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Surgical treatment of nasopharyngeal cancer - a consensus recommendation from two Chinese associations*

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Abstract

Background: Surgical treatment is playing an increasingly important role in the management of nasopharyngeal carcinoma (NPC). This consensus focuses on the indications for optimal surgery, and surgical methods in the whole process of treatment for NPC to provide a useful reference to assist these difficult clinical decisions.

Methodology: A thorough review of available literature on NPC and surgery was conducted by the Association for the Prevention and Treatment of Nasopharyngeal Carcinoma in China, International Exchange and Promotion Association for Medicine and Healthcare, and the Committee on Nasopharyngeal Cancer of the Guangdong Provincial Anticancer Association. A set of questions and a preliminary draft guideline was circulated to a panel of 1096 experienced specialists on this disease for voting on controversial areas and comments. A refined second proposal, based on a summary of the initial voting and different opinions expressed, was recirculated to the experts in two authoritative medical science and technology academic groups in the prevention and treatment of NPC in China for review and reconsideration.

Results: The initial round of questions showed variations in clinical practice even among similar specialists, reflecting the lack of high-quality supporting data and resulting difficulties in formulating clinical decisions. Through exchange of comments and iterative revisions, recommendations with high-to-moderate agreement were formulated on general treatment strategies and details of surgery, including indications and surgical approaches.

Conclusion: By standardizing the surgical indications and practice, we hope not only to improve the surgical outcomes, but also to highlight the key directions of future clinical research in the surgical management of NPC.

Key words: nasopharyngeal cancer, surgery, guideline, consensus, surgical treatment

Introduction

Nasopharyngeal carcinoma (NPC) is a head and neck cancer with a highly heterogeneous racial and geographical distribution worldwide, with the highest incidence globally found in southern China [(1)]. The non-keratinizing subtype accounts for most cases in endemic areas (>95%) and is predominantly associated with Epstein-Barr virus (EBV) infection. Although radiotherapy is still the treatment of choice for primary disease [(2)], the rapid advancement of surgical methods in recent years, including endoscopic and robotic surgery, has led to an increasingly important role of surgery in the management of NPC, especially for locally recurrent lesions or radiation-induced complications. However, most publications on NPC surgery are based on case reports or retrospective studies with a limited number of patients, leading to a lack of international consensus on the indications, optimal time, and duration for radiotherapy as well as the choice of surgical approach for NPC. Given the rich surgical experience and large number of NPC patients treated in China, the experts in the Association for the Prevention and Treatment of Nasopharyngeal Carcinoma in China, International Exchange and Promotion Association for Medicine and Healthcare, and the Committee on Nasopharyngeal Cancer of the Guangdong Provincial Anticancer Association have set up a working group aiming to compile up-to-date pragmatic recommendations on the indications and surgical approaches for NPC. After extensively reviewing the literature and carefully analyzing the failure patterns and complication rates of NPC surgery, we formulated and graded each specific surgical indication based on the best available evidence. Furthermore, we gathered the views of experienced specialists on this disease, including experts in skull base surgery, head and neck surgery, radiation oncology, and medical oncology, to build this consensus recommendation.

According to the purpose of surgical intervention, we can divide the underlying situation into three categories. The first category is for recurrent nasopharyngeal cancer after radiotherapy, including nasopharyngeal recurrence, retropharyngeal lymph node recurrence, and cervical lymph node recurrence, among which the pathological type is non-keratinizing carcinoma with EBV infection. The advantage of surgery in such cases is that it can directly remove radiotherapy-resistant lesions and avoid the damage of reirradiation. The second category comprises

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Table 1. Categories of evidence and consensus [40].

Characteristics of evidence			Specialists Consensus
Category	Level	Source	
1A	High	Rigorous meta-analysis, large randomized controlled clinical trials research	High (Support opinion ≥ 80%)
1B	High	Rigorous meta-analysis, large randomized controlled clinical trials research	Moderate (Support opinion ≥ 60% and < 80%)
2A	Moderate	Meta-analyses of average quality, small randomized controlled trials studies, well-designed large retrospective studies, case controlled study	High (Support opinion ≥ 80%)
2B	Moderate	Meta-analyses of average quality, small randomized controlled trials studies, well-designed large retrospective studies, case controlled study	Moderate (Support opinion ≥ 60% and < 80%)
3	Low	Uncontrolled single-arm clinical studies, case reports, expert opinions	Low (Support opinion < 60%)

Table 2. Recommendation criteria [40].

Recommendation level	Criterion
High	Level 1A evidence and some Level 2A evidence Notes: Our panel will take Level 1A evidence and Level 2A evidence with a high degree of consensus among our experts and good accessibility as High recommendations.
Moderate	Level 1B evidence and some Level 2A evidence Notes: Our panel will take Level 1B evidence and Level 2A evidence with a slightly lower degree of expert consensus or less accessibility as Moderate recommendations.
Low	Level 2B evidence Note: Although there is a lack of strong evidence-based medical evidence for the treatment methods being explored, the expert group has reached a moderate to high consensus and can be used as a low recommendation for clinicians.
Not recommended	Level 3 evidence Notes: For indications with low quality evidence and low expert consensus, we do not make recommendations.

rare pathological types of nasopharyngeal caner that have not been treated with radiotherapy, including salivary gland-type carcinoma and adenocarcinoma of the nasopharynx, where surgery is preferred as these types of nasopharyngeal cancer are not sensitive to radiotherapy. The third category comprises complications caused by radiotherapy including post-radiation nasopharyngeal necrosis, post-radiation rhinosinusitis, radiation-related otitis media with effusion, radiation-related encephalopathy, and radiation-related epitaxis, and the goal of surgery is to clear the diseased tissue and restore normal organ function.

Materials and methods

The following protocols were used for the evidence-based development of this guideline. First, an initial literature search on clinical outcomes of NPC patients treated with surgery up to August 2022 was performed in the PubMed, Scopus, EMBASE, CBMDISC, and China Info using the following search terms: "nasopharyngeal carcinoma" OR "NPC" OR "nasopharyngeal cancer" AND "surgery". Articles from database inception to August 2022 were independently reviewed by YR and LYP. We included prospective and retrospective studies with reported survival and/or toxicity outcomes, encompassing articles written in English or Chinese, to synthesize the evidence on specific issues related to surgical indications and strategies.

We then summarized these issues into a preliminary list of questions, which was circulated to 1096 NPC specialists including experts in skull base surgery, head and neck surgery, radiation oncology, and medical oncology from major centers across China for initial voting and exchange of comments based on a modified Delphi process [3,4]. The initial voting was performed electronically. Next, a panel of experienced specialists mostly from the Association for the Prevention and Treatment of Nasopharyngeal Cancer, the China International Exchange and Promotion Association for Medicine and Healthcare, and the Committee on Nasopharyngeal Cancer of the Guangdong Provincial Anticancer Association conducted a second round of voting on questions with moderate to low consensus in the first voting, after which they were convened to develop the guideline. The Association for the Prevention and Treatment of Nasopharyngeal Cancer, the China International Exchange and Promotion Association for Medicine and Healthcare, and the Committee on Nasopharyngeal Cancer of the Guangdong Provincial Anticancer Association are among the most authoritative medical science

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Table 3. Recommendations on the surgical treatment for nasopharyngeal cancer.

