Nasopharyngeal carcinoma: outcome of endoscopic nasopharyngectomy for local recurrence

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Abstract

Objective: Endoscopic nasopharyngectomy offers similar outcomes compared to open surgery in the primary treatment of recurrent nasopharyngeal carcinoma (NPC) without the functional and cosmetic morbidity. In this case series, we report the survival outcomes of seven recurrent NPC treated primarily with endoscopic nasopharyngectomy.

Method: Retrospective review of patients who were diagnosed with locally recurrent NPC and underwent endoscopic nasopharyngectomy from years 2010 to 2018. The extent of nasopharyngectomy was categorized based on Castelnuovo et al. and the patients were followed up to assess the survival outcome.

Result: Four patients had rT1 disease and had Type I nasopharyngeal endoscopic resection (NER), one rT2 disease who had type 3 NER, one rT3 who had type 2 NER, and one rT4 disease who had type 1 NER and post-operative chemotherapy. The 2-year overall survival (OS) was 100% and disease-free survival (DFS) was 85.71% for all stages. Only 25% of rT1 disease had post-nasopharyngectomy recurrence and the disease-free survival time was 25 months, whereas both rT2 and rT3 cases had recurrence 18 and 35 months post-operation, respectively. However, the rT4 case that received post-operative chemotherapy had no recurrence 47 months post nasopharyngectomy.

Conclusion: It is recommended that single modality treatment with endoscopic nasopharyngectomy is a good option for rT1 disease. However, for rT2 disease and above, multi-modality treatment should be considered.

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Introduction

Nasopharyngeal carcinoma (NPC) is endemic in Southern China and South East Asia with annual incidence of 15-50 cases per 100,000.[1] It is the fifth most common malignancy in Malaysia with lifetime risk for males of 1 in 143 and for females 1 in 417.[2] Current treatment modality for primary NPC is definitive radiotherapy for stage I and concurrent chemoradiotherapy for stages II,III, and IV. In Malaysia, the 5-year relative survival rates of NPC were 63.7%, 59.1%, 50.2%, and 26.9% for stages I, II, III, and IV respectively.[3] NPC has a 5-year recurrence rate between 5 to 15% and it poses a therapeutic challenge.[1] Treatment options of recurrence include re-irradiation, open surgical resection, and endoscopic resection. Re-irradiation is associated with severe complications such as cranial nerve palsies, temporal lobe necrosis, osteoradionecrosis, xerostomia, trismus, hearing and visual impairment, endocrine dysfunction, and carotid stenosis, making this option unfavourable.[1,4] Open surgery such as a trans-palatal approach, a trans-infratemporal fossa approach, midface degloving, or a maxillary swing approach, offer similar local control and overall survival compared with re-irradiation. However, this method is also associated with significant functional and cosmetic morbidity, including facial scarring, trismus, dental malocclusion, cranial nerve injuries (infraorbital nerve in maxillary swing, facial palsies in infratemporal approach), palatal defects, dysphagia, nasal regurgitation, osteonecrosis, and rupture of ICA.[1,4] The roles of platinum-based chemotherapy are still unclear, whilst the efficacy of third generation chemotherapeutic drugs (paclitaxel, docetaxel and gemcitabine) in recurrent NPC is still being tested. Other modern therapies being studied include anti-epidermal growth factor receptor (EGFR) therapy and autologous Epstein–Barr virus (EBV) targeted cytotoxic T lymphocytes therapy. Both modalities have the potential to produce optimal outcomes with minimal toxicity.[11]

Endoscopic nasopharyngectomy was first described by Chen et al in 2009 as a minimally invasive alternative for primary treatment of locally recurrent NPC (rNPC).[4] Recent studies have shown that it has similar survival outcomes to open approaches or re-irradiation.[1] Castelnuovo et al had classified nasopharyngeal endoscopic resections (NER) to three types: Type 1: resection of the posterior nasopharyngeal wall; type 2: resection superiorly extended to the sphenoid; and type 3: trans-pterygoid approach to the postero-lateral nasopharynx with removal of pterygoid plates and Eustachian tube.6 Here, we report the survival outcomes of a series of endoscopic nasopharyngectomies performed in our centre for locally recurrent NPC.

