Surgical Management of Recurrent Nasopharyngeal Carcinoma

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Current standard treatment of nasopharyngeal carcinoma (NPC) is either radiotherapy alone or combined chemoradiotherapy. Surgery in the form of nasopharyngectomy is usually only offered when there is evidence of local recurrence or persistent disease. Recurrent NPC (rNPC) can be detected earlier with the utilization of Epstein-Barr virus molecular diagnosis. This may result in early management with salvage surgery and hence improved survival. The facial translocation approach enhanced our ability to access the nasopharynx. Through a multidisciplinary approach with the collaboration of neurosurgeons, the surgical indication of salvage surgery is extended. This allowed improved respectability in locally advanced disease and involved the skull base and intracranial extension with reasonable morbidity and mortality. Endoscopic nasopharyngectomy is a choice for recurrent NPC with central roof or floor lesions with minimal lateral extension. Multivariate analysis indicated that gender, parapharyngeal space involvement, surgical margin, and the modality of adjuvant therapy impact significantly on local control. The impact on survival is indicated by the dura or brain involvement, local recurrence and modality of adjuvant therapy. It is apparent that recurrent NPC patients who underwent surgery had a significantly better survival rate than the re-radiation therapy group. *(Chang Gung Med J 2010;33:361-9)*

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Introduction of NPC

Nasopharyngeal carcinoma (NPC) is a common cancer among the Chinese.[1] NPC is a non-lymphomatous, squamous cell carcinoma that occurs in the epithelial lining of the nasopharynx. It shows varying degrees of differentiation and is frequently seen at the pharyngeal recess (fossa of Rosenmüller), posteromedial to the medial crura of the Eustachian tube opening. The tumor cell originates from the epithelial lining, and the definition of NPC strictly excludes all the other nasopharyngeal malignancies arising from lymphoid tissue or connective tissue, such as lymphomas or sarcomas.

NPC is a unique malignancy with an endemic distribution among certain well defined ethnic geographic groups. It is one of the most common head

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and neck cancers among the Chinese population but is a rare cancer among Caucasians in Europe and North America. However, a high incidence of NPC is still noted in American-born Chinese, though the incidence is lower than the Chinese who reside in the southeastern part of China.[2] These findings impose an interaction among geographic, ethnic and environmental etiologic factors. People in Taiwan, as a part of the Southeast Asia region, are affected at a rate of 5-10/100,000 per year.[3] NPC is diagnosed with clinical history, physical examination and biopsy. A typical clinical history of NPC includes unilateral or bilateral upper neck enlarged painless nodes, blood-tinged rhinorrhea, conductive hearing loss and headache.[1] Physical examination of the nasopharynx is performed in the clinic with a mirror or fiberoptic scope. A tumor mass can be visualized in the nasopharynx. Biopsy with histological proof is necessary to reach a confirmed diagnosis.

Imaging study for NPC and recurrent nasopharyngeal carcinoma (rNPC)

Imaging is required for the correct staging and treatment planning of NPC. Computed tomography (CT) and/or magnetic resonance imaging (MRI) are recommended for the diagnostic process and evaluation of the extent of the tumor.[1] MRI appears to be better than CT imaging for visualizing soft tissue invasion outside the nasopharynx, demonstrating involved retropharyngeal nodes, and identifying skull base or intracranial involvement.[4] MRI is also valuable in defining locally recurrent disease.[5,6] Asymptomatic distant metastases are not rare in the initial presentation. Thus, a pre-therapeutic work-up with positron emission tomography with [18F] fluoro-2-deoxy-D-glucose (FDG - PET) is recommended.[7]