Questions	Recommendation	Level of Evidence Quality	Results of First Voting	Results of Second Voting	Consensus	Category	GRADE of Recommendation
Indications for surgical treatment of locally recurrent NPC	1) The tumor is confined in the nasopharynx or nasal cavity, and the distance to the ICA is > 5mm.	High	Agree: 1034/1096, 96% Disagree: 47/1096, 4% Unfamiliar: 15/1096, 0%		High	IA	High
	2) The tumor invades the superficial layer of parapharyngeal space, and the distance to the ICA is > 5mm.	High	Agree: 968/1096, 89% Disagree: 102/1096, 9% Unfamiliar: 26/1096, 2%		High	IA	High
	3) The tumor invades the midline skull base bone (the bottom wall of sphenoid sinus or the bottom of pterygoid process base), and the distance to the ICA is > 5mm.	High	Agree: 875/1096, 80% Disagree: 177/1096, 16% Unfamiliar: 41/1096, 4%		High	IA	High
	4) The tumor invades the deep part of the parapharyngeal space, or invades the bone of the skull base of the parapharyngeal midline, and the distance to the ICA is less than 5mm (It is recommended to separate the ICA by direct fine anatomy, or use endoscopy through the neck as assistance to protect the parapharyngeal ICA).	Low	Agree: 681/1096, 62% Disagree: 368/1096, 34% Unfamiliar: 47/1096, 4%	Agree: 22/24, 91.7% Disagree: 2/24, 8.3% Unfamiliar: 0/24, 0%	High	IIA	Moderate
	5) The tumor is adjacent to or even invades the ICA (It is recommended to combine with BOT and ICA embolization pretreatment to avoid intraoperative ICA bleeding).	Low	Agree: 673/1096, 61% Disagree: 351/1096, 32% Unfamiliar: 72/1096, 7%	Agree: 19/24, 79.2% Disagree: 5/24, 20.8% Unfamiliar: 0/24, 0%	Moderate	IIB	Low
	6) The tumor invades the petroclival region, infratemporal fossa, middle cranial fossa, cavernous sinus or intracranial widely.	Low	Agree: 392/1096, 36% Disagree: 618/1096, 56% Unfamiliar: 86/1096, 8%	Agree: 8/24, 33.3% Disagree: 15/24, 62.5% Unfamiliar: 1/24, 4.2%	Low	III	Not recommended
Indications for surgical treatment of recurrent RPLNs	1) Simple RPLNs recurrence with intact capsule (Endoscopy-assisted trans-submandibular parapharyngeal approach is recommended).	Moderate	Agree: 886/1096, 81% Disagree: 157/1096, 14% Unfamiliar: 53/1096, 5%		High	IIA	Moderate
	2) RPLNs recurrence ≤ 1.5cm (possibly after neoadjuvant chemotherapy) with mouth opening range > 4cm (Transoral robotic surgery approach is recommended).	Low	Agree: 801/1096, 72% Disagree: 179/1096, 16% Unfamiliar: 116/1096, 11%	Agree: 19/24, 79.2% Disagree: 5/24, 20.8% Unfamiliar: 0/24, 0%	Moderate	IIB	Low
Indications for surgical treatment of CLNs recurrence	1) No invasion (encasement) of the common or ICA.	High	Agree: 1055/1096, 96% Disagree: 29/1096, 3% Unfamiliar: 12/1096, 1%		High	IA	High
	2) No direct invasion of the epidermis.	High	Agree: 1044/1096, 95% Disagree: 38/1096, 3% Unfamiliar: 14/1096, 1%		High	IA	High
	3) No direct invasion of mediastinal structures, prevertebral fascia, or cervical vertebrae.	High	Agree: 1003/1096, 91% Disagree: 62/1096, 6% Unfamiliar: 31/1096, 3%		High	IA	High

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Questions	Recommendation	Level of Evidence Quality	Results of First Voting	Results of Second Voting	Consensus	Category	GRADE of Recommendation
	4) No presence of subdermal metastases.	High	Agree: 1007/1096, 92% Disagree: 47/1096 Unfamiliar: 15/1096		High	IA	High
Indications for surgical treatment of salivary gland-type carcinoma and adenocarcinoma of the nasopharynx	1) T1-T2 tumor according to the 7th edition staging system of AJCC, which can be radically resected with negative margins (Surgery alone is recommended).	Low	Agree: 842/1096, 77% Disagree: 190/1096, 17% Unfamiliar: 64/1096, 6%	Agree: 22/24, 91.7% Disagree: 2/24, 8.3% Unfamiliar: 0/24, 0%	High	IIA	Moderate
	2) Locally advanced T3-T4 tumor according to the 7th edition staging system of AJCC (Surgery combined with adjuvant radiotherapy is recommended).	Low	Agree: 710/1096, 65% Disagree: 321/1096, 29% Unfamiliar: 65/1096, 6%	Agree: 16/24, 66.6% Disagree: 8/24, 33.4% Unfamiliar: 0/24, 0%	Moderate	IIB	Low
	3) Patients with positive lymph nodes (Surgery combined with adjuvant radiotherapy is recommended).	Low	Agree: 739/1096, 67% Disagree: 294/1096, 27% Unfamiliar: 63/1096, 6%	Agree: 17/24, 70.9% Disagree: 7/24, 29.1% Unfamiliar: 0/24, 0%	Moderate	IIB	Low

NPC = nasopharyngeal carcinoma; RPLN = retropharyngeal lymph node; CLN = cervical lymph node; AJCC = American Joint Committee on Cancer.

and technology academic groups in the prevention and treatment of nasopharyngeal cancer in China, which are composed of the most well-known and experienced scholars and experts in the field of nasopharyngeal cancer prevention and treatment in major academic centers from different parts of China. Statements with a high degree of consensus in the first round of voting were not voted on in the second round but were finally reviewed by the experts and given a final recommendation level. To ensure appropriate recommendations, criteria were set to include only members who have a good academic reputation and have published NPC-related papers in international or domestic professional academic journals, including treatment outcomes of surgery, radiotherapy, or chemotherapy, and have extensive experience specific to NPC management in the major academic centers in China. Furthermore, to ensure that the final recommendations are practical, multidisciplinary and widely applicable, our expert groups in the two rounds of voting consisted of 50% surgical experts and another 50% experts in the specific domains of radiation and medical oncology.