Methods

This study is a retrospective review of patients who were diagnosed with locally recurrent NPC and underwent endoscopic nasopharyngectomy from years 2010 to 2018. Patients were identified from the operating theatre registry and those with available medical records were reviewed. This study was approved by the Institutional Review Board of National University of Malaysia. Information regarding the patient's demographics, primary NPC stage, recurrent stage, type of nasopharyngectomy (extent of resection) performed, surgical margins, post-operative adjuvant therapy, surveillance duration, recurrence post-nasopharyngectomy, method of diagnosing recurrence, and patient's latest status were recorded.

Intraoperatively, the extent of nasopharyngeal resection is categorized based on Castelnuovo et al, and are listed as follows.[6] Type 1: superiorly to roof of nasopharynx, inferiorly to soft palate, laterally to medial border of torus tuberus , medially to midline of nasopharynx. Type 2: extent as type 1, except superior extension to roof of sphenoid. Type 3: trans-pterygoid approach to the postero-lateral nasopharynx with removal of medial pterygoid plate with medial pterygoid clearance. Posterior septectomy or partial inferior turbinectomy was performed to gain wider access to the nasopharynx. Tumour resection was performed using a microdebrider or coblator. After resection, where available, a nasoseptal flap was used for reconstruction.

Results

Our case series consisted of 7 patients with locally recurrent NPC. Table 1 lists the individual patient data. In summary, there were 6 males and 1 female. The age range was 39 years to 78 years, with mean age of 57.6 years. 4 patients were staged as rT1, one patient staged rT2, one rT3, and one rT4. All patients were N0M0.

Type 1 NER was done for 5 patients, 4 of which were staged rT1. Type 1 resection was done for one rT4 case. This was because magnetic resonance imaging (MRI) of the skull base showed that the tumour was confined to the right nasopharynx and suggestive of rT1. However, post operatively, retrospective review of the MRI revealed small tumour infiltration to the sphenopalatine foramen and encroachment of the right cavernous sinus, with perineural spread along the maxillary branch of the right trigeminal nerve. Hence, the patient was upstaged to rT4 post operatively.

Type 3 NER was performed for one rT2 case where MRI showed tumour at the left nasopharynx involving the torus tuberus and eustachian tube with fat plane loss at the anteromedial aspect of the left medial pterygoid muscle. Type 3 NER, with left modified medial maxillectomy and medial pterygoid clearance, was performed. Medial pterygoid clearance was achieved by drilling the posterior wall of the maxillary sinus and pterygoid plate. However intraoperatively, the tumour was found to involve the left nasopharynx and eustachian tube cartilage, while the medial pterygoid muscle and pterygoid plates were not involved.

Type 2 NER was performed for one rT3 case where a preoperative computed tomography (CT) scan of paranasal sinuses showed tumour confined to the left nasopharynx and superficial parapharyngeal space (initially staged as rT2). However, intra-operatively, the tumour involved the roof of the left sphenoid.

Wider access to nasopharynx was gained by performing posterior septectomy in 5 out of 7 cases. One case had partial inferior turbinectomy done for surgical access.

Out of the 7 patients, five patients achieved clear margins (four rT1 that had Type 1 NER and one rT2 that had Type 3 NER). Two patients had positive margins including one rT3 (base of skull infiltration) and one rT4 disease (intracranial extension). Both of these patients received 6 cycles of adjuvant chemotherapy.

The patients were followed up between 4 to 48 months post-surgery (mean 30.28 months). The 2-year overall survival (OS) was 100% and disease-free survival (DFS) was 85.71%. Based on retrospective chart review, there were no documented long-term complications related to the surgery during subsequent clinic follow up. All patients were still under follow up at the time of study. 57.2% (4 out of 7 patients) did not have recurrence. 3 of these patients were diagnosed with rT1 tumours and underwent Type 1 NER. The 4th patient who had no recurrence was the rT4 case that underwent type 1 NER and received post-operative adjuvant chemotherapy. He remained disease-free up to 47 months post operation.

