



Cancer of the Nasopharynx: Functional Surgical Salvage

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Published Online: May 28, 2003

Abstract. The primary treatment modality for nasopharyngeal carcinoma is radiotherapy (RT). When tumor persists or recurs at the nasopharynx or in the neck after irradiation, then further courses of radiotherapy are associated with recognized morbidities. The swallowing, speech abilities as well as the cervical musculoskeletal functions of the patient may be significantly affected. Surgical salvage of neck disease with radical neck dissection contributes to better tumor control with acceptable morbidity. For localized tumor in the nasopharynx, adequate extirpation of the disease together with the removal of paranasopharyngeal tissue is possible with the anterolateral approach. The operation is not difficult and the associated morbidity is minimal. After a median follow up of 3 years, the 82 patients who underwent this operation demonstrate that with adequate exposure and surgical salvage, satisfactory tumor control rate with good functional outcome is possible.

Nasopharyngeal carcinoma, a common cancer in Southern China, is a radiosensitive tumor and the primary treatment modality is radiotherapy (RT).

The external radiation field routinely includes both sides of the neck because this tumor has a high propensity to metastasize to the cervical lymph nodes. Patients with nasopharyngeal carcinoma commonly seek treatment only when they have one or more enlarged lymph nodes, as symptoms and signs related to early nasopharyngeal carcinoma are usually trivial. The overall 5-year disease-free survival rate after RT stands at around 50%. It ranges from 50% to 90% for early stage disease and 7% to 60% for advanced-stage cancers [1, 2].

External radiation delivered for the treatment of nasopharyngeal carcinoma inevitably affects the surrounding normal tissue. The salivary glands are usually damaged as they are within the radiation field, and all patients suffer from dry mouth. More significant late complications include neuritis affecting the cranial nerves, neuroendocrine disturbance [3], and sensorineural deafness [4]. A small number of patients may experience more serious complications, such as temporal lobe necrosis [5]. However, when the nasopharyngeal carcinoma recurs or persists after RT, a further course of radiation will cause additional damage to the important surrounding structures and affect the functional well-being of the pa-

tient. Surgical salvage of persistent or recurrent nasopharyngeal cancer avoids the complications of further RT and is aimed at providing a better functional outcome.

Surgical salvage is carried out for patients who have persistent or recurrent cancer either in the neck or at the nasopharynx with no distant metastasis. If there is disease in both the nasopharynx and the cervical lymph nodes, then there is little chance of eradicating the disease. Similarly, when there is distant metastasis, surgical therapy does not have much to offer. Before salvage surgery, it is essential to perform a metastatic work-up. The extent of tumor at the nasopharynx is assessed with endoscopic examination together with imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI). The state of disease in the cervical lymph nodes is determined through clinical examination, imaging studies, and fine-needle aspiration biopsy.

Metastatic Tumor in Cervical Lymph Nodes

The incidence of persistent or recurrent tumor localized in the cervical lymph nodes after external RT has been reported to range from 3% to 10% [6, 7]. Further doses of external RT have been employed for salvage; however, the local disease control rate for lymph nodes less than 4 cm in diameter was reported to be 51%, and the overall survival rate was only 19.7% [8]. For the second course of RT to be effective, the radiation dose has to exceed that of the first course, and the associated side effects are not negligible. Severe fibrosis of neck tissue and injury to the cranial nerves in the neck frequently lead to significant functional disabilities.

Surgical salvage in the form of radical neck dissection has been shown to control persistent or recurrent disease in the neck in 66% of patients and to attain a 5-year actuarial survival rate of 38% [9, 10]. The type of surgical therapy for salvage of neck disease depends on the extent of involvement of the tumor-bearing lymph nodes in the neck. If persistent or recurrent tumor is present only in clinically palpable cervical lymph nodes without extracapsular extension, then modified radical neck dissection or even excision of the enlarged lymph node may suffice. If the cervical lymph node metastasis involves only some levels in the neck then selective neck dissection for those levels is adequate to eradicate the disease.