The respective degree of agreement on each item was defined as high (≥80% agreement), moderate (60%~80% agreement), and low (<60% agreement) to reflect the strength of each recommendation. This process was adopted as the fundamental basis for consensus-building of recommendations, given the scarcity of high-quality, level 1 published data on this clinical problem [5].

The categories of evidence and consensus are defined according to Tables 1 and 2, while the strength of the recommendations was rated according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) system (6). The percentages of agreement in the first and second vote among the panel members (including the exact number of votes), the level of evidence quality, evidence category, and GRADE of recommendation are listed in Table 3.

Results

1. Surgical treatment of locally recurrent nasopharyngeal carcinoma

1.1 Indications

1) The tumor is confined to the nasopharynx or nasal cavity, and the distance to the internal carotid artery is > 5mm [7-12] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).

2) Limited extension to the parapharyngeal space and the distance to the internal carotid artery is > 5mm [7-12] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).

3) The tumor has invaded the midline skull base structures (the floor of the sphenoid sinus or the inferior part of the pterygoid processes), and the distance to the internal carotid artery is > 5mm [7-12] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).

4) Moderate posterolateral infiltration of the parapharyngeal space or skull base beyond the midline structures, as stated in 3, and the distance to the internal carotid artery (ICA) is between 1-5 mm [13] (ICA protection should be considered by either direct dissection or an endoscopy-assisted transcervical approach).

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(Level of evidence quality: Low; Consensus: High; Category: IIA; GRADE of recommendation: Moderate).

5) The tumor is adjacent to (i.e., less than 1 mm) or has even invaded the ICA (Pretreatment with balloon occlusion test (BOT) and ICA embolization is recommended to avoid intraoperative ICA bleeding) [13]. (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).

6) The tumor has invaded the petroclival region, infratemporal fossa, middle cranial fossa, cavernous sinus or intracranial widely [14] (Level of evidence quality: Low; Consensus: Low; Category: III; GRADE of recommendation: Not recommended).

1.2 Surgical methods

1) Endonasal endoscopic surgery

The basic principle of this approach is to completely remove the tumor with a sufficient and safe margin, under the guidance of nasal endoscopy through bilateral nasal cavities.

The posterior nasal septum can be removed to expand the operation space if the tumor is confined to the nasopharynx. The tumor should be resected together with 0.5-1.0 cm of surrounding normal tissue. To reduce the occurrence of postoperative secretory otitis media in patients with nasopharyngeal lateral wall invasion, the pharyngeal orifice of the eustachian tube can be retained as long as the tumor has not invaded the cartilage or the orifice of the eustachian tube. If the tumor has invaded the nasal septum, the nasal septum should be removed 0.5-1.0 cm away from the tumor. If the sphenoid sinus floor is invaded, the surgeon should fully open the bilateral sphenoid sinuses, and remove the inferior wall of the sphenoid sinus 0.2-0.5 cm away from the tumor. Tumors extending into the oropharyngeal space can also be surgically removed through a combined oronasal approach. After the operation, additional circumferential (usually four pieces) and deep-margin specimens should be taken for pathohistological examination. The resected wounds should be repaired with a vascularized nasal mucoperiosteal flap or temporal muscle flap to promote wound healing [15,16]. A contrast-enhanced MRI of the nasopharynx should be performed within 1 week after the operation to confirm complete resection.

While the general principle of an en-bloc resection should be followed whenever feasible, the tumor cannot be readily removed en-bloc in cases of skull base bone invasion. A high-speed micro electric drill, plasma knife, and other surgical instruments can be used for contour resection to ensure complete tumor removal with an adequate margin.

1.3 Post-operative magnetic resonance imaging (MRI) evaluation

The first postoperative MRI should be used to assess nasopharyngeal mucosal changes, adjacent soft tissue changes and bone changes. To assess nasopharyngeal mucosal changes, the presence of focal mucosal thinning and focal thickening should be evaluated. For the adjacent soft tissue changes, the presence of submucosal soft tissue volume loss and any soft tissue necrosis in the adjacent spaces should be evaluated. For the bone changes, the extent of clival bone marrow signal changes and any involvement of the neighboring bones including the petrous ridge, pterygoid plate, and C1–C2 should be evaluated. Preoperative planning surgical tumor volumes (pSTVs) need to ensure complete and effective resection of the tumor while minimizing damage to surrounding normal tissues. This volume is generally 0.5-1.0 cm outside the tumor, while the distance may be appropriately reduced to 0.2-0.3 cm when close to the bone or internal carotid artery. Surgeons should resect the entire tumor under endoscopic guidance in strict accordance with the pSTVs. Postoperative MRI should be performed to objectively evaluate the extent of tumor resection, while assessing the status of the mucoperiosteal flap. Based on the cavity visible on the postoperative MRI and the actual surgical target (aSTV), we can effectively assess the efficacy of surgery. If aSTV > pSTV, radical resection was achieved according to imaging.

2. Surgical treatment of recurrent retropharyngeal lymph node tumors

2.1 Indications

1) Retropharyngeal lymph node recurrence of tumors with an intact capsule [17] (Level of evidence quality: Moderate; Consensus: High; Category: IIA; GRADE of recommendation: Moderate).

2) The short diameter of the retropharyngeal lymph node ≤ 1.5 cm (optional neoadjuvant chemotherapy) with the ability to open the mouth > 4 cm (preferably treated with a transoral robotic surgery approach) [18] (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).

2.2 Surgical methods

1) Transoral robotic retropharyngeal lymph node dissection refers to a surgery performed orally using the da Vinci Si surgical system.

2) Transcervical endoscopic retropharyngeal lymph node dissection refers to a horizontal incision in the upper neck, followed by dissection of the lymphatic and soft tissues of level Ib and IIa to allow adequate access to the parapharyngeal space.

3) Retropharyngeal lymph node resection via a maxillary swing approach.

3. Surgical treatment of cervical lymph node recurrence

3.1 Indications

1) No invasion (encasement) of the common or internal carotid artery [19] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).

2) No direct invasion of the epidermis [19] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recom-

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mendation: High).
3) No direct invasion of mediastinal structures, prevertebral fascia, or cervical vertebrae [19] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).
4) No subcutaneous metastases [19] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).

3.2 Surgical methods

1) Radical Neck Dissection (RND)
2) Modified Radical Neck Dissection (MRND)
3) Selective Neck Dissection (SND)
4) Extended Neck Dissection (END)

4. Surgical treatment of salivary gland-type carcinoma and adenocarcinoma of the nasopharynx

The less common pathological types of nasopharyngeal cancer mainly include nasopharyngeal salivary gland-type carcinoma and nasopharyngeal adenocarcinoma, such as nasopharyngeal adenoid cystic carcinoma, nasopharyngeal papillary adenocarcinoma, and nasopharyngeal adenocarcinoma.

