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Endonasal endoscopic nasopharyngectomy for nasopharyngeal malignancies: a survival analysis

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Abstract

Introduction Nasopharyngeal cancer has a global incidence of less than 1.0 per 100,000 person-years. It originates from nasopharyngeal mucosa with the Fossa of Rosenmuller being the most common site. Radiation therapy with or without chemotherapy is an established first-line treatment modality given the sensitivity of the tumor.

Objectives The aim of our study was to report survival outcomes amongst patients undergoing endonasal endoscopic nasopharyngectomy at a tertiary care referral center.

Methods We conducted a retrospective longitudinal cohort study. We collected data on age, gender, prior treatment, histology, extent of surgery, post-operative adjuvant therapy, and recurrence and reported the survival along mean survival time using Kaplan–Meier curves and log-rank test.

Results A total of six patients, three males and three females with a mean age of 43.7 years were included in our study. Of the six, three patients underwent a salvage procedure whereas three patients received upfront definitive surgical resection. Three patients developed recurrence with a mean survival time of 19.3 months. The disease-free survival at 1 and 2 years of surgery was 88.3% and 66% respectively.

Conclusion Endonasal endoscopic nasopharyngectomy is an effective surgical procedure that can be undertaken for both salvage and primary cases. Our survival results are comparable to the literature.

Keywords Skull base, Nasopharyngeal carcinoma, Endoscopic nasopharyngectomy, Nasopharyngectomy, Survival

Main points

- Nasopharyngeal cancer has a global incidence of less than 1.0 per 100,000 person-years
- Radiation therapy with or without chemotherapy is an established first-line treatment modality given the sensitivity of the tumor.

- The aim of our study was to report survival outcomes amongst patients undergoing endonasal endoscopic nasopharyngectomy at a tertiary care referral center.
- A total of six patients, three males and three females with a mean age of 43.7 years were included in our study.
- The disease-free survival at 1 and 2 years of surgery was 88.3% and 66% respectively.

Background

Nasopharyngeal cancer is associated with Epstein-Barr Virus [1]. It has a global incidence of less than 1.0 per 100,000 person-years [2]. It originates from nasopharyngeal mucosa with the Fossa of Rosenmuller being the most common site. Radiation therapy with or

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without chemotherapy are established first-line treatment modality given the sensitivity of the tumor [3]. The inclusion of chemotherapy is reserved for late-stage disease [3]. Surgical input is usually confined to initial diagnostic biopsy or as salvage for select cases. Recurrence of nasopharyngeal carcinoma at 5 years after radiotherapy is reported as high as 56% [4] and the persistence of locoregional disease has been reported up to 20% [5, 6]. Re-irradiation of the nasopharynx is usually administered in such cases, however, it has severe complications which include osteoradionecrosis of the skull base, cranial nerve palsies, nasopharyngeal stenosis, and temporal bone necrosis, and these, coupled with life-threatening hemorrhage, do not make re-irradiation a favorable modality [7, 8].

Historically, extensive radical procedures have been employed for such cases that include, maxillary swing, mid-face degloving, transinfratemporal approaches, and intraoral trans-palatal approaches [9]. These surgical approaches are limited by narrow operative fields and surgical complications [9, 10]. Operating on previously irradiated tissue can lead to wound dehiscence and poor wound healing [11]. Moreover, trismus, facial scars, and palatal defect are among others [9, 10, 12]. Even with these caveats, surgical resection has shown promising results [13], and surgical dissection is carried out with special attention to important neurovascular bundles in close proximity, including the internal carotid artery in the lateral wall of the nasopharynx [14].

With advances in endoscopic skull base surgery, attention was given to endoscopic endonasal resection of nasopharyngeal carcinoma. The endoscopic approach provides enhanced magnification and clear visualization of the tumour aiding in achieving clear margins [10]. Additionally, it has the advantage of avoiding facial scars and preservation of masticatory functions [15, 16]. Current literature, reports similar results of endonasal endoscopic nasopharyngectomy compared to irradiation [6]. A recent meta-analysis suggests better outcomes with surgery [17]. We aimed to determine the management and outcomes of patients treated with endonasal endoscopic nasopharyngectomy at a tertiary care referral

center in the UK with special attention to disease-free survival.