To study the pathological behavior of tumor within the cervical

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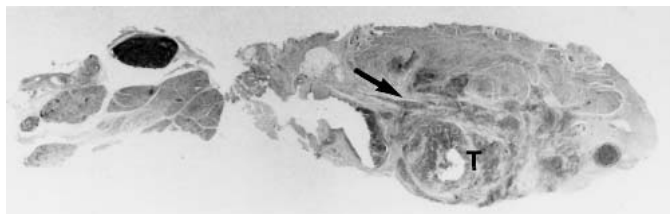


Fig. 1. Histologic section showing tumor (T) in the lymph nodes has breached the capsule and involves the surrounding tissue (arrow) (hematoxylin & eosin, $\times 20$).

lymph nodes, step-serial sections of 43 radical neck dissection specimens were carried out. The findings showed that there were six times more tumor-bearing lymph nodes in the specimen when compared with clinical examination. In addition, 70% of tumor-bearing nodes exhibited extracapsular spread (Fig. 1), and in one-third of the specimens, tumor was found to be lying close to the spinal accessory nerve or among soft tissues of the neck. In view of the extensive involvement of these tumor-bearing lymph nodes, simple excision of enlarged nodes may leave behind many foci of tumor. Because affected lymph nodes frequently involve the muscle and accessory nerve, selective or modified radical neck dissection is not adequate. Radical neck dissection, removing all tumor-bearing tissues in the neck, is considered the optimal salvage procedure for cervical nodal metastases in nasopharyngeal cancer after radiotherapy [11].

Persistent or Recurrent Cancer in the Nasopharynx

Brachytherapy

Although nasopharyngeal carcinoma is radiosensitive, some nasopharyngeal cancer persists or recurs despite radical doses of external RT. Further external RT for salvage may still be effective if the second radiation dosage is greater than that employed for the initial treatment [12]. This second course of treatment will invariably affect the surrounding tissues, leading to functional disturbances such as trismus and swallowing difficulties. The 5-year actuarial local tumor salvage rate was reported to range from 19% to 32% [13, 14].

Intracavitary brachytherapy has been found to be a useful adjunct for salvage when the location of persistent or recurrent tumor is suitable for the application of the radiation source. In many cases, the tumor extends into the lateral recess of the nasopharynx, and it is then difficult to apply the radiation source accurately to deliver the necessary tumoricidal dose. To circumvent this problem, interstitial implants such as radioactive gold grains (Au^{198}) have been inserted accurately into the tumor under direct vision [15]. For suitable patients, the probability of tumor control in the nasopharynx with this method was 80% at 5 years [16]. This technique for salvage, however, is only applicable when the persistent or recurrent tumor is superficial and not larger than 2 cm in diameter. Accurate insertion of the radiation source is mandatory for a favorable outcome, and this has to be done under general anesthesia while the medical personnel are exposed to radiation.

Surgical Resection

When the persistent or recurrent disease in the nasopharynx after external RT is not amenable to brachytherapy, either because of