Though NPC are radiosensitive tumors, they do recur after radiation therapy (RT). Local failure, either persistence or recurrence, in the nasopharynx, occurs in 10% to 30% of patients with NPC after initial RT.[8] Direct visualization with flexible endoscopy is the most sensitive modality for demonstrating mucosal recurrence in the nasopharynx.[9] However, postradiation mucositis, crust, or trismus may hinder endoscopic examination. Of note, endoscopy may miss residual or recurrent carcinoma, especially when the tumor is primarily submucosal. In one report, 27.8% of deep-seated recurrent NPC detected by MRI were not detected by endoscopy.[5] Both MRI and CT scans have a low sensitivity and moderate specificity for detecting rNPC and for distinguishing recurrence from postradiation changes.[9] MRI is superior to CT scans in differentiating postradiation fibrosis from rNPC. Early disease is difficult to differentiate because immature scars and well vascularized granulation tissues generally reveal contrast enhancement.[10] Sophisticated nuclear medicine examination, such as PET scans, appears promising for the detection of rNPC.[11] On PET scans, a viable tumor is seen as a focal area of increased FDG uptake due to its hypermetabolic activity, while radiation fibrosis is hypometabolic and appears as a focal area of decreased uptake. They may be superior to CT or MRI for detecting recurrent or residual disease.[11] However, PET cannot provide detailed anatomic information about the location of lesions, invasion of vascular and bony structures, and submucosal spread. False-positive results may occur in PET because of hypermetabolic features seen in the inflammatory process.

Current treatment of NPC

Currently available therapeutic modalities for NPC are RT, chemotherapy, or a combination of both.[12] NPC is highly radiosensitive and patients presenting with early disease have a high cure rate after RT.[12] Concurrent cisplatin based chemo-radiotherapy with or without neo-adjuvant chemotherapy has demonstrated significant survival improvement and is currently the standard treatment strategy for patients with locoregional advanced disease.[13] The treatment of NPC with current techniques of RT can achieve more than 80% local control rate.

Molecular detection of rNPC

Differentiation between locally recurrent tumor, radiation induced necrosis and scarring in the nasopharynx by direct visualization with endoscopy or radiological imaging is difficult until the tumor mass becomes grossly obvious with ulceration or asymmetric mucosal change. It has been reported that the mucosal appearance of the nasopharynx does not necessarily correlate well with the occurrence of early NPC.[14]

Epstein-Barr virus (EBV) is a double stranded DNA virus, which is closely related to NPC.[15] The presence of EBV in NPC is well documented.

Almost every NPC tumor cell carries clonal EBV genomes and expresses EBV proteins such as latent membrane proteins.[15] Quantification of plasma EBV DNA is useful for monitoring patients with nasopharyngeal carcinoma and predicting the outcome of treatment.[16]

The detection of EBV genomic LMP-1 [latent membrane protein 1 (LMP-1)] using a nasopharyngeal swab technique has a sensitivity of 81.8% and a specificity of 98.3% for predicting mucosal recurrence of NPC.[17] A mucosal recurrence should be strongly suspected if LMP-1 is present again in patients with treated NPC who had a latent disease remission of LMP-1 that exceeded 6 months, even if a nasopharyngoscopy revealed no abnormality.[18] In such situations, further investigation by punch biopsy or imaging, such as MRI or PET scans needs to be considered. Undoubtedly, detection of EBV LMP-1 by PCR assay with nasopharyngeal swabbing should be incorporated as an important part of a follow-up investigation in all NPC patients treated with radiotherapy.[19] The detection of LMP-1 again in radiation-treated patients with NPC can enhance physicians' awareness, encourage physicians to shorten patient follow up intervals, pay increased attention to changes in the nasopharynx, and even perform biopsies more frequently in suspicious nasopharyngeal mucosal areas.[18] Thus, it is reasonable to expect that mucosal recurrence may be diagnosed earlier using detection of LMP-1 as one of the follow- up screening modalities. Moreover, salvage treatment can be more successful when rNPC is treated early.[17] The role of LMP-1 as a tumor marker to monitor local or residual NPC tumors after radiation therapy has been established. In one report, of the 12 patients with local recurrence, 11 patients had positive LMP-1, including 2 cases with normal nasopharyngoscopy findings. It suggests that nasopharyngeal swabs with LMP-1 detection could detect early recurrence, and, after salvage surgery, may actually improve local control and enhance survival.[17] The detection of LMP-1 with subsequent verification of EBNA-1 from nasopharyngeal swabs in radiotherapy treated NPC patients predicted local recurrence with a sensitivity of 91.7% and a specificity of 98.6%. Nasopharyngeal swabs coupled with LMP-1 and EBNA-1 detection is simple and convenient, it proves to be a reliable method in detecting local recurrence in NPC patients after radiation therapy.[17-19] It helps to detect local recurrence in the early phases and, may improve local control as well as enhance survival of the patients.[17-19]