Methods

A retrospective longitudinal cohort study was conducted at a tertiary care center in Birmingham, United Kingdom. Ethical approval was obtained prior to conducting the study (ERC Number: CARMS-18223). Data on patients who underwent endonasal endoscopic nasopharyngectomy was collected from December 2017 until February 2021. All patients were operated on by a single surgeon with extensive experience in skull base procedures and were followed every 3 months for the first 2 years and then every 6 months. The eligibility criteria for the study were adult patients who underwent endoscopic nasopharyngectomy with diagnosed nasopharyngeal carcinoma including salivary gland carcinomas of the nasopharynx. Patients with missing records or those lost to follow-up were excluded as well as patients with very advanced tumors encasing the internal carotid artery. All the cases included in our study were discussed thoroughly in multidisciplinary discussions. None of these cases had any lymph node metastases, which were evaluated both clinically and radiologically, and no neck dissections were performed.

Surgical procedure

After induction of anesthesia and control of the airway, both nostrils were packed with 10 neuropathies soaked in adrenaline 1:10,000, on either side. Patients were moved to the operating table and neuronavigation was set up. This was followed by the head end elevated at 20° reverse Trendelenburg position. The type of nasopharyngectomy performed was categorized as per the Castelnuovo NEC grading system (types 1–3) [16] (Table 1).

Statistical analysis

We present continuous data as mean and standard deviation. Categorical data is reported in frequencies and percentages. Follow-up of patients is reported in months. Recurrence was calculated from the date of surgery to the patient presenting with a mass in the nasopharynx picked

Table 1 Castelnuovo grading system (type 1–3) for endonasal endoscopic nasopharyngectomy

Castelnuovo grading system for endoscopic nasopharyngectomy	
Type 1	Starts with the removal of the posterior portion of the nasal septum. The resection is limited to the postero-superior nasopharyngeal wall, reaching the bony floor of the sphenoid sinus superiorly and the pharyngobasilar/prevertebral fascia posteriorly
Type 2	Extends superiorly to include also the anterior wall and the floor of the sphenoid sinus. In this case, the sphenoid rostrum and the intersphenoidal septum are removed
Type 3	Extends laterally to include the lateral nasopharyngeal wall and the cartilaginous portion of the eustachian tube

up on nasal endoscopy or reported on PET scan on follow-up visits. Kaplan–Meier curve was plotted to graphically represent time to recurrence. We also reported post-operative complications following the surgical procedure. Data was analyzed on STATA version 14 (Stata-Corp LLC, College Station, TX, USA).

Results

A total of six patients were included in our study. The mean age was 43.7 ± 11.4 years. There was equal gender distribution. One patient (case 5) had previous cranial nerve palsies affecting cranial nerves IV and VI at the time of presentation. One of the patients (case 1) had a previous history of surgery followed by Intensity Modulated Radiation Therapy (IMRT). Three of the patients (cases 1, 2, and 6) were operated on as salvage procedures post radiation whereas the other three were operated upon with curative intent (cases 3–5) (Table 2).

Two patients (case 2 and 6) were operated for nasopharyngeal cancer (NPC) as a salvage procedure. Two patients (cases 3 and 4) were operated for primary mucoepidermoid carcinoma. Case no 1 was operated for adenoid cystic carcinoma and case 5 was operated for clival chordoma. En bloc resection was carried out in three patients (cases 2–4) whereas segmental resection was performed in the remaining three cases [1, 5, 6]. We were able to achieve macroscopic clear margins in all six cases however, due to segmental excision in three patients, the margin status was not commented upon by histologists (Tables 2 and 3).