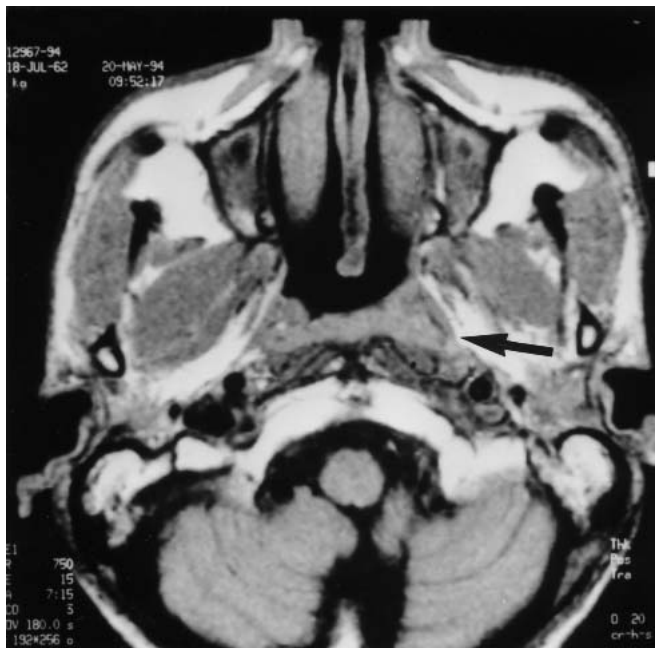


Fig. 2. Magnetic resonance imaging showing recurrent nasopharyngeal carcinoma in the paranasopharyngeal space (arrow).

location or size, then surgical resection is an alternative salvage option that does not sacrifice form and function.

Anatomically, the nasopharynx is situated in the center of the head and measures over 10 cm from the surface from all directions. The region is difficult to examine with conventional methods, although the extent of localized tumor can be assessed with endoscopic examination in combination with imaging studies such as CT or MRI (Fig. 2). It is also difficult to expose the nasopharynx adequately for tumor resection. A number of surgical approaches to the nasopharynx for resection of tumor have been described, and each one has its application, advantages, and limitations. The optimal surgical management depends on the size of the tumor, the location of the tumor, and whether it has extended to involve the paranasopharyngeal space.

Superior Approach

Exposure of the nasopharynx from the posterior is not practical because the vertebral column cannot be displaced. To approach to the nasopharynx from above, by retracting the brain upward and backward after an adequate craniotomy, however, is possible and has been reported. After resection of the lesion in the nasopharynx, the subarachnoid space is frequently in continuity with the paranasal sinuses. Reconstruction of the defect in the skull base can be achieved with pericranial flap or microvascular free flap. Ascending infection leading to meningitis, leakage of cerebrospinal fluid, formation of encephalocele, and development of diabetes insipidus have all been reported [17]. This approach is useful for resection of disease that originates within the cranium and extends down to the nasopharynx. Its application for disease localized in the nasopharynx is limited because of the extent of the surgical procedure, together with the associated morbidity and resulting functional disability.

Inferior Approach

Transpalatal. For patients who have a wide nasopharynx, exposure can be accomplished with adequate retraction of the soft palate. More extensive exposure is possible when the palate is incised in the midline and then retracted after the mucoperiosteum is lifted over the hard palate. Tumors in the nasopharynx have been successfully removed using this transpalatal approach with minimal postoperative problems [18].

Approaching the nasopharynx from the inferior aspect has the advantages that both exposure and reconstruction are relatively simple. Associated morbidity is minimal despite previous irradiation. With this approach, centrally located tumors in the nasopharynx can be exposed. It is, however, difficult to remove the tumor en bloc. The mouth and the palatal wound together limit manipulation of surgical instruments for removal of the tumor. With this approach, the lateral aspect of the nasopharynx cannot be wholly exposed to allow an oncological radical resection. Exposure of the paranasopharyngeal space is limited, and tumors that have extended lateral to the nasopharynx cannot be removed under direct vision. It is also difficult with the transpalatal approach to gain control of the internal carotid artery, which may be lying close to pathologies in the paranasopharyngeal space. This approach is not applicable in patients with trismus.

Transcervical. Use of a transcervical route has been reported for exposing the nasopharyngeal region for resection of persistent or recurrent tumor in the nasopharynx after external RT [19]. With a neck incision placed parallel to the lower border of the mandible, followed by retraction of the mandible, the parapharyngeal region can be exposed. Better exposure for resection of recurrent tumor in the region can be achieved with temporary division and retraction of the lip and the mandibular symphysis [20]. Part of the mandible and the posterior part of the maxilla may be removed for even wider exposure of the region [21]. Adequate removal of recurrent tumor is possible with this approach, but there is significant morbidity, especially when the mandible is divided.