4.1 Indications

1) T1-T2 tumor according to the staging system from the 7th edition of the American Joint Committee on Cancer (AJCC), which can be radically resected (Surgery alone is recommended with the exception of high-grade histological findings) [20,21] (Level of evidence quality: Low; Consensus: Moderate; Category: IIA; GRADE of recommendation: Moderate).
2) Locally advanced T3-T4 tumor according to the staging system from the 7th edition of the American Joint Committee on Cancer (AJCC) (Surgery combined with adjuvant radiotherapy is recommended) [21-23] (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).
3) Patients with regional nodal metastasis [22] (Surgery combined with adjuvant radiotherapy is recommended) (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).

4.2 Surgical methods

1) The surgical rationale is similar to that applied in locally recurrent nasopharyngeal carcinoma. Since salivary gland-type tumors have a high propensity for perineural invasion, the extent of excision should be appropriately adjusted to ensure adequate tumor clearance with negative margins. In select patients with positive surgical margins, renewed surgery can be considered. The indications for postoperative adjuvant radiotherapy are usually the same as for major salivary gland cancer, though there is still limited data on its efficacy. Selective neck dissection with postoperative radiotherapy should be offered to patients with regional nodal metastasis.

The results about complications caused by radiotherapy are presented in the Supplementary Materials including post-radiation nasopharyngeal necrosis, post-radiation rhinosinusitis, radiation-related otitis media with effusion, radiation-related encephalopathy, and radiation-related epitaxis.

Discussion

This is the first consensus recommendation based on a modified Delphi process for surgical treatment of nasopharyngeal carcinoma. This consensus focuses on the timing of surgical intervention, indications for optimal surgery, as well as surgical methods covering the whole process of NPC treatment to realize the international standardization of surgical treatment for this type of cancer.

Locally recurrent nasopharyngeal carcinoma

The nasopharynx resembles a six-sided cuboid, which enables three categories of surgical approaches, respectively summarized as anterior, lower, and lateral. The anterior approach can enter the nasopharynx through the nasal septum and bilateral posterior nostril area, while the lower approach can enter the nasopharynx through the soft palate, as well as laterally through the parapharyngeal space and eustachian tube area. These approaches are relatively less invasive and more commonly used, whereas maxillary swing surgery used to be popular before the emergence of nasal endoscopy. However, regardless of the surgical approach taken, the conventional external nasal approach inevitably requires excision of the normal tissue of the face, resulting in permanent sequelae for the patient (Table 4). The endonasal endoscopic approach (EEA) is now the preferred surgical option for locally recurrent NPC (Table 5). A locally recurrent NPC is generally considered resectable if the tumor is located at least 5 mm from the bilateral ICAs. These include tumors involving the nasopharynx, nasal septum, posterior nasal cavity, with mild parapharyngeal space extension, as well as those limited to the sphenoid sinus floor or the base of the pterygoid process [7-11]. For recurrent NPC confined to these resectable regions, a large-scale multicenter phase III clinical trial confirmed that 3-year overall survival (OS) was significantly higher in the surgery group (85.8%) than in the reirradiation group (68.0%) [7]. Similarly, a large-scale case-control study also showed that surgery had better clinical outcomes, including lower medical cost and less long-term side effects [11]. According to the consensus agreement, at least 80% of specialists, including radiation oncologists and medical oncologists, prefer surgery over reirradiation for these patients because of survival advantages and lesser side effects. With careful dissection, vascular intervention, and other appropriate pre-treatments, the surgical indications could be expanded to tumors within 5 mm from the

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Table 4. Efficacy and safety profiles of open surgery for recurrent nasopharyngeal carcinoma.

Author	N	rT-stage	Salvage approach	Margins (-)	Survival results (5y)	Surgical complications		
						Massive bleeding (acute or late)	Palatal fistula	Others
Vlantis et al. [41]	97	rT1-2 88% rT3-4 12%	7% TP 39% MS 36% MD 18% TCMP	48%	52% (OS)	3%	11%	15% ectropion 3% osteotomy infection
Wei et al. [42]	246	NS*	MS	78%	56% (DFS)	1%	20%	21% trismus
Bian et al. [43]	71	rT1-2 65% rT3-4 35%	10%TP 6% Lateral rhinotomy 15%Transcervical 46% MS 13% TCMP 10% Mandible ramus	rT1-2 13% rT3-4 84%	42% (OS) rT1,49%	3%	8%	4%submandible necrosis 10% severe trismus
Chan et al. [44]	338	rT1-2 72% rT3-4 28%	MS	78%	DFS: margins(+) 63% margins(-) 37%	1% (dead)	11%	41% middle ear effusion 11% trismus 10% osteoradionecrosis 7% facial numbness 7% epiphora
Tsang et al. [45]	12	rT1 67% rT3 33%	58% TORS 42% TORS+ENPG	92%	83%(2y-OS) 61%(2y-DFS)	0	8%	8% hypoxic brain damage 8% osteoradionecrosis
Ng et al. [46]	20	rT1 90% rT2 10%	Partial maxillectomy combined 95%lateral rhinotomy, 5%MD	100%	49%(DFS) 67%(OS)	5%	0	5% atlantoaxial subluxation
Chan et al. [47]	28	rT3 64% rT4 36%	EC/IC vascular bypass combined craniofacial resection with MS	46%	52%(5y-OS) 54%(5y-DFS)E	0	0	25%: prolonged diabetes insipidus or CN III/VII/X palsy

NS: not stated; TP: trans-palatal; TCMP: trans-cervico-mandibulo-palatal; MS: maxillary swing; MD: midfacial degloving; TORS: transoral robotic surgery; ENPG: endoscopic nasopharyngectomy; EC/IC: Extracranial/Intracranial; LRFS: local relapse-free survival; LPFS: local progression-free survival; OS: overall survival; DFS: disease free survival.

bilateral ICAs, and a 2-year OS rate of 88.7% has been achieved in experienced centers [13]. Recently, some teams have carried out exploratory surgical treatment for rT3 and rT4 patients with larger recurrent tumors [24]. However, the benefits of surgery for recurrent tumors close to the ICA still need to be further demonstrated by larger clinical studies.