Salvage surgery for locally recurrent NPC

The nasopharynx occupies the most cephalic portion of the upper aerodigestive tract. It is a hollow cubic space above the soft palate and posterior to the nasal cavity. It is located beneath the sphenoid sinus and upper clivus, anterior to the lower clivus and the body of the first cervical vertebra and medial to the medial pterygoid plate. The lateral wall of the nasopharynx is formed by the torus tubarius - the bulging cartilage of the medial end of the eustachian tube. The nasopharynx is lined with pseudostratified ciliated columnar epithelium. Deep in the mucosal layer is the pharyngobasilar fascia, a tough fascia surrounding the superior posterior and lateral walls. The fascia originates from the pharyngeal tubercle of the occipital bone posteriorly and inserts into the posterior sharp end of the medial pterygoid plate anteriorly. It forms the posterior boundary of the nasopharynx, and continues inferiorly as the buccopharyngeal fascia. The lateral wall of the nasopharynx is bounded by the medial pterygoid plate. It is formed by an incomplete cartilaginous ring which is deficient inferolaterally. The eustachian tube and accompanied tensor veli palatini muscle pierce through this natural defect, known as the sinus of Morgagni, on the lateral wall of the pharyngobasilar fascia to the middle ear space. As the pharyngobasilar fascia is tough and forms a good barrier, the NPC, which originates from the fossa of Rosenmüller, preferentially ascends and destroys the sphenoid sinus floor to involve the sphenoid sinus and skull base. More commonly, it invades laterally through the sinus Morgagni, extends along the eustachian tube to destroy the pterygoid plate base, and involves the parapharyngeal space and foramen ovale area. When the tumor reaches the foramen lacerum laterally, it may encase the petrous internal carotid artery. In this case it is almost impossible to achieve complete resection.

Once NPC recurs in the nasopharynx, salvage nasopharyngectomy should be the treatment of choice as there is no reason to believe that the NPC cells, which are resistant to a first course of RT, would respond to a second course of radiation, not to mention the risk of skull base osteoradionecrosis - a

potentially fatal complication of high dose RT.

Salvage nasopharyngectomy has been the mainstay of treatment after RT failure.[20-27] Surgical access to the nasopharynx has been a challenge to head and neck surgeons for years. Various surgical approaches to the nasopharynx have been developed, such as transpalatal, transmaxillary, midline mandibulotomy, transpterygoid, facial translocation, and infratemporal fossa approaches.[8] The traditional surgical approach to the nasopharynx was from the anterior inferior route. The transpalatal approach may be the most simple; however, it generally provides limited exposure of the nasopharynx and may be complicated with oronasal fistula. The transmandibular approach to the central skull base was advocated by many authors. Mandibulotomy is usually unable to provide enough exposure of the superior aspect of the rNPC. It can expose the vertical internal carotid artery before it enters the carotid canal but does not expose the petrous internal carotid artery, especially its horizontal segment, which lies behind the foramen ovale within the petrous bone. Minimally invasive endoscopic nasopharyngectomy was reported to be a feasible treatment of small mucosal recurrence.[28] However, we are very cautious in endoscopic nasopharyngectomy as the role of endoscopic surgery for skull base malignancies remains to be determined.[27] The indication of endoscopic nasopharyngectomy for rNPC includes central roof or floor lesions with minimal lateral extension.[27,28] Endoscopic nasopharyngectomy can be accomplished with laser. Parapharyngeal space or skull base bone involvement is a contraindication for endoscopic resection, and we recommend a facial translocation or even standard craniofacial resection for such recurrence.[27] There are also some excellent anterior approaches, such as the maxillary swing or mid-face degloving.[25] Both approaches to the nasopharynx are good for tumors located in the nasopharynx or for those with limited involvement of the parapharyngeal space. However, they still lack a superior exposure of the tumor, so that when a tumor attaches or destroys the pterygoid plate base or the foramen ovale area, it limits the extent of the exposure. A combined neurosurgical approach might resolve the above problems.[20,21,27,29] For example, the subfrontal approach would provide a superior exposure of the cribriform plate, fovea ethmoidalis and planum sphenoidale.[29] The subtemporal approach could provide superior exposure of the subtemporal space and also lateral exposure of the infratemporal fossa, which is ultimately important for NPC with lateral extension.[27] Although originally designed as an intradural posterior fossa approach, we found the preauricular infratemporal subtemporal approach especially useful in the lateral skull base.[27] This approach does not involve extensive petrous bone work, and only mobilizes the frontal branch of the facial nerve. It provides an excellent superior and lateral exposure of the tumor with nasopharynx and parapharyngeal space involvement. By detaching the temporalis muscle, temporarily removing the zygomatic arch and elevating the temporal lobe after craniotomy, the preauricular infratemporal subtemporal approach exposes the parapharyngeal space from both lateral and superior directions.[27] The transverse portion of the petrous internal carotid artery could be identified and preserved in this approach and may thus minimize surgical morbidity or mortality. However, patients with extensive involvement of the parapharyngeal space or infratemporal fossa by rNPC are generally not good candidates for salvage skull base surgery, as it is difficult to achieve oncologically sound surgical margins in these areas.[27] The surgical morbidity of the combined preauricular infratemporal subtemporal approach can be small. Extensive dissection or resection in the infratemporal fossa may be predisposed to postoperative trismus, which can be minimized by freeing the temporalis muscle and removing the coronoid process of the mandible.