The transpalatal and the transcervical approaches can be employed together to remove recurrent tumor in the nasopharynx. The internal carotid artery is identified in the neck and protected by a piece of gauze placed over it all the way up to the base of the skull. The combination of the two approaches has been employed with success, and associated morbidity has been reported to be minimal [22].

Mandibulotomy providing access to the space medial to its ascending ramus exposes pathology located in the paranasopharyngeal space [23]. For recurrent tumor, which often is located at a higher level, clearance of tumor superiorly may be limited. Mandibulotomy in an irradiated patient may, however, lead to significant morbidity.

Lateral Approach

Pathology in the nasopharynx including tumor in the paranasopharyngeal region can be removed via a lateral approach. This technique was first reported in 1979 [24] and was subsequently employed for the resection of post-RT recurrent nasopharyngeal carcinoma [25]. Following a radical mastoidectomy the facial nerve needs to be mobilized. The temporalis muscle is then retracted with a divided segment of the zygomatic bone and its attached masseter

muscle to expose the infratemporal fascia. The internal carotid artery needs to be exposed from the middle ear to the foramen lacerum, and so the middle meningeal artery is divided to allow retraction of the internal carotid artery. The mandibular branch of the fifth cranial nerve is divided and bone at the base of the middle cranial fossa is removed to expose the eustachian tube and the tissue of the paranasopharyngeal space. This allows removal of tumor in the nasopharynx en bloc with its surrounding tissue.

The lateral approach is suitable for recurrent tumor where the main bulk of disease is located in the paranasopharyngeal region, lateral to the nasopharynx. This operation has the advantage of enabling control of the internal carotid artery during resection, but the operative procedure requires considerable surgical expertise. The exposure of the nasopharynx achieved is also inadequate to allow radical oncological procedure to be carried out for tumors where the main bulk is located in the nasopharynx. This is particularly useful when persistent or recurrent tumor crosses the midline of the nasopharynx. With this approach it is difficult to control the resection margin at the opposite pharyngeal recess. Associated morbidity and functional disturbance are also significant, especially associated loss of hearing and damage to the Vth and VIIth cranial nerves.

Anterior Approach

To approach the nasopharynx from the front has been described. Although this is possible via the transnasal or the transtrantral route [26], the exposure achieved is not wide enough to permit an oncological resection to be carried out.

To gain increased exposure of the nasopharynx from the front, the hard palate can be fractured downward after a transverse maxillary osteotomy [27]. Pathology arising from the central skull base extended into the nasopharynx in the midline may be adequately removed with this approach [28]. Further improvements in anterior exposure can be obtained with subtotal maxillectomy or extended maxillectomy [29], whereby the coronoid process of the mandible sometimes has to be mobilized and displaced. In addition, the partial maxillectomy defect may require reconstruction. There are associated functional disabilities following all of these procedures, and none of them provide wide enough exposure of the nasopharynx to allow en bloc resection of nasopharyngeal carcinomas. Often these tumors extend through the lateral wall of the nasopharynx into paranasopharyngeal space. An anterior approach is thus only suitable for the small number of patients who have persistent or recurrent tumor localized in the central portion of the nasopharynx.

Anterolateral Approach

It is a common observation that at the completion of total maxillectomy, the nasopharynx and the paranasopharyngeal region are widely exposed. Thus after removing the maxilla, access to the nasopharynx is adequate for resection of pathologies located in the region. It has been reported that the whole maxilla may be removed to facilitate removal of tumor in this region. At completion of tumor resection, it is possible to reinsert the maxilla as a free bone graft and no bone resorption at 15 months after operation has been reported [30]. Nevertheless, this application in patients who have received a full course of radiation treatment for the primary tumor



Fig. 3. Schematic computed tomography scan showing the lateral swing of the maxilla to expose the nasopharynx and the parasphenoidal region. **Top.** Osteotomy marked with dotted line. **Bottom.** The maxilla swung laterally but kept attached to the anterior cheek flap from which it gets its blood supply.

might affect healing and significantly increases the possibility of osteoradionecrosis of the devascularized maxilla.