Recurrent retropharyngeal lymph nodes tumors

A retrospective study of 82 patients who underwent retropharyngeal lymph node resection via a maxillary swing approach reported a 5-year disease control rate (DCR) and overall disease-free survival (DFS) of 79.6 and 59%, respectively. The risks of postoperative trismus and palatal fistulae were 13.5% and 4.3%, respectively [25]. Due to the requirement of freeing the inherent maxilla to enable access to the retropharyngeal region, the surgery inevitably carries a higher risk of wound complications and may also affect facial cosmesis. To avoid these shortcomings, less invasive procedures have been investigated. In a retrospective study of 31 patients who underwent transcervical endoscopic retropharyngeal lymph node dissection, the respective rates of 2-year locoregional relapse-free survival (LRFS), distant metastasis-free survival (DMFS), progression-free survival (PFS), and OS rates were 63.9%, 95.2%, 59.9%, and 83.3%. Due to the minimally invasive treatment with endoscopic surgery, postoperative complications were significantly lower than with open surgery. The incidences of late complications, including swallowing problems, permanent nutrient tube, tongue atrophy, and shoulder problems, were 19.4%,9.7%, 9.7%, and 9.7%, respectively [17]. A similar retrospective study included 10 patients who underwent transoral robotic retropharyngeal lymph node dissection. All patients achieved negative surgical margins, and only 1 patient developed cervical recurrence after a median follow-up of 19 months [18]. Post-surgical complications were mild. Recently, several teams have performed transoral endoscopic resection of retropharyngeal lymph nodes, which is minimally invasive and may be more effective, but it is necessary

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Table 5. Efficacy of endoscopic nasopharyngectomy for recurrent nasopharyngeal carcinoma.

Author	N	rT-stage	Negative margins	Local control	Survival rate
Chen et al. [48]	6	3 rT1 3 rT2a	100%	83%	83%
Chen et al. [48]	25	10rT1 13rT2 2 rT3	96%	12% recurrence	100% (1y-OS) 86% (1y-LRFS)
Chen et al. [49]	37	17rT1N0 4 rT2aN0 14rT2bN0 2 rT3N0	97%	83% (2y-LPFS) 86% (2y-LRFS)	84% (2y-OS)
Ko et al. [50]	28	12rT1 16rT2a	89%		59% (2y-OS) rT1 91%; rT2 39%
Castelnuovo et al. [51]	8	4 rT1 1 rT2a 3 rT3		rT1-2 0% recurrence rT3 67% recurrence	88%
Ho et al. [52]	13	6 rT1 3 rT2a 2 rT2b 2 rT3	79%	38% recurrence	100%
Chen et al.* [53]	33	25rT1 8 rT2		rT1 24% recurrence rT2 50% recurrence	67%
Emanuelli et al. [54]	8	rT1	100%	13% recurrence	100% (2y-OS) 88.9% (2y-DFS)
Hsu et al. [55]	9	5 rT1 2 rT2 2 rT3	78%	11% recurrence	100% (2y-OS) 80% (2y-DFS)
You et al. [11]	72	32 rT1 27 rT2 13 rT3			77% (5y-OS) rT1 90%; rT2 60% rT3 71%
Vlantis et al. [56]	18	15 rT1 3 rT2a	83%	6% recurrence	100% (2y-OS) 90% (2y-DFS)
Liu et al. [24]	91	30 rT1 13 rT2 29 rT3 19 rT4	81%		38% (5y-OS) 65% (2y-OS) rT1 82% ; rT2 47% rT3 71% ; rT4 37%
Tang et al. [57]	55	25 rT1 20 rT2 9 rT3 1 rT4	93%	9% residual or recurrence	98% (1y-OS) 93% (1y-LDFS)
Chan et al. [58]	85	rT3	64%**		64.8% (5y-OS)
Wong et al. [59]	12	2 rT3 10 rT4	58%	100% residual or recurrence	50% (5y-OS) 25% (5y-DFS)

*: A potassium-titanyl-phosphate (KTP) laser was used in this study; **: the data contain open surgery treatment results.

to statistically analyze the relevant data after a sufficient number of cases has been collected.

Recurrent cervical lymph nodes tumors

The major differences between the reported methods lie in the extent of dissection and the resulting degree of surgical trauma. Surgical approaches that remove the least amount of normal tissue should be chosen on the premise of complete dissection. Among NPC patients with persistent or recurrent cervical lymph node tumors after radiotherapy or chemoradiotherapy, the 5-year OS rate of those who underwent RND was 38-67%, and the nodal control rate was 65-70% [26-31]. MRND can reduce the operation time and postoperative complications, such as trauma and bleeding [32]. Compared with MRND, SND can further avoid complications including shoulder pain, deformity and potential venous obstruction, significantly improving the patients' quality of life [33]. Several retrospective studies compared the clinical outcomes of RND, MRND, SND and lymph node resection. It was found that there was no significant difference in the OS rate among patients who were treated with either of these four

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methods [34-36]. Therefore, the main factor affecting the prognosis may not be related to the extent of dissection, since complete tumor removal with clear margins is the key factor affecting treatment outcomes.

Salivary gland-type carcinoma and adenocarcinoma of the nasopharynx

Due to the very low incidence of salivary gland-type carcinoma of the nasopharynx, only retrospective studies with limited numbers of patients are available. For T1-T2 lesions, patients treated with surgery had a higher 5-year OS and DFS than those treated with radiotherapy (100.0% vs. 83.3%, p=0.031; 88.4% vs. 51.4%, p=0.012, respectively). Furthermore, there was no apparent survival difference among those treated with surgery with the addition of radiotherapy [20,21]. For T3-T4 lesions, surgery followed by postoperative radiotherapy provided better outcomes than surgery or radiotherapy alone. The 5-year OS and LRFFS rates were higher in the combined modality treatment group compared with single modality treatment (73.7% vs. 66.2%, p = 0.065; (73.1% vs. 64.5%, p = 0.047, respectively) [21-23].

The prognosis of papillary adenocarcinoma is significantly better than that of adenocarcinoma (not otherwise specified (NOS)) (5-year OS: 85.7% vs. 48.8%, P=0.017) [37]. Simple operation is feasible for patients with papillary adenocarcinoma staged T1-T2, but if it has reached stage T3-T4, pre- or postoperative radiotherapy should be considered [38]. For patients with adenocarcinoma NOS (including some nasopharyngeal salivary gland-type carcinomas), the efficacy of surgery is better than that of non-surgical treatment, with respective 5-year OS rates of 75.6 and 45.5 [23], and surgery combined with radiotherapy is usually recommended for T3-T4 patients [20-22]. A recent retrospective study showed that surgery combined with postoperative radiotherapy could improve the local recurrence-free survival rate compared with surgery alone (HR, 0.39; 95% CI, 0.20–0.74; P<0.01) in T1-T2 adenoid cystic carcinoma of the nasopharynx with negative margins [39].

Conclusion

This practical guideline represents our concerted efforts to develop the best practice for NPC patients who require surgical intervention. By standardizing the surgical indications and practice, we hope not only to improve the surgical outcomes, but also to highlight key directions for future clinical research in the surgical management of NPC.

Authorship contribution

Conception and design: RY, MYC, WPW, and DMH; Provision of study materials or patients: RY, YPL, XZC, JHC, JYWC, JGF, CSH, YQH, FH, GYH, YJ, WHJ, LK, JGL, QL, YL, YHL, YTL, WTN, PKM, JWS, LT, WPW, JLY, XDZ, MYC; Collection and assembly of data: RY, YPL; Study supervision: RY, MYC, WPW, and DMH; Manuscript writing, Final approval of manuscript, Accountable for all aspects of the work: All authors.

