In their landmark study, Wei et al. [4] examined the specimens of neck dissections of 43 patients with persistent or recurrent NPC in the neck. The tumor showed aggressive behavior reflected by several factors: extracapsular spread (70% of patients), the existence of tumor cells in isolated clusters (30%) and tumor cells lying in proximity to the spinal accessory nerve (27%). The majority of tumor-bearing lymph nodes were found in the posterior triangle (72%). The authors concluded that due to this aggressive tumor behavior, an RND is indicated for the treatment of recurrent and persistent NPC in the neck.

In a later study, Wei et al. [5] have again studied the extent of nodal disease in neck dissection specimens following recurrence of NPC. They analyzed serial sections of whole-neck dissection specimens and found that all levels of the neck had the potential to be involved with level II being the most common (53%). The authors also found the incidence of extranodal extension to be 84% in this specific group of patients with extensive recurrent or persistent disease in the neck and concluded that RND is the treatment of choice with additional brachytherapy for selected patients. The analysis of their results, however, indicates that metastases at levels I or V occurred in only 4% of patients. Because their study included only patients with extensive metastases, it may be that when the disease in the neck is more limited the incidence of metastases in other levels of the neck may be even lower. However, the same authors have recently stated that the procedure of choice for patients with regionally recurrent NPC is RND because “these lymph nodes exhibit extensive involvement of the neck tissue” [6].

Similar to the salvage treatment strategies in recurrent or persistent neck disease after chemoradiation in oropharyngeal cancer, it is possible that a more selective salvage neck dissection may be effective for NPC. For example, if extranodal extension appears to be confined to one level,

could other levels at low risk such as level I be spared? Yen et al. [7] have reported a high 5-year overall survival with the salvage dissection that in many patients included levels II–V only. They also found that musculature or nerve involvement at level V or extracapsular spread of tumor was associated with a decreased survival. In a retrospective study published by Xia et al. [8], four types of neck dissection were used for 88 patients with recurrent or persistent regional disease following radiotherapy (RND, modified RND, selective neck dissection and lymph node resection).

Their results suggest that there is no difference in the outcome of the four groups of patients, and that more selective procedures may be used in certain groups of patients. Although a study of this type has an inherent bias because patients that were selected to have a more limited type of neck dissection probably had a less advanced stage disease in the neck, selective neck dissection for this group may be used instead of RND.

Because metastatic lymph nodes seem to be primarily located at levels II and V, one could argue to that selective neck dissection accompanied by the removal of the surrounding non-lymphatic tissue would suffice. For example, if a massive recurrent tumor is detected at level V involving neighboring muscles and in proximity to the spinal accessory nerve, but the other levels of the neck are free of metastases, then the neck dissection may include sacrifice of the nerve as well as wide resection of the musculature around the tumor at level V with sparing of level I, the sternocleidomastoid muscle, and/or the internal jugular vein.

Another question is whether there should be a difference in the treatment approach for recurrent versus persistent NPC in the neck. A residual neck mass at level II after radiotherapy to the entire neck for the same lymph node (no other lymph nodes detected at the time of diagnosis) may indicate a need to be “locally aggressive” and perform a neck dissection that includes the involved node as well as other adjacent structures, such as the internal jugular vein and the sternocleidomastoid muscle. But will the resection of levels IV and I of the neck result in an increased regional control or survival?

Obviously, the other levels that were clinically N0 at diagnosis have received a full dose of radiation and the question to be asked is whether we need to dissect all neck levels and whether non-lymphatic structures should be included.

Our feeling is that the neck dissection must be tailored to the patient and although the procedure of choice is currently an RND due to lack of data, one may consider less aggressive procedures in selected patients with limited persistent disease in the neck after (chemo)radiation to the neck.

## Conclusion

RND has been indicated as the standard treatment for recurrent or persistent NPC in the neck. Considering that sublevel IA is not usually involved in NPC, the dissection of this sublevel in these tumors may be considered unnecessary although dissection of this level will not add significantly to the morbidity [9]. Because there are no primary sites of the upper aerodigestive tract in which there is a high risk for involvement at all levels and sublevels, the routine use of RND should not be indicated [10]. The regional disease control for patients with persistent neck disease using selective and superselective neck dissections for advanced N2 and N3 disease after concurrent chemoradiation is well documented [11]. Although the biological behavior of tumors arising from different primary sites within the head and neck may differ, and nasopharyngeal cancer is certainly a distinct entity, it may be presumed that the same principles of surgery for recurrent or persistent neck disease may be applicable.

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