The average length of hospital stay was 4.3 ± 4.2 days ranging from 1 to 11 days. One patient developed meningitis which required inpatient antibiotic treatment. Another patient developed diabetes insipidus and stayed in the hospital for 8 days. None of our patients developed any new post-operative cranial nerve injury. Three patients developed recurrence with a mean time to recurrence of 40.3 months (Fig. 1). Mean follow-up time

Table 3 Surgery and treatment-related factors

Variable		Frequency (%)
Type of nasopharyngectomy (Castelnuovo grading)	Type 1	0
	Type 2	1 (16.7%)
	Type 3	5 (83.3%)
Type of resection	En bloc	3 (50%)
	Segmental	3 (50%)
Adjuvant therapy	Radiation therapy	2 (33.3%)
	Palliative chemotherapy	2 (33.3%)
	Proton therapy	1 (16.6%)
	No further treatment	1 (16.6%)

was 36.5 ± 19.4 months. Mean survival times along with their confidence interval are reported in Table 4.

Discussion

A total of six patients with nasopharyngeal malignancies, who had undergone endonasal endoscopic nasopharyngectomy were included in our study. We report a mean survival time of 63 months for patients who did not develop recurrence and 40.3 months for patients who developed recurrence. Our results are a representation of patients who underwent nasopharyngectomy either as a salvage or upfront primary definitive resection.

Endoscopic nasopharyngectomy is not just reserved for nasopharyngeal carcinoma [14, 18]. Recently, there has been significant work published on treating various nasopharyngeal malignancies with endoscopic resection. Castelnuovo et al. performed endoscopic resection on adenocarcinoma, adenoid cystic carcinoma, and melanoma amongst nasopharyngeal carcinoma [16]. Kamel et al. performed endoscopic nasopharyngectomy for eight cases of NPC, one of adenocarcinoma, and one case of grade II squamous cell carcinoma [18]. In our current study, we report two cases of nasopharyngeal carcinoma, two cases of mucoepidermoid carcinoma, one case of

Table 2 Characteristics of treatment of patients included in the study

Patients	Age	Gender	Previous cranial nerve palsy	Previous Radiation therapy	Surgery	Type of nasopharyngectomy [16]	Histology	Recurrence
Case 1	31	Male	No	Yes	Salvage	Type 3	Adenoid cystic Ca	Yes
Case 2	32	Male	No	Yes	Salvage	Type 2	NPC	No
Case 3	49	Female	No	No	Primary	Type 3	MEC	No
Case 4	39	Male	No	No	Primary	Type 3	MEC	No
Case 5	52	Female	Yes	No	Primary	Type 3	Clival chordoma	Yes
Case 6	59	Female	No	Yes	Salvage	Type 3	NPC	Yes

* MEC Mucoepidermoid carcinoma, NPC Nasopharyngeal carcinoma

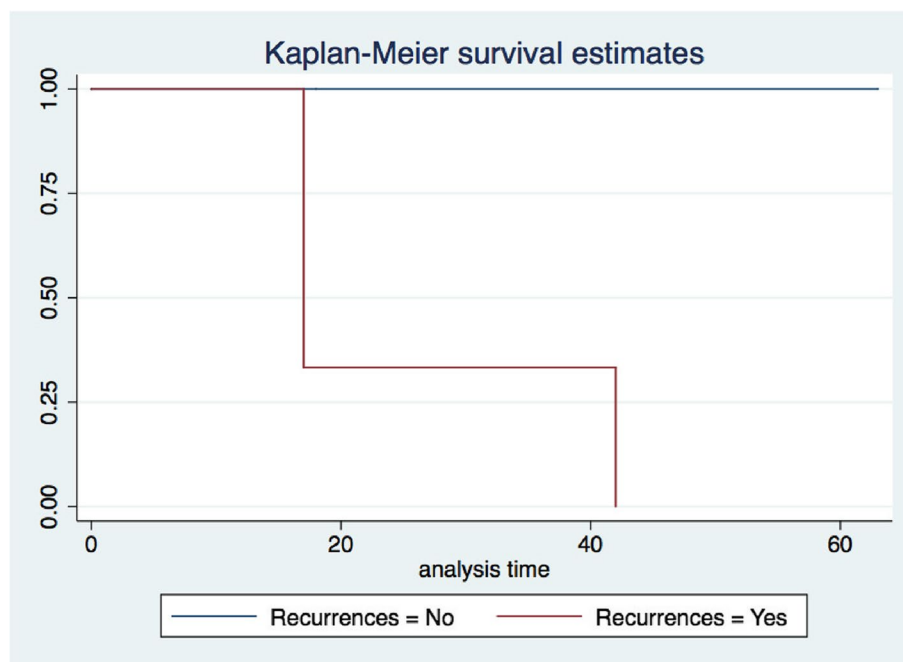


Fig. 1 Kaplan–Meier curve of disease-free survival stratified on recurrence. Patients with recurrence had a mean survival time of 40.3 months versus 63 months for patients who did not develop recurrence