The facial translocation approach, with a temporary disassembly of the facial skeleton and reinsertion and fixation of the fragment at the end of the procedure, provides an excellent surgical exposure of the skull base to facilitate extensive resectioning of tumors and reliable reconstruction.[30] Facial translocation is considered one of the best surgical approaches to the anterior and middle skull base.[30] It provides the most direct approach to the central skull base and offers generous exposure to facilitate extensive tumor resectioning with the preservation and restoration of critical structures.[30] The facial translocation approach combined with elective craniofacial osteotomies and, optionally, with neurosurgical subfrontal or subtemporal approaches can offer the exposure of almost the entire anterior and middle cranial base.[30,31] The facial translocation approach,

by translocating the facial bone segment and then reimplanting it, has its potential pitfalls. The translocated facial bone segment becomes a free bone graft if it is not left attached to the soft tissue of the cheek. Theoretically, the vascularity of the translocated bone segment could be preserved if the osteotomized facial bone segment remains attached to the soft tissue of the cheek. The approach, however, might be technically difficult, especially if the anterior wall of the maxillary sinus was removed in the previous lateral rhinotomy or Caldwell-Luc surgery. The osteotomy of the lateral wall is another technical challenge. The lateral osteotomy is usually done in a blind method and may accidentally injure the internal maxillary artery. It is difficult to control the bleeding unless the translocated facial bone is removed as a free bone graft. In the facial translocation approach, although the osteotomized facial bone segment remains vascularized by preserving the anterior cheek attachment, the blood supply of the translocated facial bone segment, which mainly derives from the facial artery, is still very redundant.[31]

There are various important surgical approaches to the skull base, such as infratemporal fossa approach,[32] maxillary swing,[24] subtotal maxillotomy approach,[33] Le Fort I osteotomy approach,[34] and facial translocation approach.[30,31] All of these are sound surgical approaches, but the facial translocation approach (or facial bone disassembly approach) has been appraised as the best surgical approach to the middle central skull base.[31] Superior extension of NPC to the skull base by directly destroying the base of the pterygoid plate is common, and from here, the tumor can invade the cavernous sinus superiorly and the foramen ovale laterally. It is crucial to realize that surgeons seldom deal with a recurrent tumor solely occupying the nasopharyngeal space. Unexpected extension to the peritubal or parapharyngeal space is common, and the surgical approach should be modified according to the preoperative magnetic resonance imaging findings and the intraoperative findings.[31] The facial translocation approach, with elective osteotomies, can flexibly fulfill the above requirements.[30] To its full extent, a unilateral facial translocation approach can offer exposure from the contralateral fossa of Rosenmüller to the ipsilateral glenoid fossa. Combined with a subfrontal approach, anterior cranial base extensions of NPC to the ethmoid sinuses and cribriform plate can be resected. When combined with a subtemporal approach, a lateral extension of NPC to the sphenoid ridge and foramen ovale area can be resected. In our department, the facial translocation approach was the surgical approach of choice for recurrent rNPC.[30,31,35-37] The indications for nasopharyngectomy included not only nasopharyngeal mucosa disease but also parapharyngeal space invasion or transcranial invasion.[20,21,27]