42.8% (3 out of the 7) cases had recurrence post NER, diagnosed between 18 to 35 months post op (mean 26 months). One rT1 case post type 1 NER with clear margins had recurrence 25 months post operation. He had recurrence at the skull base with brain metastasis and expired within 3 months due to the advanced disease.

The rT2 case underwent Type 3 NER with negative margins intraoperatively. Surveillance MRI at 18 months post-surgery showed recurrence at the posterior nasal septum extending to the left sphenoid, and a second surgery was carried out. However, 23 months post operation, he had another recurrence at the left nasopharynx, and is still alive with residual disease.

The rT3 case that had type 2 NER and 6 cycles of post-operative chemotherapy achieved remission after treatment. However, he had local recurrence at the nasopharynx 35 months after completion of chemotherapy and had received another cycle of chemotherapy. He is currently alive with residual disease.

Discussion

Surgical approaches to locally recurrent NPC include open, endoscopic, and robotic approaches.[1] The reported 5-year overall survival (OS) of traditional open resection via a maxillary swing approach were 51.9 to 62% as opposed to 78.1% in endoscopic nasopharyngectomy.[1,7] However, this may be biased as endoscopic approaches are usually reserved for early stage (rT1/2) tumours whereas open resection encompasses all rT stages.

Endoscopic approach is favoured now for early stage tumours as it offers comparable survival outcome with less destruction of surrounding tissue, facial scarring, and better preservation of function.4 However, to improve survival outcome, patient selection is essential and it is recommended that endoscopic resection be reserved for rT1, rT2, and selected rT3 (with involvement of the floor of the sphenoid) cases.[8] Exclusion criteria for endoscopic resection include significant parapharyngeal extension, internal carotid artery involvement, skull base bony invasion, significant dural involvement, cavernous sinus, and intracranial invasion.[8] Another factor that improves outcome is wider surgical exposure intraoperatively that allows for better tumour visualisation and complete resection of tumour. This can be achieved by posterior septectomy (resection of the vomer) or inferior turbinectomy.[4]

Systemic review showed that the 2-year OS for endoscopic resection ranges from 59.4 to 100% and the 2-year disease-free survival (DFS) from 57.6 to 90%.[1] Rohaizam et al reported a series of 6 patients with rT1NoMo NPC which were all able to achieve negative margins intra-operatively. There was no recurrence within the follow-up duration of 14 months.[9] Castelnuovo et al reported a series of 27 patients : 12 rT1 cases (10 had no recurrence, 1 died of disease, 1 died of other cause), 1 rT2 case (no evidence of disease), 13 rT3 cases (8 with no recurrence, 2 alive with disease, 3 died with disease), and 1 rT4 case (alive with disease) with mean follow up time of 31 months.10 Chen et al reported a large series of 37 patients diagnosed with rT1 (n=17), rT2 (n=18), and rT3 (n=2). 36 of these patients achieved negative surgical margins, 1 patient had positive margins but refused radiotherapy. During the follow

Table 1. Individual patient information.