Table 4 Mean survival time in months using the log-rank test

		Mean survival time (months)	95% Confidence interval
Recurrence	No	63 ^a	–
	Yes	40.3	26.9–53.7

^a Largest observed analysis time is censored, mean is underestimated

clival chordoma, and one patient with adenoid cystic carcinoma.

There is also controversy over primary resection of nasopharyngeal malignancy versus surgery reserved as a salvage procedure [16, 19, 20]. This debate exists due to the scarcity of evidence following surgical resection, and answering this can be achieved through meta-analysis [17]. Previously, radical procedures were employed to resect this segment of the skull base [9, 21], with higher morbidity and mortality compared to radiation therapy. With advances in endoscopic approaches, there have been reports of upfront surgical resection of skull base malignancies [22]. Castelnuovo et al. performed primary resection in five of 17 cases [16]. Lai and Chen performed primary endoscopic nasopharyngectomy in two cases [20]. Kamel et al. undertook primary resection for 2 out of 10 cases [18]. Al-Sheibani et al. reported 10 out of 20 patients undergoing resection without a prior history of any treatment [15].

We also agree with the notion of endoscopic nasopharyngectomy for the recurrence of nasopharyngeal carcinoma. Liu et al. recently reported a large cohort of 91 cases with recurrent or residual nasopharyngeal carcinoma treated with endoscopic resection [6]. Ning et al. reported nice cases of salvage endoscopic resection [23]. Macdonald et al. reported two cases of salvage resection [24]. Our study includes three patients who underwent endoscopic resection for recurrence. The practice of reserving endoscopic resection for salvage cases is rapidly changing to also include primary cases without any prior treatment history. This is attributed to growing knowledge and experience of skull base anatomy and technological advances enabling surgeons to reach deeper recesses of the skull base safely [25].

Most studies have reported en-bloc resection of tumors with frozen section clearance [19, 24, 26]; however, there are studies that have employed piece meal or segmental resections as well [18]. Tumors extending far laterally, especially near the internal carotid artery cannot be resected en bloc. Piece meal excision with an effort to achieve clear margins has also been reported. These patients are subsequently subjected to adjuvant radiation therapy [18]. We were able to achieve en bloc resection in three patients, whereas, the other three underwent segmental excision. Castelnuovo and colleagues proposed a new endoscopic nasopharyngectomy classification system [16]. Kamel et al. reported eight cases undergoing

NER type II and two cases undergoing type I [18]. Similarly, we report five cases undergoing type III and one case undergoing type II NER.

There are extensive reports on the overall and disease-free survival of patients with nasopharyngeal carcinoma undergoing radiation and chemotherapy [27, 28]. This is further stratified based on histological types and stage of disease. In contrast, there is a scarcity of data on the survival of patients undergoing endoscopic resection both as salvage or as a primary surgery [17]. Liu et al. reported an overall survival of 64.8% at 2 years and disease-free survival of 57.5% [6]. We report a disease-free survival of 83.3% at 1 year and 66% at 2 years. None of our patients during this period had mortality, so we reported 100% survival (6/6) at 63 months post-endoscopic resection.

We acknowledge some limitations of our study, the most notable is the limited patient population included in our study. This is coupled with a lower external generalizability compared to large cohort studies. We also acknowledge that we have reported the survival of patients with different histologies which can potentially skew the results as one pathology differs from the other based on its natural history. We could not stratify our data given a small sample. Moreover, we have reported a combined disease-free survival time of patients who underwent salvage procedures and those who underwent primary resection. Given our limitations, the results of our study highlight the survival time of patients undergoing endoscopic nasopharyngectomy. It provides information which can be pooled to assess survival in future meta-analyses. We propose multi-institutional studies, in collaboration with experienced rhinologists and skull base surgeons for large prospective cohort studies.