The whole nasopharynx and the parasphenoidal space can be exposed completely when the maxillary antrum together with the hard palate is displaced. This can be achieved with the appropriate osteotomies separating the maxillary antrum from the skull base. The maxillary antrum, including the hard palate on the side of the surgery remains attached to the soft tissue of the cheek (Fig. 3). The maxilla could be swung laterally as one osteocutaneous flap exposing the whole nasopharynx and the parasphenoidal region [31] (Fig. 4). En bloc resection of tumor located in the region can be achieved with confidence with this approach [32]. With the maxilla swung laterally, the internal carotid artery can be identified by palpation and dissected out under direct vision when indicated. With this exposure any bleeding from the internal carotid artery can be controlled with conventional methods. Similarly, after resecting a parapharyngeal space tumor, venous bleeding from the pterygoid plexus can also be managed with stitching. The posterior part of the nasal septum is removed with the nasopharyngectomy, and this further increases the exposure of the nasopharynx of the contralateral side. Recently, the anterior wall of the sphenoid has routinely been removed to improve the resection margin. While the

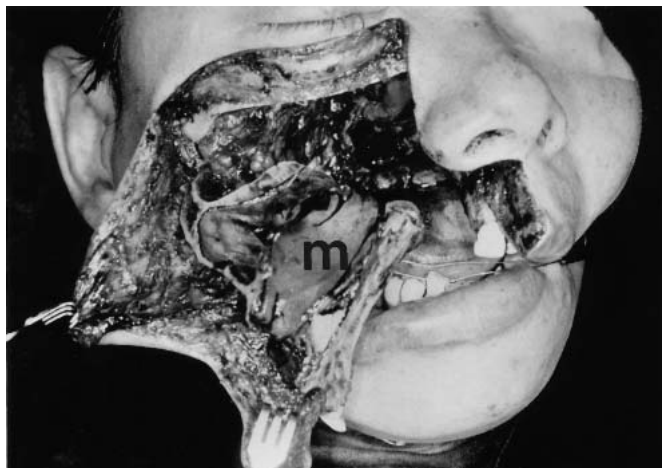


Fig. 4. Intraoperative photograph showing the laterally swung maxilla (m) to expose the nasopharynx.

maxillary antrum is swung laterally, inferior turbinectomy and inferior meatotomy are usually performed to improve subsequent drainage of the antrum and nasal cavity. After removal of tumor in the nasopharynx and its vicinity, the raw area can be grafted with the mucosa taken from the removed inferior turbinate. The maxilla attached to the anterior cheek flap can be returned to its original position and fixed to the rest of the facial skeleton with miniplates and screws. A prefabricated dental plate can also be applied to give additional stability and to contribute toward immobilizing the swung maxilla. The dental plate is then removed at 6 weeks after surgery.

Between February 1989 and June 2002, at the department of Surgery, University of Hong Kong Medical Center, Queen Mary Hospital, we have employed this anterolateral approach for resection of persistent or recurrent primary nasopharyngeal carcinoma after radiotherapy in a total of 109 patients. Among these, 82 were considered to have had a curative resection as determined with frozen section control of the resection margins. There were 66 men and 16 women; ages ranged from 27 years to 76 years (median 52 years). The histologic findings of the resected specimen were undifferentiated carcinoma in 77 patients and well-differentiated carcinoma in 5 patients. The radiation dose delivered to all patients for treatment of their primary disease ranged from 5990 to 12,250 cGy (mean 7400 cGy). All patients underwent resection of the nasopharynx on the side of the maxillary swing, and the resection crossed the midline to allow removal the mucosa just medial to the medial crura of the eustachian tube on the opposite side. In 25 patients, the parasphenoidal tissues, including the parasphenoidal lymph nodes, were removed together with the nasopharyngeal mucosa. During tumor resection, the internal carotid artery was injured in one patient and this was repaired with stitch under direct vision. He recovered with no neurological defects.