Over the years, several technical modifications of the facial translocation approach to further avoid bone graft necrosis have been designed in our department. First, three point fixation is crucial to secure and immobilize the facial bone graft otherwise the microtrauma would interfere with bone union. Second, the facial bone unit is secured to the facial soft tissue by suturing the cheek soft tissue flap to the drilling holes of the facial bone unit. Third, the lateral nasal wall can be preserved and transposed to resurface the inner aspect of the translocated facial bone unit if it is far away from the tumor and remains free of disease.[36,37] In order to prevent bone graft necrosis in the facial translocation approach for salvage nasopharyngectomy, we designed a modified facial translocation approach by using a lateral nasal flap to resurface the inner defect of the translocated facial bone graft which significantly improved the viability of the translocated facial bone graft especially in patients who underwent radiation therapy.[36,37] The use of a lateral nasal flap does not interfere with detection of early local recurrence.[36,37] We also proved that the lateral nasal wall mucoperiosteal flap is a simple and reliable flap and provides ample vascularized tissue to resurface the nude translocated facial bone segment during the facial translocation approach to the skull base and thus prevents its avascular necrosis even in circumstances following radiation therapy.[37,38]

Much effort has been devoted to salvage nasopharyngectomy in our department. We reported our first experience on salvage nasopharyngectomy on 18 patients, and the actuarial 3- year survival rate was 57%, while the local control was 78%.[20] Four of 5 patients who had skull base invasion achieved local control. There was no surgical mortality, and the morbidity was 22%. We concluded that advances in skull base surgery make the effective control of primary recurrence of nasopharyngeal carcinoma possi-

ble, and with acceptable mortality and morbidity.[20] A subsequent report based on 38 patients of rNPC who underwent nasopharyngectomy, resulted in an actuarial 3-year survival and local control rate of 60% and 72.8%, respectively.[21] Ten (83.3%) out of twelve patients with intracranial and skull base invasion achieved local control. There was no surgical mortality, and the morbidity rate was only 13.2%. The results of this study reveal a better outcome of salvage surgery than that of most published literatures of re-irradiation for rNPC.[21] With adequate exposure provided by the facial translocation approach, an integrated concept of skull base surgery, and the collaboration of neurosurgeons, we can extend our surgical indications of salvage surgery and resect many advanced lesions with acceptable mortality and morbidity.[21] Using the maxillary swing approach for the surgical resection of local recurrence, Wei et al reported actuarial rates of tumor control and overall survival at 3.5 years of 42% and 36%, respectively.[25] King et al reported their 12-year experience in the surgical treatment of recurrent NPC in 31 patients.[26] They concluded that surgical resection with postoperative RT was a better salvage treatment than re-irradiation alone for selected cases of recurrent NPC.[26]