Conflict of interest

The authors declare that they have no conflicts of interest.

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This manuscript contains online supplementary material

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SUPPLEMENTARY MATERIAL

Results

5. Surgical treatment of post-radiation nasopharyngeal necrosis

5.1 Indications

1) Necrosis of the nasopharyngeal mucosa and soft tissue without obvious skull base osteonecrosis. Tumor recurrence should be excluded (Level of evidence quality: Moderate; Consensus: High; Category: IIA; GRADE of recommendation: Moderate).
2) Localized skull base osteonecrosis at an extent not exceeding the greater wings of the sphenoid bone. No involvement of the internal carotid artery (Level of evidence quality: Moderate; Consensus: High; Category: IIA; GRADE of recommendation: Moderate).
3) Necrosis involving the carotid sheath or petrosal internal carotid artery, and thinning or deformation of the internal carotid artery, potentially accompanied by pseudoaneurysm (BOT is recommended before operation): a) for BOT-negative patients, internal carotid artery embolization pretreatment is recommended; b) for BOT-positive patients, internal carotid artery bypass grafting or stent implantation should be considered to avoid arterial rupture and massive bleeding) (Level of evidence quality: Moderate; Consensus: High; Category: IIA; GRADE of recommendation: Moderate).
4) Extensive skull base necrosis with internal carotid artery involvement with or without intracranial involvement. (BOT is again recommended, as stated in point 3. Collaboration with neurosurgeons is needed for the intracranial lesions and skull base reconstruction) (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).

5.2 Surgical methods

1) Endoscopy-guided debridement of radiation-related nasopharyngeal necrosis: This refers to the endoscopy-guided complete removal of the necrotic tissue of the nasopharynx, using a biting forceps, suction cutter or plasma knife, until the underlying healthy tissue is exposed. Bone tissue affected by osteonecrosis of the skull base can be removed using a high-speed electric micro-drill until healthy bone is exposed. The removed tissues should be sent for postoperative pathohistological examination.
2) Reconstruction using a vascularized posterior nasal septal-floor mucoperiosteum pedicled flap: The mucosal flap is usually selected from the involved side of the lesion and rotates backward to cover the nasopharyngeal wound. For patients with oropharyngeal necrosis, the ipsilateral inferior turbinate mucosa can be taken together with a septal-floor mucoperiosteum flap to achieve adequate wound coverage. If the necrotic area is too large, bilateral mucoperiosteal flaps or a temporalis muscle flap may be considered.

6. Surgical treatment of post-radiation rhinosinusitis

6.1 Indications

1) Inflammatory thickening of the mucosa of the sinuses caused by radiation therapy, with symptoms of sinusitis, persistent nasal congestion and excessive nasal discharge. The therapeutic effect is not satisfactory after at least 12 weeks of standardized drug treatment and nasal lavage [1,2] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).
2) Facial pain or pressure due to radiation induced-abnormalities affecting the drainage of ostiomeatal complex [1,2]. (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).
3) Complications affecting the cranium, orbit, etc. caused by nasosinusitis [1,2] (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High).

6.2 Surgical methods and other combined treatments

1) Removal of inflammatory secretions and crusts of the mucosa in the nasal cavity and sinuses.
2) Maxillary sinus opening
3) Ethmoid sinus opening
4) Sphenoid sinus opening
5) Frontal sinus opening surgery
6) Other auxiliary methods: Catheter-guided balloon dilatation of paranasal sinuses: This technology can alleviate sinusitis by expanding the natural sinus orifice and promoting ventilation and drainage of nasal sinuses, but it is not suitable for ethmoid sinus surgery.

7. Surgical treatment of radiation-related otitis media with effusion

7.1 Indications

1) Patients with aural fullness lasting more than 3 months with hearing loss. Tympanic effusion or eardrum perforation can be seen by otoendoscopy. The presence of middle ear effusion or suspected granulation visible on imaging examination (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High) [3,4].
2) The presence of eustachian tube dysfunction (ETS result ≤ 5 points) (Level of evidence quality: High; Consensus: High; Category: IA; GRADE of recommendation: High) [3,4].

7.2 Surgical methods and other combined treatments

1) Tympanocentesis with drainage, tympanic injection of triamcinolone acetonide and ambroxol hydrochloride, combined with

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the insertion of a ventilation tube.
2) Mastoid surgery, including mastoidotomy, radical mastoidectomy and modified radical mastoidectomy [4].
3) Tympanoplasty, including myringoplasty, ossicular chain reconstruction, exploratory tympanotomy, tympanic cavity reconstruction, or similar strategies [4].

8. Surgical treatment of radiation-related encephalopathy

8.1 Indications

1) For patients who fail medical treatment with symptoms and signs that may indicate progressive deterioration of neurocognitive function and raised intracranial pressure (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).
2) For patients with recurrent seizures or intracranial hypertension caused by progressive encephalopathy, especially in the presence of a midline shift on imaging examination (Level of evidence quality: Low; Consensus: Moderate; Category: IIB; GRADE of recommendation: Low).
3) For patients with intracranial hemorrhage, brain abscess, or a cystic lesion with a noticeable space-occupying effect, given that conservative treatments are often ineffective in these situations (Level of evidence quality: Low; Consensus: High; Category: IIA; GRADE of recommendation: High).
4) Patients with a cerebral hernia (Level of evidence quality: Low; Consensus: Low; Category: III GRADE of recommendation: Not recommended).

8.2 Surgical methods

1) Patients with mild radiation brain injury are usually first given a conservative treatment. If they fail to respond to the first-line treatment, surgical removal of necrotic brain tissue can be considered.
2) Decompressive craniotomy and debridement of necrotic brain tissue are the treatment of choice for severe brain injury.
3) Surgical methods for the treatment of radiation-induced temporal necrosis include debridement of temporal lobe lesions via the pterional approach and debridement of temporal lobe lesions via a temporal horseshoe incision.

9. Surgical treatment of radiation-related epistaxis

9.1 Indications

1) Identified location of arterial or venous hemorrhage in nasal cavity and nasopharynx (Endoscopic hemostasis is recommended) (Level of evidence quality: Moderate; Consensus: High; Category: IIA; GRADE of recommendation: High).
2) Poor control of hemorrhage after nasal packing (Anterior and posterior nostril packing is recommended) (Level of evidence quality: Low; Consensus: High; Category: IIA; GRADE of recommendation: High).
3) Patients with poor control of hemorrhage after nasal packing as well as anterior and posterior nostril packing or nasopharyngeal massive hemorrhage (Endovascular embolization is recommended) (Level of evidence quality: Low; Consensus: High; Category: IIA; GRADE of recommendation: High).