All patients survived operation and were discharged from the hospital. The follow-up period ranged from 6 to 145 months (median 37 months). Associated morbidity included a varying degree of trismus in most patients, as the pterygoid muscles had been compromised at surgery and the same region had been irradiated. Trismus usually improved with time and conservative treatment, such as the introduction of passive stretching. Palatal fistula developed in 22 patients and this was generally managed successfully with a dental plate. Palatal fistula was closed with palatal flap in three

patients successfully and all patients can take normal diet without functional disability. Two patients developed a facial sinus in the presence of an infected underlying mini-plate. Both sinuses healed after removal of the plate and screws under local anesthesia.

Eighteen patients developed recurrent tumor in the nasopharynx, 6 patients were found to have regional recurrence, and 4 other patients developed distant metastasis. The local tumor control rate was 68% at 5 years, and the 5-year actuarial survival rate for the curative group was 54%.

Salvage resection of localized persistent or recurrent tumor in the nasopharynx after radiotherapy is possible, and a satisfactory result can be achieved in suitable patients. The anterolateral approach exposes the nasopharynx and the paranasopharyngeal space adequately for en bloc removal of the disease in the nasopharynx and its vicinity. The internal carotid artery can be exposed and any bleeding appropriately controlled. The procedure is not difficult and is well within the ability of a trained otorhinolaryngologist. The associated morbidity is low, and patients normally resume swallowing and speech within 7 to 10 days after operation.

Résumé. Le traitement principal des cancers du nasopharynx est la radiothérapie. Lorsque après radiothérapie, la tumeur persiste ou récidive dans le nasopharynx ou au cou, il faut alors envisager une radiothérapie supplémentaire malgré sa morbidité bien reconnue. Toutes les fonctions du patient peuvent être atteintes et en particulier, celles de la déglutition, de la parole et musculo-squelettique. Une chirurgie de rattrapage pour une récidive ou la maladie résiduelle, associée à un curage ganglionnaire, contribue à un meilleur contrôle tumoral avec une morbidité acceptable. En ce qui concerne la tumeur du nasopharynx résiduelle ou récidivante, une excision suffisante en même temps que celle du tissu paranasopharyngé sont possibles par une approche antérolatérale. L'intervention n'est pas difficile et la morbidité associée, minime. Les résultats obtenus chez 54 patients qui ont eu ce procédé, après une médiane de survie de 3 ans, montrent qu'avec une exposition suffisante, la chirurgie de rattrapage permet d'obtenir un taux de contrôle tumoral local satisfaisant avec de bons résultats au plan fonctionnel.

Resumen. El tratamiento primario del carcinoma nasofaríngeo es la radioterapia. Cuando un tumor persiste o hace recurrencia en la nasofaringe o en el cuello luego de la irradiación, más radioterapia se asocia con reconocida morbilidad. La deglución, el habla y las funciones musculoesqueléticas del paciente se pueden ver significativamente afectadas. El salvamento quirúrgico de enfermedad cervical persistente o recurrente mediante disección radical del cuello contribuye a mejorar el control tumoral con una morbilidad aceptable. Para casos de tumor residual o recurrente en la nasofaringe, la adecuada extirpación junto con la remoción del tejido paranasofaríngeo es posible por el abordaje anterolateral. La operación no es difícil y la morbilidad es mínima. Los 54 pacientes sometidos a este procedimiento, con un seguimiento medio hasta de 3 años, han demostrado que con una exposición adecuada y el salvamento quirúrgico se pueden lograr satisfactorias tasas de control tumoral con buen resultado funcional.

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