Prognostic factors of treatment of rNPC

There have been only a few reports on the impact factors affecting the survival or local control after salvage nasopharyngectomy for rNPC. Based on 60 cases of recurrent nasopharyngeal malignancies including sarcomas and small cell carcinomas that underwent salvage nasopharyngectomy, Hsu et al. reported that recurrent T stage was the prominent prognostic factor and adjuvant radiation therapy, although showing some benefits to the patients, was not a significant impact factor.[38] They recommended surgery for rT1, rT2 or limited rT3 lesions.[38] To et al. reported on 31 patients who underwent salvage nasopharyngectomy for recurrent NPC and were followed up for more than 1 year.[39] They concluded that a high recurrent T stage, skull base involvement, repeated recurrence, nodal metastasis and positive margins were significant poor prognostic indicators. They also proved that patients with low recurrent T stage have a survival advantage and benefit most from surgery.[39] We reported the local control and overall survival outcome of 53 patients with rNPC who received salvage nasopharyngectomy and had identifiable prognostic factors.[27] In the report, fifty-three consecutive patients who had rNPC and underwent salvage surgery with curative intention from July 1993 to December 2006 were retrospectively reviewed. The follow-up time ranged from 5.1 to 142.2 months. The numbers of cases of rNPC stage were as follows: stage I, 26; stage II, 9; stage III, 10 and stage IV, 8. Fifty patients had one course of radiation therapy while 3 had two courses of radiation therapy before the salvage surgery. For the nasopharyngectomy, 2 patients underwent an endoscopic approach and 33 underwent facial translocation, while 18 had craniofacial resection. Postoperative adjuvant treatment included radiation therapy, 4 cases; radiosurgery, 8 cases; concurrent chemoradiation therapy, 7 cases; and chemotherapy, 2 cases. The 5-year local control rates were T1, 58.3%; T2, 27.8%; T3, 53.3%; T4, 75.0%; and all stages, 53.6%. The 5-year overall survival rates were stage I, 64.8%; stage II, 38.1%; stage III, 25.9%; stage IV, 46.9%; and all stages, 48.7%. Multivariate analysis revealed that gender, margin status, adjuvant treatment type and parapharyngeal space involvement were significant impact factors of local control, whereas dura or brain involvement, local recurrence and adjuvant treatment type were significant impact factors of survival.[27] In this series, the local control rate of rT2 was 27.8%, which reflected on the parapharyngeal space involvement as a prominent poor prognostic indicator on univariate analysis. There was a trend for rT1 and rT2 to have a higher local recurrence rate and for rT3 and rT4 to have a higher distant metastasis rate. However, the good local control rate of rT3 and rT4 lesions in this series may result from the commonly used craniofacial resection procedures in our hospital.[27] Nevertheless, we admit that we excluded patients with extensive dura, brain or cavernous sinus involvement, severe perineural infiltration or carotid artery encasement from skull base surgery. Thus the good outcome could be the result of cautious patient selection for salvage surgery. However, we advocate that skull base surgery has a major role in the treatment of rNPC patients, even when they have skull base involvement which was considered a relative contraindication for surgery in the past. For all oncologic surgery, margin status is always one of the most significant impact factors of local control, and we stressed that

margin status was largely determined by parapharyngeal space involvement and was a significant indicator of poor prognosis of local control and subsequently secondary local recurrence impacted the survival in a negative way.[27] Thus, we advocate that patients with extensive parapharyngeal space involvement might not be good surgical candidates and perhaps patients may benefit from concurrent chemoradiation therapy.[27]