Conclusion

Endonasal endoscopic nasopharyngectomy is a useful adjunct for treating patients with recurrent nasopharyngeal malignancies or with limited primary tumors. Recurrence was seen in 50% of our patients at 63 months. We also report a mean survival time of 40.3 months for patients who developed recurrence after undergoing endoscopic nasopharyngectomy. Moreover, the disease-free survival was 83.3% and 66% at 1 and 2 years respectively.

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Authors' contributions

HI analyzed and interpreted the data, supervised the writing process for the manuscript, and was also involved in designing the study. MOA was involved in the literature search, data collection and processing, and writing the manuscript. SKA was responsible for the concept and design of the study. All authors have read and approved the final manuscript.

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Availability of data and materials

Not applicable.

Declarations

Ethics approval and consent to participate

Ethical approval was obtained prior to conducting the study on 15th November 2017 from Queen Elizabeth Hospital Birmingham, UK. ERC Number: CARMS-18223. Written informed consent to participate was taken from all participants prior to conducting the study.

Consent for publication

Written informed consent for publication was taken from all participants prior to conducting the study.

Competing interests

The authors declare that they have no competing interests.

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References

- Thompson MP, Kurzrock R (2004) Epstein-Barr virus and cancer. *Clin Cancer Res* 10:803–821
- Chan JY, Gooi Z, Mydlarz WK, Agrawal N (2016) Risk of second primary malignancy after nasopharyngeal carcinoma in the United States: a population-based study. *Head Neck* 38:E1130–E1136
- Wei WI (2003) Cancer of the nasopharynx: functional surgical salvage. *World J Surg* 27:844–848
- Sanguineti G, Geara FB, Garden AS, Tucker SL, Ang KK, Morrison WH et al (1997) Carcinoma of the nasopharynx treated by radiotherapy alone: determinants of local and regional control. *Int J Radiat Oncol Biol Phys* 37:985–996
- Chee J, Ting Y, Ong YK, Chao SS, Loh KS, Lim CM (2016) Relapse status as a prognostic factor in patients receiving salvage surgery for recurrent or residual nasopharyngeal cancer after definitive treatment. *Head Neck* 38:1393–1400
- Liu J, Yu H, Sun X, Wang D, Gu Y, Liu Q et al (2017) Salvage endoscopic nasopharyngectomy for local recurrent or residual nasopharyngeal carcinoma: a 10-year experience. *Int J Clin Oncol* 22:834–842
- Ho AS, Kaplan MJ, Fee WE Jr, Yao M, Sunwoo JB, Hwang PH. Targeted endoscopic salvage nasopharyngectomy for recurrent nasopharyngeal carcinoma. *Int Forum Allergy Rhinol*. 2012;2(2):166–73. <https://doi.org/10.1002/alr.20111>. Epub 2011 Dec 13.
- Suárez C, Rodrigo JP, Rinaldo A, Langendijk JA, Shaha AR, Ferlito A (2010) Current treatment options for recurrent nasopharyngeal cancer. *Eur Arch Otorhinolaryngol* 267:1811–1824
- Stoker S, van Diessen J, De Boer J, Karakullukcu B, Leemans C, Tan I (2013) Current treatment options for local residual nasopharyngeal carcinoma. *Curr Treat Options Oncol* 14:475–491
- Vlantis AC, Chan HS, Tong MC, Yu BK, Kam MK, Van Hasselt CA (2011) Surgical salvage nasopharyngectomy for recurrent nasopharyngeal carcinoma: a multivariate analysis of prognostic factors. *Head Neck* 33:1126–1131
- Tsang RK, Holsinger FC (2016) Transoral endoscopic nasopharyngectomy with a flexible next-generation robotic surgical system. *Laryngoscope* 126:2257–2262
- King WW, Ku PK, Mok CO, Teo PM (2000) Nasopharyngectomy in the treatment of recurrent nasopharyngeal carcinoma: a twelve-year experience. *Head Neck*. 22:215–22
- Yoshizaki T, Wakisaka N, Muroho S, Shimizu Y, Furukawa M (2005) Endoscopic nasopharyngectomy for patients with recurrent nasopharyngeal carcinoma at the primary site. *Laryngoscope* 115:1517–1519