9.2 Surgical methods and other combined treatments

1) Endoscopic hemostasis: This approach refers to nasal packing hemostasis, high-frequency electrocoagulation hemostasis or microwave-assisted coagulation hemostasis under endoscopic observation.
2) Anterior and posterior nostril packing
3) Internal carotid artery embolization: This approach consists of three steps: General occlusion test, intensive blood pressure reduction and permanent internal carotid artery embolization.
4) Internal carotid artery stenting

Discussion

Post-radiation nasopharyngeal necrosis

The prognosis of conservative treatment alone for nasopharyngeal necrosis is generally unfavorable [5-7]. Endoscopic debridement (which can be repeated if necessary) is the mainstay of treatment for post-radiation nasopharyngeal necrosis, although its long-term efficacy remains uncertain. Most studies suggest that repeated endoscopic debridement could alleviate headaches and foul nasal odor to a variable degree in all patients. Nevertheless, the nasopharyngeal mucosa could be fully epithelized in only 25% of the cases, with 13.4-28.6% of patients achieving an apparent cure for this condition [7,8]. Another study found that the repair rate of endoscopic debridement could reach 63.2 and 50.9% in patients with mild and moderate necrosis, respectively. However, the therapeutic effect in patients with severe necrosis was poor, and the repair rate was only 17.0% [9]. Incomplete debridement and difficult wound epithelization were the main patterns of treatment failure. A vascularized mucosal flap is an effective method to improve wound healing. Many studies have shown that the addition of a vascularized mucosal flap can significantly improve the condition of nasopharyngeal necrosis, with success rates reaching 72.3-87.5% [10-12]. Therefore, endoscopy-guided debridement combined with a vascularized mucosal flap may represent the ideal treatment for nasopharyngeal necrosis. Nevertheless, large-scale phase III clinical trials, preferably with QOL assessment, are recommended to assess its efficacy. Notably, many studies found that the exposure of the internal carotid artery is an independent adverse prognostic factor of nasopharyngeal necrosis. Therefore, pre/perioperative treatments of the internal carotid artery (such as BOT and internal carotid artery embolization) are recommended [5-13].

Post-radiation rhinosinusitis

Endoscopic sinus surgery also shows a certain benefit for rhinosinusitis in patients who received radiotherapy for head

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and neck squamous cell carcinoma such as nasopharyngeal carcinoma. After the operation, the symptoms of nasal congestion or discharge were significantly improved, and the signs of rhinosinusitis in CT were alleviated [14]. In addition, the ultrastructure of the sinonasal mucosa was normalized, so that the clearance function of cilia and the mucus blanket was significantly improved [15]. A retrospective cohort study included nasopharyngeal carcinoma patients with a history of radiation therapy or chemoradiotherapy at the Stanford sinus center from 2006 to 2015. In patients with rhinosinusitis after radiotherapy, the SNOT-22 score was significantly improved 6 to 12 months after endoscopic sinus surgery compared with the control group [16]. It should be noted that radiotherapy can cause severe acute inflammation of the mucous epithelium, and surgery should be considered only after the acute response to radiotherapy has subsided (e.g., half a year after radiotherapy), and if the symptoms of sinusitis were not relieved by conservative treatment. Endoscopic sinus surgery is only one part of holistic treatment for radiation-induced sinusitis. The underlying cause of sinonasal mucosal inflammation cannot be removed or changed by surgery. Only continuous surgical cavity nursing and comprehensive drug treatment can promote the gradual morphological and functional recovery of the sinonasal mucosa.

Radiation-related otitis media with effusion

Ventilation tube insertion after radiotherapy can significantly improve the patients' hearing while reducing symptoms such as tinnitus, ear tightness and headache. The efficacy of grommet insertion is higher than 80% [3]. A randomized controlled trial confirmed myringotomy and ventilation tube insertion can significantly improve the air conducted pure tone hearing threshold and air-bone gap compared with the observation group without treatment, and the hearing of patients can be significantly improved [17]. However, the optimal time of myringotomy and ventilation tube insertion after radiotherapy in patients with nasopharyngeal carcinoma needs to be further explored. Consistent care is required after tube insertion to avoid purulent otitis media or residual tympanic membrane perforation. Nasopharynx cleaning combined with myringotomy, drainage, ventilation tube insertion and tympanic drug injection was found to be 24% more effective than myringotomy and ventilation tube insertion alone, while also significantly reducing the complications after treatment [18].

In recurrent, persistent secretory otitis media that does not respond to treatment, mastoidectomy can improve the ventilation and drainage of the mastoid space, tympanic sinus, tympanum and eustachian tube, reduce the recurrence of secretory otitis media, and improve the average air conducted pure tone hearing threshold after operation [19]. Tympanoplasty has a satisfactory therapeutic effect in patients with non-cholesteatomatous chronic otitis media, in which it can reduce the negative pressure acting on the tympanum and improve hearing [20]. However, there is still insufficient research on the effects of mastoidoplasty and tympanoplasty, with even fewer reports focusing on secretory otitis media after radiotherapy. Therefore, whether to adopt this kind of surgery should be carefully considered based on the specific situation of each patient.

Radiation-related encephalopathy

Patients with radiation-induced brain injury who are asymptomatic (i.e., diagnosed based on radiographic changes without symptoms) or mildly symptomatic should be first managed pharmacologically (including glucocorticoids, bevacizumab, and other symptomatic treatments) [21,22]. However, in patients who do not respond to drugs and show symptoms and signs of raised intracranial pressure, surgical treatment is indicated to alleviate the pressure effect. The purpose of surgery is mainly the debridement of the injured brain tissue. The post-surgical complication rate is less than 19%, and is mainly related to surgical wounds or chest infections. The recurrence rate of postoperative radiation brain injury is approximately 6.3% [23]. Furthermore, 33% of patients who initially present with a unilateral temporal lobe lesion may eventually develop bilateral lesions. There are case reports of sequential operations for bilateral lesions or unilateral surgery alone for the more severe side [24].

Radiation-related epistaxis

The efficacy of treatments for epistaxis after radiotherapy for nasopharyngeal carcinoma mainly depends on the hemostatic effect, but no related large-scale clinical trial has been reported to date. There are only a few retrospective studies, which mainly focused on massive nasopharyngeal hemorrhage. A retrospective study included 59 patients with massive nasopharyngeal hemorrhage after radiotherapy for NPC, all of whom underwent nasal packing. Among them, 50 were treated with interventional embolization and 3 received a stent with a tectorial membrane in the internal carotid artery. Among the 53 patients who underwent interventional therapy, 46 cases (86.8%) achieved effective hemostasis [25]. In another retrospective study including 32 patients, 24 were treated with anterior and posterior nostril packing to stop bleeding in the nasal cavity and nasopharynx, while 7 were treated with interventional embolization of the external carotid artery because hemorrhage was still difficult to control after nostril packing. Of the 32 patients, 25 (78.13%) were rescued eventually [26]. In addition, other retrospective studies have shown that internal or external carotid artery embolization is a further option for nasopharyngeal necrotic hemorrhage if the hemostatic effect of anterior and posterior nostril packing is poor [27-29].