REFERENCES

1. Wei WI, Sham JST. Nasopharyngeal carcinoma. Lancet 2005;365:2041-54.
2. Buell P. The effect of migration on the risk of nasopharyngeal cancer among Chinese. Cancer Res 1974;34:1189-91.
3. Department of Health. Leading causes of death from cancer in Taiwan area from 1991 to 1996. Health and vital statistics of Republic of China. Taipei: Executive Yuan, R.O.C., 1997:72-7.
4. Chong VF, Mukherji SK, Ng SH, Ginsberg LE, Wee JT, Sham JS, O'Sullivan B. Nasopharyngeal carcinoma: review of how imaging affects staging. J Comput Assist Tomogr 1999;23:984-93.
5. Ng SH, Chang JT, Ko SF, Wan YL, Tang LM, Chen WC. MRI in recurrent nasopharyngeal carcinoma. Neuroradiology 1999;41:855-62.
6. Ng SH, Liu HM, Ko SF, Hao SP, Chong VFH. Post treatment imaging of the nasopharynx. Eur J Radiol 2002;44:82-95.
7. Liu T, Xu W, Yan WL, Ye M, Bai YR, Huang G. FDG-PET, CT, MRI for diagnosis of local residual or recurrent nasopharyngeal carcinoma, which one is the best? A systematic review. Radiother & Oncol 2007;85:327-35.
8. Yu KH, Leung SF, Tung SY, Zee B, Chua DT, Sze WM, Law SC, Kam MK, Leung TW, Sham JS, Lee AW, Au JS, Hui EP, Sze WK, Cheng AC, Yau TK, Ngan RK, Wong FC, Au GK, Chan AT; Hong Kong Nasopharyngeal Carcinoma Study Group. Survival outcome of patients with nasopharyngeal carcinoma with first local failure: a study by the Hong Kong Nasopharyngeal Carcinoma Study Group. Head Neck 2005;27:397-405.
9. Chong VFH, Fan YF. Detection of recurrent nasopharyngeal carcinoma: MRI imaging versus CT. Radiology 1997;202:463-70.
10. Olmi P, Fallai C, Colagrande S, Giannardi G. Staging and follow-up of nasopharyngeal carcinoma: magnetic resonance imaging versus computerized tomography. Int J Radiat Oncol Biol Phys 1995;32:795-800.
11. Yen RF, Hung RL, Pan MH, Wang YH, Huang KM, Lui LT, Kao CH. 18-fluoro-2-deoxyglucose positron emission tomography in detecting residual/ recurrent resonance imaging. Cancer 2003;98:283-7.
12. Hao SP, Tsang NM. Chapter 11. Nasopharyngeal carcinoma. In: Guy J. Petruzzelli ed. Practical Head and Neck Oncology. San Diego, CA; Plural Publishing, 2008:175-90.
13. Cheng SH, Liu TW, Jian JJ, Tsai SY, Hao SP, Huang CH, Liu MC, Yu B, Huang AT. Concomitant chemotherapy and radiotherapy for locally advanced nasopharyngeal carcinoma. Cancer J Sci Am 1997;3:100-6.
14. Wei WI, Sham JS, Zong YS, Choy D, Ng MH. The efficacy of fiberoptic endoscopic examination and biopsy in the detection of early nasopharyngeal carcinoma. Cancer 1991;67:3127-30.
15. Cohen JI. Epstein-Barr virus infection. New Engl J Med 2000;343:481-92.
16. Lin JC, Wang WY, Chen KY, Wei YH, Liang WM, Jan JS, Jiang RS. Quantification of plasma Epstein-Barr Virus DNA in patients with advanced nasopharyngeal carcinoma. NEJM 2004;350:2461-70.
17. Hao SP, Tsang NM, Chang KP. Monitoring tumor recurrence with nasopharyngeal swab and LMP-1 and EBNA-1 gene detection in treated patients of NPC. Laryngoscope 2004;114:2027-30.
18. Tsang NM, Chuang CC, Tseng CK, Hao SP, Kuo TT, Lin CY, Pai PC. Presence of the latent membrane protein 1 gene in nasopharyngeal swabs from patients with mucosal recurrent nasopharyngeal carcinoma. Cancer 2003;198:2385-92.
19. Hao SP, Tsang NM, Chang KP, Ueng SH. Molecular diagnosis of nasopharyngeal carcinoma-detecting LMP-1 and EBNA by nasopharyngeal swab. Otolaryngol Head Neck Surg 2004;131:651-4.
20. Hao SP, Tsang NM, Chang CN. Salvage surgery for recurrent nasopharyngeal carcinoma. Arch Otolaryngol Head Neck Surg 2002;128:63-7.
21. Chang KP, Hao SP, Tsang NM, Wong SH. Salvage surgery for locally recurrent nasopharyngeal carcinoma–a 10-year experience. Otolaryngol Head Neck Surg 2004;131:497-502.
22. Fee WE, Gilmer PA, Goffinet DR. Surgical management of recurrent nasopharyngeal carcinoma after radiation failure at the primary site. Laryngoscope 1998;98:1220-6.
23. Hsu MM, Ko JY, Sheen TS, Chang YL. Salvage surgery for recurrent nasopharyngeal carcinoma. Arch Otolaryngol Head Neck Surg 1997;123:305-9.
24. Wei WI, Lam KH, Sham JST. New approach to the nasopharynx: the maxillary swing approach. Head Neck 1991;13:200-7.
25. Wei WI, Ho CM, Yuen PW, Fung CF, Sham JS, Lam KH. Maxillary swing approach for resection of tumors in and around the nasopharynx. Arch Otolaryngol Head Neck Surg 1995;121:638-42.
26. King WW. Ku PK, Mok Co, Teo PM. Nasopharyngectomy in the treatment of recurrent nasopharyngectomy and the treatment of recurrent nasopharyngeal carcinoma: a twelve-year experience. Head Neck 2000;22:215-22.