Age (years)	Gender	Initial stage	Recurrent stage	HPE	Extent of resection	Margin	Adjuvant therapy	Post op recurrence	Diagnostic method of post op recurrence	Disease free duration (months)	Survival (months)	Status
78	Male	Stage 1-T1N0M0	rT1N0M0	Type 2 (non-keratinising)	Type 1 NER -roof of nasopharynx -lateral wall FOR -soft palate -pharyngobasilar fascia	Clear	No	No	MRI	4	4	No evidence of disease
62	Male	Stage 2	rT1N0M0	Type 3 (undifferentiated)	Type 1 NER Posteriorly until pharyngobasilar fascia, superiorly until roof, medially until midline, laterally until left FOR & medial part of torus tubarus, inferiorly until level of soft palate.	Clear	No	No	CT	32	32	No evidence of disease
46	Male	Stage 1-T1N0M0	rT1N0M0	Type 3 (undifferentiated)	Type 1 NER pharyngobasilar fascia -Medial portion of torus tubarus	Clear	No	No	MRI	47	47	No evidence of disease
64	Male	Stage 3	rT1N0M0	Type 3 (undifferentiated)	Type 1 NER -roof -soft palate -medial border of torus	Clear	No	Yes	CT	25	28	Death due to advanced tumour
57	Male	Stage 2-T1N1M0	rT2N0M0	Type 3 (undifferentiated)	Type 3 NER Left modified medial maxillectomy, Medial pterygoid clearance	Clear	No	Yes	MRI	18	53	Posterior septectomy & sphenoidectomy 18 months post op. Second recurrence at left FOR 35 months after second resection. Alive with residual disease.
57	Female	Not documented	rT3N0M0	Type 1: Keratinising (moderately differentiated)	Type 2 NER Left lateral wall nasopharynx, left FOR, left roof of sphenoid	Involved (roof of left sphenoid)	Post-op chemotherapy (6 cycles)	Yes	MRI	35	48	Alive with residual tumour 48 months post nasopharyngectomy
39	Male	Stage 4b-T4N3M0	rT4N0M0	Type 3 (undifferentiated)	Type 1 NER -Midline nasopharynx extending superiorly to roof of nasopharynx, inferiorly to soft palate, laterally to torus tubarus	Involved – intracranial extension (perineural tumour at trigeminal nerve and vidian canal on MRI)	Post-op chemotherapy (6 cycles)	No	MRI	47	47	No evidence of disease

Table 2. Recurrence stage (rT stage), type of endoscopic nasopharyngectomy performed, adjuvant therapy, post-operative recurrence rate.

Recurrence stage	Number of patients	Type of endoscopic nasopharyngectomy	Adjuvant therapy	Post-operative recurrence rate
rT1	4	Type 1	Nil	25%
rT2	1	Type 3	Nil	100%
rT3	1	Type 2	Yes (chemotherapy)	100%
rT4	1	Type 1	Yes (chemotherapy)	0%

up duration (median 24 months), all rT1 cases were recurrence-free, while 5 out of the 18 rT2 cases developed local recurrence between 6 and 26 months after surgery. In the rT3 group, 1 developed distant metastasis without local recurrence. The 2-year OS, local relapse-free survival and progression free survival rates were 84.2%, 86.3%, and 82.6%.[5]

In our series, the 2-year OS was 100% and DFS was 85.71%, which is comparable with other studies. However, the majority of our patients were in early stage (rT1). Only one out of the 4 rT1 case developed recurrence (brain metastasis 25 months post op). The rT2 and rT3 diseases had local recurrence of 18 and 35 months, respectively post-nasopharyngectomy. However, the only rT4 case in our series who was diagnosed with intracranial residual tumour based on post-operative review of MRI and who received post-operative chemotherapy had no recurrence up to 47 months of surveillance.

Our study does not conflict with findings of others showing that at least in rT1 stage of recurrent NPC, endoscopic resection is superior to open approaches in terms of OS & DFS. However, rT2 stage may be challenging as the proximity of the ICA laterally makes it difficult to achieve clear resection in the parapharyngeal space.[4]

Advanced rT stage cases (rT3/T4) fair worse in local control and overall survival, and in view of the extent of disease, reirradiation with intensity modulated radiotherapy (IMRT) or chemotherapy should be considered first.[4] Chen et al had two rT3 cases where both cases had erosion of the base of the sphenoid, one case developed distant metastasis.[5] In Castelnuovo et al's series, 6 out of 14 patients with advanced T stage had recurrence, and 3 patients died due to disease.[10] Patients with rT4 generally had local failure or distant metastasis. Those with intratemporal fossa recurrence may be more amenable to surgery compared to intracranial recurrence. However, cases with infratemporal tumours require open surgical approaches due to their extensive nature.[4]

Limitations of this study include its retrospective nature, incomplete medical documentation including lack of toxicity data, small sample size, and possible selection bias as patients with unavailable medical records were excluded. That said, this study does reflect findings of other studies showing good outcomes for endoscopic resection of early stage recurrent NPC. There is insufficient data for rT3 and rT4 tumours, and whether an endoscopic approach has similar outcomes to an open approach.