14. Castelnuovo P, Nicolai P, Turri-Zanoni M, Battaglia P, Bolzoni Villaret A, Gallo S et al (2013) Endoscopic endonasal nasopharyngectomy in selected cancers. *Otolaryngology-Head Neck Surg* 149:424–430
15. Al-Sheibani S, Zanation AM, Carrau RL, Prevedello DM, Prokopakis EP, McLaughlin N et al (2011) Endoscopic endonasal transpterygoid nasopharyngectomy. *Laryngoscope* 121:2081–2089
16. Castelnuovo P, Dallan I, Bignami M, Battaglia P, Mauri S, Bolzoni Villaret A et al (2010) Nasopharyngeal endoscopic resection in the management of selected malignancies: ten-year experience. *Rhinology* 48:84
17. Yang J, Song X, Sun X, Liu Q, Hu L, Yu H, Wang D. Outcomes of recurrent nasopharyngeal carcinoma patients treated with endoscopic nasopharyngectomy: a meta-analysis. *Int Forum Allergy Rhinol*. 2020;10(8):1001–11. <https://doi.org/10.1002/alar.22552>. Epub 2020 May 25.
18. Kamel RH, Hassan MSE, Abdelfattah AE, Fouad AS, Zamzam SM (2016) Endoscopic nasopharyngectomy for nasopharyngeal carcinoma. *Pan Arab J Rhinol* 6:5
19. Chen MY, Wen WP, Guo X, Yang AK, Qian CN, Hua YJ et al (2009) Endoscopic nasopharyngectomy for locally recurrent nasopharyngeal carcinoma. *Laryngoscope* 119:516–522
20. Lai Y-S, Chen M-K (2013) Exclusively endoscopic resection of nasopharyngeal adenocarcinoma. *Clin Exp Otorhinolaryngol* 6:263
21. Bian X, Chen H, Liao L (2012) A retrospective study of salvage surgery for recurrent nasopharyngeal carcinoma. *Int J Clin Oncol* 17:212–217
22. Rohaizam J, Subramaniam S, Vikneswaran T, Tan V, Tan T (2009) Endoscopic nasopharyngectomy: the Sarawak experience. *Med J Malaysia* 64:213–215
23. Ning-i H, Ping-hung S, Siew-shuen C, Yew-kwang O, Cho-shun L (2014) Endoscopic resection concept for endoscopic endonasal nasopharyngectomy: surgical anatomy and outcome. *Chin Med J* 127:2934–2939
24. Macdonald K, Fandino M, Vescan A, Gentili F, Witterrick I (2014) Endoscopic nasopharyngectomy for locally recurrent nasopharyngeal carcinoma: how we do it. *J Otol Rhinol* 3:4
25. Ong YK, Solares CA, Lee S, Snyderman CH, Fernandez-Miranda J, Gardner PA (2011) Endoscopic nasopharyngectomy and its role in managing locally recurrent nasopharyngeal carcinoma. *Otolaryngol Clin North Am* 44:1141–1154
26. Kasemsiri P, Prevedello DMS, Otto BA, Old M, Ditzel Filho L, Kassam AB et al (2013) Endoscopic endonasal technique: treatment of paranasal and anterior skull base malignancies. *Braz J Otorhinolaryngol* 79:760–779
27. Peng H, Chen L, Li WF, Guo R, Mao YP, Zhang Y et al (2017) Tumor response to neoadjuvant chemotherapy predicts long-term survival outcomes in patients with locoregionally advanced nasopharyngeal carcinoma: a secondary analysis of a randomized phase 3 clinical trial. *Cancer* 123:1643–1652
28. Li X-Y, Chen Q-Y, Sun X-S, Liu S-L, Yan J-J, Guo S-S et al (2019) Ten-year outcomes of survival and toxicity for a phase III randomised trial of concurrent chemoradiotherapy versus radiotherapy alone in stage II nasopharyngeal carcinoma. *Eur J Cancer* 110:24–31

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