27. Hao SP, Tsang NM, Chang KP, Hsu YS, Chen CK, Fang KH. Nasopharyngectomy for recurrent nasopharyngeal carcinoma: a review of 53 patients and prognostic factors. Acta Oto-Laryngologica 2008;128:473-81.
28. Chen MK, Lai JC, Chang CC, Liu MT. Minimally invasive endoscopic nasopharyngectomy in the treatment of recurrent T1-2a nasopharyngeal carcinoma. Laryngoscope 2007;117:894-6.
29. Wang CC, Hao SP, Chen YL, Hsu YS, Jung SM. Transcranial resection of olfactory neuroblastoma. Skull Base 2005;15:163-71.
30. Hao SP, Pan WL, Chang CN, Hsu YS. The use of facial translocation technique in the management of tumors of the paranasal sinuses and skull base. Otolaryngol Head Neck Surg 2003;128:571-5.
31. Hao SP. Facial translocation approach to the skull base: the viability of translocated facial bone graft. Otolaryngol Head Neck Surg 2001;124:292-6.
32. Fisch U. Infratemporal fossa approach to tumors of the temporal bone and base of skull. J Laryngol Otol 1978;92:949-67.
33. Catalano PJ, Biller HF. Extended osteoplastic maxillotomy, a versatile new procedure for wide access to the central skull base and infratemporal fossa. Arch Otolaryngol Head Neck Surg 1993;119:394-401.
34. Williams WG, Lo LJ, Chen YR. The Le Fort I-palatal split approach for skull base tumors: efficacy, complications, and outcome. Plast Reconstr Surg 1998;102:2310-9.
35. Chen CW, Hao SP, Pan WL. Bone graft necrosis of facial translocation: Comparison of 3 different techniques. Otolaryngol Head Neck Surg 2006;135:719-23.
36. Hao SP, Pan WL, Chung TC, Kao CL. Lateral nasal wall mucoperiosteal flap: a versatile new reconstruction of the inner defect of translocated facial bone segments. Ann Plast Surg 2004;52:343-8.
37. Hao SP. Modified Facial Translocation Technique to Prevent Necrosis of Bone Graft. Laryngoscope 2002;112:1691-5.
38. Hsu MM, Hong RL, Ting LL, Ko JY, Sheen TS, Lou PJ. Factors affecting the overall survival after salvage surgery in patients with recurrent nasopharyngeal carcinoma at the primary site: experience with 60 cases. Arch Otolaryngol Head Neck Surg 2001;127:798-802.
39. To EW, Lai EC, Cheng JH, Pang PC, Williams MD, Teo PM. Nasopharyngectomy for recurrent nasopharyngeal carcinoma: a review of 31 patients and prognostic factors. Laryngoscope 2002;112:1877-82.

外科手術治療局部復發鼻咽癌

侯勝博　曾雁明[1]

鼻咽癌是以放射線照射或合併化學-放射照射來治療，倘若鼻咽癌局部復發，則可使用解救手術切除。藉由分子診斷偵測鼻咽癌細胞之 EB 病毒 DNA，可早期偵測局部復發，再早期施以解救手術，病人可望有較佳存活率。

運用顏面骨拆卸法配合神經外科的經顱手術等顱底手術，局部復發鼻咽癌的切除適應症不再只限於鼻咽腔的黏膜復發，可擴展至顱底骨頭侵犯者，甚至顱內侵犯者；而內視鏡鼻咽切除術，目前應只限於復發腫瘤位於鼻咽腔中線位置而有少量側邊侵犯的腫瘤。性別、手術切除安全範圍狀態、追加治療型式及側咽侵犯爲影響局部復發鼻咽癌手術局部控制之因素，而腦或腦膜侵犯，再次局部復發及追加治療型式爲影響存活率之因素。相對於再次放射線照射治療，局部再發的鼻咽癌若接受解救手術治療，存活率明顯較好，但這亦可能是選擇病患接受手術的結果。(長庚醫誌 2010;33:361-9)

關鍵詞：鼻咽癌，局部再發，解救手術，顱底手術，EB 病毒，預後

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