Hence, it is recommended that a prospective study with larger sample size recruiting patients from all rT stages to demonstrate the outcome of endoscopic nasopharyngectomies as compared to open approaches.

Conclusion

This case series resonates with current literature supporting endoscopic nasopharyngectomy as a reasonable option for properly selected cases of rT1N0M0 nasopharyngeal carcinoma after multidisciplinary discussion in experienced centres.

References

1. Vlantis AC, Lee DLY, Wong EWY, et al. Endoscopic nasopharyngectomy in recurrent nasopharyngeal carcinoma : a case series, literature review, and pooled analysis. Intl Forum of Allergy Rhinol .2017; (4):425-432. Available from: https://doi.org/10.1002/alr.21881
2. National Cancer Institute. Malaysian National Cancer Registry Report 2007-2011. Ministry of Health Malaysia. 2016. Available from: https://www.crc.gov.my/wp-content/uploads/documents/report/MNCRRrepor2007-2011.pdf
3. National Cancer Institute. Malaysian Study on Cancer Survival. Ministry of Health Malaysia. 2018. Available from: http://www.moh.gov.my/moh/resources/Penerbitan/Laporan/Umum/Malaysian_Study_on_Cancer_Survival_MySCan_2018.pdf
4. Ong YK, Solares CA, Lee S, et al. Endoscopic nasopharyngectomy and its role in managing locally recurrent nasopharyngeal carcinoma. Otolaryngology Clin N Am. 2011; 44(1): 1141-1154. Available from: https://doi.org/10.1016/j.otc.2011.07.002
5. Chen MY, Wen WP, Guo X, et al. Endoscopic nasopharyngectomy for locally recurrent nasopharyngeal carcinoma. Laryngoscope. 2009; 119 (3):516-22. Available from: https://doi.org/10.1002/lary.20133
6. Castelnuovo P, Dallan I, Bignami M. Nasopharyngeal endoscopic resection in the management of selected malignancies: ten-year experience. Rhinology. 2010; 48:84-89. Available from: 10.4193/Rhin09.079.
7. Zou X, Han F, Ma WJ. Salvage endoscopic nasopharyngectomy and intensity-modulated radiotherapy versus conventional radiotherapy in treating locally recurrent nasopharyngeal carcinoma. Head Neck. 2015;37:1108–1115. Available from: https://doi.org/10.1002/hed.23719
8. Monteiro E, Witterick I. Endoscopic nasopharyngectomy: Patient selection and surgical execution. Operative techniques in Otolaryngology. 2014; 25(3):284-288. Available from: https://doi.org/10.1016/j.otot.2014.04.010
9. Rohaizam J, Subramaniam SK, Vikneswaran T. Endoscopic nasopharyngectomy: the Sarawak experience. Med J Malaysia. 2009; 64:213–5. Available from: http://www.e-mjm.org/2009/v64n3/endoscopic_nasopharyngectomy.pdf
10. Castelnuovo P, Nicolai P, Turri-Zanoni M, et al. Endoscopic Endonasal Nasopharyngectomy in Selected Cancers. Otolaryngology– Head and Neck Surgery. 2013; 149(3) 424–430. Available from: 10.1177/0194599813493073
11. Xu T, Tang J, Gu M, et al. Recurrent nasopharyngeal carcinoma: a clinical dilemma and challenge. Curr Oncol. 2013; 20(5):e406–e419. Available from: https://current-oncology.com/index.php/oncology/article/view/1456/1310