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Supplementary Table 1. Recommendations on the surgical treatment for nasopharyngeal cancer specific to complications caused by radiotherapy.

Questions	Recommendation	Level of Evidence Quality	Results of First Voting	Results of Second Voting	Consensus	Category	GRADE of Recommendation
Indications for surgical treatment of post-radiation nasopharyngeal necrosis	1) Patients with a history of radiotherapy for NPC. Necrosis of nasopharyngeal mucosa and soft tissue are shown by MRI and nasal endoscopy. Nasopharyngeal necrosis should be diagnosed by pathological examination before operation. Tumor recurrence should be excluded.	Moderate	Agree: 905/1096, 83% Disagree: 135/1096, 12% Unfamiliar: 56/1096, 5%		High	IIA	Moderate
	2) Localized skull base osteonecrosis with the extent not exceeding the greater wings of sphenoid bone. No ICA involvement.	Moderate	Agree: 833/1096, 76% Disagree: 190/1096, 17% Unfamiliar: 73/1096, 7%	Agree: 24/24, 100.0% Disagree: 0/24, 0.0% Unfamiliar: 0/24, 0%	High	IIA	Moderate
	3) Necrosis involves the carotid sheath or petrosal ICA, and the ICA becomes thinner, deformed or accompanied by pseudoaneurysm (BOT is recommended before operation. Perform ICA embolization pretreatment for BOT negative patients, while perform ICA bypass grafting or stent implantation for BOT positive patients to avoid ICA rupture and massive bleeding).	Moderate	Agree: 715/1096, 65% Disagree: 249/1096, 23% Unfamiliar: 132/1096, 12%	Agree: 23/24, 95.8% Disagree: 1/24, 4.2% Unfamiliar: 0/24, 0%	High	IIA	Moderate
	4) Necrosis widely involved skull base or even intracranial, with ICA involvement. (It is recommended to combine BOT and ICA embolization pretreatment, and to collaborate with brain surgeons to remove the intracranial lesions and reconstruct the skull base).	Low	Agree: 602/1096, 54% Disagree: 334/1096, 30% Unfamiliar: 160/1096, 16%	Agree: 17/24, 70.8% Disagree: 3/24, 12.5% Unfamiliar: 4/24, 16.7%	Moderate	IIB	Low
Indications for surgical treatment of post-radiation nasosinusitis	1) Inflammatory thickening of the mucosa of the sinuses caused by radiation therapy with symptoms of sinusitis, persistent nasal congestion and excessive nasal discharge. The therapeutic effect is not satisfactory after at least 12 weeks of standardized drug treatment.	High	Agree: 1042/1096, 95% Disagree: 25/1096, 2% Unfamiliar: 29/1096, 3%		High	IA	High
	2) Facial pain or pressure due to the radiation induced abnormalities which affect the drainage of ostiomeatal complex.	High	Agree: 1053/1096, 96% Disagree: 17/1096, 2% Unfamiliar: 26/1096, 2%		High	IA	High
	3) Complications of cranium, orbit, etc. caused by nasosinusitis.	High	Agree: 1037/1096, 95% Disagree: 26/1096, 2% Unfamiliar: 33/1096, 3%		High	IA	High
Indications for surgical treatment of radiation-related the otitis media with effusion.	1) Patients with aural fullness lasting more than 3 months with hearing loss. Tympanic effusion or eardrum perforation can be seen by otoendoscopy. The presence of middle ear effusion or suspected granulationby imaging examination.	High	Agree: 1056/1096, 97% Disagree: 14/1096, 1% Unfamiliar: 22/1096, 2%		High	IA	High

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Questions	Recommendation	Level of Evidence Quality	Results of First Voting	Results of Second Voting	Consensus	Category	GRADE of Recommendation
	2) The presence of eustachian tube dysfunction (ETS result ≤ 5 points).	High	Agree: 1029/1096, 94% Disagree: 26/1096, 2% Unfamiliar: 41/1096, 4%		High	IA	High
Indications for surgical treatment of radiation-related encephalopathy	1) The effect of conservative treatment is poor, which leads to the progressive deterioration of the disease and the increase of intracranial pressure.	Low	Agree: 768/1096, 70% Disagree: 179/1096, 16% Unfamiliar: 149/1096, 14%	Agree: 19/24, 79.2% Disagree: 3/24, 12.5% Unfamiliar: 2/24, 8.3%	Moderate	IIB	Low
	2) Patients with obvious symptoms, recurrent seizures or intracranial hypertension caused by continuous progression of lesions, and obvious displacement of midline structure can be seen by imaging examination.	Low	Agree: 777/1096, 71% Disagree: 177/1096, 16% Unfamiliar: 142/1096, 13%	Agree: 17/24, 70.9% Disagree: 4/24, 16.7% Unfamiliar: 3/24, 12.5%	Moderate	IIB	Low
	3) Patients combined with hemorrhage and secondary brain abscess. Large cystic necrosis foci with obvious space occupying effect, which conservative treatments are often ineffective for.	Low	Agree: 880/1096, 80% Disagree: 107/1096, 10% Unfamiliar: 109/1096, 10%	Agree: 22/24, 91.7% Disagree: 1/24, 4.2% Unfamiliar: 1/24, 4.2%	High	IIA	High
	4) Patients combined with cerebral hernia.	Low	Agree: 700/1096, 64% Disagree: 243/1096, 22% Unfamiliar: 153/1096, 14%	Agree: 13/24, 54.2% Disagree: 7/24, 29.2% Unfamiliar: 4/24, 16.7%	Low	III	Not recommended
Indications for surgical treatment of radiation-related epistaxis	1) Location of arterial or venous hemorrhage in nasal cavity and nasopharynx can be identified (Endoscopoic hemostasis is recommended).	Moderate	Agree: 1008/1096, 92% Disagree: 67/1096, 6% Unfamiliar: 21/1096, 2%		High	IIA	High
	2) Poor control of hemorrhage after nasal packing (Anterior and posterior nostril packing is recommended).	Low	Agree: 972/1096, 89% Disagree: 103/1096, 9% Unfamiliar: 21/1096, 2%		High	IIA	High
	3) Patients with poor control of hemorrhage after nasal packing and anterior and posterior nostril packing and nasopharyngeal massive hemorrhage (Endovascular embolization is recommended).	Low	Agree: 1016/1096, 93% Disagree: 53/1096, 5% Unfamiliar: 27/1096, 2%		High	IIA	High